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Neuri 2021

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Josipa Kajić

Editors in-chief
Vinko Beg
Eva Levatić
Ljerka Delač
Bobana Samardžija

Language editors
Vinko Beg
Eva Levatić
Ljerka Delač
Bobana Samardžija

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Josipa Kajić

Welcome note

President of NeuRi 2021
Rijeka, 23 April 2021

Dear Colleagues,
I am honored to welcome you to the 10th Student Congress of Neuroscience – NeuRI 2021! These last year and a half have been extremely challenging for everyone. But, I can say confidently that all of us learned some important lessons. We have also learned to appreciate the little things, but the whole world finally found out how important science is. This is why I am honored to see so many young scientists at our NeuRi.

NeuRi has become a tradition and I'm thankful to each and everyone who was part of NeuRi in one way or another through the years. In the past nine years, NeuRi has established itself as a real platform for young scientists and neuroscience enthusiasts, and I am sure that NeuRi is here to grow even more
and stay!

I hope that through this year's program you will wander, learn and challenge yourself to think outside the box because you are the future of neuroscience.

On behalf of Organizing and Scientific Board -
Welcome to NeuRi 2021!

1 Participants of the 1st Student Congress of Neuroscience – NeuRi 2011; Faculty of Medicine, Rijeka

2 Participants of the 2nd Student Congress of Neuroscience – NeuRi 2012; Rab Psychiatric Hospital

3 Participants of the 3rd Student Congress of Neuroscience – NeuRi 2013; Faculty of Medicine, Rijeka

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Programme – NeuRi 2021

Friday, 23 April 2021 – online

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Autophagy and neurodegeneration
— David Rubinsztein

13:45 – 14:00 Break

14:00 – 15:00 **Plenary lecture**
Modern approaches in psychiatry: innovations and challenges
— Igor Salopek

15:00 – 15:15 Break

15:15 – 16:15 **Plenary lecture**
Brain machine interfaces: from basic science to neuroprostheses and neurological recovery
— Miguel Nicolelis

16:15 – 17:00 Break

17:00 – 19:00 **Sponsor lecture**
Application of robotics in neurorehabilitation
— Petra Krstičević (Meditrend)

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Vesna Šendula-Jengić: Digital psychiatry-yesterday, COVID-19, tomorrow...

11:00 – 11:15 Break

11:15 – 13:00 **Student session I**

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— Selma Terzić, Nevena Mahmutbegović
2. *Maja Mrak, Sara Belčić, Jakov Končurat, Emil Klarić, Valentino Rački, Daniela Petrić: First episode psychosis in a COVID-19 positive patient-a case report*
— Maja Mrak, Sara Belčić, Jakov Končurat, Emil Klarić, Valentino Rački, Daniela Petrić
3. *Therapy resistant depression or hospitalism; a case report*
— Sara Varljen, Tanja Grahovac Juretić, Klementina Ružić
4. *The impact of the COVID-19 pandemic on the mental health of adolescents*
— Petra Meštrić, Daniela Petrić, Ana Kaštelan
5. *Internalizing disorders in children and adolescents with autism spectrum disorders*
— Sara Milićević
6. *Video games addiction and its effect on sleep quality among college students of J.J. Strossmayer University of Osijek*
— Dorian Laslo, Terezija Berlančić, Tatjana Bačun, Dunja Degmečić

13:00 – 13:15 Break

13:15 – 14:15 **Plenary lecture**
Treatment of acute migraine attacks in children with analgesics on the World Health Organization Essential Medicines List: a systematic review
— Livia Puljak

14:15 – 14:30 Break

14:30 – 16:00 **Student session II**
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— Emir Begagić, Lejla Čejvan, Hakija Bečulić:
2. *Outcome of deep brain stimulation in Parkinson's disease in an elderly patient-case report*
— Mario Hero, Vladimira Vuletić
3. *Uncommon supratentorial anaplastic glioneuronal tumor in a pediatric case of Li-Fraumeni syndrome*
— Kamelija Horvatović, Filip Jadrijević-Cvrlje, Goran Mrak, Kamelija Žarković
4. *Doppler flow velocity measurements in the extracranial carotid arteries in healthy adults*
— Lea Vrhovnik, Sanja Kovačić, Slavica Sović, Ivana Martinović
5. *A case report of a novel GNB1 mutation and the response to deep brain stimulation*
— Gloria Rožmarić, Mario Hero, Valentino Rački, Vladimira Vuletić
6. *Bacterial endocarditis complicated with multiple embolic cerebral infarctions and multiple organ failure syndrome*
— Iva Sabljić, Mihael Mišir

16:00 – 16:30 Break

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— Lara Batičić, Edvard Bedoić, Dijana Detel:
2. *Regions of proteins critical to their aggregation in mental illness*
— Simone Ruhije Bertoša, Patricia Estañol Cayuela, Beti Zaharija, Nicholas J. Bradshaw
3. *Co-aggregation of proteins involved in mental illness*
— Mihaela Bergman, Maja Juković, Bobana Samardžija, Tina Fartek, Beti Zaharija, Nicholas J. Bradshaw
4. *Integrative analysis of tumor suppressor CHUK in diffuse gliomas of the brain*
— Petar Brlek, Anja Bukovac, Anja Kafka, Nives Pećina-Šlaus
5. *Investigating the mechanisms of TRIOBP-1 aggregation in mental illness*
— Anja Hart, Tina Fartek, Beti Zaharija, Maja Odorčić, Nicholas J. Bradshaw
6. *Obesity, deformities, cognitive deficit and developmental delay in five patients with BDNF gene mutation; a case report*
— Tomislav Glavan, Jasmine Knoll, Ivana Mihalek, Olaf Bodamer
7. *Immunohistological analysis of the propagation of the tau protein oligomers and fibrils in the rat brain*
— Emina Horvat Velić, Lea Langer Horvat, Goran Šimić
8. *DISC1 and FUS: linking proteins from mental and neurodegenerative illnesses through aggregation*
— Martina Jeremić, Beti Zaharija, Ines Gvoić, Nicholas J. Bradshaw

9. *Olfactory bulb – potential drug target for Alzheimer disease: an update*
— Dalia Vađunec, Jelena Osmanović Barilar
10. *Nanotechnology-based quantifications of nanoparticles from human cerebrospinal fluid: comparison of Atomic Force Microscopy and Tunable Resistive Pulse Sensing*
— Ivona Vidović, Marko Perčić, Vedrana Krušić, Kristina Grabušić, Mladenka Malenica
11. *Design, synthesis and in silico evaluation of potent and selective dopamine D4 receptor ligands*
— Pegi Pavletić, Fabio Del Bello, Wilma Quaglia, Gianfabio Giorgioni, Alessandro Piergentili

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2. *Anterocollis – a side effect of a drug or atypical parkinsonism-case report*
— Luka Ivanovski, Magda Gajski, Vladimira Vuletić
3. *Neuropathic pain as a complication of COVID-19*
— Petra Ivančević, Lea Kajba, Petra Jurić, Romana Marušić, Anamarija Soldo Koruga
4. *Case report-Acute symptomatic seizures caused by alcohol abuse and electrolyte disbalance*
— Tin Karakaš, Maša Kopušar, Mirna Karakaš, Miljenko Crnjaković

5. *Niemann-Pick disease type C-case report*
— Marija Olujić, Romana Marušić, Svetlana Tomić
6. *Microsatellite instability signatures in human meningioma*
— Nika Šlaus, Petra Petanjek, Amadea Tuđen, Petar Brlek, Anja Kafka, Anja Bukovac
7. *The severity of SARS-CoV-2 infection in multiple sclerosis patient treated with B-cell depletion therapy*
— Anamaria Dukić, Nikola Erceg, Tereza Gabelić
8. *Segawa's dystonia-the importance of properly diagnosing rare diseases*
— Nikola Erceg, Anamaria Dukić, Srđana Telarović
9. *Parkinsonism in spinocerebellar ataxia type 1 – the importance of diagnostic algorithm*
— Matea Hodonj, Srđana Telarović
10. *Possible COVID-19 associated rapid onset of Alzheimer's disease: a case report*
— Valentina Juraga, Juraj Jug
11. *From side-effects to a rare syndrome-case report*
— Petra Jurić, Petra Ivančević, Lea Kajba, Dora Karl, Romana Marušić, Anamarija Petek Erić
12. *Obstructive sleep apnea in a patient with acromegaly*
— Petra Jurić, Ivana Jurić, Lea Kajba, Romana Marušić, Dorian Östrreicher, Stjepan Jurić
13. *The role of videourodynamic study in patients with neurological disorders: a case report*
— Dora Karl, Romana Marušić, Petra Jurić, Ivana Radoja
14. *From dementia to glioblastoma*
— Romana Marušić, Anamaria Bukulin, Petra Jurić, Lea Kajba, Petra Ivančević, Hrvoje Bradvica
15. *Research of neuroregenerative mechanisms on primary cortical cell cultures derived from Monodelphis domestica*
— Marta Pongrac, Matea Ivaničić, Antonela Petrović, Ivana Tomljanović, Jelena Ban, Miranda Mladinić Pejatović

16. *Adverse cutaneous reactions to antiepileptic drugs: a five-year retrospective study*
— Lara Vasari, Sandra Peternel
17. *A case report of postnatally diagnosed hydranencephaly*
— Veronika Šikić, Zara Miočić, Marko Kovačević
18. *Use of anxiolytics in medical students at the Faculty of Medicine Osijek*
— Romana Marušić, Marija Olujić, Petra Jurić, Dora Karl, Tatjana Bačun, Dunja Degmečić
19. *Diagnosis and monitoring of intraventricular hemorrhage by ultrasound in premature infants*
— Tomislav Perković, Marina Perković
20. *Command hallucinations in schizoaffective disorder*
— Nika Pušeljić, Nora Pušeljić, Tatjana Bačun, Ivana Jurić, Dunja Degmečić
21. *Correlations between clinical and metabolic variables and smoking among antipsychotic- naïve first-episode and nonadherent chronic patients with psychosis*
— Sara Huskić, Sergej Nadalin, Vjekoslav Peitl, Dalibor Karlović, Lena Zatković, Alena Buretić-Tomljanović
22. *Art as an assistive method in diagnosing schizophrenia in children and adolescents*
— Sara Belčić, Maja Mrak, Valentino Rački, Daniela Petrić

9:30 – 9:45 Break

9:45 – 12:00 **Student session IV**
1. *Guillain-Barré syndrome and COVID-19-case series*
— Benjamin Herrlich, Antonio Kondrić, Valentino Rački, Mira Bučuk, Olivio Perković, Vladimira Vuletić
2. *Coherence in narrative discourse of people with aphasia and traumatic brain injury*
— Marija Jozipović, Valentina Rosković, Sanja Habus

3. *Case report-Reversible cerebral vasoconstriction syndrome in a postpartum patient*
— Maša Kopušar, Tin Karakaš, Miljenko Crnjaković
4. *Giant cell arteritis (GCA): a case report*
— Martin Angjelov, Olivera Kujundzieva, Gordana Kiteva-Trenchevska
5. *Non-pharmacological treatment of Alzheimer's disease in an aging population*
— Lorena Zavidić
6. *Peroneal nerve lesion associated with SARS-CoV-2 infection-case report*
— Marija Janev, Danica Gobin, Berislav Barbalić
7. *Application of Lokomat in neurorehabilitation*
— Mark Tomaj, Mile Marinčić, Petra Krstičević
8. *Assessment of quality of life in people with aphasia*
— Valentina Rosković, Marija Jozipović, Andrea Adašević
9. *Glucose transporter type 1 deficiency syndrome: a case report*
— Ema Šlabek, Ivana Kolić, Igor Prpić
10. *Perinatal stroke: case report*
— Ema Šlabek, Ivana Kolić, Iva Bilić Čače
11. *Severe carbon monoxide poisoning: a case report*
— Dora Šimić, Kristina Lah Tomulić

12:00 – 12:15 Break

12:15 – 14:15 **Workshops**
I. *Awareness – the foundation of mental health*
— Mihael Kozina
II. *Back pain – Where? How? Why?*
— Domagoj Gajski
III. *Neurological consequences of COVID-19 infection*
— Avindra Nath

14:15 – 15:00 Break

15:00 – 16:00 **Plenary lecture**
Intraoperative computed tomography (CT) and augmented reality (AR) in cranial and spinal surgery
— Mirza Pojskić

16:00 – 16:15 Break

16:15 – 17:15 **Plenary lecture**
Neurochemical coding: How 'clever' are neurons?
— Ivica Grković

17:15 – 17:30 Break

17:30 – 18:30 **Plenary lecture**
Protein aggregation in major mental illness
— Nicholas J. Bradshaw

18:30 – 19:00 **Closing and award ceremony**

Plenary lectures

David Rubinsztein

Autophagy and neurodegeneration

Cambridge Institute for Medical Research, UK Dementia Research Institute, University of Cambridge, Cambridge, United Kingdom

Intracellular protein aggregation is a feature of many late-onset neurodegenerative diseases, including Parkinson's disease, tauopathies, and polyglutamine expansion diseases (like Huntington's disease (HD)). Many of these mutant proteins, like that causing HD, cause disease via toxic gain-of-function mechanisms. Therefore, the factors regulating their clearance are crucial for understanding disease pathogenesis and for developing rational therapeutic strategies. We showed that autophagy induction reduces the levels of mutant huntingtin and attenuated its toxicity in cells, and in *Drosophila*, *zebrafish*, and mouse HD models. We have extended the range of intracellular proteinopathy substrates that are cleared by autophagy to other related neurodegenerative disease targets, like alpha-synuclein in Parkinson's disease and tau in various dementias and Alzheimer's disease. After summarising some of our recent work on autophagosome biogenesis and its regulation, I will describe how autophagy is compromised in certain neurodegenerative diseases. I will then consider how autophagy induction may be a powerful therapeutic approach for some of these conditions.

CONTACT dcr1000@cam.ac.uk

Igor Salopek

Modern approaches in psychiatry: innovations and challenges

Karlovac General Hospital, Department of Psychiatry; Faculty of Medicine, University of Rijeka, Department of Social Sciences and Humanities in Medicine; Integrative Mental Health Center

Learning from life, the specificity of each moment, including the first part of the "Century of the Mind" brings the inevitability of constant change, and thus developmental adjustments. Medicine is at the forefront of this, not bypassing psychiatry, which is only seemingly slower. Especially psychiatry which implies biopsychosocial causes and the same therapeutic approaches to help people with cognitive, emotional, and behavioral psychopathological dysfunctions. Therefore, today and in the future, dynamic psychiatric models should include an emphasis on preventive and public health activities with the concept of positive psychiatry and destigmatization of persons with mental disorders. The interaction of institutional and non - institutional capacities must emphasize psychiatry in the community with: mental health centers, mobile, hybrid - telepsychiatric, and day hospital multidisciplinary teams dedicated to the person going through the recovery process, empowerment, and improvement of quality of life. In addition to the challenges of continuously increasing number of people with anxiety-depressive disorders, dementia, addictions (especially behavioral-digital), psychocyborgization, psychiatry based on excellent and innovative clinical practices intertwined with neuroscientific translational achievements plays an extremely important role in medicine of the 21st century.

CONTACT igor.salopek@gmail.com

Miguel Nicolelis

Brain machine interfaces: from basic science to neuroprostheses and neurological recovery

Duke School of Medicine Professor in Neuroscience; Depts. of Neurobiology, Neurology, Biomedical Engineering, and Psychology and Neuroscience

In this talk, I will describe how state-of-the-art research on brain-machine interfaces makes it possible for the brains of primates to interact directly and in a bi-directional way with mechanical, computational, and virtual devices without any interference of the body muscles or sensory organs. I will review a series of recent experiments using real-time computational models to investigate how ensembles of neurons encode motor information. These experiments have revealed that brain-machine interfaces can be used not only to study fundamental aspects of neural ensemble physiology, but they can also serve as an experimental paradigm aimed at testing the design of novel neuroprosthetic devices. I will also describe evidence indicating that continuous operation of a closed-loop brain machine interface, which utilizes a robotic arm as its main actuator, can induce significant changes in the physiological properties of neural circuits in multiple motor and sensory cortical areas. This research raises the hypothesis that the properties of a robot arm, or other neurally controlled tools, can be assimilated by brain representations as if they were extensions of the subject's own body.

CONTACT nicoleli@neuro.duke.edu

Petra Krstičević

Application of robotics in neurorehabilitation

Meditrend, Zagreb, Croatia

Robotic neurorehabilitation is a part of new technologies enabling training in high-dosage and high-intensity. It is finding use in the rehabilitation of patients with motor deficits as a result of neurological disease or condition. Neuroplasticity is the grounds for rehabilitation and recovery of sensorimotor functions after brain damage. Rehabilitation robots are divided into four main categories: assistive robots, robotic prostheses, robotic orthosis, and therapy robots. The latter help and improve movement in patients facilitating recovery, taking part in therapy, and evaluating patient's improvement. Robotic devices can incorporate patient's engagement in high dosage in comparison to standard therapy. Many devices utilize implemented software with games and challenges that additionally motivate patients and yield higher dedication to the rehabilitation process. Applications of the Tyromotion device will be presented. Furthermore, devices and their functions will be demonstrated with an opportunity to try robot-assisted therapy first-hand. This lecture and workshop aim to characterize robotic neurorehabilitation, indications for its use as well as contraindications, in addition to an overview of robotic devices most commonly used for therapeutic purposes in Croatia.

CONTACT office@medi-trend.com

Vesna Šendula-Jengić

Digital psychiatry -yesterday, COVID-19, tomorrow...

Rab Psychiatric Hospital, Rab, Croatia

The introduction of technology into psychiatry, the branch of medicine dealing with the most intricate and elusive part of a human - the mind, very quickly made its way from revolutionary to normal, and even to necessary. The Covid-19 pandemic situation significantly accelerated the adoption of many technological solutions in psychiatry and certainly brought many benefits. The fast development of the technical field is not surprising, but the question remains - how quickly can a human adapt to new technology, accept novel approaches, and fully benefit from them. Is technology outpacing us? Are we being pushed into the water before we have learned to swim? Does medical school prepare one for the new approaches in the treatment of mental illness in the digital environment? What about the education of both the providers as well as the users of the services? The rules of privacy ethics are not the same in the digital environment. There is also the issue of inequality of accessibility of the digitally provided services. The accessibility of digital technology (devices, software, high-speed internet) is affected by a number of factors, such as the socio-economic status, physical disability, or mental state of the potential user of the services. How digital is psychiatry today, how digital might it become in the future, and what are the pitfalls of this process? Technology undoubtedly offers a myriad of fantastic solutions and possibilities in the diagnostics and treatment of mental illness. However, while admiring their potential, we should not lose sight of the ethical, legal, and other issues they might entail.

CONTACT vesna.sendula@gmail.com

Milka Jeric[1], Nives Surjan[2], Antonia Jelicic Kadic[2,3], Nicoletta Riva[4], Livia Puljak[2,5*]

Treatment of acute migraine attacks in children with analgesics on the World Health Organization Essential Medicines List: a systematic review

[1] Department of Dermatovenerology, General Hospital Zadar, Zadar, Croatia;
[2] Laboratory for Pain Research, University of Split School of Medicine, Split, Croatia
[3] Department of Pediatrics, University Hospital Split, Split, Croatia
[4] Department of Pathology, Faculty of Medicine and Surgery, University of Malta, Msida, Malta
[5] Department for Development, Research and Health Technology Assessment, Agency for Quality and Accreditation in Health Care and Social Welfare, Zagreb, Croatia
*** Current affiliation: Catholic University of Croatia, Zagreb, Croatia**

It has been indicated that there are few reliable trials about pharmacological interventions to relieve the pain of migraine in children and that using paracetamol or NSAIDs as first-line agents is “widely accepted good clinical practice during acute attacks unless contraindicated”. The World Health Organization Essential Medicines List (WHO EML) contains a limited number of analgesics. Two analgesics for the treatment of acute migraine attacks in WHO EML for children are ibuprofen and paracetamol. We searched Embase, CDSR, CENTRAL, DARE, and MEDLINE databases up to 18 April 2017. We analyzed randomized controlled trials (RCTs) and systematic reviews (SRs) about the efficacy and safety of ibuprofen or paracetamol for the treatment of acute migraine attacks in children. We conducted meta-analysis and assessments of evidence with GRADE, Cochrane risk of bias tool, and AMSTAR. Three RCTs (201 children) and 10 SRs on ibuprofen and/

CONTACT livia.puljak@unicath.hr

or paracetamol for acute migraine attacks in children were included. Meta-analysis indicated that ibuprofen was superior to placebo for pain-free at 2 h or pain relief at 2 h, without difference in adverse events. There were no differences between paracetamol and placebo, or ibuprofen and paracetamol. Ten SRs that analyzed various therapies for migraine in children were published between 2004 and 2016, with discordant conclusions. Limited data from low-quality RCTs indicate that ibuprofen and paracetamol might be effective analgesics for treating migraine attacks in children. The inclusion of ibuprofen and paracetamol as antimigraine medicines for children in the WHO EML is supported by indirect evidence from studies in adults. This study began as a diploma thesis of a pharmacy student. Systematic reviews and methodological studies analyzing biomedical research are an excellent opportunity for students to gain research experience. These types of studies require low resources and are time- and place-independent.

CONTACT livia.puljak@unicath.hr

Mirza Pojskić

Intraoperative computed tomography (CT) and augmented reality (AR) in cranial and spinal surgery

Department of Neurosurgery,
Philipps University Marburg, Germany

Progress in computed tomography (CT) technology, as well as increasing demand and interest in the neurosurgical community in spinal intraoperative imaging, has led to a renaissance of intraoperative CT (iCT). Neuronavigation is a routine method in neurosurgery. The use of augmented reality (AR) in neurosurgical procedures has its roots in superimposing the optical image in operating microscopes. For more than 20 years, (AR) based on head-up displays (HUD) of operating microscopes is clinically available. Registration accuracy is the main factor influencing overall navigation accuracy. Standard fiducial- or landmark-based patient registration is user-dependent and error-prone. Intraoperative imaging offers the possibility for user-independent patient registration. We present our experience with iCT-based neuronavigation with the application of AR for cranial as well as for spinal procedures (neurooncology, skull base, vascular, deep brain stimulation, degenerative and infectious disease). For CT scanning, we applied a 32-slice movable CT scanner (AIRO, Brainlab, Munich, Germany), which is closely integrated into a navigation setup consisting of a ceiling-mounted double monitor navigation system (Curve, Brainlab, Munich, Germany) in combination with a dual-display system (Buzz, Brainlab, Munich, Germany) for further visualization of co-registered images. Segmentation of anatomical target structures of interest (tumors, nerves, vessels, ventricles, vertebra, spinal cord, aorta) which were visualized by AR, was based on preoperative magnetic resonance and computed tomography (CT) images, that were in cranial cases rigidly registered with a 3D image data set using the image fusion element (BrainLab) or non rigidly fused to low-dose intraoperative CT (iCT) data in spinal cases. In addition to superimposing the 3-D objects in the operating microscope, the fused datasets are visualized in the spinal navigation application. In cranial and spinal procedures, iCT proved to be a straightforward, automatic, and highly reliable navigation registration device. Low-dose CT protocols allowed to reduce the patient radiation exposure for the registration scan, without decreasing registration accuracy. A microscope-based AR greatly supports the surgeon in understanding the 3-D anatomy, thereby facilitating surgery.

CONTACT mirza.pojskic@uk-gm.de

CONTACT mirza.pojskic@uk-gm.de

Ivica Grković

Neurochemical coding: How 'clever' are neurons?

Department of Anatomy, University of Split School of Medicine

Co-localization and co-release of various neuroactive substances (mainly neuropeptides) with classical neurotransmitters (like acetylcholine and/or noradrenaline) have been well documented in various parts of the nervous system. A functional significance of co-localized substances lies in the fact that the unique combinations of substances could be interpreted as potential 'chemical codes'. The functionally specific chemical codes that were found can be utilized to identify the final common (autonomic) pathway for the transmission of messages from the central nervous system to the peripheral effector targets/organs. These pathways consist of specific subpopulations of preganglionic neurons that provided inputs to functionally distinct postganglionic neurons. Retrograde neuronal tracing in combination with multiple immunohistochemistry for the detection of various neuroactive substances was combined in order to produce function/projection-specific pathways. Specificity of neuron-to-neuron projections was established using electron microscopy. This approach was then used to discover what happens to the autonomic neurons when target tissues are 'shifted' so that neurons are 'forced' to innervate completely new target tissue. Do they adjust their 'chemical fingerprint' to the new tissue and how? What happens to neurons if the target tissue (like the myocardium) is damaged? Answers to all these questions will be illustrated by presenting the original research conducted in the 'Laboratory for experimental neurocardiology' at the University of Split School of Medicine.

CONTACT ivica.grkovic@mefst.hr

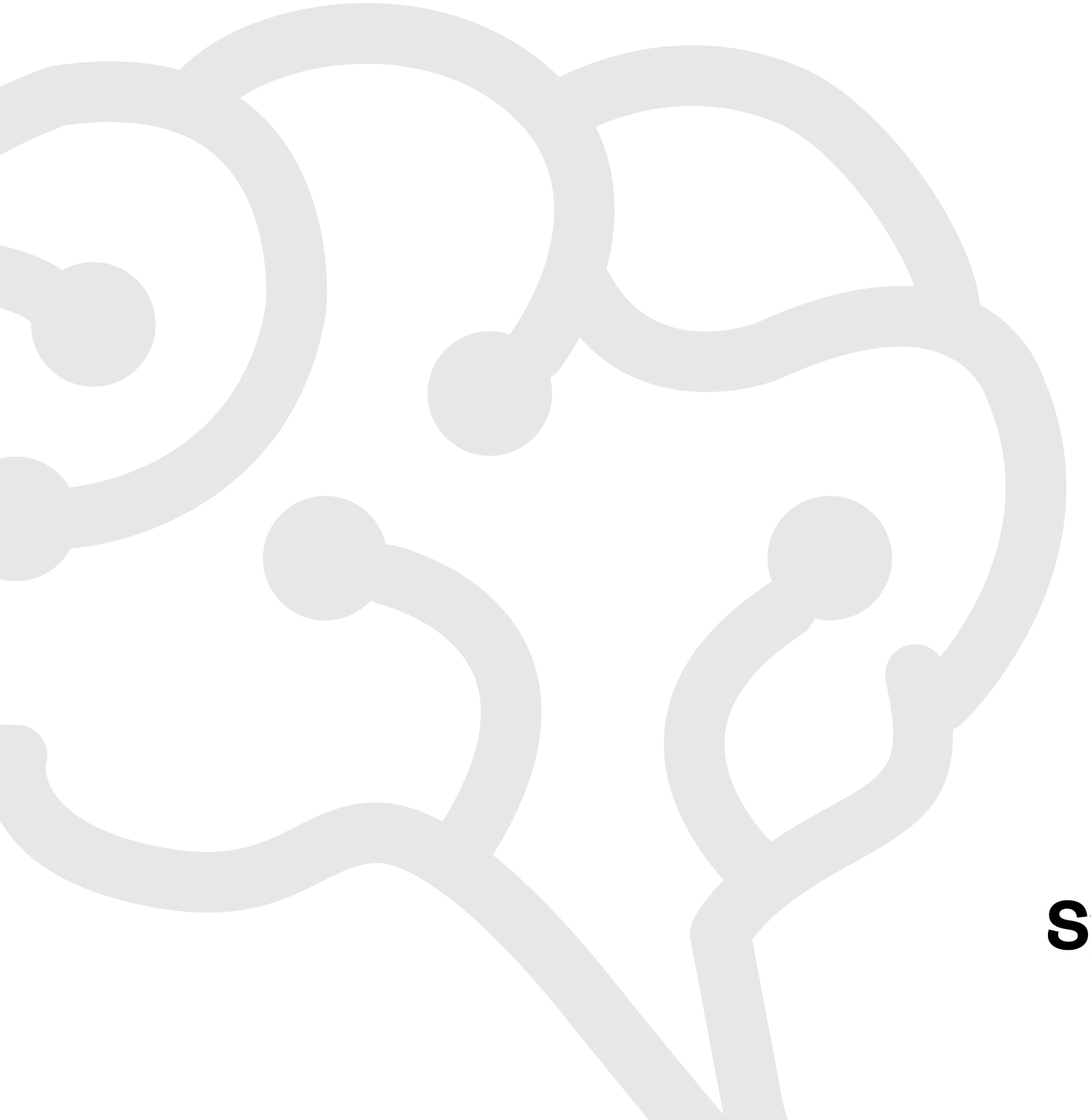
Nicholas J. Bradshaw

Protein aggregation in major mental illness

Department of Biotechnology, University of Rijeka

Major mental illnesses, such as schizophrenia and major depressive disorder, are devastating conditions and are among the largest causes of disability, both regionally and internationally. This problem is made significantly worse by the lack of biological tests available to diagnose them, and the comparatively small range of effective medications to treat them. It is therefore vital that we gain a greater understanding of what the biological events are that underlie these conditions. The genetic background to these conditions has been thoroughly investigated but has proven to be highly complex, with few obvious targets for new drugs or therapies. We, and our collaboration partners, have therefore been attempting to complement this approach by also studying proteins involved in major mental illness. Specifically, we have been investigating the existence of misfolded protein aggregates in these disorders, comparable to similar neurotoxic aggregates in neurodegenerative diseases such as Alzheimer's or Parkinson's disease. Several proteins have now been identified that appear to specifically form aggregates in the brains of patients with schizophrenia, bipolar disorder and/or depression. These are all brain-expressed proteins that, when functioning normally, are involved in either synaptic function and/or neurodevelopment. In many instances, one isoform or variant of the protein readily forms aggregates in cell culture and/or animal models, while others do not. For several of the proteins, specific regions of the protein have been shown to be essential for aggregation. Work is now ongoing to determine how the aggregation of these proteins occurs, and what their consequences are for the normal function of neurons and the brain. While still at a comparatively early stage, the study of protein aggregation in mental illness is showing promise. Studies in larger brain collections, as well as further biochemical characterization of the proteins, are now required to determine their ultimate relevance for diagnosis and/or treatment of major mental illness.

CONTACT nicholas.b@uniri.hr



Symposia

Selma Terzić[1], Nevena Mahmutbegović[2]

Schizophrenia and/or epilepsy; a case report

[1] Faculty of Medicine, University of Sarajevo, Bosnia and Herzegovina;
[2] Neurology Clinic, Clinical Center of Sarajevo University, Bosnia and Herzegovina

Up to 30% of the patients diagnosed with epilepsy will have some form of a psychiatric condition. Incidence of schizophrenia-like psychosis mainly increases in temporal lobe epilepsy. On the other hand, the clinical presentation of temporal epilepsy can present with different psychiatric symptoms that can overshadow the epileptic manifestation leading to misdiagnoses. Our aim is to present a case of a 28-year-old patient who has been diagnosed with schizophrenia and treated for 8 years. The first symptoms occurred in 2008 with a strike of fear, followed by a jump through a window, which was understood as a suicide attempt. In November 2011, two convulsive attacks were recorded for the first time. Overall, the patient had 17 hospitalizations in a psychiatric hospital. His diagnoses were hebephrenia and epilepsy. Magnetic resonance imaging (MRI) of the brain was normal. Electroencephalography (EEG) repeatedly showed moderate severity dysfunction of the fronto-temporo-occipital region. It was evident, from the patient's history, that the aura was typically manifested in the form of structured auditory and visual hallucinations. Visual illusions as macropsia or micropsia were followed with characteristic vegetative symptoms. Focal seizures followed by a head toss to the right and spasms of the left hand were recorded in May 2014. After therapy revision, the patient was seizure free, psychologically and affectively adequate, and completely functional in his environment. Better understanding of mechanisms of temporal epilepsy may enable early identification of patients and adequate therapeutic strategies.

Keywords Psychosis; Schizophrenia; Temporal Lobe Epilepsy

CONTACT selmicte@hotmail.com

Maja Mrak[1], Sara Belčić[1], Jakov Končurat[1], Emil Klarić[1], Valentino Rački[2], Daniela Petrić[3]

First episode psychosis in a COVID-19 positive patient; a case report

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] Clinic of Neurology, Clinical Hospital Center Rijeka, Croatia
[3] Clinic of Psychiatry, Clinical Hospital Center Rijeka, Croatia

The clinical manifestation of SARS-CoV- 2 infection is typically marked with respiratory symptoms. However, there are numerous varying neuropsychiatric symptoms that can be present at onset, due to the neurotropic characteristics of the virus. We present an atypical clinical manifestation of SARS-CoV- 2 infection dominated by acute psychotic symptoms. A 20-year-old previously healthy man with no personal or family history of mental illness presented with new-onset psychosis. At admission, he was manifestly psychotic, uncooperative, resisting care while entering tied and handcuffed on the stretcher, half-naked at the verge of agitation, was staring, and was non-communicative. The PCR test for COVID-19 was positive. During his stay in the hospital, he was subfebrile and febrile with normal oxygen saturation and without chest X-ray abnormalities. His psychotic symptoms initially improved with antipsychotics and benzodiazepines and further improved with the resolution of COVID-19 symptoms. There is a growing number of reports regarding new-onset brief psychotic disorders in COVID-19 positive patients, without previous mental illness and without a positive family history. The onset of physical manifestations varied from days to weeks, with mostly mild COVID-19 symptoms and delusions as the most dominant

CONTACT maja.mrak@student.uniri.hr

manifestation. SARS-CoV-2 infection has been shown as a trigger for a psychotic episode. We would like to emphasize the diversity of the clinical manifestation of SARS-CoV-2 infection. Special attention should be given to patients with no previous history of psychiatric disorders.

Keywords Psychiatry; Psychotic Disorders; SARS-CoV-2

CONTACT maja.mrak@student.uniri.hr

Sara Varljen[1], Tanja Grahovac Juretić[2], Klementina Ružić[2]

Therapy resistant depression or hospitalism; a case report

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] Department of psychiatry at Clinical Hospital Centre Rijeka, Croatia

Therapy resistant depression is a form of depression that is resistant to therapy with antidepressants, i.e., there is a weak therapy answer to at least two different pharmacological treatment methods with antidepressants from different pharmacological groups. The aim of this case report is to demonstrate a 64-year-old patient who is in psychiatric treatment for a long period because of symptoms from the depressive disorder spectrum. The patient has been hospitalized several times in different psychiatric clinics. The patient undergoes regular psychiatric checkups and is under psychotropic medication. She was treated with different combinations containing an antidepressant in combination with an anxiolytic and antipsychotic drug. She also underwent transcranial magnet stimulation therapy. During the hospitalization period, an improvement in the patient's mental wellbeing was noticed, unfortunately after being discharged her condition intensified and got worse in domicile surrounding, respectively. Hospitalism is a psychoneurotic behavior of repeated visits to the hospital. It can manifest itself as a loss of interest in performing daily activities and overcoming challenges of daily life because all of the patients' needs are met in the hospital setting. Dominant symptoms in her clinical presentation include weakness, apathy, and fatigue. The patient complains of a feeling of constant discomfort in the body, she has troubles with sleeping and loss of appetite. With this case report, we intended to point out a high probability of hospitalism being present in this patient.

Keywords Depression; Transcranial Magnetic Stimulation

CONTACT sara.pilj.varljen@student.uniri.hr

Petra Meštrić[1], Ana Kaštelan[1,2], Daniela Petrić[1,2]

The impact of the COVID-19 pandemic on the mental health of adolescents

[1] Faculty of Medicine, University of Rijeka, Rijeka; [2] Clinical Department of Psychiatry, Clinical Hospital Centre of Rijeka, Rijeka

It has been a year since the World Health Organization declared the COVID-19 pandemic. The pandemic affected all aspects of life, from existential to social and cultural. The spread of the infection causes fear of illness and death, along with fears related to financial securi

CONTACT petramestric@gmail.com

ty. There is growing evidence of a significant negative impact of the pandemic on the mental health of adolescents, and consequently of an increased need for psychiatric care. The detrimental impact of the pandemic is thought to be mediated not only by the aforementioned fears but also by social distancing measures aimed at preventing the spread of the infection. Socialization among peers and establishing close relationships outside the family are the main psychological tasks of adolescence. Therefore, measures that limit socialization can be particularly detrimental to the psychological development and mental health of adolescents. The purpose of this paper is to briefly review the results of scientific research that indicate the negative effects of a pandemic on the mental health of young people, as well as their growing need for psychiatric care during a pandemic.

Keywords Adolescent; COVID-19; Health; Pandemics; Psychiatry

CONTACT petramestric@gmail.com

Sara Milićević

Internalizing disorders in children and adolescents with autism spectrum disorders

University of Belgrade, Faculty for Special Education and Rehabilitation, Belgrade, Serbia

CONTACT saramilicevic13@gmail.com

Mental disorders, especially internalizing, are common in the population of people with autism spectrum disorders. This comorbidity is usually a characteristic of children and adolescents. Nevertheless, observing the fact that the symptoms of depression, anxiety, or obsessive-compulsive disorder are often misinterpreted with the manifestation of autism spectrum disorders, it is difficult to establish the right diagnosis. The aim of this paper is to show the prevalence of internalizing disorders in the population of children and adolescents with autism spectrum disorders, the symptoms of the most frequent internalizing disorders, as well as the profile of persons at greater risk of this diagnosis. Scientific papers and journals with the topic of internalizing disorders, autism spectrum disorders, and their comorbidities, published in the previous decade, were analyzed. Summarizing the data, the results indicate that the frequency of these disorders is higher than in the typical population, as well as in the population of persons with other types of disorders, such as ADHD and intellectual disability. In addition, anxiety and depression are the most common disorders within this population. Furthermore, symptoms that indicate the presence of these disorders can be altered behavior and classic symptoms experienced by the typical population, such as depressed mood, avoidant behavior, and irritability. The vast majority of authors emphasize high intelligence, male gender, negative experience in social relations, unsupportive environment, and older age as typical characteristics of these people. It can be concluded that there is not much available information on internalizing disorders of this population, regarding the importance of this topic for the future establishment of differential diagnosis, education, and rehabilitation of these children and adolescents. It is very important to prioritize introspection and communication about emotions in the future work with this population in favor of easier recognition and treatment of these disorders.

Keywords Anxiety; Autistic Disorder; Child; Depression

CONTACT saramilicevic13@gmail.com

Dorian Laslo[1], Terezija Berlančić [1,2,3], Tatjana Bačun[1,4], Dunja Degmečić[1,5]

Video games addiction and its effect on sleep quality among college students of J.J. Strossmayer University of Osijek

[1] Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [2] Department of obstetrics and gynecology, General County Hospital Nasice, Nasice, Croatia; [3] Faculty of Economics in Osijek, Josip Juraj Strossmayer; University of Osijek, Osijek, Croatia [4] Department of Endocrinology, University Hospital Centre Osijek, Osijek, Croatia; [5] Department of Psychiatry, University Hospital Centre Osijek, Osijek, Croatia

In the last couple of years, video games (VG) have become largely accessible, and more and more people started playing them as a result of fun, boredom, or stress relief. They are most popular among children, teenagers, and young adults. However, in many cases instead of providing fun, they have become an addiction that obstructs them in their everyday life and sleeping schedule, resulting in poor sleep quality. The aim of this study was to investigate the frequency of VS addiction and its effect on the sleep quality of college students. This online, anonymous questionnaire study was done during one month by the use of a specially designed questionnaire, which contained Problematic Online Gaming Questionnaire Short Form (POGQSF), Sleep Quality Survey (SQS), and demographic data questions. There was a total of 230 participants currently studying at the University of Osijek. There were 42,60% (98/230) males. Age median was 22 years with a minimum being 18 and a maximum of 44 years. 16,5% (38/230) were classified as having problematic gaming habits according to POGQSF, acquired point median was 23 points, the minimum was 12, and the maximum was 55 points. Regarding SQS median of acquired points was 28, minimum was 13, and maximum 64 points. The study has shown that students who were classified as having problematic gaming habits according to POGQSF had poorer sleep quality p=0,007, also female students had poorer sleep quality p=0,014. VG addiction disturbs sleep quality in college students of the University of Osijek.

Keywords Addictive Behavior; Sleep; Students; Video Games

CONTACT dorian.laslo123@gmail.com

Emir Begagić[1], Lejla Čejvan[1], Hakija Bečulić[2]

Open resection of rare and big Schwannoma of brachial plexus branches

[1] University of Zenica, Faculty of Medicine, Zenica, Bosnia and Herzegovina
[2] Cantonal Hospital Zenica, Department of Neurosurgery, Bosnia and Herzegovina

Schwannomas are encapsulated tumors that originate from Schwann cells and develop slowly. Tumors can develop in any nerve, but tumors of the brachial plexus are the most uncommon, accounting for less than 5% of all schwannomas. A 29-year-old woman presented with a mass on the left upper arm's posteromedial side. It's a localized mass, solid to the touch, of the upper arm which causes distal paresthesia. A Magnetic Resonance Imaging scan revealed a mass along with the medial head of the triceps brachial muscle. This tumor affects the ulnar, radial, and musculocutaneous nerves on radiography. The brachial artery and vein were first removed from the tumor, during resection. The ulnar nerve and the musculocutaneous nerve are isolated. A simple origin infiltrates the radial nerve, and preserved fibers were successfully dissected. Since more than half of the radial nerve is preserved, there is no

CONTACT begagicem@gmail.com

need for a sural graft. The patient's left dorsiflexion was reduced after surgery. The patient made a full recovery after physical therapy. The first treatment option was open surgery due to the tumor's size and presence in surrounding structures. The prompt therapy aided in the avoidance of neurological deficits. The benign nature of the tumor was confirmed by pathohistological analysis, which revealed dominant Antoni A areas and a less myxoid hypocellular portion (Antoni B areas). Because of the minimal dorsiflexion of the left hand, the recovery phase included physical therapy. Separation of non-infiltrated nerve fibers and rehabilitation process represents a safe protocol that results in a positive outcome.

Keywords Brachial Plexus; Neoplasms; Neurosurgical Procedures; Schwannoma

CONTACT begagicem@gmail.com

Mario Hero[1], Vladimira Vuletić[1,2]

Outcome of deep brain stimulation in Parkinson's disease in an elderly patient-case report

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] Clinic of Neurology, KBC Rijeka, Rijeka, Croatia

Parkinson's disease (PD) is a chronic progressive neurodegenerative disease characterized by the deposition of abnormal aggregates that cause significant loss of dopaminergic neurons in the pars compacta of the substantia nigra. The aim of this case report is to present the outcome of deep brain stimulation (DBS) through a period of 2,5 years in a seventy-eight-year-old female patient suffering from drug-resistant PD. We present the case of a 74-year-old patient who was interested in DBS due to drug-resistant PD. The disease manifested itself in the form of a tremor of the left arm and leg and significantly impaired her quality of life. At the age of 75, she was embedded with DBS in the subthalamic nuclei (STN) bilaterally. At the first postoperative check-up, it was found that there was almost no tremor after stimulation, and the speech was orderly. Electrode stimulations were placed on the right (D 0- 2.1 V 90 ys 130 Hz) and on the left (L 8- 0.8 V 90 ys 130 Hz). Over a period of 2.5 years, the patient was regularly monitored, and electrode stimulation was changed twice. At the last check-up, she stated that she performed her daily activities without hindrance, and in her free time, she was even knitting, which she couldn't do before. Also, the patient was well cognitively preserved. The level of electrode stimulation was right (D 0–2.4 V 90 ys 130 Hz) and left (L 8- 1.0 V 90 ys 130 Hz). In carefully selected candidates, who have been suffering from drug-resistant PD for many years, age above 70 years should not be a contraindication for DBS STN. The presented case shows that DBS STN can be helpful in reducing symptoms and thus significantly improve the quality of life in such patients.

Keywords Deep Brain Stimulation; Parkinson's Disease; Subthalamic Nucleus

CONTACT mario.hero10@gmail.com

CONTACT mario.hero10@gmail.com

Kamelija Horvatović[1], Filip Jadrijević-Cvrlje[2], Goran Mrak[3], Kamelija Žarković[4]

Uncommon supratentorial anaplastic glioneuronal tumor in a pediatric case of Li-Fraumeni syndrome

[1] School of Medicine, University of Zagreb, Zagreb, Croatia; [2] Department of Oncology, Children's Hospital Zagreb, Zagreb, Croatia; [3] Department of Neurosurgery, University Hospital Centre Zagreb, Zagreb, Croatia; [4] Department of Pathology, University Hospital Centre Zagreb, Zagreb, Croatia

CONTACT kamelija2h@gmail.com

Li-Fraumeni syndrome (LFS) is a rare hereditary disorder commonly associated with mutations in tumor suppressor gene TP53 resulting in inadequate proliferation regulation and predisposition for development of multiple malignant neoplasms, including brain tumors. A 15-year-old boy experiencing persistent headaches followed by nausea in duration of 3 weeks was admitted to UHC Zagreb after brain MRI revealed right frontotemporoparietal multilobular expansive process with perifocal edema and inhomogeneous postcontrast opacity along with a coexisting lesion located in the fourth ventricle. Craniotomy and neurosurgical extirpation of the tumor tissue was performed, without postoperative complications and neurological deficit. PHD successfully classified the infratentorial neoplasm as ependymoma gradus IIB. Histologically, the tissue supratentorial tumor (ST) consisted of polymorphic, irregular multinuclear, and spindle cells along with clusters of atypical glia and tissue necrosis. Immunohistochemistry of the tissue revealed positive signal for glial fibrillar protein (GFAP), p53, β-tubulin, synaptophysin, and vimentin, whereas Ki67 measured proliferation activity showed 76%. The exact determination of the ST remains uncertain but is described as primary, anaplastic glioneuronal tumor gradus III. Most probable diagnosis might be anaplastic ganglioglioma or less likely anaplastic pleomorphic xanthoastrocytoma. Methylation profile was also examined in UHC Heidelberg where similarities with inflammatory myofibroblastic tumors were concluded, score 0.9. However, mentioned results did not match previous immunohistochemistry and histological findings. The patient underwent genetic testing, and LFS was identified. According to the newly found disorder, avoidance of radiotherapy was recommended, and everolimus was administered. Four months later relapse of the ST occurred and was immediately neurosurgically treated. PHD analysis revealed matching characteristics as previously extirpated ST. The exact determination of the ST in this patient suffering from LFS remains unclear. The ST neoplasm consists of polymorphic glial, neuronal, and gigantic cells along with sarcoma features. The entity might not be previously described in the literature.

Keywords Ependymoma;
Li-Fraumeni Syndrome;
Primary Malignant Brain Neoplasm;
Supratentorial Tumor

CONTACT kamelija2h@gmail.com

Lea Vrhovnik[1], Sanja Kovačić[2], Slavica Sović[3], Ivana Martinović[4]

Doppler flow velocity measurements in the extracranial carotid arteries in healthy adults

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia; [2] General Hospital Zabok and Hospital of Croatian Veterans, Department of Neurology, Zabok, Croatia; [3] University of Zagreb, Andrija Štampar School of Public Health,Zagreb, Croatia; [4] University Hospital Centre Zagreb, Department of Neurology,Intensive Care Unit, Zagreb, Croatia

Carotid Doppler ultrasonography is a powerful modality for evaluating the pathology of carotid arteries. A vast range of hemodynamic data can be generated by Doppler ultrasound: maximum velocities values as peak systolic velocity (PSV), end-diastolic velocity (EDV), and Doppler indices, resistive index (RI), and pulsatility index (PI). To establish Doppler reference data and to investigate the development of hemodynamics in the extracranial internal carotid arteries (ICA) related to age, we performed a descriptive cross-sectional, observational study on 227 (102 men and 125 women) healthy adults from 28 to 86 y old. Angle-corrected flow velocities PSV, EDV were measured and waveform parameters calculated, RI and PI, in all the arteries. We divided the examinee into three age groups (20-39 years, 40-59 years, and above 60 years). Associations of age and analyzed variables were presented as Pearson's correlation coefficients. Side-to-side and gender differences in distribution of variables were analyzed with Student t-test for dependent variables. In the ICA flow velocities decreased significantly during aging in both gender (PSV; r -0.8124, EDV; r -0.7857), the RI statistically increased (r 0.6777), while age-related PI changes were not statistically significant (r 0.5127). There were no significant side-to-side differences in flow velocities

CONTACT lvrhovnik@student.uniri.hr

and hemodynamic indices. The 20–39 age group showed statistically significant higher PSV and EDV values, and lower RI values in females (p<0.005), while other two groups 40-59 and above 60 showed no statistically significant gender differences. PI showed no statistical gender difference related to age groups. The reference data provided here, combined with the published data from other reports give us the means to survey the physiological age-dependent evolution of the extracranial brain supplying arteries. In the evaluation of hemodynamic changes in patients with cerebrovascular disease, we consider the existence of data on normal values to be crucial.

Keywords Blood Flow Velocities; Doppler Ultrasonography; Internal Carotid Arteries; Reference Ranges

CONTACT lvrhovnik@student.uniri.hr

Gloria Rožmarić[1], Mario Hero[1], Valentino Rački[1,2], Vladimira Vuletić[1,2]

A case report of a novel GNB1 mutation and the response to deep brain stimulation

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] University Hospital Center Rijeka, Rijeka, Croatia

Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions, leading to abnormal involuntary movements or postures. Dystonia is in some cases caused by genetic mutations, most commonly occurring with TOR1A, THAP1, GCH1, and KMT2B mutations, but only a few cases have been reported with a GNB1 mutation. The rare cases reported up to now in the literature had developmental delay, hypotonia, or dystonia, with dystonia being infrequent in these patients. We present a 27-year-old woman with a history of difficulty walking, abnormal neck posture, and head jerks since childhood. She was diagnosed with dystonia at the age of 14. The symptoms became more severe over time, affecting her entire body and interfering with the majority of her everyday activities. She underwent DBS of the globus pallidus internus (GPi) at the age of 22 after failing to respond to several oral medications. DBS helped with neck rigidity and head posture, but difficulty walking and involuntary shaking of both hands were still present. Genetic testing performed at the age of 27 showed a heterogeneous, probably pathogenic variant c.352G>C in the GNB1 gene that led to the replacement of aspartate with histidine at the 118th position in the amino acid sequence. This variant isn't described in the single nucleotide polymorphism database nor in the genome aggregation database. In this case report, we describe a novel c.352G>C variant in the GNB1 gene. To the best of our knowledge, we present the second case of a GNB1-dystonia treated with GPi DBS. Furthermore, it is important to emphasize the difficulties in treating the patient with both oral and invasive treatment techniques.

Keywords Childhood Onset Dystonia; Deep Brain Stimulation; GNB1 Protein

CONTACT gloria.rozmaric@gmail.com

Iva Sabljić[1], Mihael Mišir[2]

Bacterial endocarditis complicated with multiple embolic cerebral infarctions and multiple organ failure syndrome

[1] University of Josip Juraj Strossmayer in Osijek, Faculty of Medicine, Osijek; [2] University Hospital Center Osijek, Croatia

The objective of this clinical case report is to highlight possible neurologic complications of bacterial endocarditis, such as cerebral embolism linked

CONTACT ivasabljicc@gmail.com

to meningoencephalitis, brain abscess, and secondary microhemorrhage. Additionally, this case was complicated by sepsis and multiple organ failure syndrome (MOFS). A 34-year-old man was admitted to the hospital with altered mental status in terms of unusual and strange behavior and disorientation. He was febrile for four days followed by vomiting on the second day of illness. On clinical examination signs of meningism were positive. Initial CT imaging showed a change corresponding to encephalitis. Clinical laboratory test results indicated sepsis, thrombocytopenia, disseminated intravascular coagulation, and possible liver and kidney damage while liquor analysis indicated staphylococcus bacterial infection. After brain MR imaging showed septic microembolism, bacterial endocarditis was suspected. Subsequently, transesophageal ultrasonography was done and aortic valve vegetations were found. Further on, aortic valve replacement surgery was performed. Control MR pointed on brain abscess with possible AV malformation or aneurism of the middle cerebral artery and temporal zone of hemorrhage due to erosion of the vessel wall (septic emboli). It was decided that neurosurgical treatment in terms of abscess aspiration would not be performed until the encapsulation of abscess. In the following days, the patient's neurological and circulatory status got worse despite of the strict treatment protocol. Abdominal CT confirmed the ischemic injury of the kidneys, spleen, and liver. After progression on the CT scan, decompressive craniotomy and external ventricular drainage were performed. Ultimately, coma and brain stem areflexia ensued. The patient died even treatment strategy was adequate and following the guidelines.

Keywords Bacterial Endocarditis; Embolic Infarction; Middle Cerebral Artery; Multiple Organ Failure

CONTACT ivasabljicc@gmail.com

Lara Batičić[1], Edvard Bedoić[2], Dijana Detel[1]

Neuroimmunomodulation mediated by DPP IV/CD26 in murine experimental colitis

[1] Department of Medical Chemistry, Biochemistry and Clinical Chemistry, Faculty of Medicine, University of Rijeka, Brace Branchetta 20, 51000 Rijeka, Croatia; [2] Faculty of Medicine, Integrated undergraduate and graduate university study Medicine, University of Rijeka, Brace Branchetta 20, 51000 Rijeka, Croatia

Dipeptidyl peptidase IV (DPP IV/CD26) is a multifunctional protein and serine protease which plays a crucial role in physiological and pathological conditions. Neuropeptide Y (NPY) is considered to have a role in the regulation of immune and inflammatory events. Vasoactive intestinal peptide (VIP) has a potential protective effect on the intestinal mucosa. Both VIP and NPY are gut-brain peptides and DPP IV substrates. A causal connection between DPP IV/CD26 and inflammatory events has been proposed but the mechanisms of these interactions are still unclear. Our hypothesis was that DPP IV/CD26 could affect the neuroimmune response at the systemic and local levels during colitis development and resolution in mice. Our aim was to evaluate the possible role of DPP IV/CD26 and the relevance of the gut-brain axis in a colitis model in mice. A model of Crohn's disease has been induced in CD26 deficient and wild type (C57BL/6) mice using 2,4,6-trinitrobenzenesulfonic acid (TNBS). Experimental animals were monitored daily and sacrificed on crucial days of colitis. NPY and VIP concentrations and protein expressions likewise DPP IV/CD26 enzymatic activity have been determined among the gut-brain axis, on local and systemic levels, by ELISA and Western blot techniques. Our study revealed constitutionally significantly ($p<0.05$) higher serum VIP concentrations in CD26 deficient compared to wild-type mice. Maximum values were determined in the acute phase of colitis in serum, colon, and brain. NPY concentrations in the

CONTACT lara.baticic@uniri.hr

colon were increased in both mice strains in acute inflammation as well, with significantly ($p<0.05$) higher values in CD26 deficient mice. DPP IV/CD26 enzymatic activities among the gut-brain axis were also found to be altered in the acute phase of the disease. Obtained results indicate a causal connection between levels of VIP and NPY, inflammatory events, and the activity of DPP IV/CD26. The relevance of the gut-brain axis has been confirmed. DPP IV/CD26 has been shown to play an important neuroimmunomodulative role in colitis pathogenesis and should be further evaluated in order to develop new potential therapeutical approaches.

Keywords Colitis; Colon; Neuroimmunomodulation; Neuropeptide; Trinitrobenzenesulfonic Acid

CONTACT lara.baticic@uniri.hr

Simone Ruhije Bertoša[1], Patricia Estañol Cayuela[2], Beti Zaharija[1], Nicholas J. Bradshaw[1]

Regions of proteins critical to their aggregation in mental illness

[1] **University of Rijeka, Department of Biotechnology, Rijeka, Croatia**
[2] **Universitat Autònoma de Barcelona, Faculty of Biosciences, Barcelona, Spain**

Mental illnesses are common health conditions, associated with problems functioning in the family, work, and social environments. These illnesses may be chronic, and they involve distress caused by changes in emotions, thoughts, and/or behaviors. Examples of mental illnesses include schizophrenia, major depressive disorder, psychoses, and bipolar disorder. Even though most mental illnesses patients can be treated, very little is known about their biology, their genetic component, or their physiological cause. There are many possible biological mechanisms by which mental illnesses may develop, one of them being the aggregation of specific proteins, which form insoluble aggregates in the brain and disrupts its correct functionality. Understanding protein aggregation may be directly linked with critical protein regions, which cause their aggregation. These critical protein regions could therefore potentially be targets for future treatment of specific mental illnesses. In this study, we aim to identify which protein regions cause specific proteins to aggregate, which may lead them to be involved in mental illness. To do this, we are cloning fragments of the genes encoding these proteins, and then expressing protein fragments in human cell lines. These are subsequently analyzed by immunofluorescent microscopy to determine the presence of protein aggregates in the cells. So far, we have found that an unstructured region in the center of the protein DISC1 (Disrupted in Schizophrenia 1) forms the basis for its aggregation. DISC1 is a protein that takes part in scaffolding protein and regulates neurodevelopment. We are expanding our research to try and determine critical regions of other proteins of interest in mental illnesses. Further research on the biology of mental illnesses would potentially provide new means for their diagnosis, treatment, and prognosis.

Keywords Human DISC1 Protein; Mental Disorders; Pathological; Protein Aggregation; Proteostasis

CONTACT simone.bertosa@student.uniri.hr

Mihaela Bergman, Maja Juković, Bobana Samardžija, Tina Fartek, Beti Zaharija, Nicholas J. Bradshaw

Co-aggregation of proteins involved in mental illness

University of Rijeka, Department of Biotechnology, Rijeka, Croatia

Chronic mental disorders (CMD), including bipolar disorder, major depression disorder, and schizophrenia, are complex conditions characterized by both genetic and non-genetic elements. However, their underlying biological causes remain relatively unknown. Determining a specific biological cause for any of these illnesses may provide us with a drug target whose design would be the next step in defeating these illnesses. Over the past several years, a number of studies proposed the presence of disturbed proteostasis as a possible pathological cause of non-genetic cases of chronic brain disorders. The idea of aggregation of one or multiple proteins (co-aggregation) derived from research that established that disturbance of proteostasis in the brain could be one of the key features for developing such disorders. Providing evidence of co-aggregation of certain proteins could give us more insight into understanding the biological causes of specific brain disorders. We are investigating the presence of co-aggregates through expressing proteins of interest firstly in neuroblastoma cell line, SHSY5Y, and, if proteins are proven to co-aggregate, testing brain tissue samples for expression of these aggregated proteins. Previous studies characterized a number of proteins that are known to misassemble in CMD, which are CRMP1, dysbindin-1, DISC1, NPAS3, and TRIOBP-1. We have already seen some proteins co-aggregate, such as DISC1 with CRMP1 and dysbindin-1, while others do not such as TRIOBP-1 with DISC1 and CRMP1. We are now expanding these studies to investigate the co-aggregation between other proteins found in CMD and to look at whether their aggregation affects other known interaction partners. We are hoping that the results of our research will contribute to understanding the biological causes of CMD and possibly lead to subsequent research on designing drugs that could effectively treat those illnesses.

Keywords Mental Disorders; Protein Aggregation; Proteostasis; Schizophrenia

CONTACT mihaela.bergman@student.uniri.hr

Petar Brlek,
Anja Bukovac,
Anja Kafka,
Nives Pećina-Šlaus

Integrative analysis of tumor suppressor CHUK in diffuse gliomas of the brain

University of Zagreb, School of Medicine, Department of Biology, Croatian Institute for Brain Research, Zagreb, Croatia

Diffuse gliomas are primary brain tumors with aggressive biological behavior, poor prognosis, and lack of effective treatment methods. Although inhibitor of nuclear factor kappa-B kinase subunit alpha (IKK-α) plays an important role through NF-κB and AKT signaling in different types of cancer, the importance of this serin kinase in diffuse glioma is still unknown. Using the cBioPortal (https://www.cbioportal.org/) platform for large-scale analysis, 751 samples (62 diffuse astrocytomas, 129 anaplastic astrocytomas, and 560 glioblastomas) revealed changes in copy number aberrations (CNA), methylation, and mRNA expression of CHUK gene that encodes for IKK-α. CNA of CHUK were found in 75% of total samples and 99% of them were hemizygous deletions. The highest number of hemizygous deletions had glioblastomas with alterations in 88% of samples. Spearman's test showed a statistically significant correlation between linear CNA data and tumor grade ($r=-0.511$; $p<0.001$). Likewise, a significant positive correlation was observed between CHUK methylation and tumor grade (Spearman's $r=0.796$, $p<0.001$) as well as a negative correlation between mRNA expression and tumor grade (Spearman's $r=-0.351$, $p<0.001$). These results suggest that hemizygous deletions and gene methylation inactivate this tumor suppressor during diffuse glioma progression to higher grades. The log-rank test showed higher, both overall and disease-free survival in dif-

CONTACT pbrlek@gmail.com

fuse glioma without CHUK deletions ($p<0.001$). These results demonstrate the important role of CHUK in the progression of diffuse glioma as well as the specific molecular signature of each pathohistological type examined in this study. Also, we suggest that CHUK CNA status could be used as a molecular marker for prognosis and potential treatment target in patients with diffuse glioma.

Keywords Astrocytoma; Glioma; Glioblastoma; I-kappa B kinase; NF-kappa B

CONTACT pbrlek@gmail.com

Anja Hart, Tina Fartek, Beti Zaharija, Maja Odorčić, Nicholas J. Bradshaw

Investigating the mechanisms of TRIOBP-1 aggregation in mental illness

University of Rijeka, Department of Biotechnology, Rijeka, Croatia

Schizophrenia is a chronic mental illness, characterized by severe symptoms such as delusions, hallucinations, disorganized speech, lack of motivation, and unpredictable behavior. The development of schizophrenia is caused by genetic and environmental factors. The complexity of these factors has made it difficult to develop new methods for the successful treatment of patients. Recent research has shown that disruption of proteostasis may also impact the progression of schizophrenia. Disruption in proteostasis causes certain proteins to misfold and therefore aggregate if the cell fails to degrade them. Aggregation is a process in which insoluble large structures known as aggregates are formed. So far, five proteins have been identified that may aggregate in schizophrenia. Among these five is TRIO and F-actin-binding protein (TRIOBP-1), our protein of interest. Using C-terminally truncated constructs, it was discovered that the critical region for aggregation of TRIOBP-1 is located in the central region of the protein. As a next step, we expressed different truncated variants of TRIOBP-1 in neuroblastoma cells and are using immunofluorescent microscopy to visualize aggregation. In this way, we have now narrowed down the critical region for aggregation to a sequence of less than 10 amino acids. Our most recent findings suggest that the presence of the PH domain at the N-terminus causes aggregation, indicating that TRIOBP-1 has two aggregation domains. By generating a TRIOBP-1 mutant with the minimal number of mutations required to prevent aggregation we will be able to generate model systems for studying TRIOBP-1 aggregation, the first of which will be Drosophila melanogaster. This will allow us to better understand the role of TRIOBP-1 in the progression of schizophrenia.

Keywords Schizophrenia; TRIOBP-1; Protein Aggregation; Mental Illness

CONTACT anjahart5@gmail.com

Tomislav Glavan[1], Jasmine Knoll[2], Ivana Mihalek[1], Olaf Bodamer[2]

Obesity, deformities, cognitive deficit and developmental delay in five patients with BDNF gene mutation; a case report

[1] **University of Rijeka, Faculty of Medicine, Rijeka, Croatia**
[2] **Boston Children´s Hospital, Massachusetts**

CONTACT tomislav.glavan@student.uniri.hr

In this article, we present a cohort of five patients with mutations located in the *BDNF* gene. BDNF is a nerve growth factor that plays an important role in the differentiation, maturation, and survival of neurons. However, it is known that not only the mature form but prepro-*BDNF* and perhaps the pro-domain of the protein itself have an important role in the nervous system by modulating neurogenesis, apoptosis, and synaptic plasticity. Another important function of *BDNF* is performed within the appetite-regulating and energy homeostasis centers of the hypothalamus, where it has an anorexigenic role. The first patient has a maternally inherited nonsense mutation in the mature domain of the *BDNF* gene with moderate global developmental delay and striking obesity (BMI Z score +5 at 2 years old). She has some repetitive behaviors with occasional temper tantrums and some dysmorphic facial features. Patient 2 with a de novo missense variant has autistic features, frequent temper tantrums, and anxiety. It is the obesity that is again striking (Wt was >2SD at 16 months). Patients 3 and 4 are siblings that have a maternally inherited nonsense variant and global developmental delays but do not have striking obesity. Dysmorphic facial features are also present. The last patient has a de novo missense variant. She has obesity (BMI 97th percentile, Z +1.82), cognitive disability (IQ 77), and behavioral challenges such as abnormal aggressive, impulsive, and violent behavior. No dysmorphic features are present. The goal of this case report is to research the connection between various *BDNF* mutations detected in these five patients and their consequences on energy homeostasis, cognitive functions, and mental & physical development. By doing so, more insight could be gained into the function and importance of not only mature *BDNF* but also its prepro-form and domains it is comprised of.

Keywords Brain-Derived Neurotrophic Factor; Developmental Disabilities; Nerve Growth Factors; Obesity

CONTACT tomislav.glavan@student.uniri.hr

Emina Horvat Velić[1], Lea Langer Horvat[2], Goran Šimić[2]

Immunohistological analysis of the propagation of the tau protein oligomers and fibrils in the rat brain

[1] University of Zagreb Faculty of Science, Department of Biology, Croatia
[2] University of Zagreb School of Medicine, Croatian Institute for Brain Research, Department of Neuroscience, Croatia

Alzheimer's disease is a neurodegenerative disease and one of the most common causes of dementia syndrome. There are many theories about the possible mechanisms of development and progression of Alzheimer's disease, one of which is the tau hypothesis. This theory suggests that the hyperphosphorylated tau protein triggers a cascade of events leading to cytoskeletal destruction, synaptic dysfunction, and the death of neurons. In this pilot work, we investigated the propagation of pathological tau fibrils and oligomers injected into the medial entorhinal cortex of six Wistar rats using immunohistochemical visualization of phosphorylated tau at Ser202/Thr205 epitope, using AT8 antibody. Three coronal levels (bregma -8.04, -6.84, -5.64) were analyzed by using Nissl-stained adjacent slides at 4, 8, and 11-month post-injection. The preliminary results obtained during this study will be discussed during the oral presentation.

Keywords Alzheimer's Disease; Dementia; Immunohistochemistry; Tau Protein

CONTACT ehvelic@stud.biol.pmf.hr

Martina Jeremić,
Beti Zaharija, Ines Gvoić,
Nicholas J. Bradshaw

DISC1 and FUS: linking proteins from mental and neurodegenerative illnesses through aggregation

University of Rijeka, Department of Biotechnology, Rijeka, Croatia

Chronic mental illnesses, such as schizophrenia, bipolar disorder, or depression, have overlapping genetic backgrounds and symptoms. These illnesses are manifested as disruptions of mental health (cognitive, emotional, and behavioral) from various etiological factors. Neurodegenerative disorders such as amyotrophic lateral sclerosis (ALS) or Alzheimer's disease are well known to be associated with occurrence of protein aggregation. Recent studies suggest that this same biological state, in which misfolded proteins aggregate, may be found in mental illnesses as well. The Disrupted in Schizophrenia 1 (DISC1) protein has been identified in protein aggregates from the brain tissue of patients suffering from schizophrenia, bipolar disorder, and depression. We are investigating the interaction of DISC1 with the Fused in Sarcoma protein (FUS) in protein aggregates. FUS has been found in protein aggregates of various neurodegenerative illnesses, including ALS and frontotemporal dementia (FTD). This interaction, therefore, provides an interesting biological link between mental illnesses and neurodegenerative disorders. We compared wild-type and mutated FUS protein with DISC1 in cultured mammalian cells. Microscopic examination of cells overexpressing these two proteins showed them to co-aggregate. Mutations of FUS protein have been described as contributing to neurodegenerative disorders, and in this case, only mutated FUS co-aggregated with DISC1. Additionally, we examined co-aggregation of fragments of DISC1 with the FUS protein, in order to determine which domains of this protein are involved in co-aggregation. From the data we obtained so far, we can conclude that co-aggregation of DISC1 and FUS protein is dependent on C-terminal regions of DISC1. These results can help explain biological connections between neurodegenerative disorders and mental illnesses while explaining aspects of the overlap in symptoms of these illnesses and the difficulty of making specific diagnoses.

Keywords Amyotrophic Lateral Sclerosis; Mental Disorders; Neurodegenerative Diseases; Protein Aggregates; Schizophrenia

CONTACT martinajeremic@gmail.com

Dalia Vađunec[1],
Jelena Osmanović Barilar[2]

Olfactory bulb – potential drug target for Alzheimer disease: an update

[1] **University of Zagreb, Faculty of Pharmacy and Biochemistry, Department of Pharmacology, Zagreb, Croatia;** [2] **University of Zagreb, School of Medicine, Department of Pharmacology, Zagreb**

Literature data suggest that olfactory dysfunction could be one of the earliest clinical symptoms in Sporadic Alzheimer disease (sAD). The exact pathophysiological mechanism is not yet fully clarified, but it could be associated with hyperphosphorylation of tau protein and GSK3β. Therefore, the aim of this study was to continue research of possible relationship between changes of insulin receptor (IR), insulin-degrading enzyme (IDE), tau (t-tau), phosphorylated tau (p-tau), glycogen synthase kinase 3 beta (t-GSK3β) and phosphorylated glycogen synthase kinase 3 beta (p-GSK3β) in the olfactory bulb (OFB) at different time points and doses after the streptozotocin-intracerebroventricularly (STZ-icv) treatment which is sAD representative animal model. Male

CONTACT daliavad@gmail.com

Wistar rats were injected with STZ-icv (0.3, 1, 3 mg/kg) or vehicle (controls) and sacrificed six and nine months after the treatment. Protein expressions of IR, IDE, tau, p-tau, GSK3β, and p-GSK3β in OFB were measured by Western blot. Data were analyzed by Kruskal-Wallis and Mann-Whitney U test ($p<0.05$). Dose of 0,3mg/kg first decreased IR (-40.6%) and ratio of p/tau 396 (-33.7%) after 6 months, then increased IR (+121.6%) and p/t-GSK3β (+195.7%) ratio after 9 months after STZ-icv. Other investigated proteins remain unchanged at dose of 0,3mg/kg STZ-icv. Dose of 1mg/kg decreased ratio of p/tau 396 (-52.7%) was found 6 months after STZ-icv. Other investigated proteins remain unchanged. Dose of 3mg/kg decreased ratio of p/t-tau 396 (-44.4%) 6 months after STZ-icv. Decrement of IDE (-31.6%) was found 9 months after STZ-icv. Increased ratio of p/t- GSK3β (+88%) 9 months after STZ-icv was found. The increased phosphorylation of tau protein 6 months after the STZ- icv treatment was independent of STZ-icv dose. Interaction of IR decrement with increased tau phosphorylation in olfactory bulb was seen only at the dose of 0.3 mg/kg. And there was no connection between GSK-3β activity and tau phosphorylation indicating the involvement of some other factors like MAP kinase signaling pathway.

Keywords Alzheimer Disease; Animal Model; Gsk 3 beta; Olfactory Bulb; Tau Protein

CONTACT daliavad@gmail.com

Ivona Vidović[1], Marko Perčić [2,3], Vedrana Krušić[4], Kristina Grabušić[4], Mladenka Malenica[4]

Nanotechnology-based quantifications of nanoparticles from human cerebrospinal fluid: comparison of Atomic Force Microscopy and Tunable Resistive Pulse Sensing

CONTACT ivona.vidovic@student.uniri.hr

[1] **University of Rijeka, Department of Biotechnology, Rijeka, Croatia**
[2] **University of Rijeka, Faculty of Engineering, Rijeka, Croatia**
[3] **University of Rijeka, Centre for Micro- and Nanosciences and Technologies, Rijeka, Croatia**
[4] **University of Rijeka, Faculty of Medicine, Rijeka, Croatia**

Nanoparticles are natural components of body fluids and include diverse nanosized structures produced by various tissues and secreted for different purposes. Extracellular vesicles (EVs) are currently the most intensively studied type of nanoparticles because of their potential usage as diagnostic and prognostic markers. Namely, EVs are secreted by practically all cells and their molecular composition reflects the type and state of originating cells. However, research of EVs is hampered due to lacking methods for precise and reliable quantification. The goal of our study was to improve EV size measurement in their natural environment by applying novel technologies able to measure individual nanoparticles directly and in the liquid phase. Such quantification is obtained by Tunable Resistive Pulse Sensing (TRPS) and Atomic Force Microscopy (AFM). We determined the size and concentration of EVs in cerebrospinal fluid (CSF) from patients with severe traumatic brain injury (TBI), a condition in which EVs have been previously described to change their physical properties. TRPS measurements of the CSF sample showed a mean EV diameter of 61.5 nm ± 22.8 nm and an EV concentration of 1.31 x 109 particles/ml. The same CSF sample was used for the AFM measurement for which we introduced a novel protocol in tapping mode to obtain images in a liquid environment. Particle diameter distribution was calculated from a 1.5 x 5 µm image containing 100 nanoparticles, resulting in mean diameter of 66.7 nm ± 21.9 nm. However, no EV concentration was determined by AFM since the detected signal does not include volume measurement. Thus, the current AFM technology is not suitable to measure EV concentration. Overall, our results show that both AFM and TRPS nanotechnologies provide comparable EV diameter measurements. Yet, TRPS brings a clear advantage in a more reliable measurement of EV concentration. This research will further contribute to the characterization of quantitative changes of nanoparticles in biofluids.

CONTACT ivona.vidovic@student.uniri.hr

Keywords Extracellular Vesicles (EVs); Traumatic Brain Injury (TBI); Cerebrospinal Fluid (CSF); Atomic Force Microscopy (AFM); Tunable Resistive Pulse Sensing (TRPS)

CONTACT ivona.vidovic@student.uniri.hr

Pegi Pavletić, Fabio Del Bello, Wilma Quaglia, Gianfabio Giorgioni, Alessandro Piergentili

Design, synthesis, and in silico evaluation of potent and selective dopamine D4 receptor ligands

University of Camerino, School of Pharmacy, Medicinal Chemistry Unit, Camerino, Italy

Dopamine is a catecholamine neurotransmitter involved in a variety of physiological functions, through interactions with five different G protein-coupled receptors (DRD1-DRD5). Among them, dopamine receptor D4 (DRD4) has emerged as a potential target in the treatment of eating disorders, drug addiction, and cancer. The common pharmacophore of DRD4 ligands consists of a lipophilic moiety linked by a spacer to a piperidine or a piperazine basic function and an aromatic terminal. For the purpose of this research, we have modified the aromatic terminal of the recently published DRD4 ligand D12 that contains all the parts of the general pharmacophoric model of DRD4. Modifications included the substitution of methyl, methoxy, nitro, and chlorine groups in ortho, meta, and para positions of the aromatic terminal of D12. All the compounds will be assessed for their DRD4 binding affinity and selectivity over DRD3 and DRD2. The purpose of this research was to determine whether the selectivity for DRD4 over DRD2 and DRD3 can be predicted using an in silico approach. We have used Autodock Vina software for docking studies and UCSF Chimera program to determine the strength of binding of the ligands to DRD2, DRD3, and DRD4. In particular, hydrogen bonds and Van Der Waals forces were assessed. Our results show the discrepancies in the binding of the ligands to the receptors according to their position of substituents (ortho, meta, or para). These discrepancies follow a pattern for the compounds substituted in the para-position of the aromatic terminal, showing structure inversion in ligands` placement within the orthosteric and the extended binding pocket of DRD4. Further in silico investigations, as well as biological studies, are necessary to prove our results and establish a reliable pattern.

Keywords Dopamine; Human DRD4 Protein; Molecular Model

CONTACT pegi.pavletic@unicam.it

Benjamin Herrlich[1], Antonio Kondrić[1], Valentino Rački[2], Mira Bučuk[2], Olivio Perković[2], Vladimira Vuletić[2]

Guillain-Barré syndrome and COVID-19-case series

[1] Faculty of Medicine, University of Rijeka, Rijeka, Croatia
[2] Clinic for Neurology, Clinical Hospital Centre Rijeka, Rijeka, Croatia

The WHO declared the outbreak and pandemic of SARS-CoV-2 in March of 2020. The peak of COVID-19 infections in Croatia occurred during November and December of 2020. GuillainBarré syndrome is a known complication of numerous viral infections. Four patients with COVID-19 have developed Guillain-Barré syndrome in our center thus far. We aim to present those cases systematically. Four patients between the age of 50

CONTACT herrlich.benjamin@web.de

and 66 were hospitalized in the Clinic for Neurology, Clinical Hospital Centre Rijeka, due to the emergence of neurological symptoms such as progressive ascending weakness of extremities, paresthesia, and areflexia. All four patients have tested positive for SARS-CoV-2 via a PCR test. All of these patients have, according to the apparent clinical presentation, laboratory analysis, and nerve conduction studies, been diagnosed with Guillain-Barré syndrome, acute inflammatory demyelinating polyneuropathy variant with comparable severity. Management and outcome: All four patients have been treated accordingly with intravenous immunoglobulins and physical therapy, with a solid recovery through a short timeframe. None of them suffered from long-term consequences to our knowledge. There is growing evidence that the infection of SARS-CoV-2 can cause Guillain-Barré syndrome. In concert with existing studies, this paper aims to estimate the possibility of this link based on the aforementioned cases in terms of symptomatology, time of onset, and laboratory findings.

Keywords COVID-19; Guillain-Barré Syndrome, SARS-CoV-2

CONTACT herrlich.benjamin@web.de

Marija Jozipović[1], Valentina Rosković[1], Sanja Habus[2]

Coherence in narrative discourse of people with aphasia and traumatic brain injury

[1] **Faculty of Education and Rehabilitation Sciences University of Zagreb, Zagreb, Croatia**
[2] **The Special Hospital for Medical Rehabilitation in Krapinske Toplice, Krapine, Zagreb, Croatia**

CONTACT marija.jozipovic.1996@gmail.com

Aphasia is an acquired language impairment typically caused by stroke. It occurs as a result of damage to specific brain regions, affecting one or more aspects of language. Traumatic brain injury (TBI) is an injury caused by external physical force or violent movement of the head. TBI often results in cognitive, physical, behavioral, and communication difficulties. Discourse analysis, including the study of coherence, can provide information needed to understand the language manifestation of aphasia and TBI. Coherence refers to the ability to maintain thematic unity and semantic connectedness of discourse at the propositional level. The notion of impaired coherence in discourse of people with TBI is widely accepted. On the other hand, there has been considerable debate of whether such deficits exist in discourse of people with aphasia. This research studied the global coherence in narrative discourse of people with aphasia and TBI assuming that no difference would be found. The study included the analysis of transcripts of 6 subjects (3 with aphasia and 3 with TBI). All of them were patients in The Special Hospital for Medical Rehabilitation in Krapinske Toplice. Data analysis was performed in the CLAN, using a 4-point subjective scale to measure global coherence. Statistical data processing was done in IBM SPSS Statistic – version 26 (t-test). No statistically significant difference was found in the coherence of discourse of the participants with aphasia and participants with TBI ($p > 0,05$). That confirmed the initial hypothesis. Therefore, it seems possible that different background difficulties are manifested in the same way. In other words, language pathology in people with aphasia and deficits of executive functions in people with TBI both result in impaired narrative organization and production. However, due to a small sample of participants and lack of control of the sociodemographic and clinical factors, caution in generalization of results is needed.

Keywords Aphasia; Language; Narration; Traumatic Brain Injury

CONTACT marija.jozipovic.1996@gmail.com

Maša Kopušar[1], Tin Karakaš[2], Mirna Karakaš[3], Miljenko Crnjaković[3]

Case report-Reversible cerebral vasoconstriction syndrome in a postpartum patient

[1] Faculty of Medicine, University of Rijeka, Croatia; [2] School of Medicine, University of Zagreb, Croatia; [3] Department of Neurology, University Hospital Dubrava, Zagreb, Croatia

Reversible cerebral vasoconstriction syndrome (RCVS) is a group of medical conditions characterized by severe thunderclap headaches. It can occur with or without seizures and focal neurological deficits and constriction of cerebral arteries which resolve spontaneously in 1-3 months. Female population with history of migraines and past pregnancies is more frequently affected. A 39- year old female patient, admitted to the Emergency Department (ER) after dizziness, tingling sensations of the right side of the body, blurred vision, nausea, and headaches. She also gave birth 8 days before the symptoms appeared. Birth went smoothly without any complications. The patient has a history of migraines. She is being treated for rheumatoid arthritis with methylprednisolone. At the age of 27, she recovered from pericarditis. Smoking habit (half a pack per day), penicillin and diclofenac allergies were also noted during the examination. Throughout the physical examination, disorientation, ocular deviation, and right arm paresis were present. Glasgow coma scale was 13, otherwise, the vital signs were normal. Leucocytes and D- dimers were significantly elevated. Lumbar punction revealed no abnormalities in cerebrospinal fluid. CT and MR angiography and color doppler ultrasound findings were unremarkable. Electroencephalography (EEG) was dysrhythmic frontocentrotemporaly, predominantly on the left side. Diagnosis was made of reversible cerebrovascular vasoconstriction syndrome. The patient was treated with nonsteroidal antiinflammatory drugs and saline solution both intravenous. The clinical presentation of RCVS is usually dramatic and sudden, but otherwise benign. Diagnosis is based upon clinical, brain imaging, and angiographic features. Also worth noting are the triggering factors such as physical exertion, acute stressful or emotional situation, childbirth, and orgasm. Treatment is mostly supportive. If left untreated it could culminate in massive strokes, brain edema, and permanent brain damage.

Keywords Migraine; Postpartum Period; Thunderclap Headache

CONTACT Kopusar.masa10@gmail.com

Martin Angjelov[1], Olivera Kujundzieva[1], Gordana Kiteva –Trenchevska[2]

Giant cell arteritis (GCA); a case report

[1] "Ss. Cyril and Methodius" University in Skopje, Faculty of Medicine, Skopje, North Macedonia
[2] PHI University Clinic of Neurology, "Ss. Cyril and Methodius" University in Skopje, Faculty of Medicine, Skopje, North Macedonia

Giant cell arteritis (GCA) is a rare form of large and medium vessel vasculitis, mainly involving the extracranial branches of the carotid arteries, especially the temporal artery. Clinical manifestation is due to the Inflammation of the arterial wall conducts to luminal occlusion and tissue ischemia. A female patient aged 69, was presented with major symptoms of pain in the eye, expanding through half portion of her face (cheek, jaw, and temporal area). The initial diagnosis was affirmative for Cluster headache. Corticosteroid treatment was

CONTACT martinmkd95@gmail.com

prescribed and the patient goes well. After, cutting off corticosteroids, the patient got the same worse presentation as the previous one. The patient was immediately sent to the University Clinic of Neurology for further investigations. Because of her anamnesis, and due to high sedimentation rate and suspicion of autoimmune disease, Giant cell arteritis was diagnosed, by excluding other differential diagnostic entities with neurophysiological, imaging, and ultrasound methods. EEG was normal, CT and MRI did not detect any structural brain lesions. Doppler of the carotid and vertebral arteries was without significant hemodynamic changes. We didn't receive permission for temporal artery biopsy (TAB) as after corticosteroid treatment the patient's status improved. As with other autoimmune diseases the immunosuppressive treatment should be long-lasting, with the addition of bone health protection, protection from increased gastric acid secretion, blood pressure control, and blood sugar concentration regulation. Nowadays, for avoiding the side effects of long corticosteroid treatment tocilizumab is the best-proven immunomodulation cure for this disease. Corticosteroid-related treatment complications are common in GCA. Our case illustrates the potential for diagnostic dilemma between GCA and Cluster headache (CH) and the need to consider CH as a potential differential diagnosis in those newly presenting with headaches, even in the elderly and relapsing headaches in subjects with a diagnosis of GCA.

Keywords Cluster Headache; Giant Cell Arteritis; Temporal Artery; Vasculitis

CONTACT martinmkd95@gmail.com

Lorena Zavidić

Non-pharmacological treatment of Alzheimer's disease in an aging population

CONTACT lzavidic@student.uniri.hr

University of Rijeka, Faculty of health studies, Rijeka, Croatia

Dementia includes various neurological diseases characterized by memory loss and cognitive dysfunction. There are over 50 different forms of dementia and the differences between these forms can be divided into primary and secondary forms. Alzheimer's disease, as a primary form of dementia, occurs in 50-70% of cases. It is marked by severe cortical atrophy and deposition of amyloid plaques into the brain. Symptoms are often difficult to notice due to benign age forgetfulness. Unfortunately, medicines that can delay the progression of the disease are not discovered yet. The aim of this review article was to investigate the available literature about dementia, especially Alzheimer's disease and nonpharmacological methods of treatment, as well as make a conclusion on the effects of cognitive training and vitamin D on the progress of Alzheimer's disease. A search of the literature was conducted in online libraries: PubMed, Google Scholar, and Hrčak using the following keywords: dementia, Alzheimer's disease, crossword, vitamin D. Studies that I found have shown that daily vitamin D supplementation can improve cognitive function and reduce beta-amyloid related biomarkers in elderly people with Alzheimer's disease by promoting phagocytosis of amyloid plaques. Another study has shown a significant correlation between hypovitaminosis D and developing different types of dementia. This study has shown that vitamin D deficiency can predict the onset of dementia within 7 years in older female members. Another study that I found showed that brain training through fulfilling crosswords and sudoku has been effective in the process of brain neuroplasticity as well as computerized cognitive training. Reading can increase semantic memory over the following hours of the same day. There is strong evidence that shows that a higher cognitive reserve is associated with a reduced risk of developing dementia. It is very important to recognize symptoms of Alzheimer's disease on time so it could be treated well. Crossword puzzles, sudoku, and entering at least 20 ng/mL of vitamin D have neuroprotective effects and can prevent the occurrence of Alzheimer's disease.

Keywords Alzheimer's Disease; Amyloid Plaques; Cognitive Reserve; Dementia; Vitamin D

CONTACT lzavidic@student.uniri.hr

Marija Janev[1], Danica Gobin[1], Berislav Barbalić[2]

Peroneal nerve lesion associated with SARS-CoV-2 infection-case report

[1] **Faculty of Medicine, University of Rijeka, Rijeka**
[2] **Clinical Department of Anesthesiology, Intensive Care and Pain Relief, Clinical Hospital Centre of Rijeka, Rijeka**

Pandemic caused by severe acute respiratory syndrome corona virus (SARS-CoV-2) is a contagious disease that can affect any organ system but is typically manifested in the respiratory tract. Neurological manifestations, such as neuropathies, have also been reported. Using the example of COVID-19 positive patient who developed a bilateral peroneal nerve lesion, we aim to point out potential connection between infection with SARS-CoV-2 and neurological complications. A 47-year-old male patient, without history of chronic diseases, is referred to the Emergency room due to dyspnea, dry cough, and fever of 38.8 C. PCR detected SARS-CoV-2 infection, and interstitial pneumonia was confirmed by X-ray. Due to worsening of symptoms, patient was hospitalized with the diagnosis of acute respiratory failure. In the ICU the patient was initially treated with non-invasive ventilation but was later intubated due to constant decreased oxygen saturation levels. After improvement of the patient's condition, active physical therapy was initiated and the lag of the left hand in relation to the right was detected. During hospitalization, progressive weakness in both legs occurred and neurological examination showed paraparetic gait and muscle atrophy. Pathognomonic signs of foot drop and inability to bend the foot upward at the ankle confirmed diagnosis of bilateral peroneal nerve lesion. Due to the suspicion of Guillain-Barré Syndrome (GBS), vitamin tests, immunological tests, and Electromyoneurography (EMNG) were performed. Results showed the absence of antibodies to gangliosides, but hypovitaminosis D and EMNG indicated GBS. The patient was discharged home with required physical therapy and further monitoring from a physiatrist. Since this patient was previously healthy and has never been neurologically treated, it is possible that COVID-19 caused dysregulation of immune system, which could explain the pathogenesis of GBS and peroneal lesion.

Keywords Electromyography; Gait Disorders, Neurologic; Guillain-Barre Syndrome; Peroneal Neuropathies; SARS-CoV-2

CONTACT marijajanev96@gmail.com

Mark Tomaj[1], Mile Marinčić[2], Petra Krstičević[3]

Application of Lokomat in neurorehabilitation

[1] **Poliklinika Glavić, Zagreb, Croatia**
[2] **Visoka škola Ivanić Grad, Ivanić Grad, Croatia**
[3] **Physio Borovci, Zagreb, Croatia**

With the development of information and sensor technology, the application of various robots in medicine is expanding every day. In the rehabilitation of people with neurological impairments, traditional rehabilitation methods are still most commonly used, although robotics are increasingly being used in neurorehabilitation today. Robotics is used in addition to conventional neurorehabilitation and as a supplement to occupational therapy under educated medical supervision. Neurorobotics is an assisted rehabilitation for the upper and lower extremities with the goal of recovering impaired motor skills to assist people with neurological impairments

CONTACT mark.tomaj@gmail.com

in performing activities of daily living. Robots allow a large number of movement repetitions, the intensity, and specificity of stimulation, the duration of stimulation, which will facilitate certain functions of everyday life for the patient. Repetitive active exercise and training stimulate neuronal plasticity and changes of adaptations of synapses, nerve cells, or even entire cerebral areas to restore lost movements. The advantages of neurorobotics are not only related to the locomotor system, such as increasing range of motion, strength but also improving attention, motivation based on audiovisual stimulation, which enhances the patient's neurorehabilitation process. This paper will present the influence of Lokomat, a robotic therapeutic device, on the rehabilitation of the lower extremities. Lokomat, as a supplement to the usual rehabilitation of people with neurological impairments, has improved recovery outcomes as well as motor response, indicating the results of numerous studies. Recent research proves that Lokomat has become an inevitable component for the rehabilitation of neurological patients. Neurological patients who receive robotic-assisted walking training in addition to classical rehabilitation, achieve easier independent walking than those who did not have training at Lokomat. Continuous monitoring of the development of robotics in medicine is crucial for the work of health professionals in neurological rehabilitation with the help of Lokomat. In addition to presenting the core features of Lokomat robots, at the very end of the paper we will briefly look at the different opinions and attitudes when it comes to modern technologies in medicine and their use. We will look upon the media, then articles from the field of science and profession, trying to give guidelines for examples in the future when talking about modern technologies and their application in medical practice.

Keywords Bioethics; Ethics; Lokomotion; Neurological Rehabilitation

CONTACT mark.tomaj@gmail.com

Valentina Rosković,
Marija Jozipović,
Andrea Adašević

Assessment of quality of life in people with aphasia

Faculty of Education and Rehabilitation Sciences University of Zagreb, University of Zagreb

The quality of life has been at the center of attention of numerous researchers and scientists for years. WHO defines it as "an individual's perception of position in life within the context of culture and set of values they live in, and relating to their goals, expectations, standards, and worries." Aphasia is an acquired language impairment that results from damage to specific brain regions, affecting one or more aspects of language, typically caused by stroke. Aphasia undoubtedly affects one's quality of one's life, but it yet remains unknown in which aspects and how to measure it. The main issue of measuring the quality of life in people with aphasia is that self-assessment often requires understanding and production of language and process of information recall. On the other hand, trying to overcome these obstacles by using significant others in the assessment of quality of life of people with aphasia is problematic. That is because quality of life represents the subjective construct interpreted differently by every individual. Besides mentioned problems, it is unknown how aware are the clinicians of the necessity to assess the quality of life in planning therapy and its outcomes for people with aphasia. Even the ones willing to implement quality of life assessment in their clinical work feel they lack practice, knowledge, resources, and/or time to do so. However, despite the obstacles, scientists and clinicians should have in mind that assessment of quality of life enables the preparation of efficient therapy and the estimation of its effectiveness. Due to the speech and language difficulties com-

CONTACT roskova4@gmail.com

monly found in people with aphasia, big importance lies within the speech therapists, professionals who can adjust the particles in assessment of quality of life and so ease the stressful situation. All of the above implies the necessity of education of speech therapists in this field.

Keywords Aphasia; Self-Assessment; Symptom Assessment; Quality of Life

CONTACT roskova4@gmail.com

Ema Šlabek[1], Ivana Kolić[2], Igor Prpić[1,2]

Glucose transporter type 1 deficiency syndrome: a case report

[1] **University of Rijeka, Faculty of Medicine, Rijeka, Croatia**
[2] **Clinical Hospital Center Rijeka, Department of Pediatrics, Rijeka, Croatia**

Glucose transporter type 1 deficiency syndrome (GLUT1-DS) is caused by heterozygous mutations in the SLC2A1 gene. The gene is encoding the glucose transporter protein type 1. Mutations in this gene reduce the amount of glucose available in the brain, resulting in cerebral energy deficiency. Epilepsy is a common feature of the disease, affecting 80–90% of the patients. Seizures typically begin in the first year of life. The ketogenic diet is the standard treatment for GLUT1-DS. The aim of this case is to present an infant who was early diagnosed and successfully treated. An 11-months-old infant was hospitalized for myoclonus treatment. The child was born from uneventful pregnancy and delivery at term. At the age of 4 months, he had short-term twitches of the head, arms, and legs during sleep and normal daily activities. The neurodevelopment was within the normal range. Electroencephalography showed abnormal epileptiform activity with the ictal recording of generalized spike-waves discharges, normal background activity, and no signs of encephalopathy. The magnetic resonance imaging of the brain was within normal limits. In an extensive diagnostic process, hypoglycorrhachia was found and genetic testing was scheduled. The results revealed deletion of one SLC2A1 gene and the diagnosis of GLUT1-DS was confirmed. Treatment included levetiracetam before the confirmed diagnose and later only modified Atkins diet. Early introduction of modified Atkins diet maintained seizure-free period without antiseizure medications and normal cognitive development in follow-up period at the age of 24 months. Any epilepsy with an early onset and/or signs of movement should urge the physician to consider the possibility of GLUT1-DS as a treatable metabolic disorder. A poor response to antiepileptic drugs, cognitive decline, and/or a dramatic response to a ketogenic diet are highly suggestive of the diagnosis. Since the condition is treatable, early diagnosis of the affected patients is critical for clinical practice.

Keywords Glucose Transporter Type 1; Epilepsy; Diet Therapy

CONTACT ema.slabek311@gmail.com

Ema Šlabek[1], Ivana Kolić[2], Iva Bilić Čače[1,2]

Perinatal stroke: case report

[1] **University of Rijeka, Faculty of Medicine, Rijeka, Croatia**
[2] **Clinical Hospital Center Rijeka, Department of Pediatrics, Rijeka, Croatia**

CONTACT ema.slabek311@gmail.com

Perinatal stroke is an acute neurologic condition with potential long-term consequences caused by a vascular-related cerebral injury that occurs between 20 weeks of pregnancy and 28 days after birth as a result of arterial ischemic stroke, cerebral venous thrombosis, and primary intracerebral hemorrhage. It is a major cause of permanent neurologic disability. Preeclampsia, diabetes, chorioamnionitis, and smoking are among the maternal risk factors. The aim of this case is to preset an infant with perinatal stroke. A male infant was born at 37 gestational weeks (GW). Pregnancy was uneventful until 35 GW when unilateral ventriculomegaly was noticed. He was born by cesarean with an Apgar score of 10/10 and was admitted to neonatal intensive care unit for observation and initial work-up. The child was in good general condition. Cranial ultrasound revealed asymmetric ventriculomegaly and pseudocystic frontotemporal formations on the left side. The findings indicated hematoma resorption due to the prenatal hemorrhagic stroke. Neurological status was normal for age. Magnetic resonance imaging (MRI) showed an enlargement of the left lateral ventricle with intraventricular marginal hemosiderin deposits on both sides due to earlier hemorrhage. Hemosiderin deposits were also visible in the area of the left basal ganglia in the posterior part of the internal capsule. The results revealed an ischemic lesion with hemorrhage in the germinal matrix zone. The diagnosis of perinatal stroke was confirmed, and further observation, diagnostic procedure, and follow-up were recommended. Perinatal stroke is a common cause of neurological disability in children. It may manifest in the neonatal period with seizures, altered mental status, and sensorimotor deficits. The outcome varies depending on the severity, anatomic localization, and other factors not yet well characterized. The recommended imaging method is MRI and it should be used in all neonates suspected of having a perinatal stroke.

Keywords Ischemic Stroke; Magnetic Resonance Imaging; Perinatal Care

CONTACT ema.slabek311@gmail.com

Dora Šimić [1], Kristina Lah Tomulić [1,2]

Severe carbon monoxide poisoning: a case report

[1] **University of Rijeka, Faculty of Medicine, Rijeka, Croatia;**
[2] **Clinical Hospital Center Rijeka, Department of Pediatrics, Rijeka, Croatia**

The clinical findings of carbon monoxide (CO) poisoning are highly variable and largely nonspecific. CO precipitates an inflammatory cascade that results in central nervous system lipid peroxidation and delayed neurologic sequelae (DNS). The aim of this case is to present a child with acute altered mental status and progressive cognitive dysfunction due to CO poisoning. A seventeen-year-old boy was admitted to pediatric intensive care unit (PICU) due to altered mental status of unclear etiology. Arterial blood gas test showed combined acidosis with elevated carboxyhemoglobin (COHb) level of 24.8% and normal oxygen saturation. Extensive diagnostics revealed the initial signs of acute respiratory distress syndrome (ARDS) and cardiac ischemia. Patient was diagnosed with severe carbon monoxide poisoning, so invasive mechanical ventilation with 100% oxygen and hyperbaric oxygen therapy was indicated. Control COHb level was 12,8% four hours after oxygen therapy and 1,2% after hyperbaric oxygen therapy. MRI of the brain showed ischemic changes. Electroencephalography showed low voltage activity with generalized slow waves. On the seventh day, patient was extubated and transferred to the neuropediatrics department. A psychological evaluation showed significant difficulties in verbal reasoning and expression, working memory, and speed of information processing. Since neurological sequelae are possible following resolution of acute symptoms, patient needed regular neuropediatric and psychological examination. Some of them are diffuse demyelination of the brain accompanied by lethargy, behavior changes, forgetfulness, memory loss, and parkinsonian features. Severe CO toxicity produces neurologic symptoms and other systemic manifestations. COHb levels between 30% and 70% lead to loss of consciousness and eventually death. In the absence of concurrent trauma or burns, physical findings in CO poisoning are usually confined to alterations in mental status, so a careful neurologic examination is crucial. The treatment of severe CO poisoning is 100% oxygen and hyperbaric oxygen therapy.

Keywords Carbon Monoxide Poisoning; Child; Hyperbaric Oxygenation

CONTACT dora.simic1@gmail.com

Poster session

Lea Kajba[1], Petra Ivančević[1], Petra Jurić[1], Romana Marušić[1], Anamarija Petek Erić[1,2]

Impact of COVID-19 pandemic on the mental health of students

[1] **Faculty of Medicine Osijek, Osijek, Croatia**
[2] **Clinical Hospital Center, Department of Psychiatry, Osijek, Croatia**

The global state of "new-normal" reflected upon all levels of human functioning. The burden of the ongoing pandemic probably affected most school children, adolescents, and young adults (students). To investigate how a year of pandemic impacted the functioning and mental health of students on the Faculty of Medicine in Osijek. The research was conducted among medical students (1st to 6th year) at the Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek (Croatia). It was constructed as an online survey with the following sections: socio-demographic questions, inventory for assessing the various emotional disturbances – Depression and Anxiety Stress Scale – 21 item (DASS-21), instrument for assessment of COVID-19 impact on mental functioning – COVID-19-Impact on Quality of Life scale (COV19-QoL) and inventory for personality assessment - International Personality Item Pool - 50 item (IPIP-50, Croatian Translation of the 50-Item Lexical Big-Five Factor Markers for Self-Report). The survey was equally distributed and accessible to female and male students. There were no specific inclusion criteria and the only exclusion criteria were chronic and severe mental illnesses. The participation was anonymous and each participant was asked for consent in order to participate in the survey. All the data were statistically processed with adequate

CONTACT lea.kajba@gmail.com

statistical software. In the research participated 92 students (66.3% female and 33.7% male students). 25% of students were positive on coronavirus and 40.2% were in self-isolation. Students reported a number of academic and everyday difficulties. 19.6% consume alcohol and 2.2% use psychoactive drugs more often since the onset of the pandemic. Moreover, 2.2% started using anxiolytics. The majority of students experienced various emotional disturbances (markedly depressive and anxious difficulties) due to the overall negative perception of the COVID-19 pandemic on their quality of life somewhat correlated with specific personality traits.
The COVID-19 pandemic is making a significant negative impact on mental health, so it's necessary to support the mental health and well-being of medical students.

Keywords Anxiety; COVID-19; Mental Health

Luka Ivanovski[1], Magda Gajski[1], Vladimira Vuletić [1,2]

Anterocollis – a side effect of a drug or atypical parkinsonism-case report

[1] **Faculty of Medicine, University of Rijeka, Croatia**
[2] **Clinical hospital center Rijeka, Rijeka, Croatia**

Anterocollis is characterized by disproportionate flexion of the head over the trunk. It can present as one of the symptoms of atypical parkinsonism but it can also present as a side effect of dopamine agonist drugs. The aim of this case report is to present a patient with Parkinson's disease and anterocol-

CONTACT ivanovski.luka15@gmail.com

lis and a differential diagnostic approach in determining the cause of anterocollis. A 61-year-old patient diagnosed with Parkinson's disease was taking the Azilect (rasagiline), PK Merz (amantadine sulphate), and dopamine agonist Eminens (ropinirole) as his therapy. Four years after the onset of symptoms and a slow continuous increase in Eminense dosage the patient developed a new symptom - anterocollis. Due to the suspicion of the Eminens to be the cause of anterocollis the dosage was gradually decreased from 14 mg to 8 mg. The reduction of Eminens led to the increase of tremor in the left hand while anterocollis was still present. The patient was referred for magnetic resonance imaging (MRI), positron emission tomography fluorodeoxyglucose (PET FDG) and dopamine transporter scan (DAT scan), and since there were no signs of atypical parkinsonism the suspicion of the dopamine agonist as the cause of anterocollis increased. Due to the still present anterocollis, it was decided to completely exclude Eminens from the therapy and at the same time introduce a new antiparkinsonian drug containing levodopa – Madopar (levodopa and benserazide). That did not reduce the tremor but it resulted in complete resolution of the anterocollis. Dopamine agonist-induced anterocollis should be considered when encountering anterocollis in Parkinson's disease patients. If the drug is responsible for anterocollis, its withdrawal may improve symptoms, as was the case with the presented patient. For additional treatment, an increase in the dosage of levodopa is advised.

Keywords Dopamine agonist; Levodopa; Parkinson's disease

CONTACT ivanovski.luka15@gmail.com

Petra Ivančević[2], Lea Kajba[2], Petra Jurić[2], Romana Marušić[2], Anamarija Soldo Koruga [1,2]

Neuropathic pain as a complication of COVID-19

CONTACT petraivancevic100@gmail.com

[1] **University Hospital Center Osijek, Department of Neurology, Osijek, Croatia**
[2] **Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia**

A characteristic of COVID-19 is that it often causes neurological complications (peripheral or central), either through direct invasion of the nervous system or through postviral immune reactions. Therefore, a COVID-19 infection may be linked to an exacerbation of a previous neurological deficit or de novo neurological symptoms or disorders. This case describes a 31-year-old man, without previous chronic illness or neurological comorbidities. Since November last year, he started experiencing burning pain in the upper back, neck, and right arm, regardless of sleeping position, denying provoking factors. The pain began to occur several times a day, especially during the night and started to become more severe. Due to close contact with an infected family member, the patient tested positive for SARS-CoV-2 ten days after the occurrence of pain but did not have fever or any other symptoms of acute infection. Because of continuous allodynia and pain, the patient became anxious with impaired concentration. During the entire duration of the mentioned symptoms, no other neurological or physical signs or symptoms were reported or observed. The patient appears for the first examination by a neurologist in January this year due to more intense pain. Examination showed no deviations in physical, mental, cognitive, and neurological status. Magnetic resonance imaging of the brain, cervical and thoracic medulla shows no changes, as well as electroencephalography. Complete laboratory tests show no deviations. Serological blood testing for human immunodeficiency virus, hepatitis B and C, herpes simplex virus type 1 and 2, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, and Borrelia burgdorferi was negative. The patient was prescribed pregabalin and tricyclic antidepressant. Since the performed test did not prove the etiology of pain and taking into account the time of onset of pain, there is a possibility that the etiology of pain is associated with SARS-Cov-2 infection.

Keywords Allodynia; COVID-19; Neuropathic Pain

CONTACT petraivancevic100@gmail.com

Tin Karakaš[1], Maša Kopušar[2], Mirna Karakaš[3], Miljenko Crnjaković[3]

Case report - Acute symptomatic seizures caused by alcohol abuse and electrolyte disbalance

[1] **School of Medicine, University of Zagreb, Croatia**
[2] **Faculty of medicine, University of Rijeka, Croatia**
[3] **Department of Neurology, University Hospital Dubrava, Zagreb, Croatia**

Hyponatremia refers to a condition that is caused by serum sodium concentration that is less than 135 mmol/l. It is a common electrolyte imbalance that mostly presents itself with other comorbidities (chronic alcoholism, malnutrition, pneumonia, heart, liver, and renal failure) but can also be seen as an isolated abnormality. According to the serum sodium levels, this condition can be classified as mild (130-134 mmol/l), moderate (125-129 mmol/l) and profound (<125 mmol/l) Neurologic symptoms become apparent when the sodium levels reach 120 mmol/l. A 60- year old male patient, presented to the Emergency Department (ER), was found on a kitchen floor while having a motor, tonic-clonic seizure of unknown onset that lasted for 3-4 minutes. The patient has a known alcohol abuse problem. No medication usage has been noted in his medical history. Vital signs were borderline normal including blood pressure of 145/80 mm/Hg, heart rate 80/min, blood oxygen saturation 98%, body temperature 36.3C°, and glucose 7.4 mmol/l. Glasgow coma scale was 10. During the neurological examination, the patient was unresponsive to physical and verbal contact, hypertonic with hyperactive reflexes without clonus and meningeal sign was positive. Biochemistry tests showed signs of hyponatremia (107 mmol/l) and hypoosmolarity (223mOsm), also, urine sediment was positive for glucose and ketones. Emergency head computed tomography (CT) was negative. Lumbar puncture excluded acute inflammation of central nervous system. The patient was treated with diazepam. After the diagnosis was made of acute hyponatremia, further treatment was continued at the internal diseases department. Hyponatremia is often seen during the late stage of liver cirrhosis due to kidney impairment and antidiuretic hormone secretion and as the dilutional effect of excessive alcohol usage. Sodium concentration should be corrected slowly using hypertonic solutions at a rate of 0.5 mmol/l/h to avoid central pontine myelinolysis and permanent brain damage.

Keywords Alcoholism; Hyponatremia; Osmolar Concentration; Seizures

CONTACT Karakastin@gmail.com

Marija Olujić[1], Romana Marušić[2], Svetlana Tomić[3]

Niemann-Pick disease type C-case report

[1] **Osijek Health Center, Osijek, Croatia**
[2] **Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia**
[3] **Department of Neurology, Clinical Hospital Centre Osijek, Croatia**

Niemann – Pick disease type C (NPC) is a rare autosomal recessive disorder caused by a mutation in the NPC1 gene in 95% of cases leading to the accumulation of cholesterol in lysosomes. In the perinatal period and infancy, visceral symptoms with hepatosplenomegaly, jaundice, and pulmonary infiltrates predominate as clinical features. From late childhood onwards, neurological manifestations and psychiatric symptomatology dominate. The estimated incidence is 1: 100000. We present a 42-year-old female patient without a family history of neurological or psychiatric diseases. She has always been hyperactive and hand tremor

was noticed already in childhood. Till her early thirties family notices that she performs fine motor skills "with a spasm", is unstable in gait, and has problems with swallowing and speech. She became paranoid, restless, anxious, and had difficulty sleeping. In the neurological examination vertical palsy of the downward gaze is observed, with saccadic horizontal smooth movements and hypometric horizontal saccades. She is dysarthric with trunk and limb ataxia, incontinent, mildly demented, and paranoid. Magnetic resonance of the brain shows atrophy of the cerebrum and cerebellum, corpus callosum, and brainstem. There has no polyneuropathy. Dopamine transporter scan presents discrete asymmetry of the striatal dopamine transporter. Abdominal ultrasound presents mild hepatosplenomegaly. Genetic testing reveals mutation on c.2974> C p.(Gly992Arg) and c.1042c>T p.(Arg348) and diagnosis of NPC was confirmed. Due to its clinical variability, sometimes is not easy to diagnose an NPC and distinguish it from individual psychiatric illnesses. A detailed neurological examination and a comprehensive history are of great importance in making the diagnosis.

Keywords Autosomal Recessive; Niemann-Pick Disease, Type C

CONTACT molujic9@gmail.com

Nika Šlaus[1], Petra Petanjek[2], Amadea Tuđen[1], Petar Brlek[3], Anja Kafka[4], Anja Bukovac[4]

Microsatellite instability signatures in human meningioma

CONTACT slausnik@gmail.com

[1] University of Zagreb, School of Medicine, Zagreb, Croatia; [2] University of Rijeka, Faculty of Medicine, Rijeka, Croatia; [3] University of Zagreb, School of Medicine, Department of Biology, Croatian Institute for Brain Research, Zagreb, Croatia; [4] University of Zagreb, School of Medicine, Department of Biology, Croatian Institute for Brain Research, Zagreb, Croatia

The defect in the functioning of the postreplicative mismatch repair (MMR) increases the genome's overall mutational frequency and is reflected in a phenomenon called microsatellite instability (MSI). MSI can be detected by the microsatellite gene markers and the instability is evident from different numbers of microsatellite repeats in tumor tissue when compared to normal blood DNA. One of the major mismatch repair genes - MLH1 is responsible for MMR and when mutated or lost the system does not work correctly. We decided to investigate if MMR gene MLH1 is associated with the overall frequency of MSI. The overall MSI on 7 different loci in the genome of 35 meningioma patients of different histo-pathological subtypes and grades was investigated and compared to large deletions of the MLH1 gene. Microsatellite markers used were: D3S1611, D16S3399, D3S1262, D16S752, D16S3025, D18S66, and D18S819. Large deletion of MLH1 was analyzed by the loss of heterozygosity (LOH) method. A relatively high presence of microsatellite instability in meningioma patients, when compared to their autologous blood DNA, was detected. 25 patients showed MSI at least one of the seven different investigated loci of the genome (71.4%). MLH1 was struck by large deletion or LOH in 7 meningioma cases (20%). When comparing overall MSI to the LOH of the MLH1 gene we found that four cases that harbored MLH1 deletions also showed MSI (57.1%). However, MSI was not associated with any histological subtype and was evenly distributed among different grades. The found deletions of the MLH1 gene indicate malfunctioning of the MMR system in investigated meningiomas. This was further supported by the relatively high overall incidence of MSI. Our study helps to better understand the genetic profile of human meningiomas and may shed information on the clinical course, response to therapy, and survival outcomes.

Keywords Meningioma; Microsatellite Instability (MSI); Mismatch Repair (MMR), MLH1, Loss of Heterozygosity

CONTACT slausnik@gmail.com

Anamaria Dukić[1], Nikola Erceg[1], Tereza Gabelić[1,2]

The severity of SARS-CoV-2 infection in multiple sclerosis patient treated with B-cell depletion therapy

[1] **School of Medicine, University of Zagreb, Croatia**
[2] **University Hospital Centre Zagreb, Department of Neurology, Croatia**

At the time of the current pandemic, there is a concern about the outcome of SARS- CoV-2 infection in patients with multiple sclerosis (MS) that are treated with immunomodulatory or immunosuppressive therapies. We present a case of a 35-year-old female patient that was diagnosed with relapsing-remitting MS in 2015. She first started the treatment with glatiramer acetate, which is an immunomodulatory medication. She had no relapses and was clinically stable. Three years later, due to disease activity and progression, ocrelizumab treatment was introduced. Ocrelizumab is an immunosuppressive treatment that targets CD20 marker on B lymphocytes causing profound and sustained B-cell depletion. Therefore, in ocrelizumab treated patients there is an increased risk of bacterial as well as viral infections. In July 2020 the patient completed the 4th cycle and was doing excellent. Unfortunately, two months after the last infusion, she tested SARS-CoV-2 positive. She developed serious symptoms, such as high fever above 39.50C, headache, muscle pain, severe fatigue, nausea, anosmia, and ageusia. A few days later, she developed pneumonia which was confirmed by X-ray. She was treated with azithromycin and methylprednisolone for five days. After 15 days, she eventually got better. Optimal management of MS must remain a key consideration. Only a minority of SARS-CoV-2 positive patients treated with ocrelizumab develop a severe form of infection. Nevertheless, we have to be alert with patients on B-cell depletion therapy because it was demonstrated that it is increasing the risk for more serious

CONTACT dukic.anamaria@gmail.com

forms of infections. To prevent that, it is necessary to vaccinate these patients. However, due to the reduced number of B lymphocytes, decreased response to the vaccine is expected because of the inability to develop specific antibodies. It is essential to treat every patient individually and to consider their age, comorbidities, and risk for developing a severe type of SARS-CoV-2 infection.

Keywords Multiple Sclerosis; Ocrelizumab; SARS-CoV-2

CONTACT dukic.anamaria@gmail.com

Nikola Erceg[1], Anamaria Dukić[1], Srđana Telarović[1,2]

Segawa's dystonia -the importance of properly diagnosing rare diseases

[1] **University of Zagreb, School of Medicine, Zagreb, Croatia**
[2] **University Hospital Centre Zagreb, Department of Neurology, Zagreb, Croatia**

Segawa dystonia (SD) is dopa-responsive dystonia that is caused by a deficiency of guanosine triphosphate cyclohydrolase I. There are autosomal dominant and autosomal recessive forms. Typically, this disease starts around the age of six and leads to dystonic hypertonus of one leg. Symptoms are mild in the morning, but their intensity rises during the day. By the age of 18, dystonia can involve all four extremities. Signs of parkinsonism can occur, such as tremor, bradykinesia, and rigidity. The diagnosis of SD is made according to the patient's history, genetic testing, and positive re-

CONTACT nikolaer7@gmail.com

sponse to levodopa therapy. A 19-year-old male patient was diagnosed with SD at the age of 8. He presented with idiopathic torsional dystonia that is resolved by levodopa therapy. On the last check-up, there was no hyperkinesis. During the walk, the right leg is in mild internal rotation with pes excavatus. On the left leg, there is pes planovalgus. The trunk is in torsion and shows increased physiological lordosis. There is also difficulty walking on heels. He draws the Archimedean spiral more slowly. The prevalence of SD is estimated to 1/1000000 people worldwide. The disease remains unrecognized in people with mild symptoms, or the symptoms are attributed to another disease. There are cases where patients with this disease have been misdiagnosed with cerebral palsy (CP). That is because it has a higher frequency and people are more aware of it. CP is a nonprogressive neurological disease that cannot be cured, but physical and occupational therapy is performed. SD responds well to levodopa therapy, which eliminates the symptoms, and improves the patient's quality of life. It is necessary to conduct a detailed examination to prescribe adequate therapy. Typical history and rapid improvement on levodopa therapy, as in our patient, makes it easier to diagnose rare diseases.

Keywords Dystonia; Levodopa; Rare Diseases

CONTACT nikolaer7@gmail.com

Matea Hodonj[1], Srđana Telarović[1,2]

Parkinsonism in spinocerebellar ataxia type 1 – the importance of diagnostic algorithm

[1] **School of Medicine, University of Zagreb, Zagreb, Croatia**
[2] **Department of Neurology, University Hospital Centre Zagreb, Zagreb, Croatia**

Tremor is an involuntary muscle contraction resulting in shaking movements and might affect one or multiple parts of the body. It has higher prevalence in the older population, but it can occur at any age. This hyperkinesis has various etiology such as neurodegenerative disorders (like Parkinson's disease), multiple sclerosis, use of certain medicines, and some genetic disorders, like spinocerebellar ataxia (SCA). In this case report, we present a patient with SCA type 1. A 43-year-old female reported clumsiness and tremor in her right hand. She also dragged her right leg behind. She doesn't have a history of dopamine blocker intake. Family history revealed signs of parkinsonism such as tremor and feet deformation at her mother's side. The patient's neurological status showed hypomimia, mild bradykinesia, and hypokinesia. She had postural and static tremor with 6-8 Hz frequency. Impoverishment of synkinesis of the right hand was noticed while walking. Fast alternating hand movements were slower and with reduced amplitude on the right. As a result of such signs and symptoms, ataxia and parkinsonism were diagnosed. Serum copper, 24-hour urine copper, ceruloplasmin test, thyroid gland ultrasound, ophthalmological evaluation, and examination of Kayser-Fleischer ring and molecular genetics of SCA – 1,2,3,6,7 and Friedreich's ataxia are required tests for young patients with tremor and were performed in this case. Molecular genetic tests showed positive SCA1 with intermedial allele which subsequently proved spinocerebellar ataxia type 1 as a current diagnosis. The patient was administered a low dose of levodopa – 250 mg daily and reported amelioration of symptoms, allowing regular exercise with only mild hypomimia and tremorless ataxia. Tremor is a movement disorder causing disability and reducing the quality of life. Etiology and treatment options vary and depend on signs and symptoms present in each patient. Systematical approach and complete diagnostic algorithm are essential, especially in younger patients with a hereditary background.

Keywords Algorithms; Parkinsonian Disorders; Spinocerebellar Ataxias; Tremor

CONTACT tea.hodonj@gmail.com

Valentina Juraga[1], Juraj Jug[2]

Possible COVID-19 associated rapid onset of Alzheimer's disease: a case report

[1] **University of Zagreb, School of Medicine, Zagreb, Croatia**
[2] **Health Center Zagreb West, Zagreb, Croatia**

Recent studies show that immune response and excessive inflammation in COVID-19 may accelerate the progression of brain inflammatory neurodegeneration. Elderly individuals are more susceptible to severe outcomes after COVID-19 infection. Our patient is a previously healthy 78-year-old male who was hospitally treated for COVID-19 infection. On admission, he was diagnosed with bilateral pneumonia and he was given ceftriaxone, dexamethasone, remdesivir, low-molecular-weight heparin, and oxygen. Shortly after the admission the patient entered a type of delirium state, consiliary psychiatrist was consulted and the patient was prescribed quetiapine and alprazolam. After 9 days his condition improved, and he was released from the hospital. Ten days after the hospital release the patient fell, hit his head, and lost consciousness. His CT scans showed no signs of ischemia, hemorrhage, or expansion and for that reason, he was conservatively treated in hospital and fully recovered after 3 days. In the next two months, the patient started rapidly losing memory and was referred to a neurologist. On MoCa test he scored 20/30, his cognitive electric potentials were slightly changed, color doppler of carotid and vertebral arteries was without any significant changes. Neurologist control was set for 8 to 10 months to monitor cognitive function without therapy. In the following month, his cognitive state worsened. The patient visited our practice almost every day and repeated that he never got his referral papers for a hospital specialist check-up from his doctor. He became aggressive and he didn't recall he was

CONTACT valentina.juraga@gmail.com

at the same place every day saying almost the same words. He didn't notice any changes in his lifestyle. The patient was sent back to the neurologist earlier than was planned. This case report serves as a foundation for further research of COVID-19 effects on the brain and its potential as a factor for neurodegeneration and possible cause of dementia.

Keywords Cognitive Impairment; COVID-19

CONTACT valentina.juraga@gmail.com

Petra Jurić[1], Petra Ivančević[1], Lea Kajba[1], Dora Karl[1], Romana Marušić[1], Anamarija Petek Erić[1,2,3]

From side-effect to a rare syndrome-case report

[1] **Faculty of Medicine Osijek, J.J. Strossmayer, University Osijek, Croatia**
[2] **Clinical Hospital Centre, Department of Psychiatry, Osijek, Croatia**
[3] **Faculty of Dental Medicine, J.J. Strossmayer, University of Osijek, Croatia**

Schizophrenia is a severe, chronic mental disorder with typical onset in late adolescence or early adulthood. It has a profound impact on the affected individual and society. The core symptoms are positive, negative, affective, and cognitive ones. Psychiatry today manages the treatment of schizophrenia with a first and second generation of antipsychotics. Although extrapyramidal movement disorders are less common with the second generation, the risk of their occurrence is still possible. A rare, but clinically highly similar syndrome to the extrapyramidal movement disorder that can also mimic the

CONTACT valentina.juraga@gmail.com

symptoms of schizophrenia is Fahr syndrome. It is a rare disorder characterized by abnormal deposits of calcium in the control movement areas, including the basal ganglia and the cerebral cortex. We present a 53-year-old male patient who has been diagnosed with schizophrenia for more than 20 years. For the last year and a half, he had developed barely noticeable tremors of his upper limbs, which were treated as a possible antipsychotic side-effect. Before his last inpatient treatment, the illness exacerbated and he was admitted with the following symptoms: agitation, insomnia, disorganized behavior, paranoid ideas towards his close family members. The most impressive finding was a severe tremor of his upper limbs (which intensifies during aimed motion), thorax, and head, but also postural tremor of the left foot, which all continued during the first days of hospital treatment. The computed tomography (CT) scan showed calcification in the basal ganglia and cerebellar area which is correlated with Fahr syndrome. The magnetic resonance imaging (MRI) scan confirmed suspected Fahr syndrome. During the literature review, we have found only a few case reports in which Fahr syndrome is often misdiagnosed as schizophrenia. However, we wanted to emphasize that it is crucial to have an integrated and personalized approach, as well as the importance of considering differential diagnosis, especially to chronic schizophrenic patients.

Keywords Antipsychotic Agents; Basal Ganglia Calcification; Schizophrenia

CONTACT valentina.juraga@gmail.com

Petra Jurić[1], Ivana Jurić[1], Lea Kajba[1], Romana Marušić[1], Dorian Östrreicher[1], Stjepan Jurić [1,2,3]

Obstructive sleep apnea in a patient with acromegaly

CONTACT petra.juric.os@gmail.com

[1] **Faculty of Medicine Osijek, J.J. Strossmayer, University Osijek, Croatia**
[2] **Clinical Hospital Centre, Department of Neurology, Osijek, Croatia**
[3] **Faculty of Dental Medicine, J.J. Strossmayer, University of Osijek, Croatia**

Acromegaly is a rare disease caused by hypersecretion of growth hormone (GH), mostly caused by a pituitary adenoma, which leads to excessive production of insulin-like growth factor 1 (IGF-1). GH and IGF-1 hypersecretion lead to craniofacial abnormalities and tissue growth in the upper respiratory tract, including macroglossia, tonsil and adenoid hypertrophy, nasal obstruction, and laryngeal anomalies. These changes result in an increased incidence of predominantly obstructive sleep apnea (OSA) which is characterized by recurrent episodes of complete or partial obstruction of the upper airway leading to reduced or absent breathing during sleep. The standard diagnostic test for OSA is Polysomnography (PSG). We present a case of a 73-year-old female patient who was hospitalized due to transient global amnesia and unusual breathing while sleeping. The patient was unable to be woken up by her husband. She has been snoring for years, but lately, it has become more frequent. Her medical history includes diabetes mellitus type 2 and hypertension. Physical examination revealed macroglossia, enlarged hands, feet, and facial features. Computed tomography (CT) scan and magnetic resonance imaging (MRI) scan showed an expansive tumor in the suprasellar region (20mm x 19mm x 18mm). Endocrine tests showed an increased level of insulin-like growth factor (IGF-1) and growth hormone (GH) that confirmed pituitary macroadenoma and the diagnosis of acromegaly. Treatment included somatostatin which led to a decrease in IGF-1 level. Due to suspicion of OSA, PSG was performed. Apnea hypopnea index (AHI) was 61,4/h. Diagnosis of severe OSA was confirmed and CPAP (continuous positive airway pressure) machine was initiated. Since then, AHI has decreased to 5,1/h, and the snoring has stopped. Acromegaly is a rare cause of OSA, but OSA is a common complication of acromegaly. This case report highlights the significance of the early diagnosis of OSA in patients with acromegaly to prevent cerebrovascular complications of OSA.

Keywords Acromegaly; Growth Hormone; Sleep Apnea

CONTACT petra.juric.os@gmail.com

Dora Karl[1], Romana Marušić[1], Petra Jurić[1], Ivan Radoja[1],

The role of videourodynamic study in patients with neurological disorders: a case report

[1] **University of Zagreb, School of Medicine, Zagreb, Croatia**
[2] **Health Center Zagreb West, Zagreb, Croatia**

Chiari malformations (CM) are complex brain abnormalities most commonly presenting with sliding of the cerebellar tonsils through the foramen magnum, consequently interfering with the normal flow of cerebrospinal fluid. CM can cause various problems including lower urinary tract symptoms (LUTS), which have a high prevalence in patients with neurological disorders. LUTS are often unrecognized and underreported in neurological patients. Videourodynamic study (VUDS) is one of the most important diagnostic methods. We present a 24-year-old female patient with a history of myelomeningocele and Arnold-Chiari malformation (ACM) surgery who was admitted to our department of urology for VUDS due to symptoms of overactive bladder syndrome (OAB) and underactive bladder syndrome (UAB), and suspicion of vesicoureteral reflux (VUR). After birth, she underwent surgery for the myelomeningocele of the sacral region and hydrocephalus with ventriculoperitoneal shunt insertion. She is immobile and has been performing intermittent urethral catheterization (IUC) since she was five years old. At the age of 15, she underwent decompression surgery because of ACM. She has been taking mirabegron for a year because of the OAB. We performed VUDS according to the ICS standards. Uroflowmetry showed reduced flow rates (<1 ml/s). Cystometry showed reduced bladder compliance (22 ml/cmH2O), reduced cystometric capacity (240 ml), and no signs of detrusor overactivity. There were no flow or detrusor contractions during the pressure flow study. During the VUDS the bladder imaging showed no bladder wall trabeculation or diverticulum, no detrusor contractions, and no signs of passive or active VUR. The patient was discharged from our department with a recommendation to continue IUC 6 times a day with mirabegron therapy. Patients with neurological disorders and a combination of UAB and OAB symptoms are at long-term risk of secondary upper urinary tract damage. Follow-up VUDS should be considered in these patients to prevent complications.

Keywords Arnold-Chiari Malformation; Intermittent Urethral Catheterization; Overactive Urinary Bladder; Underactive Urinary Bladder; Urodynamics

CONTACT dora734@gmail.com

Romana Marušić[1], Anamaria Bukulin[2], Petra Jurić[1], Lea Kajba[1], Petra Ivančević[1], Hrvoje Bradvica[3]

From dementia to glioblastoma

[1] **University of Josip Juraj Strossmayer in Osijek, Faculty of Medicine, Osijek, Croatia**
[2] **Specialistic Family Medicine Practice Romana Bogojević, Osijek, Croatia**
[3] **Department of Neurology, Clinical Hospital Center Osijek, Osijek, Croatia**

Dementia is the most common neurodegenerative disorder affecting approximately 5% of the population over 65 years of age. It is characterized by loss of memory, worsening of judgment and thinking, and weakening of emotional control with preserved consciousness. They can be divided into vascular, infectious, dementias caused by metabolic diseases and de-

CONTACT romana.marusic55@gmail.com

generative ones, the most common of which is Alzheimer's disease. We present an 80-year-old patient suffering from type 2 diabetes mellitus, arterial hypertension, rheumatoid arthritis, prostate hyperplasia, and being monitored by a surgeon for an abdominal aortic aneurysm. The patient complains of speech, memory, and anxiety disorders. He states that he has a feeling that he lacks words, that he has a harder time composing sentences, and that he is very forgetful and slow. He noticed a deterioration in vision in his right eye. In the neurological status, hemianopsia on the right, motor dysphasic speech, pronounced nominal aphasia are observed. In the anterior supination position, the left arm is discreetly placed lower. A native and postcontrast computed tomography (CT) of the brain was performed, where an expansive process measuring 53x47x50 mm was found occipitally to the left, which was marginally imbibed with centrally present necrosis on postcontrast images. This change suggests the diagnosis of glioblastoma. Due to the high age and extensive comorbidities, neurosurgery is not recommended. The patient opted for symptomatic therapy and there was a slight improvement in symptoms. Due to the high frequency of dementia in elderly patients, it is sometimes not easy to find the cause of dementia, so a detailed neurological examination and a comprehensive history are of great importance.

Keywords Anxiety; Dementia; Glioblastoma

CONTACT romana.marusic55@gmail.com

Marta Pongrac[1], Matea Ivaničić[1], Antonela Petrović[1], Ivana Tomljanović[1], Jelena Ban[1], Miranda Mladinić Pejatović[1]

Research of neuroregenerative mechanisms on primary cortical cell cultures derived from Monodelphis domestica

CONTACT mirandamp@biotech.uniri.hr

[1] **University of Rijeka, Department of Biotechnology, Rijeka, Croatia**

The inability to regenerate and self-repair the mammalian central nervous system (CNS) after the injury is one of the greatest challenges of modern neurobiology. CNS injury in adult mammals induces cell death and neurodegeneration and consequently leads to the impairment of neuronal networks. Disrupted neuronal connectivity and signal transduction in damaged regions cause severely impaired overall function. Furthermore, pathophysiological response after the CNS injury is characterized by inflammation and glial scar formation. Standard models for studying mammalian CNS in vitro are primary dissociated neuronal cultures, which are predominantly prepared from various CNS regions of immature rodents (mice and rats). We recently proposed the primary cortical neuronal cultures derived from neonatal gray South American short-tailed opossums (Monodelphis domestica) as a novel model for investigating the cellular and molecular basis of regeneration. Opossums are marsupials able to successfully regenerate the spinal cord after an injury in the first two weeks of their life, after which the regenerative capacity of their spinal tissue is abruptly lost. We prepare our primary cell cultures from cortices of postnatal day (P) 3-5 and P16-18 opossums since those ages differ in regenerative capacity after spinal cord injury. Almost pure neuronal cultures are obtained using the P3-5 opossums, while mixed cultures of neurons and glia are obtained from P16-18 opossums' cortex. With different conditions, cells can be kept in a proliferative state or directed to differentiate into neurons or glial cells. Progenitor and neural stem cells, like radial glia cells (RGCs) and neurospheres, retain the neurogenic potential even after a few days in vitro. These neuronal and non-neuronal cell cultures allow the study of developmental and regenerative mechanisms involved for example in RGC differentiation, and in the neurite (re-)growth and cell migration after injury in vitro.

Keywords Cortex; Opossums; Neural Stem Cells; Primary Cell Culture; Regeneration

CONTACT mirandamp@biotech.uniri.hr

Lara Vasari[1], Sandra Peternel[2]

Adverse cutaneous reactions to antiepileptic drugs: a five-year retrospective study

[1] **University of Rijeka, Faculty of Medicine, Rijeka, Croatia**
[2] **Department of Dermatovenerology, University Hospital Center Rijeka, Croatia**

Cutaneous adverse drug reactions (cADRs) have complex pathogenesis and diverse morphology and therefore these reactions represent a diagnostic challenge. CADRs occur in up to 8% of individuals taking drugs and in 2-3% of hospitalized patients. Timely recognition and appropriate treatment of these reactions, some of which can be life-threatening, have great importance in clinical practice. In addition to antibiotics and non-steroidal antirheumatics, antiepileptic drugs (AEDs) are one of the three drug groups that most commonly cause cADRs. In this retrospective study, we aimed to investigate the incidence of cADRs triggered by the use of AEDs at the Department of Dermatovenerology in the Clinical Hospital Center (CHC) Rijeka for the period of five years. The hospital information system of CHC Rijeka was searched according to the generic and brand names of all registered AEDs. In this study, we included all patients diagnosed with a medicamentous exanthema induced by AEDs who were examined and/or treated at the Department of Dermatovenerology in CHC Rijeka from 1st January 2015 to 31st December 2019. A total of 20 patients with cADRs were found. Most reactions were triggered by carbamazepine intake (11 patients), lamotrigine triggered eruptions in six patients, while oxcarbazepine, pregabalin, and phenytoin each triggered cADR in one patient. The most common skin reaction was maculopapular rash in eight patients, followed by Drug Reaction with Eosinophilia and Systemic Symptoms in four patients and urticaria in three patients. Other skin reactions were: photodermatitis, fixed drug erythema, erythroderma, acute generalized exanthematous pustulosis, and granuloma annulare. The results of this retrospective study indicate a high incidence of cADRs triggered by AEDs, which in five out of 20 patients caused severe skin reactions that were accompanied by internal organ involvement and were life-threatening.

CONTACT lara_vasari@hotmail.com

Keywords Antiepileptics; Adverse Drug Reactions; Carbamazepine; Exanthem; Lamotrigine

Veronika Šikić[1], Zara Miočić[1], Marko Kovačević[1,2,3]

A case report of postnatally diagnosed hydranencephaly

[1] **School of Medicine, Josip Juraj Strossmayer University, Osijek, Croatia**
[2] **School of Dental Medicine and Health Sciences, Josip Juraj Strossmayer University, Osijek, Croatia**
[2] **Department of Neurosurgery, Osijek Clinical Hospital Center, Osijek, Croatia**

Hydranencephaly is a rare malformation of the central nervous system in which the cerebral mantle is partially or completely absent and replaced by a fluid-filled membranous sac. According to pathogenesis, the most frequent cause of brain damage is occlusion of the internal carotid artery. In the differential diagnosis extreme hydrocephalus, alobar holoprosencephaly, and porencephalic cyst should be considered. A 9-month-old female infant, with previously diagnosed hydranencephaly, came to our facility for the evaluation of the possibility of neurosurgical treatment. Despite a rapid increase in head circumference after birth, surgical treatment was

CONTACT lara_vasari@hotmail.com

not performed in previously visited facilities. Considering neuroradiological examination and existing symptoms, it was decided to set an internal cerebrospinal fluid (CSF) drainage which reduced head circumference by 0,5 cm within a few days. Hydranencephaly is a severe brain malformation that raises ethical questions about whether to perform or not any surgical treatment considering its expectations and the patient's prognosis.

Keywords Cerebral Cortex; Hydranencephaly; Hydrocephalus; Malformation

CONTACT veronika.sikic1@gmail.com

Romana Marušić[1], Marija Olujić[2], Petra Jurić[1], Dora Karl[1], Tatjana Bačun[1,3], Dunja Degmečić[1,4]

Use of anxiolytics in medical students at the Faculty of Medicine Osijek

[1] **University of Josip Juraj Strossmayer in Osijek, Faculty of Medicine, Osijek, Croatia**
[2] **Osijek Health Center, Osijek-Baranja County, Osijek, Croatia**
[3] **Clinical Hospital Centre, Department of Internal Medicine, Osijek, Croatia**
[4] **Clinical Hospital Centre, Department of Psychiatry, Osijek, Croatia**

Anxiolytics remove the feeling of fear and tension and are used to symptomatically treat anxiety, panic attacks, and insomnia. Overuse of anxiolytics is concerning, though almost no data concerning their usage in students are available. The aim was to examine the use, prevalence, and attitudes about benzodiazepines. The research was conducted during February 2021 on a sample of 222 students from the 1st to 6th year of Medicine at the Faculty of Medicine Osijek. An anonymous questionnaire was created to record and examine the data. Of the 222 respondents, 64% are women and 36% are men. Of the total number of respondents, 19% use benzodiazepines. According to the T-test, female and male respondents significantly differ in benzodiazepine usage ($p<0,01$); 81% of females: 19% of males. The most commonly used benzodiazepines are alprazolam (52%) and diazepam (38%). 52% of respondents use it for anxiety, 28% for insomnia, and 12% for panic attacks. 49% of respondents cite the upcoming exam as the most common event preceding taking anxiolytics, 22% dissatisfaction with themselves, 13% family problems, and 6% problems in a love relationship. 58% report taking benzodiazepines once every few months, 17% once a month, 15% once a week, and 4% every day. 1st and 2nd-year students have the most negative attitude towards the use of benzodiazepines, while 6th-year students use them the most. All respondents were familiar with the possibility of developing addiction and tolerance when taking benzodiazepines daily. The results of this study showed a controlled and rational use of anxiolytics in students. Negative attitudes towards benzodiazepines are predominantly held by students in the lower years of study, while their use increases at higher years. Awareness and rational use of these drugs among medical students is important because they are future doctors whose decisions will affect their patients

Keywords Anxiety; Anxiolytics; Benzodiazepines; Medical Students

CONTACT romana.marusic55@gmail.com

Tomislav Perković[1], Marina Perković [2]

Diagnosis and monitoring of intraventricular hemorrhage by ultrasound in premature infants

CONTACT tomislavperkovic95@gmail.com

[1] **University of Zagreb, Faculty of Medicine, Zagreb, Croatia**
[2] **Special Hospital for Pulmonary Diseases, Zagreb, Croatia**

Ultrasound examination of the brain in infants is possible due to the existence of the fontanelles and cartilage zones on the infant's head. Anterior fontanelle provides a view for up to 6 months of age, and its closure is expected between 9 – 16 months of age. This method allows us to track intracranial hemorrhage or hypoxemic brain changes in premature infants, without radiation, sedation, or anesthesia. We report a case of a male infant, born in 34. week by a C-section, with an Apgar score of 10/10. Three days after birth, appeared short-term apnea that spontaneously regressed. A brain ultrasound was performed which confirmed voluminous left choroid plexus, corresponding to class II hemorrhage. In the first months of life, the infant had slower neuromotor development compared to its age. Significantly better findings were observed on a control brain ultrasound at 3 months of age. The child was involved in physical and occupational therapy programs that encouraged motor and sensory advancement and later visited speech therapists and psychologists. At the age of 3, the child reached neuromotor development appropriate for its age. To conclude, brain ultrasound is indicated in premature infants and children with postnatal complications. Unfortunately, because of technical reasons, the procedure isn't routinely performed on all newborns. It would allow prompt diagnosis of congenital malformation, hydrocephalus, clinically intractable bleeding, and screening for the children with increased risk for neuromotor development issues or behavioral and learning disorders. Such children could be promptly covered with needed diagnostic and therapeutic procedures which would improve the results of psychomotor development of children at risk.

Keywords Brain; Hemorrhage; Infant; Point-of-care Testing; Ultrasonography

CONTACT tomislavperkovic95@gmail.com

Nika Pušeljić[1]; Nora Pušeljić[2]; Tatjana Bačun[1,3]; Ivana Jurić[1]; Dunja Degmečić [1,4]

Command hallucinations in schizoaffective disorder

[1] **University of Zagreb, Faculty of Medicine, Zagreb, Croatia**
[2] **Special Hospital for Pulmonary Diseases, Zagreb, Croatia**

Schizoaffective disorder is a specific mental disorder involving both psychotic and affective symptoms. During acute psychosis in schizophrenia, the appearance of command hallucinations is possible. Command hallucinations are verbal hallucinations in which the affected individual hears specific instructions. The aim of this case is to show how discontinuation of long-term therapy in schizoaffective disorder can lead to strong imperative hallucinations. A 35-year-old female with schizoaffective disorder was admitted to the Department of Psychiatry because of severe command hallucinations. She has positive psychiatric heredity. Her sister suffers from schizophrenia while both parents are alcoholics. She has been hospitalized in psychiatry several times in the last two years since her diagnosis was determined. The last hospitalization was a month before the onset of command hallucinations. Since that she adhered to the prescribed pharmacotherapeutic regimen and the only change was the exclusion of depot preparation of paliperidone palmitate. During the examination, she was frightened, suspicious, contactable after encouragement with a prominent low mood. She admits hearing voices that were insulting her and telling her to kill herself. On presentation, the patient was in consciousness, contactable, oriented in place and time but slow to questioning. Psychomotor tension, anxiety, and depressive mood were noted. During hospitalization, she was treated with a combination

CONTACT nika.puseljic1@gmail.com

of psychopharmaceuticals (aripiprazole, diazepam, flurazepam, lamotrigine, biperidine) with re-introduction of the depot preparation paliperidone palmitate. Upon discharge, the patient was significantly psychomotorly calm without the imperative hallucinations described at admission. This case clearly shows how the abrupt exclusion of long-term depot therapy in patients with schizoaffective disorders can affect the onset of powerful deceptions that can result in imperative suicidal ideas. It is also important to emphasize that monitoring patients with schizoaffective disorder after discontinuation of any psychopharmaceutical plays an important role in preventing poor outcomes.

Keywords Hallucinations; Schizophrenia; Paliperidone palmitate

CONTACT nika.puseljic1@gmail.com

Sara Huskić[1], Sergej Nadalin[2], Vjekoslav Peitl[3], Dalibor Karlović[3], Lena Zatković[4], Alena Buretić-Tomljanović[2]

Correlations between clinical and metabolic variables and smoking among antipsychotic-naïve first-episode and nonadherent chronic patients with psychosis

[1] **Faculty of Medicine, University of Rijeka, Rijeka, Croatia**
[2] **Department of Medical Biology and Genetics, Faculty of Medicine, University of Rijeka, Rijeka, Croatia**
[3] **Department of Psychiatry, Sestre Milosrdnice University Hospital Center and Catholic University of Croatia, Zagreb, Croatia**
[4] **Hospital Pharmacy, Clinical Hospital Center Rijeka, Rijeka, Croatia**

CONTACT nika.puseljic1@gmail.com

Interaction between smoking and antipsychotic medications could potentially affect treatment efficacy, and promote metabolic side effects. Previous data are inconsistent regarding the effects of smoking on clinical psychopathology among antipsychotic-naïve or minimally medicated patients with first-episode psychosis, and there are no reports describing the effects of smoking on metabolic parameters among unmedicated patients with first-episode psychosis or chronic psychosis. Here we aimed to elucidate the influence of smoking on clinical psychopathology and metabolic parameters of psychosis among unmedicated patients. We investigated the contribution of smoking status towards Positive and Negative Syndrome Scale (PANSS) scores and metabolic syndrome-related parameters (plasma lipid and glucose concentrations, and body mass index) among two groups of unmedicated patients with psychosis from the Croatian population: antipsychotic-naïve first-episode patients and nonadherent chronic patients. Information about smoking status and antipsychotic nonadherence was obtained via self-report. PANSS data were obtained while patients were in a psychotic state during the illness requiring hospitalization. Plasma total cholesterol, LDL cholesterol, HDL cholesterol (HDL-c), triglyceride, and glucose levels were determined after a 12-hour fasting period. Compared with nonsmoking antipsychotic-naïve first-episode individuals, antipsychotic-naïve smokers exhibited significantly lower depression factor scores, and significantly higher triglyceride levels and triglyceride/HDL-c ratio ($p < 0.05$). Compared with nonsmoking nonadherent chronic individuals, nonadherent smokers exhibited significantly lower negative symptoms and negative factor scores, and lower HDL-c levels. Contributions of smoking to clinical and metabolic parameters ranged from ~3.4% to 10%. Our present results indicated that smoking may be a protective factor against clinical psychopathology, and a risk factor for metabolic parameters, among unmedicated patients with first-episode psychosis and chronic psychosis.

Keywords Antipsychotic Agents; Psychotic Disorders; Schizophrenia; Smoking

CONTACT huskicsara@gmail.com

Sara Belčić[1], Maja Mrak[1], Valentino Rački[2], Daniela Petrić[3]

Art as an assistive method in diagnosing schizophrenia in children and adolescents

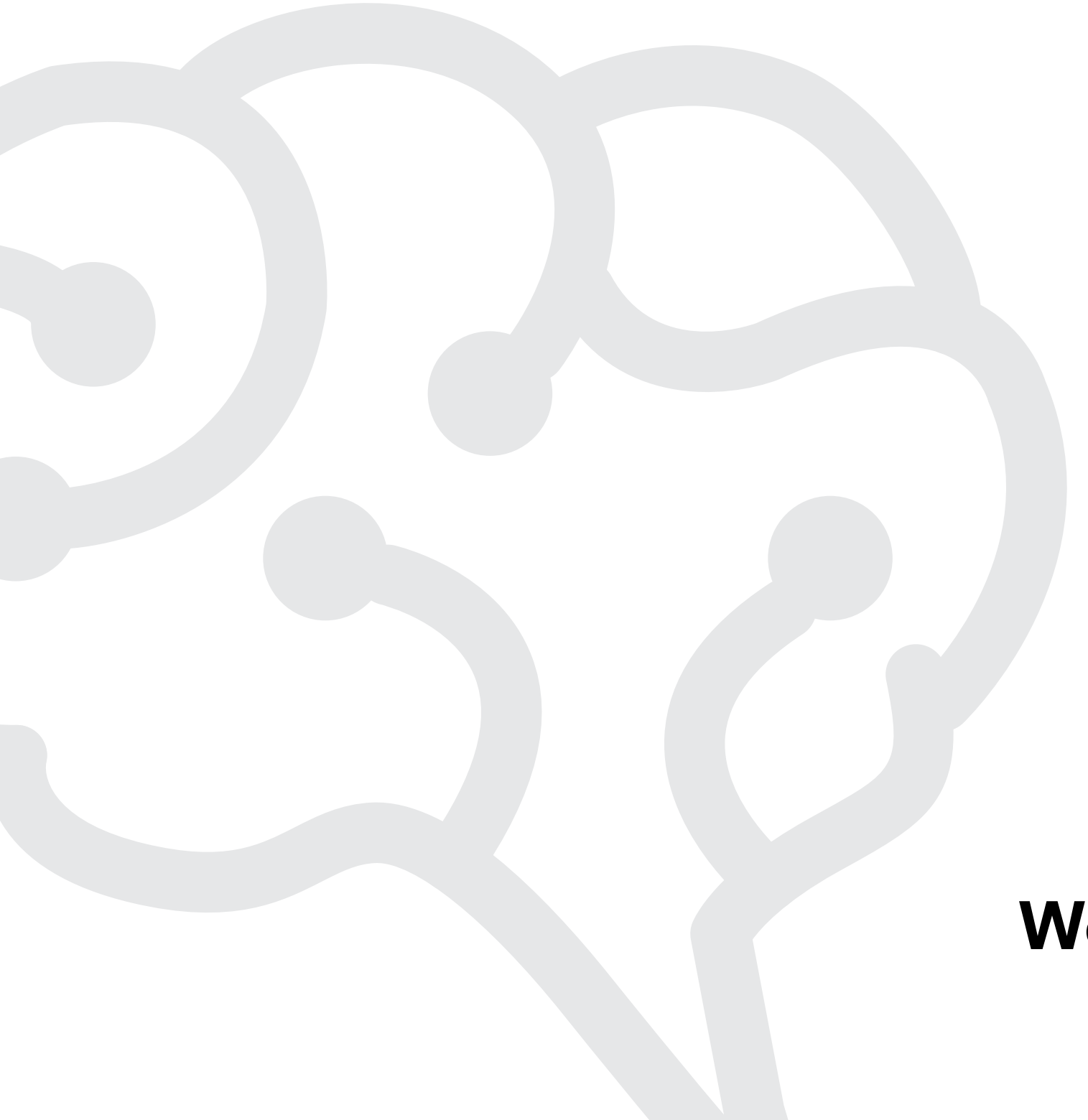
[1] **Faculty of Medicine, University of Rijeka, Rijeka, Croatia**
[2] **Department of Neurology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia**
[3] **Department of Psychiatry, Clinical Hospital Centre Rijeka, Psychiatry Clinic, Rijeka, Croatia**

Art as a creative therapeutic form of self-expression can play a meaningful role in clinical practice. The process of creating art is like holding a mirror as opposed to the creator, offering an opportunity to face problems through a background of the actual conflict. Childhood schizophrenia is characterized by onset before the age of 13. It poses many diagnostic challenges as children having a problem verbalizing their symptoms. A 13- year- old female patient came to our center with a two-year history of anxiety, self-destructive behavior, and affective disorder. Eventually, she started to voice several paranoid delusions and her parents also noticed new strange behaviors. While hospitalized, there was a lack of verbalization and action throughout the whole treatment process, she also voiced suicidal thoughts for a month. We decided to encourage her to channel her emotions in drawings when she drew ominous figures. The following months were better, further dose adjustments of medication led to an improvement in quality of life, which we noticed in the content of her drawing. The role of art in mental healthcare is considered positive, as it enhances the well-being of both the staff and patients. Multiple studies showed so far the therapeutic benefits of art therapy in schizophrenia. A recent meta-analysis concluded that there is no beneficial effect for positive symptoms, only a slight benefit in negative symptoms. On the other hand, there is a lack of literature that investigates the use of art therapy in diagnosing schizophrenia. Art was instrumental in making a diagnosis in this case, as the patient did not voice her psychopathology that was present for a while. The contents of her drawings enabled us to follow the improvement. Therefore, we propose art as a tool to assist in the diagnosis of schizophrenia in children and adults.

Keywords Art Therapy; Childhood Schizophrenia; Diagnosis

CONTACT sara.belcic@student.uniri.hr

CONTACT sara.belcic@student.uniri.hr



Workshops

Mihael Kozina

Awareness – the foundation of mental health

BoliMe

There is no single definition of awareness. The question is how is it so difficult to define awareness when we all think we know what it is or at least we had the experience of awareness. Awareness helps us to become more alive and real. But are we aware all the time? Why are we not in contact with ourselves most of the time? What are the dangers of such a life? The aim of the workshop is to raise awareness of the connection between awareness and mental health. We plan to achieve the set goal through short exercises, conversation, and connecting the insights we gain with modern scientific findings. We expect active participation.

CONTACT mihael.kozina@gmail.com

Domagoj Gajski, Krešimir Rotim

Back pain – Where? How? Why?

Clinic for Neurosurgery, KBC Sestre Milosrdnice

There is no single definition of awareness. The question is how is it so difficult to define awareness when we all think we know what it is or at least we had the experience of awareness. Awareness helps us to become more alive and real. But are we aware all the time? Why are we not in contact with ourselves most of the time? What are the dangers of such a life? The aim of the workshop is to raise awareness of the connection between awareness and mental health. We plan to achieve the set goal through short exercises, conversation, and connecting the insights we gain with modern scientific findings. We expect active participation.

Avindra Nath

Neurological consequences of COVID-19 infection

Clinical Director, NINDS, NIH; Director, Translational Neuroscience Center, NINDS, NIH

Chief, Section of Infections of the Nervous System, NINDS, NIH

Neurologic complications of SARS-CoV-2 infection can occur during the acute phase of the illness from multi-organ involvement presenting as an encephalopathy. These patients often have a prothrombotic state and can develop occlusion of multiple arteries and venous systems simultaneously. The virus causes widespread endothelial damage which underlies many of the manifestations. This can be further complicated with hemorrhagic lesions. Viral encephalitis is rare, although the possibility that the virus may enter the brain via the olfactory pathways has been widely speculated. Some may develop immune-mediated syndromes such as acute disseminated encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, transverse myelitis, Guillain Barré Syndrome, or myositis. The underlying immune pathogenesis of these syndromes is distinct. Some others are developing a constellation of chronic symptoms termed, Long-Haul COVID that resembles myalgic encephalomyelitis/chronic fatigue syndrome. The possibility of persistent/restricted viral replication as an underlying pathophysiological mechanism has been considered. Even though most children develop mild symptoms from the infection, a multi-systemic inflammatory syndrome that includes neurologic manifestations is being recognized. Early recognition and treatment is key to the effective management of these patients.

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