Abstract book

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WELCOME NOTE

Dear colleagues,

It is an honor to write these words for the last time in the role of the President of NeuRi. NeuRi has become a real neuroscientific institution for students, and I can not be more proud of that. My mission was to offer students a way to improve their scientific writing and presenting skills. Each year participants surprise me with their will to learn. Learning and improvement are what is motivating us to keep organizing NeuRi events.

Special thanks goes to everyone standing behind the scenes of this project, from organizing, and scientific committees, to our sponsors, and everyone else who made this possible overcoming countless obstacles on the road. We have proven that NeuRi is here to stay and help mold future scientists.

My work here is done, and once more I want to thank everyone whom I've met during my NeuRi journey. This will be an unforgettable part of my life.

I hope as always, 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 the Organizing and Scientific Board -

Welcome to NeuRi 2023!

Josipa Kajić
President of NeuRi 2023
Rijeka, 21 April 2023

PROGRAM – NeuRi 2023

Friday, 21 April 2023 – Faculty of Medicine Rijeka

11:00 – 13:00	Registrations
13:15 – 13:45	Opening ceremony
13:45 – 14:00	Group photo
14:00 – 14:45	Plenary lecture
	Ingrid Škarpa-Prpić: PostCOVID-19 era – challenges in neurology
14:45 – 15:00	Coffee break
15:00 – 15:45	Plenary lecture
	Raghavan Narasimhan: Lateralization and Meta-Control in Pigeons
15:45 – 16:00	Coffee break
16:00 – 16:45	Plenary lecture
	Nenad Šestan: What makes us human? Development and evolution of the prefrontal cortex
16:45 – 17:00	Elderease
17:00 – 18:00	Dinner
18:00 – 18:45	Plenary lecture
	Tina Bregant: Music in our brain
18:45 – 19:30	NeuRi TALK – Women in neuroscience (Moderator: Maja Krištafor)
20:00	Pub quiz & Beer pong @ FOSS

Saturday, 22 April 2023 – Rab

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11:00 – 12:00	Plenary lecture
	Paola Čargonja and Matea Iglić Debelić: The little devil from inside?
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12:15 – 13:00	Student session I
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	2. Adriana Adamović, Patricija Belužić, Džana Bjelić, Jelena Benčić, Filip Mustač, Darko Marčinko: Conversion Disorder as a Condition at the Intersection Between Neurology and Psychiatry
	3. Ema Gudelj, Ante Periša, Karlo Dalić, Nataša Đuran, Jakša Vukojević: Patient with impairment in social functioning exhibiting stereotyped motor behaviour: a diagnostic challenge

13:00 – 14:00	Lunch
14:00 – 15:30	Sightseeing
15:30 – 16:00	Free time
16:30	Drive to Rijeka
22:00	NeuRi Party @ STOP

Sunday, 23 April 2023 – Faculty of Medicine Rijeka

07:30 – 08:00 Breakfast

08:00 – 10:00 Poster session

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2. Ivana Pavičić, Filip Rokic, Oliver Vugrek: S-adenosylhomocysteine (SAH) hydrolase deficiency and disruption of semaphorin neuronal signaling (SEMA3A gene)

3. Marija Babić, Maria Banović, Ivana Berečić, Ena Španić, Vana Vukić, Željka Vogrinc, Jadranka Sertić, Nina Barišić, Goran Šimić: Change of total tau protein in CSF of SMA patients after nusinersen treatment

4. Maria Banović, Ivana Berečić, Marija Babić, Ena Španić, Vana Vukić, Željka Vogrinc, Jadranka Sertić, Nina Barišić, Goran Šimić: Levels of NFL protein in CSF of SMA patients treated with nusinersen

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6. Lea Cofek: Iron Dyshomeostasis and Brain Functions – A Literature Review

7. Ana Prica, Vesna Kerek, Miloš Jovičić: Paraneoplastic encephalitis of the brain stem: a case report

8. Antonia Vukšić, Zrinka Vuksan-Ćusa, Klara Bosnić, Dora Vogrinc, Marijana Udovičić: The connection between the Mediterranean diet, gut microbiota, and risk of Alzheimer's or Parkinson's disease

9. Lucija Lučev, Luce Lumezi, Romana Perković: Radiological differences between Frontotemporal dementia (FTD) subtypes

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11. Gracia Grabarić, Manuela Frančić, Melita Klaić, Romana Perković, Jakob Nemir, Fran Borovečki: Parkinson's disease patient selection for advanced treatment options

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13. Matea Lukić, Matea Smajić, Martina Kos: PRRT2 Mutation - A Cause of Benign Familial Infantile Epilepsy

14. Lucija Relja, Barbara Barun: A case report of narcolepsy with cataplexy

15. Matea Smajić, Matea Lukić, Petra Smajić, Martina Kos: Case report of Radiologically isolated syndrome (RIS)

16. Marijana Udovičić, Dora Vogrinc, Zrinka Vuksan-Ćusa, Antonia Vukšić, Sandra Morović: Cognitive status of patients with memory loss at first neurology visit

17. Dora Vogrinc, Marijana Udovičić, Antonia Vukšić, Zrinka Vuksan-Ćusa: The role of endocannabinoids in migraine pathogenesis regarding future treatment

18. Luce Lumezi, Lucija Lučev, Ana Hrkać-Pustahija: Leptomeningeal carcinomatosis in a patient with pancreatic neuroendocrine tumor

19. Patricija Belužić, Adriana Adamović, Martina Bešter, Džana Bjelić, Karolina Režek Tomašić: Diffuse axonal injury: presentation of traumatic brain injury following polytrauma

20. Džana Bjelić, Jelena Benčić, Adriana Adamović, Patricija Belužić, Sandra Ćulap, Sara Bognar, Karolina Režek Tomašić: Cervical spine injury after ground-level fall

21. Marta Grgat, Kristijan Harak, Lidija Hunjet, Lana Ivanišević, Viktorija Antolović: Case presentation: Extreme macrocrania due to severe congenital hydrocephalus

22. Marta Klarić, Anja Janković, Vera Klarić: Mental health battle in a 10 year old girl caused by Covid-19 pandemic

23. Iva Badurina-Dudić, Mersad Muminović, Marina Letica Crepulja: Complex post-traumatic stress disorder as a new diagnosis category

24. Zrinka Vuksan-Ćusa, Antonia Vukšić, Klara Bosnić, Dora Vogrinc, Marijana Udovičić: The correlation between breastfeeding in infancy and mental health problems in adolescence and adulthood

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Ira Milošević: Targeting endocytic pathways in Parkinson's disease

Plenary lecture

Lara Pilepić: What we (don't) know about language processing in the brain

10:45 – 11:00 Coffee break

11:00 – 11:45 Student session II

1. Marko Gavrančić, Dražen Juraj Petrović, Dinko Mitrečić: Influence of hydrogen peroxide on expression of γH2AX in neural stem cells

2. Lena Zatković, Sergej Nadalin, Sanja Dević Pavlić, Vjekoslav Peitl, Dalibor Karlović, Jelena Rebić, Alena Buretić-Tomljanović: PLA2G4C rs1549637 polymorphism and metabolic syndrome-related parameters among patients with schizophrenia under

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12:00 – 12:45	Student session III
	1. Alen Šarić, Barbara Kolbah: Epileptic seizure resulting in cervical trauma led to discovery of underlying spina bifida and hamartoma
	2. Ana Prica, Alen Rončević, Nenad Koruga: Meningioma of the anterior cranial base: a case report
	3. Hrvoje Barić, Zoya Jelovečki Đokić, Marina Kljajić, Guy Alush: Morbidity other-than-cranial-nerve deficits in surgical treatment of petroclival meningiomas
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13:30 – 13:45	Coffee break
13:45 – 14:30	Student session IV
	1. Doris Dragić, Kristina Lah Tomulić: Autoimmune encephalitis – case report
	2.Kristijan Harak, Marta Grgat: Clinical characteristics and diagnosis of mitochondrial membrane protein-associated neurodegeneration (MPAN)
	3. Loren Serdarović, Karla Schwarz, Eva Stanec, Srđana Telarević: Severe Clinical Presentation of Huntington Disease in a Patient With Incomplete Penetrance
14:30 – 15:30	Lunch
15:30 – 17:00	Workshops
	I. Traumatic brain injury – a practical approach (Matej Bura and Jan Maroević)
	II. Self-Care for future doctors: a mental health workshop (Tajana Kukolj, Ida Štimac, Josipa Batur)
17:15 – 17:30	Closing and award ceremony

Plenary lectures

PostCOVID-19 era – challenges in neurology

Ingrid Škarpa-Prpić
Department of Neurology, Clinical Hospital Centre Rijeka, Rijeka, Croatia

The Covid-19 pandemic has definitely changed our world, and we faced the challenges of treating patients initially with the “unknown”, and now with the post-pandemic period often called the “new normal” in which new challenges are imposed in clinical neurological practice.

Acknowledging the wide range of symptoms in the current post-pandemic period, we encounter the recognition and treatment of new neurological complications and the treatment of existing ones, both acute and chronic neurological diseases.

At the same time, such conditions are a challenge to research and the application of new therapeutic and new technologies in Neurology.

Lateralisation and Meta-Control in Pigeons

Raghavan Narasimhan, Martina Manns
Ruhr University Bochum, Bochum, Germany

Brain lateralization is the specialization of certain cognitive functions in either the left or right hemisphere of the brain (Güntürkün et al., 2020; Vallortigara & Rogers, 2005, 2020). In a lateralized brain, there is always a possibility of decision conflict, wherein the two hemispheres propose different solutions for a given problem. This gives rise to the concept of meta-control where one of the hemispheres dominates decision-making and controls the behavior. Yet, the neuronal mechanisms mediating meta-control and their ontogenetic foundations are currently unclear (Manns M, Otto T, & Salm L, 2021). Pigeons are often used as an animal models for investigating lateralization since the optic nerves are completely crossed so that the two brain hemispheres can be trained and tested independently simply by occluding one eye. Similar to mammals, pigeons display left-hemispheric dominance for visuomotor control or discrimination accuracy while the right hemisphere is specialized in spatial processing (Güntürkün et al., 2020). In this work, we explore meta-control and the possibility of manipulating behavior involving meta-control by optogenetically stimulating specific forebrain areas. A color conflict test which gives rise to meta control is used and this is coupled with optogenetic manipulation, trying to answer the question of whether the decision pattern could be modulated when the pigeons are presented with conflict stimuli. This may allow disentangling the impact of intra- and interhemispheric mechanisms mediating meta-control.

What makes us human? Development and evolution of the prefrontal cortex

Nenad Šestan
School of Medicine, Yale University, USA

The question of what makes human beings unique has fascinated humankind throughout modern history. Today, we view the brain as the core component of human identity, making an understanding of this organ crucial to explaining our species' characteristics. What distinguishes humans from other species is largely thought to reside in the unique features of brain development, especially in the wiring of the immensely complex neural circuits that underlie our cognitive and motor abilities. In my presentation, I will describe some of our recent efforts to better understand the molecular and cellular basis of how neurons acquire distinct identities and form proper connections in the cerebral cortex. This region, located on the outside of the mammalian brain, is responsible for processing our senses, executing motor functions, and facilitating higher-order cognitive abilities like language. The prefrontal cortex (PFC) will be specifically highlighted for its role in cognitive control, and the significance of retinoic acid signaling in the evolution and development of the PFC will be explored. The presentation will also examine how these complex developmental processes have been modified in human evolution and may be vulnerable to compromise in neuropsychiatric conditions.

Music in our brain

Tina Bregant
CIRIUS-Centre for Education and Rehabilitation of Physically Handicapped Children and Adolescents, Kamnik, Slovenia

Sounds surround us all our lives. We recognize signals in some sounds, and some signals are recognized by humans as music and in some cases even as singing. On St. Gregory's Day, March 12th, our grandmothers say that birds get married. Although the process of learning to sing in songbirds has attracted the attention of several fields from ethology, behavioral ecology, genetics, and neurobiology, it still remains an evolutionary puzzle. The learning of birdsong has attracted much scientific interest because of its similarity to the process of language acquisition. Humans and songbirds share the ability to learn vocal production through imitation – a trait not found in our closest relatives, the apes (Bolhuis 2013). There are remarkable behavioral, neural, and genetic similarities between the acquisition of speech in human infants and the learning of birdsong. In humans, there is a language-related brain network that includes several functional circuits. The nervous system's response to music is more complex than the sound itself. In some respects, it is similar to speech perception, but in others, it is completely different. The music consists of a sequence of tones, and its perception depends on the perception of the relationship between sounds. The rhythm, harmony, and color of the sound are also important in the response of the cerebral cortex. Music performance is a natural and ubiquitous human skill that requires specific and unique types of control over motor systems and perception. Current knowledge of sensory-motor interactions is very important, but may not be sufficient to explain the unique demands placed on these systems by a musical performance. In the talk, we browse through our brain: evolutionary from birds to humans and in our brain from mirror neurons to auditory pathways. With music we try to deal with the stresses of modern digital-driven life just the way more than 400 years ago, William Shakespeare said that "Music can raze out the written troubles of the brain".

This Little Devil from Inside?

Paola Čargonja, Matea Iglić Debelić
County Hospital Insula, Rab, Croatia

Eating disorders are serious health conditions that significantly affect physical and mental health. These conditions include problems with the way you think about food, diet, weight and body shape, and behavior related to nutrition. Symptoms can affect health, emotions, and ability to function in important areas of life. If not treated effectively, eating disorders can become long-term problems and, in some cases, cause death. Eating disorders affect several million people at any given time, often women aged 12 to 35. There are several types of eating disorders of which the most common are anorexia nervosa, bulimia nervosa, overeating disorder (binge eating disorder), avoidant restrictive food intake disorder (ARFID), and other specified feeding and eating disorders (OSFED). Eating disorders are not Choices. In treatment, a multidisciplinary approach is important, which includes a psychiatrist, nutritionist/dietitian, and internist, which is important for people with eating disorders so they can re-establish healthy eating habits and recover their emotional and mental health.

Targeting endocytic pathways in Parkinson's disease

Ira Milosevic[1,2]

[1]Wellcome Centre for Human Genetics, Nuffield Department of Medicine (NDM), University of Oxford, Oxford, UK

[2]Multidisciplinary Institute for Ageing (MIA), Coimbra, Portugal

Membrane trafficking at the synapse is among the most complex, rapid, and tightly regulated processes in cell biology, and it is linked to several brain diseases including Parkinson's disease (PD), the second most common neurodegenerative disorder. Specifically, neuronal cells rely on endocytosis and synaptic vesicle (SV) recycling to sustain high rates of activity. The main pathway of SV recycling, clathrin-mediated endocytosis, builds on a clathrin coat formation and dissociation. Mutations in two uncoating factors, auxilin, and synaptojanin-1, were found to cause early-onset PD. Auxilin is recruited to the clathrin coats due to the action of synaptojanin-1, which is itself brought to clathrin-coated pits by the key endocytic adaptor endophilin-A. Curiously, endophilin-A is directly linked to PD and neurodegeneration - it is altered in the cortex of PD patients, and it interacts with two hallmark PD proteins, the E3 ubiquitin ligase Parkin and the leucine-rich repeat kinase LRRK2, the most commonly disrupted gene in familial PD. We have reported that a partial loss of endophilin-A in mice results in neurodegeneration, ataxia, altered gait and motor coordination, defective SV recycling, impaired autophagy, and shorter lifespan. Building on data generated by a comprehensive cell biology tool kit including biochemistry, microscopy at different scales, and genome editing tools, I will propose in this talk that the impaired synaptic membrane trafficking results in selective neurodegeneration of dopaminergic neurons and/or neurons with long axons in PD. Further work on the potential synergistic function of several PD-linked proteins on the synaptic endocytic pathway will also be presented. By defining the molecular and cellular networks in which these proteins operate, we hope to identify strategies for reversing the cellular vulnerabilities that cause PD or increase disease risk.

What we (don’t) know about language processing in the brain

Lara Pilepić

Intensive Neurological Care Unit, Clinical Hospital Center Sestre Milosrdnice, Zagreb, Croatia

For normal speech and language functioning there are a number of individual but connected brain processes working in the background of a multimodal cognitive function that is language. The knowledge that language is lateralized and localized in specific left hemisphere areas is in Croatia still used as a basis for diagnostics and rehabilitation of language disorders in patients with stroke. Recent neurolinguistic research determined that in healthy individuals both brain hemispheres are responsible for normal language functioning. The latest research even emphasizes a more dominant role of the right hemisphere in some language activities seen during fMRI. In Croatia, not one large neurolinguistic research used a standardized aphasia battery in combination with brain imaging techniques in the acute phase of a stroke to determine brain areas responsible for speech and language. The aim of this lecture is to explain how both hemispheres interact in language processing, give students a more modern view of how to examine patients with speech and language impairment and show results of the newest neurolinguistic Croatian study on stroke patients.

Symposia

Caregiver's needs in pediatric palliative care in Istria and Primorje-Gorski kotar county

Maja Ploh[1,2], Lea Petranović[3], Duška Petranović[1,4]

[1]Faculty of Medicine, University of Rijeka, Rijeka, Croatia

[2]Istrian Health Centers, Pula, Croatia

[3]Faculty of Architecture, University of Zagreb, Zagreb, Croatia

[4]Department of Internal Medicine, Division of Hematology, University Hospital Center Rijeka, Rijeka, Croatia

Introduction

The World Health Organization describes pediatric palliative care as the active total care of the body, mind, and spirit of a child with a life-limiting disease, also supporting the family. Annually, 10/10,000 young people up to 19 years old are affected by an incurable illness, with an annual mortality rate of 1/10,000 young people. The main aim of this study is to investigate the needs of caregivers, in families taking care of a child with a life-limiting disease.

Materials and Methods

Our study engaged 50 participants, 18 to 60 years old, involved in the care of a person up to 18 years old with a life-limiting disease. Participants anonymously answered a questionnaire with 25 questions, based on their personal opinion and life experience related to medical care, social possibilities, and quality of life after facing a child's diagnosis.

Results

Our study revealed that caregivers take care of a child usually spend 20 hours per day in caring activities. Participants notice lack of rest as the most pronounced problem in the caring process, and 86% of them point out that they face a lack of education in caring techniques, in particular 60% experience a lack of education in handling an emergency in their child's care. All participants assert that they need psychological assistance, and 74% of them point out that they need a better-organized health and social care network to easily manage their demanding situation.

Discussion/Conclusion

Daily care of a child with a life-limiting disease is a challenging situation for each family member, the uppermost for a caregiver. A health worker and society should question and listen to a child's and caregiver's needs, to improve end-of-life support for a child and its relatives.

Keywords:

Adolescent; Caregivers; Child; Needs Assessment; Terminally Ill

Conversion Disorder as a Condition at the Intersection Between Neurology and Psychiatry

Adriana Adamović[1], Patricija Belužić[1], Džana Bjelić1, Jelena Benčić[1], Filip Mustač[2], Darko Marčinko[1,2]

[1] School of Medicine, University of Zagreb, Zagreb Croatia

[2] Department of Psychiatry, University Hospital Centre Zagreb, Zagreb, Croatia

Introduction

Conversion disorder, also known as functional neurological symptom disorder (FND), is a disorder at the interface between neurology and psychiatry characterized by physical and sensory symptoms, with no underlying neurologic pathology. The most common ones are paralysis, numbness, blindness, deafness, and seizures. The symptoms significantly impact a patient's ability to function, therefore a multidisciplinary approach should be included in diagnosis and treatment.

Case Report

A 39-year-old female was referred to psychiatry because of an eating disorder, depressed mood, and somatization complaints like severe headaches and abdominal twinges. During the previous 4 years, she has been afraid of swallowing solid or liquid food independently, connecting her fear of choking to a traumatic event from childhood. Her past medical history shows that she has been treated under the diagnosis of personality disorder, non-specific (F60.9), inorganic psychosis (F29), and conversion disorder (F44) during the last 10 years. During her childhood, she had several febrile convulsions and vasovagal syncope. During hospitalization, she had sudden syncope one morning after taking her therapy. She felt nausea in the epigastrium and had briefly blurred vision after which she does not remember the period of one minute. Heteroanamnestically she was sitting and her hands started shaking with her eyes open, indicating a coarse tremor. Her blood pressure was 90/50 mmHg. In consultation with a neurologist, an epileptic seizure was excluded and further tests are recommended. Her therapy has been modified including intravenous diazepam and parenteral nutrition. Also, psychoanalytic psychotherapy was carried out in which she actively began to understand herself and her relationships with other people. There was a gradual improvement in her condition. Therapy after discharge included SSRI (sertraline), sulpiride, diazepam, olanzapine, and enteral nutrition.

Discussion/Conclusion

Conversion disorder can be presented with multiple symptoms imitating various neurological conditions and it is usually connected with traumatic events in childhood or unresolved intrapsychic conflict. Neurological symptoms without known neurological cause can indicate to psychosomatic disorder and should be included in differential diagnoses.

Keywords:

Conversion Disorder; Eating Disorder; Epileptic Seizure; Psychosomatic Disorder; Vasovagal Syncope

Patient with impairment in social functioning exhibiting stereotyped motor behavior: a diagnostic challenge

Ema Gudelj, Ante Periša, Karlo Dalić, Nataša Đuran, Jakša Vukojević
University Psychiatric Hospital Vrapče, Zagreb, Croatia

Introduction
Pervasive Developmental Disorder Otherwise Not Specified is a disorder in which a patient has impaired communication skills or stereotyped behavior but does not meet the criteria for any of the disorders formally defined in that class. Despite being the most common pervasive developmental condition, it is the least researched. We present a case of a patient who has a particular clinical presentation and thus presents a diagnostic challenge.

Case Report
A 47-year-old male patient presented to the psychiatric ward with repetitive movements, regressive disinhibited behavior, impairment in social functioning, and difficulties forming complete sentences. Neurodevelopmental and behavioral issues such as delayed psychomotor development, adaptation issues, social withdrawal, impairment in understanding social situations, regressive behavior, and motor disturbances began in his childhood. Deviations on the projective test used in psychological assessment, among other things, indicate stereotypical performance. During his life, he was managed under different diagnoses such as disorganized schizophrenia, unspecified nonorganic psychosis, organic dissociative disorder, other acute and transient psychotic disorders, and obsessive-compulsive disorder. His condition was managed by discontinuing fluphenazine and clozapine, increasing olanzapine dosage, and introducing clonazepam.

Discussion/Conclusion
Repetitive movements are a symptom of many psychiatric and neurodevelopmental disorders. Stereotypies are distinguished from other hyperkinetic movement disorders by prolonged, involuntary, rhythmic movement patterns and the absence of premonitory urges. The pharmacological intervention reduced psychomotor agitation and improved verbal communication.

Keywords:
Disorganized schizophrenia; Hyperkinetic Movement; Obsessive Compulsive Disorder; Pervasive Development Disorder; Stereotyped Behaviour

Influence of hydrogen peroxide on expression of γH2AX in neural stem cells

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Introduction
γH2AX is a phosphorylated histone that serves as a marker of double-stranded DNA breaks. Our hypothesis was that rising concentrations of hydrogen peroxide (H2O2), an equivalent of oxidative stress, would cause DNA damage in vitro cultivated neural stem cells, visible in increasing γH2AX expression and cell death.

Materials and Methods
Neural stem cells (NSCs) were isolated from murine embryos, passaged as neurospheres, then dissociated and plated in a 24-well plate. After 48 hours in the differentiation medium, cells were grown in three groups with two technical replicates (control, 100 μM H2O2, 1000 μM H2O2). After 24-hour treatment with H2O2, NSCs were fixated with 4% paraformaldehyde solution and then stained for immunocytochemistry with γH2AX-specific antibody alongside DAPI nuclear dye. Images were taken with Moticam - light microscope right before and 24 hours after H2O2 treatment. Fluorescent confocal images were taken by Olympus FV3000.

Results
Cells treated by hydrogen peroxide exhibited changes typical for cytotoxicity: a smaller concentration of H2O2 caused a decrease in cell adherence to the glass with a visibly higher proportion of pycnotic nuclei. Number of cells counted by DAPI positivity, compared to the control, decreased by 45,0%. Concentration of 1000 μM of H2O2 led to a dramatic lack of adherent cells, with almost all remaining cells exhibiting pycnotic nuclei. Number of cells compared to the control decreased by 78,8%. ImageJ and Imaris analyses of confocal images revealed a rise in the percentage of γH2AX-positive cells with increasing H2O2 concentration with statistical significance (ANOVA $p<0.05$).

Discussion/Conclusion
In this study, we confirmed our hypothesis that hydrogen peroxide induces DNA damage on NSCs in vitro. Analyses of light microscopy images revealed clear signs of cytotoxicity. This was confirmed by cell quantification which revealed that a rising concentration of hydrogen peroxide led to decreased number of DAPI-positive cell count, i.e., a lower number of viable cells. With a rising concentration of hydrogen peroxide, we found that there is a rise in the percentage of γH2AX-positive neural stem cells which implies a higher occurrence of double-stranded DNA breaks.

Keywords:
Neural Stem Cells; Hydrogen Peroxide; gamma-H2AX protein mouse; Cell Death; Microscopy, Confocal

PLA2G4C rs1549637 polymorphism and metabolic syndrome-related parameters among patients with schizophrenia under antipsychotic treatment

Lena Zatković[1], Sergej Nadalin[2,3], Sanja Dević Pavlić[4], Vjekoslav Peitl[2,5], Dalibor Karlović[2,5], Jelena Rebić[6], Alena Buretić-Tomljanović[4]

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Introduction

By playing a role in signal transduction and membrane phospholipid homeostasis, phospholipases (PLA2s) participate in a variety of physiological processes, including dopaminergic neurotransmission and insulin secretion. Patients with schizophrenia frequently exhibit abnormal signaling of dopamine and other neurotransmitters and are more likely to experience weight gain, lipid disturbances, and glucose dysregulation. Antipsychotic medication use (specifically, the use of second-generation antipsychotics) has also been linked to metabolic disturbances in schizophrenia. We previously found that rs1549637 polymorphism, an A/T polymorphism within intron 16 of the PLA2G4C gene (19q13.3), in interaction with one polymorphism of the PLA2G6 gene, predicts an elevated schizophrenia risk. We also found that PLA2G4C rs1549637 polymorphism influences the clinical expression of schizophrenia, as measured by the Positive and Negative Syndrome Scale (PANSS), in male patients. Here, we investigated whether metabolic syndrome-related parameters such as body mass index (BMI) and plasma total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, and glucose levels might be influenced by the PLA2G4C polymorphism among Croatian patients with schizophrenia under antipsychotic treatment. To our knowledge, this is the first study investigating the possible relevance of the PLA2G4C polymorphism in metabolic syndrome-related parameters.

Materials and Methods

Genotyping was performed in 277 schizophrenic patients (males/females: 143/134) by polymerase chain reaction/restriction fragment length polymorphism analysis. Plasma total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, and glucose levels were determined after a 12-hour fasting period. We conducted separate analyses for males and females to account for a possible interaction of the metabolic measurements with gender.

Results

Total cholesterol and LDL cholesterol levels in females and triglyceride levels in males were elevated i.e. in the borderline high category relative to the reference values for the Croatian population, and mean BMI values were in the overweight range in both genders. Male patients manifested lower total cholesterol and HDL cholesterol levels and higher triglyceride levels than female patients ($p > 0.05$). The PLA2G4C polymorphism was not associated with any of the metabolic parameters among male or female patients ($p > 0.05$).

Conclusion
Our results indicate that PLA2G4C polymorphism may not be of relevance in metabolic syndrome-related parameters among patients with schizophrenia under antipsychotic treatment. Environmental factors such as the use of antipsychotic medication and cigarette smoking, by modulating PLA2 activity, might have masked the effect of PLA2G4C polymorphism on metabolic syndrome-related parameters.

Keywords:
glucose; lipids; phospholipases A2, gene polymorphism; schizophrenia

Growth Associated Protein 43 in the acute phase of recovery after severe traumatic brain injury

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Introduction
Traumatic brain injury (TBI) occurs when an external force, such as the impact of the head during a fall or traffic accident, causes damage to the brain tissue. One of the main challenges in TBI treatment is whether and how neuro-recovery can be supported. However, biomarkers that could indicate underlying processes toward neuro-recovery are still lacking. Our aim is to investigate whether Growth Associated Protein 43 (GAP43) has the potential to become a biomarker for neuro-recovery. GAP43 is required for axonal regeneration and is regarded as crucial for regenerative response in the nervous system.

Materials and Methods
The study involved severe TBI (sTBI) patients whose treatment required an external ventricular drain and whose family member signed the informed consent. Drained cerebrospinal fluids (CSF) were collected daily and combined into pools day (d) 1–2, d3–4, d5–6, and d7–12 which were used together with protein lysate of SH-SY5Y cells to detect GAP43 by western blot.

Results
A total of 35 CSF samples from 5 sTBI patients, 4 males, and 1 female, with a median age of 33 years (range 19–49) were included. Intracellular GAP43 was detected in SH-SY5Y protein lysate in the form of three bands with comparable intensity. However, GAP43 in CSF-pools was found as a single band corresponding in size to the largest band detected in SH-SY5Y. The highest level of GAP43 in CSF was detected in d1–2 followed by lower and comparable GAP43 levels in d3–4, d5–6, and d7–12.

Discussion/Conclusion
This is a preliminary analysis of GAP43 protein in CSF of sTBI patients. Our results indicate that GAP43 is present in CSF as a single form in comparison to three forms detected in SH-SY5Y cells which are of neuronal origin. Further studies should determine GAP43 levels in individual CSF samples from sTBI patients.

Keywords:
Biomarkers; Cerebrospinal Fluid; GAP-43 Protein; Nerve Regeneration, Traumatic Brain Injury

Epileptic seizure resulting in cervical trauma led to discovery of underlying spina bifida and hamartoma

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Introduction:
Epilepsy is occasionally caused by congenital malformations such as periventricular nodular heterotopia (PNH), and it can present in young adulthood with a refractory course. Nodular heterotopia is associated with other congenital malformations like spina bifida which can lead to some very rare tumors in the spinal cord.

Case Report:
We report a young female patient with a fracture of the C4 vertebrae and subluxation as sequelae to an epileptic attack. Epilepsy in our patient is known to be caused by left PNH. The fracture was managed with anterior C4/C5 fusion and cage implantation. Postoperative MRI revealed a syringomyelia C5/C6 and spina bifida occulta from C5 to C7, along with two posterior epidural masses that were radiologically described as hematomas. Surgical resection and analysis revealed that they were an ependymal cyst and probably a spinal hamartoma or teratoma. At presentation, the patient was severely tetraplegic, but after physical rehabilitation, she completely recovered her neurological function.

Discussion/Conclusion:
Around 2% of epilepsy is caused by nodular heterotopia, but resistance to the classic therapy makes this condition a big challenge for treatment. Refractory epilepsy leads to the accumulation of falls and increases the risk of some serious fractures. Spine fractures can lead to serious consequences, but they are rare, especially in the cervical region. So, awareness of, and adaptation to this kind of epilepsy is crucial. Cervical spinal dysraphism is the rarest form of spina bifida accounting for 1-5% of all spinal dysraphism. Spina bifida is associated with other congenital malformations like mentioned nodular heterotopia, but also with some forms of tumors. Due to the lack of conclusion in the pathological description of the second mass, the probability of spinal hamartoma or teratoma is discussed, although both tumors are extremely rare in the spinal canal.

Keywords:
Spina Bifida Occulta; Periventricular Nodular Heterotopia, Spinal Cord Trauma, Drug-Resistant Epilepsy, Spinal Cord Tumors

Meningioma of the anterior cranial base: a case report

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Introduction

A meningioma is the most common primary brain tumor that arises from the meninges (arachnoid cap cells), accounting for up to 30 percent of all brain tumors. It is mostly benign with slow progression, often over many years without causing symptoms. There are three groups of meningiomas according to the World Health Organization (WHO): grade I – low-grade tumors are the most common; grade II – atypical meningiomas and grade III – anaplastic meningiomas. The relative 5-year survival rate for atypical and anaplastic meningiomas is up to 64%. The degree of surgical resection of meningiomas is established by Simpson grade.

Case Report

We present a case of 75- a year – old male patient treated by ophthalmologists due to vision disturbances and loss of visual acuity. Due to the gradual progression of these symptoms, the patient underwent computer tomography (CT) and magnetic resonance imaging (MRI) scans which revealed a giant tumor of the anterior cranial base with concomitant compression of the optic chiasm and anterior cerebral arteries. The patient underwent surgical treatment under general anesthesia. The tumor was completely removed with complete preservation of cranial nerves and vascular structures. A postoperative CT scan confirmed complete tumor removal. Pathological analysis confirmed meningioma grade I.

Discussion/Conclusion

Most meningiomas are benign and remain silent until their anatomic location or diameter causes significant symptoms; grades II and III are relatively uncommon. Oncological treatment is more needed in the treatment of the higher grades of meningiomas, also the patient's age, residual tumor, and its location can dictate further treatment.

Keywords:

meningioma, primary brain neoplasm, meninges

Morbidity other-than-cranial-nerve deficits in surgical treatment of petroclival meningiomas

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Introduction

We recently published a meta-analysis on cranial nerve morbidity and mortality in surgically treated petroclival meningiomas (PCMs) across 3553 cases in 73 case-series. Petroclival meningiomas are skull base meningiomas that arise in the upper two-thirds of the clivus at the petroclival junction. These tumors are especially difficult to treat due to their location. Available treatments consist of radiotherapy, surgery, or a combination of both. We decided to expand the analysis on other-than-cranial nerve deficit morbidity in this report.

Materials and Methods

73 case-series that were published before February 7, 2021, were included in the meta-analysis. We extracted data on postoperative speech disturbances, tracheostomy, gait disturbances, motor deficits, cognitive deficits, CSF leak, infection, hydrocephalus, seizures, cerebrovascular incident (CVI), deep venous thrombosis (DVT) and pulmonary embolism (PE). Inclusion criteria are as follows: a) a case-series of at least 10 patients with PCMs defined as “true PCMs” or “PCMs”. One study could report on more than one cohort of patients (e.g., with different surgical approaches) or PCM patients could be a subset of a larger series including other tumor locations – as long as data on different procedures/PCM patients were reported separately with the same scrutiny regarding the outcomes and comprised at least 10 patients, each cohort was treated as a separate item; full-text articles in English or German language; numerical data on one of the outcomes of interest. Data on overall preoperative as compared to the postoperative clinical outcome was also included. Data were summarized as absolute/relative frequencies. Incidence of postoperative morbidity was compared between supratentorial, infratentorial, and combined surgical approaches, as well as overall morbidity incidence. Proportions were compared using the Chi-square test (Table 1).

Results

Morbidity incidence was reported from 6 to 59%. The incidence of morbidity ranged from 1.7 to 25.5%. There were significant differences between the supra- and infratentorial surgical approach groups in the incidence of speech deficits, gait disturbance, motor deficit, cognitive deficit, CSF leak, cerebrovascular incidents, and pulmonary embolism. Overall clinical outcome was reported in 27.8-47.1% of publications. Between the supra- and infratentorial groups differences were significant between the proportion of patients who clinically worsened or were unchanged postoperatively, but not in the proportion of patients who improved.

Discussion/Conclusion

Roughly half of the patients experienced overall clinical improvement following PCM surgery- a contrast given that the mortality rate was within the same range until the 1970s (7). The most

common morbidity as reported in 48% of the cohorts, was motor disturbance (paresis/plegia), developed by 25% of patients, and significantly more common among the cohorts predominantly operated on via a supratentorial approach. Gait disturbances were statistically significant and higher with the supratentorial approach with an incidence of 18.9%. Inconsistent terminology and defintion of motor deficits versus gait impairment across articles could account for the similarity in reported incidences (1). Improved clinical outcome was not significant between approaches, however, worsened clinical outcome was significantly increased in the supratentorial approach. The increase in gait disturbance incidence within the supratentorial group could account for the worsened clinical outcome, as gait dysfunction can severely impact patient quality of life.

Keywords:
Petroclival meningiomas, supratentorial approach, infratentorial approach, brain tumors, neurosurgery

Autoimmune Encephalitis in Pediatric Patients Linked to Positive Epstein-Barr Virus Serology – Case Report

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Introduction

Autoimmune encephalitis (AIE) is an inflammatory brain disease. The annual incidence of AIE and acute disseminated encephalomyelitis (ADEM) is 1,54 and 2,49 children/million, respectively. There are three known common autoantibodies. But like in this case not all children have a known autoantibody which makes the diagnosis difficult. A rare disease agent can be the Epstein-Barr virus (EBV). The overall incidence of neurological complications in EBV is <7%. In this case, the exact pathogen is unknown, but because of positive Epstein-Bar virus antibodies, this case is linked to it.

Case Report

A two-year-old, from an uneventful pregnancy and with normal psychomotor development, was brought to the emergency department on the fourth day of fever and hospitalized the same day due to an altered state of consciousness. Using the AVPU scale of consciousness the patient did not respond to pain stimulus. An initial lab exam showed elevated infection parameters. She was described as somnolent, with bilateral ophthalmoplegia, positive Brudzinski and Babinski sign. Because of serious deterioration in the state of health, from the third day on the child was mechanically ventilated. A series of serology tests conducted over the next days revealed negative results for Covid-19/Influenza panel and meningitis/encephalitis panel, while anti-EBV IgG was positive. The electroencephalogram (EEG) displayed posterior asymmetries. And the magnetic resonance imaging (MRI) showed increased T2 FLAIR signal in the thalamic region, tegmentum mesencephali, and periaqueductal, which progressed to the fronto-parieto-occipital cortex and the internal capsule. The treatment included intravenous immunoglobulin and plasmapheresis with corticosteroids. The child recovered on the twelfth day of the disease.

Discussion/Conclusion

The incidence of autoimmune encephalitis in the pediatric population is rising. In case of a fever and altered consciousness, a rare differential diagnosis may be autoimmune encephalitis. Treatment is complex and the outcome is uncertain. In some cases, full recovery can be achieved, like in this case.

Keywords:

Autoimmune Diseases; Child; Encephalitis; Immunoglobulin; Epstein-Barr Virus

Clinical characteristics and diagnosis of mitochondrial membrane protein-associated neurodegeneration (MPAN)

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Introduction
Mitochondrial membrane protein-associated neurodegeneration (MPAN) is a rare disorder that is estimated to affect less than 1 in 1 million people. The aim of this case report is to show the most common symptoms of the disease, the differential diagnosis, and the potential benefit of skin biopsy in the diagnostic process.

Case Report
We discuss the case of a 12-year-old female patient who came to the general practice complaining of involuntary muscle cramping and muscle stiffness. Past medical history showed only allergic rhinitis. Since she was engaged in intense sports activity, she was advised to occasionally take magnesium and vitamin B complex pills.

During the course of 15 months, muscle cramps began to worsen and she presented with hand tremor, hyperreflexia, postural instability, dysarthria, bilateral optic atrophy, swallowing difficulty, and progressive cognitive decline. Skin biopsy revealed axonal spheroids and bubble-like features on degenerating axons. Brain MRI showed parenchymal volume loss and iron deposits mainly in the globus pallidus and substantia nigra.

By the time her 2 years younger sister presented with similar symptoms, the neuro pediatrician suspected a hereditary component of the disease. Differential diagnoses included other neurodegenerative diseases with brain iron accumulation. Genetic testing confirmed the mutation in the C19orf12 gene and the final diagnosis was made.

Discussion/Conclusion
MPAN is a rare progressive neurodegenerative disease whose symptoms usually begin in childhood and adolescence. The diagnosis is established by proving the mutation of the C19orf12 gene. Active monitoring of such patients is required to prevent possible secondary complications of the disease, the most common of which is pneumonia.

Keywords:
Iron deposits, MPAN, neuropediatrics, skin biopsy

Severe Clinical Presentation of Huntington Disease in a Patient With Incomplete Penetrance

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Introduction
Huntington disease (HD) is an autosomal dominant progressive neurodegenerative disease caused by the expansion of CAG triplets on chromosome 4. It manifests in predominantly hyperkinetic movement disorders, as well as psychiatric and cognitive symptoms. The typical clinical picture is presented in patients with 40 or more CAG triplet repeats, better known as complete penetrance. Penetrance refers to the probability that a clinical condition will occur in a patient with a particular genotype. Repeats between 36 and 39 are incompletely penetrant and cause a mild clinical picture at a later age, or the disease does not manifest at all. The intermediate genotype ranges between 30 and 35 triplets, and the disease does not manifest in those patients.

Case Report
We present a case of a male patient who, at the age of 44, developed stiffness and difficulty walking which was demonstrated in small steps, along with difficulty lifting his legs. Shortly after the initial symptoms, slurred speech, difficulty swallowing, along with involuntary movements of fingers and orofacial musculature appeared. Genetic analysis showed 36 repeats and a diagnosis of HD was made with a predominantly hypokinetic-rigid presentation. Antipsychotic treatment was induced. Over the next 12 years, the disease severely progressed. The patient became immobile, dysarthric, uncommunicative, incontinent, and dependent on others' help, with frequent urinary tract infections and the development of pressure ulcers.

Discussion/Conclusion
Even though the course of the disease is typical, a severe clinical picture with an early onset of symptoms is highly unexpected in patients with incomplete penetrance. Considering this patient has 36 repeats, which is at a lower margin for the disease presentation, the premature development of disability which significantly lowers the quality of life is highly uncommon. Finally, the dominance of hypokinetic-rigid symptoms is another peculiarity.

Keywords:
CAG, Huntington disease, penetrance

Posters

The role of Rey-Osterrieth Complex Figure Test in assessment and diagnosis of dementia

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Introduction
One of the goals of neuropsychological assessment is to determine the extent to which brain damage affects cognitive abilities. It is one of the key steps that help clinicians establish a working diagnosis. One of the frequently used tests for examining visual-spatial construction abilities, visual-perceptual abilities, and visual memory is the Rey-Osterrieth Complex Figure Test (ROCF). In addition, ROCF also measures organization, planning, and self-monitoring.

Materials and Methods
To find recent literature, we have searched ScienceDirect database according to keywords such as "Rey-Osterrieth Complex Figure Test", "dementia" and "neuropsychological assessment". We included research papers that used ROCF as an assessment tool for signs of dementia, five of them in total.

Literature Review
Research shows that there are significant differences in ROCF performance between healthy people and people with dementia and that the test performance differs qualitatively and quantitatively between people with different types of dementia. Moreover, it is found that ROCF can indicate the presence of mild cognitive impairment, a condition that often precedes the development of different types of dementia, which is extremely useful since early detection of the disease is essential for early treatment and rehabilitation. Different characteristic signs of dementia can be seen based on the patient's performance, but also how the progression of the disease, i.e. the increasing deterioration of specific brain areas, can be monitored by repeated use of ROCF. Intending to optimize the scoring and interpretation of performance on this test, researchers and clinicians are working on developing digital scoring systems. A decision support system (DDS) is a system that aims to standardize the qualitative and quantitative evaluation of a patient's work using artificial intelligence (AI).

Discussion/Conclusion
ROCF is a useful tool in neuropsychological assessment and can detect early signs of cognitive dysfunction which can help in the more precise diagnosis of different types of dementia.

Keywords:
Neuropsychological Tests; Cognitive Dysfunction; Dementia

S-adenosylhomocysteine (SAH) hydrolase deficiency and disruption of semaphorin neuronal signaling (SEMA3A gene)

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Introduction
SAH (S-adenosylhomocysteine) is a byproduct of the transmethylation reactions and is normally hydrolyzed by SAH hydrolase to maintain the balance of S-adenosylmethionine (SAM) and SAH, which is a potent inhibitor of many methyltransferases. The neurological symptoms of SAH hydrolase deficiency can vary widely. Accumulation of SAH can have widespread effects on cellular pathways including the semaphorin neuronal signaling pathway (SNSP). Semaphorins are a family of proteins that regulate neuronal growth cone guidance and synapse formation, and their signaling is important for the proper development and function of the nervous system. Semaphorin 3A (SEMA3A) has been shown to play a role in axon guidance during development and in neuronal plasticity in the adult brain. SNSP is involved in cell survival, proliferation, differentiation, and migration.

Materials and Methods
We performed RNAseq experiments on AHCY-deficient MCF7 cells using NGS-based approaches on Illumina platforms. Differential expression data were analyzed using Ingenuity Pathway Analysis software. Core analysis was performed. Total cell RNA was extracted from 1 × 106 cells. Two different cell passages were used to extract RNA both for shAHCY and shCTRL cells and treated as a biological replicate.

Results
Fifteen differentially expressed networks were identified. We found a predicted effect of AHCY down-regulation on the expression of the SEMA3A gene with a z score -2.

Discussion/Conclusion
AHCY deficiency results in lower transcription of the SEMA3A gene. Altered methylation patterns as a result of AHCY aberrant activity are associated with changes in gene expression that may affect SEMA3A. These findings suggest that SAH hydrolase deficiency can lead to disruptions in semaphorin signaling and could contribute to the neurological symptoms of this disorder. Limitations of this study: further research is needed to better understand the underlying mechanisms of this relationship on the protein level.

Keywords:
S-adenosylhomocysteine, SAH hydrolase deficiency, Semaphorins, Neuronal plasticity, Gene expression

Change of total tau protein in cerebrospinal fluid (CSF) of patients with spinal muscular atrophy (SMA) after nusinersen treatment

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Introduction
In this study, we aimed to investigate the effect of nusinersen treatment on the level of total tau (t-tau) protein in cerebrospinal fluid (CSF) of patients with spinal muscular atrophy (SMA). SMA is an autosomal recessive disease characterized by degeneration of the spinal cord anterior horn motoneurons, caused by the homozygous deletion or mutation of the survival motor neuron 1 gene (SMN 1). We also analyzed the existence of an association between CSF t-tau and genetic biomarkers of SMA (the number of copies of the 7th exon of the SMN2 gene and the number of copies of the NAIP gene), scores on scales for the assessment of motor functions, duration and type of SMA.

Materials and Methods
The study included 30 patients with SMA types 1, 2, and 3, treated at the University Hospital Centre Zagreb. CSF samples were collected by lumbar puncture, T-tau concentration in CSF was determined using Enzyme-Linked Immunosorbent Assay (ELISA). The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) and Hammersmith Functional Motor Scale Expanded (HFMSE) were used to measure their motor function. Genetic analyses were done using the Multiplex ligation-dependent probe amplification method (MLPA). Statistical data analysis was done using the SPSS program, version 19.0.1 (SPSS, Chicago, IL, USA).

Results
After the nusinersen treatment, CSF t-tau levels were significantly decreased. There were no significant differences in CSF t-tau levels between patients with different genetic biomarkers of SMA. Additionally, t-tau levels did not correlate with the scores on the COOP-INTEND scale and HFMSE scale. There was no association of CSF t-tau with duration or type of SMA.

Discussion/Conclusion
Since there was a statistically significant decline in its average values with the administration of nu-

sinersen, CSF t-tau protein turned out to be a statistically significant prognostic and theragnostic biological marker of a successful response in patients with SMA. However, t-tau did not correlate with genetic biomarkers of SMA, scores on scales for the assessment of motor functions, duration, and type of SMA.

Keywords
Cerebrospinal fluid, Genetics, Spinal muscular atrophy, Tau protein, Therapy.

Levels of NFL protein in CSF of SMA patients treated with nusinersen

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Introduction
In this study, we aimed to determine if cerebrospinal fluid (CSF) neurofilament light chain (NFL) levels change after treatment of patients with spinal muscular atrophy (SMA) with nusinersen. We also analyzed if NFL levels are associated with genetic biomarkers of SMA (the number of copies of the NAIP gene and the number of copies of the 7th exon of the SMN2 gene). We additionally tested if there is a correlation between CSF NFL levels and the scores on scales for the assessment of motor functions in SMA patients, type, and duration of the disease.

Materials and Methods
In this study, 30 participants were treated for SMA at University Hospital Centre Zagreb. Before nusinersen administration, CSF samples were collected by lumbar puncture. The CHOP-INTEND (The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders) scale and the HFMSE (The Hammersmith Functional Motor Scale Expanded) scale were used for measuring motor functions in SMA patients. Patients with SMA type 1 were tested with the CHOP-INTEND scale, while patients with SMA type 2 and 3 were tested with the HFMSE scale. Protein concentrations in cerebrospinal fluid were determined using enzyme-linked immunosorbent assay analyzes (ELISA, Enzyme-Linked Immunosorbent Assay). Statistical data analysis was performed using the statistical program SPSS, version 19.0.1 (SPSS, Chicago, IL, USA).

Results
CSF NFL levels were moderately decreased in SMA patients after nusinersen treatment, so NFL protein has been shown to be a moderately good biomarker for monitoring the response of patients with SMA to the effect of nusinersen. NFL levels correlated negatively with CHOP-INTEND scores, and positively with the duration of the disease. There was no association of CSF NFL levels with genetic biomarkers of SMA and type of disease.

Discussion/Conclusion
Since there was a negative correlation between NFL levels and the number of points on the CHOP-INTEND scale, NFL proved to be a statistically significant prognostic biological marker of favorable therapeutic response in patients with SMA. In addition, NFL levels were positively correlated with the duration of the disease.

Keywords
cerebrospinal fluid, genetics, neurofilament light chain, spinal muscular atrophy, therapy

S100 calcium-binding protein B (S100B) in cerebrospinal fluid (CSF) of spinal muscular atrophy (SMA) patients treated with nusinersen

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Introduction

The main goal of this study was to evaluate the effect of nusinersen treatment in patients with spinal muscular atrophy (SMA) on cerebrospinal fluid (CSF) S100 calcium-binding protein B (S100B) levels. We also wanted to ascertain if there is an association of CSF S100B with genetic biomarkers of SMA, scores on the Hammersmith Functional Motor Scale Expanded (HFMSE), and The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) scales for the assessment of motor functions in SMA patients, type and duration of SMA.

Materials and Methods

30 SMA patients were involved in this study at the University Hospital Centre Zagreb. Before administering nusinersen, patients' CSF samples were taken by lumbar puncture. CSF S100B concentration was determined by Enzyme-Linked Immunosorbent Assay (ELISA). To assess motor functions in SMA patients, we used the CHOP-INTEND and the HFMSE scales. All genetic analyses were accomplished using the Multiplex Ligation-dependent Probe Amplification (MLPA) method. Statistical data analysis was performed in the SPSS program, version 19.0.1 (SPSS, Chicago, IL, USA). Due to deviation in data distribution, non-parametric tests were used.

Results

CSF S100B levels did not change significantly in SMA patients after the treatment with nusinersen. Additionally, S100B levels neither correlated with scores on HFMSE and CHOP-INTEND scales nor showed association with genetic biomarkers of SMA (the number of copies of the NAIP gene and the number of copies of the 7th exon of the SMN2 gene). S100B levels did not differ between patients with different types of SMA. However, S100B levels positively correlated with the duration of the disease.

Discussion/Conclusion
S100B protein did not show characteristics of an informative biological marker for the therapeutic response of patients with SMA during nusinersen therapy, given that the administration of nusinersen did not affect S100B levels after administration. Also, no association was established between S100B protein and SMA genetic biomarkers. Nevertheless, S100B values positively correlated with the duration of the disease.

Keywords
Cerebrospinal fluid, Genetics, S100B, Spinal muscular atrophy, Therapy

Iron Dyshomeostasis and Brain Functions – A Literature Review

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Introduction
Iron is an essential micronutrient involved in numerous physiological processes. In the brain, it participates in crucial processes such as oxidative metabolism, myelination, and the biosynthesis of neurotransmitters. Hence, dyshomeostasis in iron concentration significantly affects brain functions. Therefore, the aim of this review is to highlight the importance of maintaining brain iron homeostasis for normal brain functions and the prevention of iron-related brain disorders.

Materials and Methods
The PubMed database was searched only for Reviews published between the years 2013 and 2023, up to February 2023, using the keyword "iron" in combination with "homeostasis", "deficiency", "overload", "brain", "oxidative stress", "neurodegeneration", "multiple sclerosis", "demyelination", "Parkinson's disease", "Alzheimer's disease." The search has yielded 5478 results. Among them were 70 articles related to brain functions and they were analyzed for this review.

Literature Review
Iron is the most abundant trace metal in the brain, supporting the brain's high need for energy. Its homeostasis is maintained by the coordinated action of many proteins, such as transferrin, hephaestin, hepcidin, and ferroportin. When some of these molecular mechanisms are disturbed, iron overload or deficiency occurs. Iron deficiency leads to cerebral hypoxia, insufficient neurotransmitter synthesis, and impaired myelination, leading to cognitive decline and dementia. It is usually associated with aging, but recent studies show a correlation between iron deficiency and neurodevelopmental decline in children. On the other hand, brain iron overload generates oxidative stress, making the brain more susceptible to neurodegenerative processes. The magnetic resonance imaging showed brain iron deposits in neurodegenerative diseases, such as multiple sclerosis, Parkinson's disease, and Alzheimer's disease, and correlated iron accumulation with the severity of the disease.

Discussion/Conclusion
In conclusion, systemic and brain iron homeostasis regulation is crucial for ensuring normal functions of the central nervous system. Disturbances of cellular or molecular mechanisms of brain iron homeostasis can lead to serious central nervous system disorders.

Keywords:
Brain; Homeostasis; Iron; Iron Overload; Neurodegenerative Diseases

Paraneoplastic encephalitis of the brain stem: a case report

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Introduction

Paraneoplastic neurological syndromes (PNSs) are comprised of immune – mediated nervous system ailments triggered by an underlying malignancy. Each PNS has its own distinct clinical presentation. Once a connection between cancer and the immune-mediated effects affecting the cerebral hemispheres is established, the term paraneoplastic encephalitis (PE) is used.

Case Report

A 62-year-old female patient with a medical history of breast and lung cancer was admitted to the Department of Neurology after presenting with encephalopathy, dystaxia, and nystagmus, followed by stupor, nuchal rigidity, and periodic tonic-clonic seizures. No pathomorphological substrate was confirmed upon emergency intracranial evaluation. Initially, respiratory insufficiency due to pulmonary embolism was considered as the cause, however, following the negative computer tomography angiography, further testing was needed. Next, a lumbar puncture was performed, which confirmed signs of acute inflammation (elevated cell count and proteins), hence antibiotic/antiviral treatment was started. Antibodies for neurotropic viruses came back negative, as well as the bacterial analysis of cerebral spinal fluid (CSF), so the treatment was stopped. An initial electroencephalogram (EEG) showed lateralized periodic discharges (LPDs) frontocentrotemporoparietally on the left. Magnetic resonance imaging (MRI) performed two weeks later showcased subacute bilateral lesions in the middle cerebellar peduncles and on the ventral pons, which were at the time described as ischemic. After the symptomatic therapy of anticonvulsants, antipsychotics, corticosteroids, and sedatives, the patient's state significantly improved, although moderate memory impairment and confabulations remained. No changes to the patient's condition were reported two months later at the check-up. Further, oncologic treatment was recommended. In recent developments, the patient's status has gotten worse, leaving her nearly immobile.

Discussion/Conclusion

A few weeks ago, onconeural and autoimmune encephalitis antibody panels came back negative. Based on the patient's history of malignant disease, and the workup, it is likely that the cause of her state was paraneoplastic brain stem encephalitis. Even with the negative panels, the patient fits the diagnostic criteria.

Keywords:

paraneoplastic syndromes, encephalitis, electroencephalogram

The connection between the Mediterranean diet, gut microbiota, and risk of Alzheimer's or Parkinson's disease

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Introduction Alzheimer's disease (AD) and Parkinson's disease (PD) are the two most prevalent neurodegenerative diseases without cure. The Mediterranean diet (MeDi) may be beneficial for health overall and for healthy brain aging. Gut dysbiosis can be mitigated by consuming a diet high in fiber and polyphenols, such as MeDi, by increasing beneficial gut bacteria. With no curative therapies for AD or PD, attention should focus on preventative measures such as modifiable lifestyle factors such as the Mediterranean diet.

Materials and Methods We analyzed databases on PubMed, and the Web of science using the keywords „gut microbiota ", „Alzheimer's disease ", and „Parkinson's disease ".

Literature Review Through a systematic literature review on MeDi adherence and AD or PD risk, we found an overall reduction of risk in disease development with MeDi adherence. Dysbiosis, which is represented by a decrease in the number of bacteria that produce short-chain fatty acids (SCFA), can lead to various adverse effects. Increased inflammation and intestinal and brain-blood barrier permeability resulted from dysbiosis stemming from diets high in fat and low in fermentable fiber. These changes induced by the intestinal microbiota can allow the passage of normally blocked bacteria and bacterial endotoxins into circulation. One such Lipopolysaccharide (gram-negative bacteria) binding protein has been found to be elevated in the serum of PD patients and lipopolysaccharide has been found in postmortem brain tissues. Further, endotoxins can promote amyloid-β and tau aggregation, neuropathology in AD patients, and α-synuclein production and aggregation in PD patients. Differences in gut microbiota have been observed between healthy controls and cases of neurological disorders including PD and AD.

Discussion/Conclusion Our review found that adherence to the MeDi reduces the risk of AD and PD and helps preserve intestinal eubiosis. However, to confirm these findings further research is required.

Keywords
Microbiota, Alzheimer's disease, Parkinson's disease, diet, protective effect

Radiological differences between Frontotemporal dementia (FTD) subtypes

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Introduction

Frontotemporal dementia (FTD) is a heterogenous group of disorders characterized by progressive changes in behavior, language, and cognition associated with frontotemporal lobar degeneration. There are 2 clinical variants based on the symptoms most prominent early in the disease onset: behavioral variant (BV) and primary progressive aphasia (PPA). PPA is further classified into semantic variant PPA (svPPA), nonfluent agrammatic PPA (nfaPPA), and logopenic variant PPA (lvPPA).

Materials and Methods

The search of the PubMed database was conducted using "frontotemporal dementia AND neuroimaging", "frontotemporal dementia AND MRI" and "frontotemporal dementia AND radio*". All the articles had those terms in the title and were published between 2017. and 2023.

Literature Review

In around 30% of patients, FTD is a hereditary disease, and the radiological changes can be found 8 to 10 years before the onset of the symptoms. The majority of genetic FTD relates to a mutation in three genes: C9orf72, GRN, and MAPT.

In the behavioral variant, changes can be found in the prefrontal cortex, anterior temporal lobes, and limbic and subcortical regions, but the amygdala, striatum, and anterior insula are structures most affected by the atrophic changes.

Typically, degeneration is asymmetrical and it's more pronounced in the right hemisphere. The exception is the left ventrolateral temporal lobe which is generally more atrophic than the right.

The semantic variant presents with asymmetric atrophy of the anterior temporal lobes and the language-dominant hemisphere is usually more impacted.

The hallmark of non-fluent agrammatic PPA is frontal lobe atrophy of the dominant hemisphere with pars opercularis, insula, middle frontal gyrus, and the supplementary motor area being the most affected.

Discussion/Conclusion

FTD is diagnosed using clinical examination, cognitive testing, and magnetic resonance imaging which showcases frontotemporal atrophy, but each FTD subtype has its own neuroimaging characteristics. In some cases, it's even possible to suspect which gene mutation caused FTD based on clinical presentation and radiological changes.

Keywords

Frontotemporal Dementia, Neuroimaging, Magnetic Resonance Imaging

Non-compliance with Wilson disease

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Introduction
Wilson disease is a multisystem disease that occurs due to an inherited disorder of copper metabolism. Hepatic, neurological, ophthalmic, and psychiatric symptoms are the most common clinical presentation.

Case Report
We present a case of a 30-year-old woman who has been diagnosed with Wilson disease at the age of 11.

In the beginning, the patient has had primarily gastroenterological symptoms but over the years the neurological symptoms appeared too.

The patient noticed dystonia and tremor in the hands. Moreover, there had been difficulties in speech and balance, as well as hypersalivation. On the physical exam dysarthric speech, postural tremor of the hands, and mild generalized hypertonia presented as rigidity were found.

The patient was not able to do the heal-to-toe walk test and the retropulsion was noted while performing the Romberg test. The patient walked with a wide-based gait and the right limbs dropped in the anti-gravitational positions.

MRI (Magnetic Resonance Imaging) showed hyperdense signals in the mesencephalon and bilaterally in the putamen and thalamus, while the ophthalmological exam discovered bilateral Kayser-Fleischer rings. These findings indicated that the copper was now being accumulated in the brain and eyes. Zinc by itself was no longer a sufficient treatment so penicillamine and physical therapy were added.

On the follow-up annual control, only the slight dysarthria was found. On the MRI there was a complete regression of the basal ganglia changes.

Unfortunately, over the years our patient stopped using the medications regularly and symptoms came back. She noticed a worsening in her balance, coordination, and movement. Furthermore, hyperdense signals in the basal ganglia appeared once again, and the serum levels of copper raised, while the serum levels of ceruloplasmin remained low. Regarding her neurological exam, dysarthria, dystonic posture of the right hand, and wide-based gait were found.

Discussion/Conclusion
This case shows how quickly deterioration can occur if the treatment is not used regularly.

Keywords
Hepatolenticular Degeneration, Patient compliance, Penicillamine, Dysarthria, Basal ganglia diseases

Parkinson's disease patient selection for advanced treatment options

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Introduction

Parkinson's Disease (PD) is a neurodegenerative disorder of the dopaminergic neurons in the substantia nigra. Multiple advanced treatment options exist and are not used as much as they maybe should be. In most countries, there are no official national guidelines, and a considerable number of doctors treating these patients are not well-informed about them. We aim, through this review, to make an algorithm proposing when these device-aided therapies should be considered.

Materials and Methods

This review was conducted using PubMed with combinations of the keywords: Parkinson's disease treatment, device-aided therapy, apomorphine, levodopa-carbidopa intestinal gel (LCIG), levodopa-entacapone-carbidopa intestinal gel (LECIG), and deep brain stimulation (DBS).

Literature Review

Complications of advanced PD are difficult to treat with oral therapy. In case of early morning dystonia and akinesia or unpredictable off periods that need a quick fix, an apomorphine pen can be suggested. When the pen is needed more than 10x/day, an apomorphine pump should be considered. More invasive, LCIG can be introduced initially as well, particularly if gastric emptying dysfunction or "freezing of gait" exists. If the patient had a good effect from oral entacapone, LECIG is recommended. DBS can be advised for patients with tremor-resistant PD under 70 years (or older with no cognitive decline or MRI (magnetic resonance imaging) changes). Another substantial problem in advanced PD is dyskinesia which can be treated with an apomorphine pen or pump when trying to avoid more invasive procedures. LCIG can be started as monotherapy and later other drugs can be added, or we can introduce LECIG.

Discussion/Conclusion

Transitioning to advanced therapy methods at the right time is crucial in treating Parkinson's disease. A simple and clear algorithm for treatment is needed for these patients to preserve a satisfying level of their quality of life for as long as possible.

Keywords

Apomorphine; Carbidopa, levodopa drug combination; Deep Brain Stimulation; Drug Therapy; Parkinson Disease

Neurosarcoidosis features in an adult man

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Introduction

Neurosarcoidosis refers to a type of sarcoidosis, defined as a multisystem inflammatory disease of unknown etiology predominantly affecting lymph nodes and lungs, with the involvement of the central or peripheral nervous system. Considering the manifestation variability depending on affected nervous system areas, neurosarcoidosis diagnosis may be difficult or delayed mimicking other neurological conditions.

Case Report

A 39-year-old male patient has been referred for occasional episodes of right-sided limb-ascending paresthesias accompanied by nocturnal enuresis, blurred vision, and gait instability. During the patient's interview, he reported his father's lung-affecting sarcoidosis. Additionally, the previous ophthalmologic assessment showed bilateral temporal and upper quadrant visual field defects. Neurological examination revealed the intentional tremor with an ataxic wide-based gait. Hereafter, cerebrospinal fluid (CSF) analysis demonstrated increased total cell count, significantly elevated levels of total proteins (1,55 g/L), intrathecal oligoclonal band synthesis, and slightly decreased levels of glucose (2,10 mmol/L). Afterward, magnetic resonance imaging (MRI) depicted increased subcortical and periventricular parietal T2/FLAIR signals with the same characteristics noticed on the left side around the anterior horn of the lateral ventricle and putamen. The T1 post-contrast sequence revealed diffuse perimedulary veins imbibition, and multiple minor subcortical signal drops were detected in the susceptibility-weighted imaging (SWI) sequence. Also, the patient underwent an endocrine evaluation where hypogonadism was found following gonadotropic hypophysis insufficiency. Consequently, all of these findings were attributed to neurosarcoidosis leading to the patient's methylprednisolone-based therapy prescription.

Discussion/Conclusion

Even though that is a rare entity, it should be kept in mind while evaluating patients with multiple non-specific CNS symptoms of longer duration. Sometimes, despite many diagnostic procedures, MRI is one of the most important methods to confirm our suspicion of neurosarcoidosis.

Keywords

Cerebrospinal fluid; magnetic resonance imaging; paresthesia; sarcoidosis

PRRT2 Mutation - A Cause of Benign Familial Infantile Epilepsy

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Introduction
Benign familial infantile epilepsy is an autosomal-dominant seizure disorder that occurs in infancy and in which seizure onset occurs at a mean age of 6 months. In the majority of cases, mutations in the proline-rich transmembrane protein 2 (PRRT2) gene located at 16p11.2 has been found.

Case Report
We present a five-month-old infant who was hospitalized at the Clinic due to suspected afebrile convulsions manifested by staring and atony, after which the child falls asleep. The child has no perinatal risk factors, but the family history is positive for epilepsy and febrile seizures that the mother's father and mother have. Upon admission, only mild hypotonia of the right hand is visible, and the laboratory findings are normal. During hospitalization, all tests performed, including brain magnetic resonance imaging and an electroencephalogram were normal, but focal-type seizures still occurred frequently, later with impaired consciousness as well. Therefore, it was decided to introduce permanent therapy with levetiracetam, after which the seizures completely disappear. He was discharged from the hospital but brought again after a few days due to repeated seizures. Because the tests were normal, it was assumed that the relapse occurred due to an insufficient dose of the drug. The doses of levetiracetam were increased and the condition was improved. Genetic testing using the Invitae panel proved the PRRT2 pathogenic mutation.

Conclusion
PRRT2, a presynaptic membrane protein that plays an important role in cell exocytosis and neurotransmitter release, is highly expressed in the human brain, especially in the cerebral cortex, basal ganglia, and cerebellum. The dysfunction of this gene has been proposed to cause dysregulation of neuronal excitability and cerebral disorders. Understanding the pathophysiological mechanism of this protein is still ongoing, but could be a big step in moving from symptomatic treatments to therapeutic options targeting their specific pathophysiologic alterations.

Keywords
Anticonvulsants, Benign Neonatal Epilepsies, Epileptic seizures, Levetiracetam, Genetic testing

A case report of narcolepsy with cataplexy

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Introduction

Narcolepsy is a chronic neurological disorder that impairs the brain's ability to control sleep-wake cycles which consequently leads to overwhelming sleepiness throughout the day. People who suffer from narcolepsy may experience cataplexy which is a temporary loss of muscle tone triggered by strong emotions. These symptoms result in poor sleep efficiency and restrict the person from engaging in daily activities.

Case Report

A 49-year-old female was admitted to the neurology department due to excessive daytime sleepiness, episodes of unpredictable loss of voluntary muscle control, and weakness. The patient reported that she first started noticing symptoms after childbirth 17 years ago. She described them as a sudden loss of face, neck, and arms muscle tone with strabismus when laughing. The patient is also a diabetic who developed glaucoma. Repetitive scintillating scotoma lasting up to 20 minutes occurred occasionally followed by exhaustion and intermittent headaches without nausea or vomiting. During the last two years, her problems aggravated being more frequent and severe. She would fall asleep in less than 15 minutes and woke up in the middle of the night being unable to fall back asleep. Additionally, she had approximately 4 hours of sleep per night and hypnagogic hallucinations. Obstructive sleep apnea was excluded. The electroencephalogram showed normal electrical activity without bursts of theta rhythm brainwaves. However, a polysomnogram and multiple sleep latency tests confirmed that her symptoms are a manifestation of narcolepsy. Pathological changes visible on brain MRI were indicative of chronic small vessel disease. Our patient was given sodium oxybate 2.25g x2 per os therapy to which she responded successfully. Alternative therapy is modafinil and duloxetine. Active surveillance was recommended in order to adjust drug dosing if necessary.

Conclusion

The main purpose of this report is to emphasize the importance of recognizing early signs of narcolepsy. Although incurable, proper medications can minimize the symptoms of narcolepsy.

Keywords:

cataplexy; narcolepsy; neurology; polysomnography; sleepiness

Case report of Radiologically isolated syndrome (RIS)

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Introduction

Radiologically isolated syndrome (RIS) is a rare condition that is characterized by Magnetic resonance imaging (MRI) results of white matter lesions that fulfill McDonald criteria for Multiple sclerosis (MS) but with a complete absence of any clinical symptoms typical for MS.

Case Report

We present a case of a 14-year-old girl, who is 183 cm tall and weighs 80 kg. On January 2022, an endocrinologist because of excessive height examined her, even though her parents are also of tall stature. Since hormone testing showed normal levels of insulin-like growth factor 1 (IGF-1), MRI was performed. After non-specific MRI findings of focal cortical dysplasia, a control MRI was recommended 6 months later. She collapsed on July 2022, when a hemodynamically insignificant atrial septal defect secundum was founded. She has not suffered from any other neurological symptoms. The repeated MRI showed lesions that are disseminating in space (hyperintensities in the subcortical white matter, in the knee at the left side, and splenium on the right side of corpus callosum) and lesions that are disseminating in time (subcortical white matter, corpus callosum, cervical medulla). Because of these incidentally found results, following the guidelines for demyelinating disease of the central nervous system, a complete clinical evaluation was performed. There were no other pathological findings. She has not experienced any other symptoms since then, including fatigue, numbness and tingling, problems with intellectual activities, etc. She has no family history of demyelinating diseases.

Discussion/Conclusion

Regarding the fact that the girl does not have any clinical manifestations, has no subjective complaints, and has a completely normal finding of cerebrospinal fluid, stated MRI findings are considered as RIS. It is important to control these patients regularly because there is a high risk of conversion to clinically definite MS.

Keywords

Central Nervous System, Demyelinating Disease, Incidental Findings, Magnetic Resonance Imaging, Multiple Sclerosis

Cognitive status of patients with memory loss at first neurology visit

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Introduction
Cognitive loss in one or more areas, such as memory, language, and visuospatial processing, can significantly impact daily independence and is referred to as dementia. With dementia incidence expected to triple by 2050, early identification and monitoring of cognitive function are crucial. The Montreal Cognitive Assessment (MoCA) is a brief cognitive screening tool used in clinical settings to assess various aspects of cognitive function, including attention, concentration, memory, language, and visuospatial abilities. Mild cognitive impairment (MCI) is the term used to describe cognitive deterioration with residual independence. In this study, we aimed to determine the prevalence and stage of MCI in patients referred to a neurologist for the first time, using the MoCA as a screening tool.

Materials and Methods
MoCA test was performed on 48 participants. The results were analyzed using descriptive statistics.

Results
Among the 48 participants, 40% (19) were found to have mild cognitive impairment (MCI), with 74% (14) of those being female and 26% (5) being male. Moderate cognitive impairment was present in 35% (17) of all participants, while 6% (3) displayed severe cognitive impairment. Only 19% (9) showed no cognitive impairment, with 56% (5) of those being female and 44% (4) being male.

Discussion/Conclusion
The study showed 40% of patients present with MCI at the time of their first visit.

Number of patients who present with signs of dementia at the time of their first visit was 81%. Our results confirm that dementia is a leading socioeconomic and public health issue with patients presenting with signs of dementia at the time of their first assessment.

Better care for patients requires more education on disease prevention, early recognition, and treatment. Early detection and treatment enhance life quality and reduce cognitive decline in MCI patients. Limitations of the study include small sample size and the lack of follow-up to determine MCI progression to dementia.

Keywords
Dementia; MCI; MoCA; dementia screening; cognitive decline

The role of endocannabinoids in migraine pathogenesis regarding future treatment

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Introduction
Migraine is a primary headache disorder characterized by severe pulsatile pain, accompanied by nausea, vomiting, photophobia, or phonophobia. According to GBD (Global Burden of Disease) data from 2019, migraine is regarded as one of the conditions with the highest negative impact on quality of life. The endocannabinoid system (ECS) is a complex network of chemical signals and cellular receptors involved in different pathways (e.g. glutamatergic, serotoninergic, and inflammatory) included in the pathophysiology of a migraine attack. The aim of this review was to present ECS as a potential target for migraine pain drug development.

Materials and Methods
A literature search was conducted, using PubMed and Google Scholar data, on ECS influence in migraine with a focus on the new approach in pain management.

Literature Review
Most of the current evidence supports the trigeminovascular hypothesis in the pathophysiology of migraine attacks. It proposes that abnormal activation of the trigeminal nerve leads to the releasement of neuropeptides, which cause dilation and inflammation of blood vessels in the brain, resulting in pain. The ECS modulates the trigeminovascular system (TGVS) by stimulating specific receptors (CB) of endocannabinoids (eCBs). The most prevalent eCBs are 2-arachidonoylglycerol (2-AG) and anandamide (AEA) which act primarily on CB1 (predominantly expressed in neurons) and CB2 (mainly expressed in immune cells) receptor isoforms. During a migraine attack, prolonged activation of the TGVS ultimately causes sensitization of higher-order neurons, leading to persistent nociceptive signaling. All three key meningeal structures (nerves, vessels, and mast cells) can act as targets for the action of pCBs (phytocannabinoids) or eCBs thus opening the door for selective pharmaceutical treatment.

Conclusion
Modulation of the ECS, particularly in the processing of nociceptive signals in the TGVS, suggests a promising approach to control migraine pain, potentially limiting the undesired side effects of new treatments. However, to confirm this, future experimental research should be conducted.

Keywords
migraine, endocannabinoids, headache, therapy, pain

Leptomeningeal carcinomatosis in a patient with pancreatic neuroendocrine tumor

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Introduction
Leptomeningeal carcinomatosis (LC) is a metastatic infiltration of the cerebrospinal fluid, pia, and arachnoid by tumor cells. It can occur in every tumor type and up to 5% of patients with a solid malignancy will develop LC. The incidence is thought to be increasing.

Case Report
We present a case of a 65-year-old woman who had been diagnosed with gastric adenocarcinoma. The patient underwent Billroth II resection and adjuvant chemotherapy.

Two months later she was admitted to the hospital because of obstructive jaundice and pancreatic neuroendocrine carcinoma with multiple liver metastases was found. Local lymph nodes were also affected, but there were no more distant metastases found.

The patient now presents to the emergency department with aphasia and visual hallucinations that have lasted for several days. Meningeal tests are negative and the neurological exam shows some speech comprehension difficulties and moderate frontal headache with nausea. Laboratory tests show pancytopenia and high C-reactive protein. Native and post-contrast computed tomography scans of the brain show no signs of dissemination or acute ischemic lesions, however, a contrast magnetic resonance imaging (MRI) scan of the brain is ordered. It shows pathological leptomeningeal imbibition bilaterally in cerebellar folia, brainstem, and in the supratentorial region including the inferior frontal gyrus, which confirms that the patient has leptomeningeal carcinomatosis. No intra-axial tumor is shown.

Considering her medical history and current condition, systemic oncological treatment is no longer indicated and the patient is discharged to her own home where she is supposed to receive palliative care.

Discussion/Conclusion
This case is an example of how neurological symptoms such as aphasia and visual hallucinations can be a sign of disseminated malignant disease. When oncologic patients are presented with non-specific neurological symptoms that they never had before, leptomeningeal carcinomatosis should always be considered as one of the possible diagnoses. LC has a high mortality rate and this patient passed away several weeks after being diagnosed.

Keywords
Leptomeningeal Carcinomatosis, Neuroendocrine Tumors, Pancreatic Neoplasms, Aphasia, Hallucinations

Diffuse axonal injury: presentation of traumatic brain injury following polytrauma

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Introduction

Traumatic brain injury (TBI) refers to external trauma inflicted on the brain and, following the Glasgow Coma Scale (GCS), is classified into 3 stages: mild (GCS 13-15), moderate (9-12), and severe (3-8). Neuroimaging methods are used to define the localization and severity of the injury. TBI can be treated surgically or conservatively, depending on the results of radiological and clinical examinations.

Case Report

A 17-year-old female patient was brought to the Emergency Department (ED) after suffering severe injuries in a vehicular collision. Upon admission, she was unconscious with a GCS of 4 (eye-opening 1, verbal response 1, motor response 2). Computerized tomography (CT) scan of the brain and cervical spine showed hematomas in the right basal ganglia, subarachnoid hemorrhage collections in the right temporal and parietal lobes, and diffuse parenchymal edema. The next CT scan, issued after a 6-hour interval, showed significant progression of the hematomas. Because of the progression, the neurosurgery team placed an intraparenchymal probe to measure intracranial pressure (ICP). The patient was hyperventilated and their electrolyte values were closely monitored. ICP values stayed within the normal range (6-14 mmHg), thus the probe was removed after 4 days. The following CT scans showed almost complete resorption of hematomas. A magnetic resonance imaging (MRI) scan was issued 2 weeks after admission, confirming the presence of diffuse axonal injury (DAI). The following week, the patient regained consciousness and was able to spontaneously open their eyes. Later on, they started responding to simple verbal cues (yes/no questions) by nodding or shaking their head. The rehabilitation process plans to be carried out in another institution.

Discussion/Conclusion

With TBI being the leading cause of death in trauma patients, its adequate and apt treatment is crucial to the patient's survival. When choosing a more conservative approach, regular neuroimaging check-ups play a key role in recognizing potentially fatal complications of TBI. They are especially important in cases where raised ICP is not present to indicate progression of bleeding and/or edema and, consequently, deterioration of the patient's state.

Keywords

Cerebral Hemorrhage; Diffuse Axonal Injury; Neuroimaging; Polytrauma; Traumatic Brain Injury

Cervical spine injury after ground-level fall

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Introduction

Ground-level falls are defined as a slip, trip, or fall in which the patient either impacts an object or the floor at the same level at which they are standing. Not to be taken lightly, head injuries, fractured bones, and occasionally lifelong disability can result from these falls.

Case Report

A 65-year-old man was admitted to the emergency room (ER) after a ground-level fall. At the admission, he was conscious, had a Glasgow Coma Scale (GCS) of 15 (eye-opening 4, verbal response 5, motor response 6), and was tachycardic, and hypotensive. Continuous noradrenaline infusion was started immediately. The patient was paraplegic (Medical Research Council (MRC) scale 0/5 on lower limbs) and had paresis of the upper limbs (MRC scale 2/5). Also, there was a loss of sensation from the T4 spinal level downward. Brain computed tomography (CT) showed multiple neurocranium and viscerocranium bone fractures, but there were no signs of intracranial hemorrhage, ischemia, or hydrocephalus. CT of the cervical spine showed no fracture of the vertebrae, but there was a protrusion of the disc osteophyte complexes at the C3/C4 and C5/C6 levels. An urgent magnetic resonance imaging (MRI) revealed compressive edema and significant spinal canal stenosis from the C3 to C6 levels due to protrusion of disc osteophyte complexes. To decompress the spinal canal, discectomy with spondylodesis was performed at the C5/C6 level, and a laminectomy of the C3, C4, and C5 vertebrae. An 8-day follow-up MRI revealed no more spinal canal compression, although it did reveal myelopathy. The patient was awake, had a 1/5 MRC in the upper limbs, and no motor activity could be detected in the lower limbs. Also, reflexes were enhanced, with positive Babinski and Hoffman signs on both sides. However, the patient reported symmetrical sensations throughout the trunk and all limbs, indicating an improvement in sensory function. The treatment has been continued in the Intensive Care Unit (ICU).

Discussion/Conclusion

Since the patient's American Spinal Cord Injury Association (ASIA) grade initially was A (no motor, no sensory, no sacral sparing), the possibility of functional improvement following urgent surgical treatment is between 10% and 15%. In conclusion, even though ground-level falls seem to be relatively harmless, this case demonstrates that they can result in long-term disability.

Keywords:

Accidental Falls, Paraplegia, Paresis, Spinal Injury, Spinal Stenosis

Case presentation: Extreme macrocrania due to severe congenital hydrocephalus

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Introduction

Congenital hydrocephalus is one of the most common central nervous system anomalies manifested by excessive cerebrospinal fluid (CSF) accumulation within the ventricular system of the brain.

Case Report

Our patient is a six-year-old girl who was born as the fifth child from an irregularly controlled, high-risk pregnancy by an emergency cesarean section due to polyhydramnios and idiopathic congenital hydrocephalus with hydranencephaly and raised intracranial pressure (ICP). Shortly after birth, a ventriculoperitoneal (VP) drainage system was successfully implanted. Unfortunately, the patient's head circumference continued to grow and CT and MRI scans showed further progression of hydrocephalus and thinning of the brain tissue.

At the age of 10 weeks and with a head circumference of 67 cm, the infant was transferred to another hospital where a second VP drainage system was implanted and also failed to stabilize the hydrocephalus. Further treatment was complicated by shunt meningitis when both internal drainage systems were removed and external ventricular drainage was installed. Even with continuous external drainage, hydrocephalus could not be controlled and it was estimated that the possibilities of surgical treatment were exhausted.

The patient was transferred to a specialized hospital for chronic childhood diseases for long-term palliative treatment and care. Her hydrocephalus eventually reached an arrested form, albeit at a cost of an extremely large head circumference.

Discussion/Conclusion

This case report shows that despite timely and appropriate therapeutic intervention, the expected treatment outcomes may not be achieved. In that case, it's important to assess "harm to benefit" ratio and adopt a suitable palliative care plan if necessary.

Keywords

cerebrospinal fluid shunt, congenital hydrocephalus, neurosurgery, palliative care, ventriculoperitoneal shunt

Mental health battle in a 10-year-old girl caused by COVID-19 pandemic

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Introduction
It is well known that covid pandemic can cause acute or chronic damage to various organ systems. We have also witnessed its tremendous impact on children's mental health. This case report is about how a 10-year-old girl took up her fight with it.

Case Report
A 10-year-old girl, with proper psychomotor development, had no more severe pain or psychological problems until the onset of the covid pandemic. She is in the fourth grade, an excellent student, and calm, cooperative, and orderly behavior. Six months after the outbreak of the covid pandemic, her mother and brother carried her barefoot to the infirmary. She was afraid to walk and shower because she thought there were ants and bugs on the floor and in the drops of water. She was extremely depressed and agitated. She didn't hang out with children and banned her parents to go out of the house because she was afraid of infection. Everyday life became impossible.

In therapy, an antidepressant (sertraline, first 50, then 100 mg) was prescribed, and intensive psychotherapy (drawing) was given twice a week.

The antidepressant helped to improve mood and had a calming component. Psychotherapy worked through the stressor in a way that was available to her. She explained her drawings, which were dark at first, but later were lighter. By 4 weeks, the girl becomes satisfied.

Discussion/Conclusion
In a pandemic situation, children also suffer and they don't understand what is happening. Adults are busy with the newly created situation, taking care of work and everyday life, often they do not talk to children and children develop fear which is the cause of clinical disorders. Finally, in unusual life situations, it is important to explain the situation to the children in a way they can understand so that they could more easily cope with the new life challenges.

Keywords
Children, pandemic, fear, psychotherapy, antidepressants

Complex post-traumatic stress disorder is a new diagnosis category

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Introduction

Complex post-traumatic stress disorder (CPTSD) is a disorder that includes three symptom clusters of post-traumatic stress disorder (PTSD) (reexperiencing, avoidance, and hyperarousal) and additional three symptom clusters that represent Disturbances in Self- Organization (affective dysregulation, negative self-concept, and disturbances in relationships). In the new edition of the International Classification of Diseases (ICD-11), CPTSD is classified as a new disorder, separated from PTSD.

Case Report

D. M., a forty-nine-year-old patient started getting psychiatric treatment in 2001 because of post-traumatic symptoms. He voluntary joined the army as a minor during the Homeland War (HW) in which he participated until it ended. DM family experienced great losses during The Second World War and, during the HW, several members joined the army. The patient's symptoms started occurring after he got back home from the battlefield. He was included in different kinds of PTSD treatment: day hospital, prolonged group therapy, outpatient treatment, and several hospitalizations with continuous use of the prescribed pharmacotherapy. Over the years of treatment, the patient continuously showed, in addition to basic PTSD symptoms, all the additional symptoms that are linked to CPTSD: a tendency for self-isolation and social withdrawal with difficulties in maintaining close relationships despite his good effort, low frustration tolerance and difficulties in controlling his emotions, severe negative self-perception and strong feeling of guilt. Furthermore, patient developed psychosomatic symptoms, which, with all the above-mentioned symptoms, interfered with the patient's normal functioning in several important life aspects (family, work, and social relationships).

Discussion/Conclusion

Prolonged trauma as well as repeated trauma, particularly during an early age, can have a significant impact on the development of CPTSD. In addition, it is important to describe a characteristic broader spectrum of symptoms of CPTSD in relation to PTSD. The change in diagnosis should certainly be accompanied by changes in the approach to treatment.

Keywords

PTSD; ICD – 11; War-Related Trauma; Psychological Trauma

The correlation between breastfeeding in infancy and mental health problems in adolescence and adulthood

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Introduction

Studies have shown that breastfeeding has numerous benefits for both children and their mothers. Breastfeeding protects the child against infections, reduces the risk of obesity and diabetes, and aids their cognitive development. Furthermore, adults who were breastfed experienced better cardiovascular health, and lower blood pressure and cholesterol than those who were not. Little is known about whether the positive effect of breastfeeding on physical health also extends to mental health. This systematic review aimed to assess the evidence available for the association of breastfeeding in infancy and mental health problems later on.

Materials and Methods

Various papers were analyzed using the PubMed database. A literature search was carried out using the following terms for breastfeeding: breastfeed, breast-feed, breastfed combined with the following keywords: mental health, mental health problems, and mental disorders.

Literature Review

The majority of the reviewed studies suggest that individuals who were breastfed for more than 6 months had a lower risk for both major depression and more severe depressive symptoms in adulthood while the association with anxiety symptoms differed between aforementioned studies. Furthermore, data suggest that breastfeeding for at least 6 months may have a significant protective effect on anxiety and depressive symptoms in early adolescence. Interestingly, one study found gender-specific associations between being breastfed and mental health outcomes since it has been found that breastfeeding contributed to adult psychological well-being in women but not in men.

Discussion/ConclusionOur findings seem to indicate that breastfeeding is inversely associated with mental health problems, especially depression or depressive symptomatology. These findings provide additional reasons to encourage breastfeeding as a beneficial factor for both mental and physical health. Further research should continue to investigate the full extent of the benefits of breastfeeding for mothers and their children and explore ways to support and promote breastfeeding in all communities.

Keywords

anxiety, breastfeeding, depression, education, mental healthWorkshops

Workshops

Traumatic brain injury -a practical approach

Matej Bura, Jan Maroević

Traumatic brain injury is the most common cause of death and disability in young people. Patients with severe traumatic brain injury (TBI) have a significant risk of hypotension, hypoxemia, and brain swelling which are considered secondary brain injuries. If these sequelae are not prevented or treated properly, they can exacerbate brain damage and increase the risk of death. Major improvements in outcomes can be achieved for such patients before they reach the hospital. In our workshop, we will be focusing on the set of skills that are crucial in the management of traumatic brain injury and those are assessing the Glasgow coma scale, securing the airway, and quick interpretation of head CT scan. The workshop will take place on manikins simulating the real scenarios that you may encounter one day in clinical practice.

Self-Care for Future Doctors: A Mental Health Workshop

Tajana Kukolj, Ida Štimac, Josipa Batur

Overthinking, procrastination, anxiety - the holy trinity of every medical student. You study in theory about everything from the books, but in reality, you can't think of anything to help yourself? The workshop is a part of the "Inside Out" project. Repeat with us why it is important to take care of mental health and maintain mental hygiene, learn how to love yourself, and remind yourself of how small daily activities can improve your inner space. Take 90 minutes just for yourself, join us, and learn simple mental health tricks to help yourself on daily basis!

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