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# Abstract book

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11th Student Congress of Neuroscience - Neuri 2022  
Rijeka – Rab – onsite and online  
22 – 24 April 2022

## IMPRESSUM

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# NeuRi

## Student Congress of Neuroscience

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## COMMITTEES

### ORGANIZING COMMITTEE

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## WELCOME NOTE

Dear colleagues,

It is an honor to write these words once more. NeuRi has become a real neuroscientific institution for students, and I can not be more proud of that. 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.

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 2022!

**Josipa Kajić**  
**President of NeuRi 2022**  
**Rijeka, 22 April 2022**

## PROGRAM – NeuRi 2022

### Friday, 22 April 2022 – Faculty of Medicine Rijeka and online

13:00 – 14:30	Registrations
14:30 – 15:00	Opening ceremony
15:00 – 15:15	Group photo
15:15 – 16:15	Plenary lecture <b>Vladimir Trkulja:</b> Medical marihuana use in neurological diseases
16:15 – 16:30	Coffee break
16:30 – 17:30	Plenary lecture <b>Dražen Domijan:</b> Neural foundations of numerical competences
17:30 – 18:30	Dinner
18:30	Beer pong and Quiz night

### Saturday, 23 April 2022 – Rab and online

06:30	Drive to Rab
11:00 – 12:00	Plenary lecture <b>Vesna Šendula-Jengi:</b> COVID-19 and mental health: a multifaceted connection
12:00 – 12:15	Coffee Break
12:15 – 13:30	<b>Student session I</b> <ol style="list-style-type: none"><li>1. Mirna Jozinović: Mental health of students in the COVID-19 pandemic</li><li>2. Paola Danjek, Nikolina Runje, Lidija Iličić: Physicians' attitudes, knowledge and some misconceptions regarding the use of augmentative and alternative communication with patients with complex communication needs: a pilot survey</li><li>3. Andrea Racetin, Nika Ribarić, Jelena Sušac: Acute post-COVID-19 psychosis following corticosteroid administration: a case report</li><li>4. Nika Ribarić, Andrea Racetin, Jelena Sušac: Case report of the LSD induced psychosis in 21-year-old</li><li>5. Sara Huskić, Sergej Nadalin, Vjekoslav Peitl, Dalibor Karlović, Lena Zatković, Alena Buretić-Tomljanović: Clinical and metabolic implications of disease onset among unmedicated patients with schizophrenia</li></ol>

6. Vesna Zarezovski, Filip Kolenković: Alcohol Consumption in COVID-19 pandemic

7. Anton Malbašić, Vinko Michael Dodig, Robert Martinez, Dora Cesarec, Robert Marčec: Benzodiazepine Utilisation in Croatia - Time to Sound the Alarm?

8. Nikoleta Marlais, Denis Mulabdić, Aleksandar Savić, Jelena Sušac: Hikikomori syndrome – severe social withdrawal or prodromal psychosis?

9. Petar Žauhar, Tea Škoda, Sandra Knežević, Roberta Žauhar Bačić: Postpartum Psychosis Following an Urgent C-section

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

### Sunday, 24 April 2022 – Faculty of Medicine Rijeka and online

8:45 – 09:00	<b>Breakfast</b>
09:00 – 10:15	<b>Student session II</b> <ol style="list-style-type: none"><li>1. Mihovil Joja, Jan Homolak, Melita Šalković-Petrišić: Intestinal redox parameters in the Alzheimer's disease rats receiving oral d-galactose</li><li>2. Maja Juković, Beti Zaharija, Bobana Samardžija, Nicholas J. Bradshaw: TRIOBP-1 co-aggregates with DISC1, a major protein implicated in chronic mental illnesses</li><li>3. Ana Sorić, Maja Živković: Pharmacogenetic approach in the treatment of depression and breast cancer</li><li>4. Tin Jagoić, Vedrana Krušić Alić, Siniša Zrna, Maša Biberić, Lara Valenčić, Kristina Grabušić: Dynamics of antioxidative enzymes in cerebrospinal fluid of patients with severe traumatic brain injury - a pilot study of potential biomarkers for neuro-recovery</li><li>5. Nermina Kamarić, Mario Stojanović, Borna Puljko, Anja Bukovac, Kristina Mlinac Jerković, Nives Pećina-Šlaus, Svjetlana Kalanj Bognar: Tracing neuroplastin in glioblastoma</li><li>6. Marija Piknjač: Association of cognitive ability with glutamate and insulin signaling in a rat model of Parkinson's disease</li></ol>
10:15 – 10:30	Coffee break

10:30 – 11:45	<b>Student session III</b> 1. Tamanna Agarwal: Neuro-oncological Symptoms Worsening Post COVID-19 Vaccine 2. Martin Angjelov, Mihail Petrov, Nikolay Velinov, Nikolay		
Gabrovsky:	Surgical evacuation of bilateral frontal abscesses followed by 3D-printed PEEK cranioplasty: A case report 3. Kristina Štajminger, Arian Širac, Domagoj Dlake: Neurofibromatosis Type 1: a case report 4. Saaz Sahani: Recurrent hemorrhage: an atypical presentation of cerebral cavernous malformations in an adolescent 5. Antonela Geber, Vesna Galjuf, Maksimilijan Mrak, Vladimir Kalousek: A case report of visual field defect due to unruptured internal carotid artery aneurysm 6. Antea Kršek, Lara Batičić: Long term medical and physiotherapy approach to the treatment of Spina bifida 7. Ana Prica, Nenad Koruga: Recurrent medulloblastoma in an adult patient – a case report	report	2. Sara Smeraldo, Zanë Demiri, Arijan Verbić: Respiratory syncytial virus encephalitis in children – case report 3. Dora Cesarec, Anton Malbašić, Vinka Potočki, Sandro Gašpar: Comparison of Nervous System Agents Utilisation in Croatia in Prepandemic 2019 and Pandemic 2020 4. Lea Čorluka, Zvonimir Popović: Atypical neurodegenerative disease presentation with corticobasal degeneration – a case
11:45 – 12:00	Coffee break	with	5. Mia Grgić, Marija Ratković, Marinko Dikanović: Relapsing-remitting multiple sclerosis and response to glatiramer acetate therapy 6. Matej Lovrić, Sijana Demirović: OSA in a 14-year old patient
12:00 – 13:00	<b>Student session IV</b> 1. Lucia Bekić, Mirella Graffel: Vascular dementia and/or depression in hypertensive and obese patient with psychic deterioration 2. Lea Kalajžić, Valentino Rački, Vladimira Vuletić: Patient with YY1-related dystonia treated with deep brain stimulation: a case report 3. Lucija Karaman, Leonardo Hršak, David Bonifačić: Neurological symptoms and complications associated with COVID-19: Case report 4. Marija Magdalena Šamal: Effect of non-invasive neurostimulation on some aspects of executive function 5. Arian Širac, Kristina Štajminger, Mirna Karakaš: Third cranial nerve palsy in a COVID-19 patient	spectrum	growth hormone deficiency and enuresis – a case report 7. Robert Martinez, Ivan Martinez, Leona Blaži, Kristijan Kaniški, Robert Marčec: Double seronegative neuromyelitis optica disorder in a 35-year-old female 8. Klara Radović, Gloria Rožmarić, Valentino Rački, Vladimira
		Vuletić:	Exacerbations of advanced Parkinson's disease after COVID-19 infection in patients treated with invasive therapies – case report 9. Gloria Rožmarić, Klara Radović, Valentino Rački, Vladimira Vuletić: Functional neurological disorder in Parkinson's disease treated with deep brain stimulation: a case report 10. Tea Škoda, Petar Žauhar, Jelena Radić Nišević: Migrainous stroke; a myth or a reality? – case report 11. Klara Vranešević, Jelena Radić Nišević: Neuronal ceroid lipofuscinosis type 2; treatment of an incurable disease- case
13:00 – 13:15	Coffee break	report	12. Petar Žauhar, Sandra Knežević, Zoran Rumboldt: Trigeminal neuralgia associated with solitary pontine/brainstem lesion (SPL-TN) - Case report
13:15 – 14:15	Plenary lecture <b>Dubravka Švob Štrac:</b> Neurosteroids and their therapeutic potential in brain disorders	16:15 – 18:15	Workshops I. <b>Bioinformatic transcriptome analysis</b> (Andrea Gelemanović) II. <b>Stress – how it affects our brain and body and how can we deal with it</b> (Tina Bregant)
14:15 – 15:15	Lunch	18:15 – 18:30	Closing and award ceremony
15:15 – 16:15	<b>Student session V</b> 1. Zanë Demiri, Sara Smeraldo, Jelena Radić Nišević: Niemann-Pick disease type C- progressive neurological deterioration in a 10-year-old girl – Case report		



# Plenary lectures



# Medical marihuana use in neurological diseases

## Vladimir Trkulja

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The use of cannabinoid decoctions in human medicine has a thousand-year history - from simple phytocannabinoid preparations observed in ancient China and Indian folk medicine - to semi-synthetic and synthetic compounds that have been intensively researched for several decades (mostly in the 1980s - 2000s) in academic institutions and the pharmaceutical industry. Contrary to the claims of the activist lay public, the endogenous cannabinoid system and the possibilities of its pharmacological modulation for the purpose of treating or preventing disease have been investigated in considerable detail. Most efforts have focused on central nervous system function/disorders - and this is the main topic of this brief review: molecular foundations (or biological rationale) and medical clinical experience with the use of certain cannabinoid preparations in the treatment of neurological conditions/disorders. Most of the experience is related to pain - problems, attempts of application in neurodegenerative diseases (multiple sclerosis, Parkinson's disease, Huntington's disease), and epilepsy. The current state of evidence that would suggest that pharmacological (or "phytopharmacological") intervention in the cannabinoid system could significantly improve the treatment of any of these conditions is scarce or non-existent, and there are clear indications that previous attempts have failed. But no one can rule out the possibility that the situation will change significantly in the (near) future.

# Neural foundations of numerical competences

## Dražen Domijan

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In a modern, technologically advanced society, numerical competences are of great importance to an individual's wellbeing. This talk will review recent data on three distinct cognitive and neural systems that support our ability to understand and manipulate natural numbers and to perform single-digit mental arithmetic. The first system relies on the symbolic representation of exact numbers, and it is specific to adult humans. This system is assumed to be located in the left angular gyrus. It contains a verbal store used to comprehend and produce spoken number names and is also a repository for learned arithmetical facts and tables. Another system, also known as a number sense, is present in preverbal infants and in other animal species. It enables representation of approximate number magnitudes such as a number of objects in a visual scene. Number sense is supported by two mechanisms: neural integrators and spatial representation known as a mental number line. Functional neuroimaging points to the involvement of the horizontal segment of the intraparietal sulcus in all tasks that require some form of numerical processing. In addition, single-unit recordings revealed the existence of neurons tuned to specific numerosities in frontal and parietal cortices. The third system enables fast and accurate enumeration or subitization of small sets of objects. This system is closely related to attention and working memory because it depends on visual indexing or object individuation. Functional neuroimaging suggests that the temporo-parietal junction plays an important role in subitization. At the end of the talk, I will examine recent studies on the possible interactions between three number processing systems. To conclude, neuroscientific studies revealed a complex network of cortical areas that support the representation of numbers. Further studies are needed to elucidate whether and how these networks cooperate and integrate their outputs during online numerical processing. Such findings may inform design of future intervention programs aimed to help children who struggle with math and who suffer from math anxiety.

# COVID-19 and mental health: a multifaceted connection

## **Vesna Šendula-Jengić**

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Since the first registered case on November 17, 2019, Covid-19 has spread worldwide like wildfire, and although it has been two and a half years since the outbreak, the pandemic hasn't ceased yet. The current statistics report almost half a billion Coronavirus cases, but the impact of the disease actually goes beyond that number. Covid-19 presents itself with a wide variety of symptoms – neurological, respiratory, psychiatric, digestive, dermatological, and to all those, we can add the impact it has had on the population in general, even on those who haven't contracted the disease. Namely, there has been a major impact of this pandemic on the mental health of the population worldwide. World Health Organization reports a tremendous 25% increase in the global prevalence of anxiety and depression in the first year of the pandemic. At the same time, there are some sources that report a beneficial effect of Covid-19 on mental health. The relationship between Covid-19 and mental health is multifaceted and intricate, and in many aspects still not clear. This paper will report the current findings regarding the impact of Covid-19 on mental health and discuss some still unanswered issues. Particular emphasis will be placed on specific examples and the clinical experience in County Hospital Insula.

# Neurosteroids and their therapeutic potential in brain disorders

## **Dubravka Švob Štrac**

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Neurosteroids are neuroactive steroids synthesized within the brain from cholesterol, which are converted first into pregnenolone and then into other endogenous steroids. Their synthesis occurs both in glia and neurons in many brain regions, including the hippocampus and neocortex. A variety of neurosteroids are present in the brain, including pregnane, androstane, and sulfated neurosteroids. Their actions are generally not mediated via classic steroid hormone receptors but through other mechanisms, such as neuronal membrane neurotransmitter receptors and ion channels. Neurosteroids are endogenous regulators of neuronal excitability and affect many biological functions including modulation of neural plasticity, learning and memory processes, emotions, behavior, and seizure susceptibility, as well as responses to stress, anxiety, and depression. Therefore, they provide tremendous opportunities as novel therapeutic approaches to various brain disorders, such as epilepsy, anxiety, depression, and Alzheimer's disease. Currently, there is a high level of interest in neurosteroid therapeutics and several clinical trials are in progress for different neuropsychiatric disorders. In addition to natural neurosteroids and drugs enhancing neurosteroid synthesis, several synthetic analogs have shown potential for therapeutic use, since they demonstrate many advantages, such as improved bioavailability and efficacy, acceptable pharmacokinetics with longer half-life, and lack of active metabolites that can cause reproductive side effects. This talk will provide an overview of neurosteroids, their impact on the brain, as well as their therapeutic potential for various brain disorders. Moreover, some results of our own research regarding the neuroprotective actions of neurosteroids in brain injury and dementia will be presented.



# Symposia

# The mental health of students in the COVID – 19 pandemic

**Mirna Jozinović**

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The change in everyday life caused by the outbreak of Coronavirus 19 has significant negative consequences for individuals' mental (psychological) health. The growing threat to the mental health of children and young people is particularly emphasized and investigated. Therefore, the main goal of this review is the general insight and impact of coronavirus on students' mental health to develop a school prevention program to develop an awareness of the importance of caring for and maintaining mental health. For the review, the parameters of questionnaires and tests were used to test the level of anxiety and depression. Databases of complete texts and data from the field of biomedicine and health and social sciences were searched. Early recognition and early behavioral interventions, due to the perceived many threats to students' mental health and understanding of how teachers and schools are expected to provide answers from different perspectives, educate them on recognizing first symptoms. The first step is to investigate the current state of mental health of students in schools to organize preventive activities.

Keywords: Educational Early Intervention; Mental Health; SARS-CoV-2; Students

# Physicians' attitudes, knowledge and misconceptions on augmentative and alternative communication

**Paola Danjek, mag. logoped. <sup>1,2</sup>, Nikolina Runje, mag. logoped. <sup>2</sup>, Lidija Iličić, mag. rehab. educ. <sup>3,2</sup>**

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Augmentative and alternative communication (AAC) supplements or compensates for speech and language impairments. A variety of tools and techniques, such as manual signs, picture communication boards, letter boards, and speech-generating devices, are used to support the communication of individuals with complex communication needs (CCN). Speech-language pathologists (SLPs) and special education need teachers (SEN teachers) are trained for recognizing individuals with CCN and for implementing AAC. Complex communication needs can be a result of developmental disabilities, such as autism spectrum disorder, cerebral palsy, and intellectual disability, as well as acquired impairments after a cerebrovascular incident, traumatic brain injury, or neurodegenerative diseases. This study aimed to reveal Croatian physicians' attitudes regarding the use of AAC with patients with CCN, to find out how much physicians know about AAC, and to detect if physicians have some misconceptions about AAC and individuals with CCN. The study was conducted in March 2022 on a sample of 49 examinees with different medical specialties working in various parts of Croatia. The required data and information were collected using a self-constructed questionnaire designed specifically for this study. The collected data were analyzed using quantitative and qualitative methodology. The preliminary results have revealed that even though Croatian physicians display some amount of agreement with some misconceptions they generally report positive attitudes towards AAC. Pearson's correlation test has shown a statistically significant correlation between attitudes and misconceptions ( $r=-0,364$ ,  $p=0,01$ ). Physicians with more positive attitudes report less agreement with misconceptions. Previous research has shown that using AAC in clinical settings significantly mitigates communication obstacles for patients with CCN, increases the patient's safety, and lowers hospital costs and risks of medical errors. Future research should investigate the reasons behind persisting misconceptions and negative attitudes in order to successfully implement positive AAC practices with patients with CCN.

Keywords: Communication; Neurological Rehabilitation; Physicians

# Acute post-COVID-19 psychosis following corticosteroid administration: a case report

**Andrea Racetin<sup>1</sup>, Nika Ribarić<sup>1</sup>, Jelena Sušac<sup>1,2</sup>**

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Glucocorticoids are widely used in the treatment of endocrine as well as non-endocrine disorders. Unfortunately, these agents are connected with numerous side effects, impacting various organ systems, including severe neuropsychiatric consequences like psychosis, mania, depression, disorientation, or suicide attempt. Due to the COVID-19 (Coronavirus Disease 2019) pandemic, the use of glucocorticoids is increased. Therefore, clinicians should be aware of neuropsychiatric symptoms and perform a detailed history and physical examination on all patients presenting with psychiatric symptoms in the context of COVID-19. A 39-year-old woman with hypothyroidism and postpartum depression in her past psychiatric history was admitted to the psychiatric hospital for treatment of an acute psychotic episode. Previously, she was hospitalized and treated at University Hospital for Infectious Diseases „Dr.Fran Mihaljević“ due to SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) pneumonia. The patient did not indicate any psychiatric symptoms during the initial admission. After the discharge home, she struggled with anxiety and insomnia. Also, she was re-admitted five days later, presenting with acute psychosis following intravenous dexamethasone administration for nine days. The patient presented with psychomotor agitation, delusions, and suicide threats. The treatment was continued with olanzapine, diazepam, and psychotherapy with significant improvement. Acute psychosis after COVID-19 is a new and emerging diagnosis with no consensus on management strategy. Clinicians should be careful with corticosteroid administration, especially in patients with past psychiatric history. This case highlights the importance of follow-up in patients with a predisposition to neuropsychiatric side effects because they typically develop within 1 or 2 weeks after starting high-dose corticosteroid treatment.

Keywords: Acute Psychosis; Corticosteroid; COVID-19

# Case report of the LSD induced psychosis in 21-year-old

**Nika Ribarić<sup>1</sup>, Andrea Racetin<sup>1</sup>, Jelena Sušac<sup>1,2</sup> MD**

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Overdosing with LSD (lysergic acid diethylamide) is generally very rare. Even though LSD usage was mostly widespread in the 1970s the interest in this substance had a recent uprising. Nowadays, there is a great interest in the therapeutic potential of micro-dosing of LSD and other psychedelics. Some studies have shown the possible therapeutic potential of LSD in the management of alcoholism, depression, anxiety, and PTSD (posttraumatic stress disorder). However, this case presents an LSD-induced schizophreniform reaction. A 21-year-old male patient was brought by ambulance. He had previously been hospitalized for a head contusion in the neurosurgery department. A head contusion occurred in a car accident. Afterward, due to decompensation of the mental state in the form of acute psychotic behavior, the patient was hospitalized in the psychiatry department. The patient was conscious however disoriented in space and time. Both behavior and mood could be described as dysphoric. Psychomotor agitation was present. A conversation was established with the encouragement of the examiner. The patient was not aggressive or suicidal, but he had auditory hallucinations for the time being in hospitalization. In a later conversation, the patient admits to consuming LSD and recalls the exact dates of the consumption. The patient admitted that he wanted to expand his awareness to be even more efficient at work. It is suspected that the LSD consumption provoked the development of schizophrenic psychosis. On the other hand, affective distance as well as social retraction, speak in favor of endogenous psychosis. After the patient's discharge from the hospital, it is advisable to continue treatment for which the patient is motivated. Sometimes it is hard to distinguish between already existing but undiagnosed schizophrenia and drug-induced psychosis. If the symptoms precede drug usage, then psychotic episodes are not considered to be induced by drugs. It is important to emphasize that psychotic drug-induced episodes can only be triggered in people that already have an underlying condition.

Keywords: Drug overdose; Lysergic Acid Diethylamide; Substance-Induced Psychoses

# Clinical and metabolic implications of disease onset among unmedicated patients with schizophrenia

**Sara Huskić<sup>1</sup>, Sergej Nadalin<sup>2</sup>, Vjekoslav Peitl<sup>3,4</sup>, Dalibor Karlović<sup>3,4</sup>, Lena Zatković<sup>5</sup>, Alena Buretić-Tomljanović<sup>6</sup>**

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Patients with early onset of schizophrenia ( $\leq 18$  years) reportedly manifest greater cognitive impairment and increased negative symptom severity compared to those with adult-onset ( $> 18$  years). Antipsychotic medications are the main class of medication to treat schizophrenia patients and many of them have been causatively linked to iatrogenic negative symptoms, cognitive impairment, and metabolic disturbances, such as weight gain, lipid disturbance, and glucose dysregulation. To elucidate the potential associations between the onset of schizophrenia (early vs. adult), clinical psychopathology, and metabolic parameters, among unmedicated schizophrenia patients, may be of clinical relevance when prescribing antipsychotic medications. We investigated whether and to what extent the onset of schizophrenia might contribute to Positive and Negative Syndrome Scale (PANSS) scores, body mass index values, and plasma lipid and glucose concentrations among two groups of unmedicated patients from the Croatian population: antipsychotic-naïve first-episode patients ( $N = 64$ ) and nonadherent chronic patients ( $N = 107$ ). Age of onset was defined as the patient's age at their first hospital admission due to a psychotic episode, at which the diagnosis of schizophrenia was first used. PANSS data were recorded during a psychotic state of the illness requiring hospitalization. Plasma total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, and glucose levels were determined after a 12-hour fasting period. The onset of schizophrenia was significantly associated with negative factor scores only. Specifically, patients with early onset of schizophrenia manifested higher negative factor scores compared to those with adult-onset ( $P < 0.01$ ). After adjustment for the possible effect of gender, age, illness duration, and number of psychotic episodes, the onset of schizophrenia accounted for ~8% of the variability of the negative factor. Our present results suggest that medications that are more effective for negative symptoms should be considered when prescribing antipsychotic medications to unmedicated patients with early onset of schizophrenia.

Keywords: Age of Onset; Antipsychotic Agents; Schizophrenia

# Alcohol consumption in COVID-19 pandemic

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The harmful use of alcohol is determined not only by the volume but also by the frequency of drinking. The volume of alcohol consumption and the pattern of drinking affect both health and social outcomes. According to the Standardized European Alcohol Research (RAR-HA-SEAS) prevalence of excessive episodic drinking in Croatia, at least once a month in the last 12 months, was 11% and was the highest in the age group 18-34 years (17%). Beginning in March 2020, in an attempt to contain the spread of the novel coronavirus, local governments throughout the World initiated orders for individuals to stay at home and shelter in place. Added to the financial uncertainty posed by job loss and expiring unemployment benefits, many people have also experienced the emotional strains of prolonged social isolation, loneliness, depression, and even suicidal ideation as stay-at-home restrictions were extended or re-initiated to curb surging infection rates. The COVID-19 pandemic has brought major challenges to healthcare systems and public health policies globally, as it requires novel treatment and prevention strategies to adapt to the impact of the pandemic. The pandemic has resulted in changes in patterns of drinking, an increase in alcohol withdrawal, disruption in access to care, and an increase in illicit alcohol availability.

Keywords: Alcoholism; COVID-19; Pandemic



# Benzodiazepine Utilisation in Croatia - Time to Sound the Alarm

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For the past ten years, nervous system drugs (N category) have been among the top 3 Anatomical Therapeutic Chemical (ATC) categories used in Croatia, both in terms of financial consumption and utilization. Most of the utilization in the N drug category is due to the high usage of benzodiazepines (N05BA and subcategories), with diazepam being ranked 6th among drugs with the highest utilization in 2020. The continuous increase in benzodiazepine utilization, taken in the context of their addictive potential, could lead to a public health crisis in the near future. Therefore, we aim to explore current trends in the utilization of benzodiazepines and forecast future ones, with the goals of raising awareness of this growing problem and the need for immediate action. Data was collected from annual drug utilization reports published by the Croatian Agency for Medical Products and Medical Devices regarding the utilization (defined daily dosage, DDD/1000 pop./day) of benzodiazepines (N05BA and subcategories) from 2010 to 2020. An autoregressive integrated moving average (ARIMA) model was used to forecast utilization from 2021 to 2032, based on retrieved utilization data. Benzodiazepine utilization in Croatia is increasing continuously from 2010 to 2020, with an average yearly increase of 2.42%. According to the results of the ARIMA model, in 2032 the utilization is forecasted to reach 102,08 [95,19; 108,97] DDD/1000 pop./day. From 2010 to 2020, looking at the utilization of individual benzodiazepines, the utilization of alprazolam and diazepam are continuously increasing and seem to drive the increasing utilization of this drug group, while the utilization of other drugs is stagnant or decreasing. If no measures are taken, benzodiazepine utilization in Croatia will most likely continue to increase and in 2032 may be greater than 100 DDD/1000 pop./day. Public health measures should be taken to avoid such a scenario.

Keywords: Benzodiazepines; Drug Utilization; Public Health

# Hikikomori syndrome – severe social withdrawal or prodromal psychosis?

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Hikikomori is a Japanese term defining an extreme form of socio-spatial isolation lasting 6 months or longer with the apparent absence of other mental health problems. The condition predominantly manifests in young males transitioning into adulthood, with etiology believed to be linked with traumatic childhood experiences, introverted personality types, and avoidant attachment styles. Individuals typically self-isolate in their parents homes with a heterogeneous symptomatology that includes anxiety, mistrust, depressive mood, and loss of drive. A cardinal feature of hikikomori is escapism through excessive internet use and video game addictions to relieve dysphoric moods. Notably, there is a significant overlap between hikikomori symptoms with those of prodromal psychosis, making an isolated definitive diagnosis difficult. A 23-year-old patient presented with social withdrawal and a video game addiction lasting several years. His compulsion led to him quit his job to facilitate more time for gaming. On examination, he was anxious with a depressive mood, and without any noticeable signs of psychosis. His avoidant personality traits led him to find an escape from stressors in excessive gaming and consequent self-isolation. At 25, he was hospitalized after developing auditory hallucinations directing him to harm himself and others. He was diagnosed with F23.2—acute schizophrenia-like psychotic disorder. Contemporary understanding reveals symptomatic similarities between hikikomori and different psychiatric illnesses, leading to uncertainties as to whether it is a primary or secondary disorder. A secondary clinical picture typically manifests with social isolation coupled with other psychiatric conditions such as prodromal psychosis, negative symptoms of schizophrenia, and Internet addiction.

Keywords: Internet Addiction; Psychotic Disorders; Social Anxiety Disorder

# Postpartum Psychosis Following an Urgent C-section

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Postpartum psychosis is a rare but serious mental disorder affecting 0.1% of new mothers. Typically develops with a sudden onset in the first two weeks after delivery. Symptoms often include loss of inhibition, depression, paranoia, hallucinations, delusions, and in severe cases suicidal ideas and even thoughts of infanticide. Case report: 37-year-old primigravida, with a history of migraines, was admitted to the Clinic of Obstetrics and Gynaecology, Clinical Hospital Centre Rijeka during 39th week of gestation because she developed signs of mild preeclampsia. Due to favorable obstetrical findings and satisfactory foetal condition, the labor was induced with prostaglandin gel and the patient was transferred to the delivery room where epidural analgesia was administered. Due to persistent high blood pressure and cardiotocography signs of foetal distress, it was decided to undertake an urgent cesarean section. The operation was successful and a healthy female child was born, APGAR score 10/10. Two days later the patient started complaining that the medical staff was whispering about her calling her crazy, and a drunk. Psychiatric assessment found the patient feeling exhausted and worried about the impression she was leaving on the staff; active contact was periodically being lost and there were signs of intrapsychic conflict. Due to repeated difficulties, the patient was transferred to the Psychiatric Clinic where she received quetiapine and alprazolam therapy for postpartum psychosis, and reaction to severe stress and adjustment disorder. Patient's parents and partner were both contacted and, with all parties agreeing to provide sufficient care and assistance, the patient was released the next day. Patient was scheduled for further psychiatric evaluation. Conclusion: Postpartum psychosis has to be differentiated from, much more common, "baby blues" or postpartum depression for the danger it poses to the mother and child. Patient has to be evaluated for potential underlying conditions, such as bipolar disorder, and has to be deemed safe for potential auto and hetero-aggressive behavior.

Keywords: Antipsychotic Agents; Emergency Psychiatric Services; Female, Postpartum Period; Psychotic Disorder

# Intestinal redox parameters in the Alzheimer's disease rats receiving oral d-galactose

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Intracerebroventricular administration of streptozotocin (STZ-icv) to rats causes cognitive deficits with accompanying pathological changes reminiscent of those found in sporadic Alzheimer's disease. Interestingly, unlike chronic parenteral administration of D-galactose which is found to accelerate cognitive decline in aging rodents by increasing oxidative stress, chronic oral administration of D-galactose prevents cognitive impairment in STZ-icv rats. Aim To assess the effects of oral D-galactose on redox parameters along the intestinal tract in control and STZ-icv rats. Methods Three-month-old male Wistar rats (N=40) were split into two groups treated bilaterally by intracerebroventricular injection of either streptozotocin (STZ, 3 mg/kg) or vehicle (CTR- control). Animals were further assigned into a group receiving daily oral galactose solution (200 mg/kg) or vehicle (tap water). After two months, rats were euthanized and the proximal duodenum, distal ileum, and distal colon (N = 20) were dissected and stored at -80°C. Lipid peroxidation was assessed by thiobarbituric acid reactive substances (TBARS), catalase activity was assessed indirectly by quantification of the carbonato-cobaltate (III) complex, low molecular weight thiols (LMWT), and total protein sulfhydryls (SH) were measured with 5,5'-dithio-bis(2-nitrobenzoate). Total antioxidant capacity was evaluated by nitrocellulose redox permanganometry (NRP) and ABTS(2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) assay. Results In the duodenum, LMWT, and SH were decreased in groups receiving galactose, and catalase was decreased in STZ-icv animals. In the ileum, the only noticeable change was a decrease in TBARS in the galactose-treated STZ-icv group compared to the non-treated STZ-icv rats. In the colon, D-galactose treatment reduced catalase and TBARS, while NRP and SH were decreased only in the galactose-treated STZ-icv group compared to non-treated STZ-icv rats. Conclusion The effect of oral D-galactose administration on redox parameters differs between parts of the intestine, with a slight shift in the colon and no prominent effect on the small intestine. The intestines of the STZ-icv rats seem to respond differently to oral D-galactose.

Keywords: Alzheimer's Disease; Galactose; Intestine; Redox; Streptozotocin



# Pharmacogenetic approach in the treatment of depression and breast cancer

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Depression is a significant and prevalent comorbidity in breast cancer patients especially affecting the course of the disease and patient's quality of life. The literature describes very few studies looking at the efficacy of antidepressant medications in this population despite the impact of depression in patients with breast cancer. The purpose of this case study is to emphasize the importance of pharmacogenetics as a useful tool in selecting the appropriate drug and successfully treating both diseases. In this paper, a case study of a 57-year-old woman diagnosed with breast cancer during 2017 is shown. She was treated by surgery, irradiation, and tamoxifen as prophylaxis. In 2018 she developed a major depressive disorder characterized by decreased mood, lethargy, and anhedonia followed by cognitive impairment and social dysfunction as well. Antidepressant treatment was started with escitalopram but was discontinued because of adverse drug reactions like nausea and diarrhea. The next treatment choice was sertraline, but because of the same reason, it was also stopped. Antidepressants and tamoxifen are metabolized by cytochrome isoenzyme CYP2D6 in the way that tamoxifen is a substrate and the two mentioned SSRI drugs are inhibitors of CYP2D6. So, pharmacogenetic analysis was performed. It turned out that she was an intermediate metabolizer of the enzyme CYP2C19 and the substrate's concentration at the beginning of the treatment was higher than normal. According to the recommendations, the next treatment option was medication from another antidepressant group: serotonin and norepinephrine reuptake inhibitors (SNRI)- venlafaxine, a weak inhibitor of CYP2D6 which doesn't influence tamoxifen's metabolism. In conclusion, symptomatic and functional remission of depression occurred with venlafaxine and at the same time, there was no increased risk of malignant disease relapse in which the contribution of the knowledge about pharmacogenetic factors was crucial. In long term, pharmacogenetic analysis, implemented in daily clinical practice, could help in the treatment of breast cancer comorbidities such as depression.

Keywords: Breast Cancer; Depression; Drug Interactions; Pharmacogenetics

# Dynamics of antioxidative enzymes in cerebrospinal fluid of patients with severe traumatic brain injury - a pilot study of potential biomarkers for neuro-recovery

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Severe traumatic brain injury (TBI) is intracranial damage triggered by physical impact and continued by resulting in detrimental processes like excitotoxicity, inflammation, and oxidative stress. Currently, only supportive care is available for patients with TBI because there are no specific approaches approach to treatment or biomarkers that would indicate the degree of brain damage is still lacking. Putative biomarker candidates are antioxidative enzymes that which play a key role in eliminating oxidative stress molecules to stop further fulminant cell damage. To characterize cerebrospinal fluid (CSF) levels of 5 antioxidant enzymes during the acute phase of recovery in severe TBI patients. Patients and methods Adult TBI patients were enrolled if their treatment required ventriculostomy and a family member provided informed consent. The cerebrospinal fluid was collected in 24-hour intervals and analyzed by western blot analyses followed by Ponceau staining and immunodetection for superoxide dismutase 1 (SOD1), peroxiredoxin-2 (PRDX-2), PRDX-6, deglycase 7 associated with parkinsonism (PARK7) and catalase. The study included 9 patients aged 19 to 83 years, 2 were females. Ventriculostomy was applied up to 10 days after an injury resulting in a collection of 66 CSF samples in total. We detected high levels of SOD1, PARK7, catalase, and PRDX-2 and -6 in at least one CSF per patient. PARK7 and catalase were detected in the majority of the CSFs. SOD1, PRDX-2, and -6 showed diverse dynamics whereby the first several consecutive days were often positive. Discussion Our pilot study shows that SOD1, PARK7, catalase, and PRDX-2 and -6 are present at various levels in CSF during the first 10 days after TBI. Further research with a larger number of patients and a more detailed characterization including quantification of enzyme levels in CSF could reveal biomarker potential of antioxidative processes.

Keywords: Biomarkers; Cerebrospinal Fluid; Oxidative Stress; Traumatic Brain Injury

# Tracing neuroplastin in glioblastoma

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Astrocytomas are the most common type of brain tumors. Glioblastoma, also known as grade IV astrocytoma, accounts for the most frequent malignant brain tumors which are known to develop rapidly and invade neighboring brain tissue. The poor 5-year survival rate of patients marks glioblastoma as an almost invariably fatal disease. Still, due to its heterogeneity, the etiology of glioblastoma remains unknown. With its high resistance to a variety of therapies, there is an urgent need for new molecular targets which would be used in precise treatments. It is known that one of the mechanisms of glioblastoma invasion is cell-cell interactions. One of the most prominent cell adhesion glycoproteins in brain tissue is neuroplastin (Np) which is involved in synaptic plasticity, but also related to the regulation of calcium homeostasis as an auxiliary subunit of plasma membrane Ca<sup>2+</sup>-ATPase (PMCA). Neuroplastin was also found to promote tumor invasion in metastatic breast tumors. In this work, we used Western blotting in order to investigate the expression of neuroplastin and PMCA4 in different types of astrocytoma, with emphasis on glioblastoma samples. The results were compared with those from healthy brain tissue. Our preliminary results of astrocytoma tissue and control tissue (n=29 and 5) showed that neuroplastin signal intensity is greatly decreased in tumors ( $p < 2.3 \times 10^{-9}$ ). PMCA4 signal intensity correlated with low neuroplastin signal ( $p < 0.01$ ). Interestingly, in calcified tumor tissue, we observed no neuroplastin signal but PMCA4 signal intensity ranged from no signal ( $p < 0.0001$ ) to greater than in control tissue ( $p < 0.0002$ ). This certain heterogeneity concerning PMCA4 is probably due to calcification process progression. Our results suggest that the Np-PMCA4 axis of calcium homeostasis maintenance is severely disturbed in astrocytoma tumors, especially glioblastoma, and could be a new target for therapy.

Keywords: Astrocytoma; Glioblastoma; Neuroplastin; PMCA4

# Association of cognitive ability with glutamate and insulin signaling in a rat

## model of Parkinson's disease

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Parkinson's disease, in addition to being considered a motoric disorder, can be manifested by the appearance of a cognitive deficit. Glutamate and insulin signaling dysfunction is involved in the development of cognitive deficit in Alzheimer's disease. One of the main goals of this thesis was to investigate cognition in a rat model of Parkinson's disease as well as its association with brain glutamate and insulin signaling, induced by bilateral intrastriatal injection of 6-hydroxydopamine, which is a toxin used for the selective depletion of dopaminergic neurons. Three months after 6-hydroxydopamine treatment, animals were subjected to motoric and cognitive tests such as RotaRod, Passive avoidance, and Morris Water Maze, and then sacrificed. Expression of tyrosine hydroxylase and proteins involved in insulin and glutamate signaling were assessed in the hippocampus, hypothalamus, and striatum using immunofluorescence, Western blot, and ELISA methods. Cognitive and motor deficits were observed three months after the administration of 6-hydroxydopamine, while protein expression involved in insulin signaling remained largely unchanged. Motor and cognitive deficits were observed as well as a decrease in tyrosine hydroxylase expression and  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor activation in the hippocampus and striatum, while dopaminergic nuclei in substantia nigra were preserved. These findings suggest a possible association between glutamate signaling dysfunction and cognitive deficit in a rat model of Parkinson's disease.

Keywords: Cognitive Disorder; Glutamate Receptor; 6-hydroxydopamine; Insulin Signaling Pathway; Tyrosine Hydroxylase

# Neuro-oncological Symptoms Worsening Post COVID-19 Vaccine

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It is well established that vaccines do not come free of adverse effects. The presenting case is one such statistical anomaly.

A 60-year-old woman with a history of colon carcinoma, without metastasis, presented in late June 2021 to her oncologist with complaints of headache, nausea, double vision, and vertigo within a week of being administered her first dose of the COVID-19 vaccination. She was referred to the neurology department and a CT scan and MRI were performed. A lesion was found in the right cerebellar hemisphere, suspected to be a metastasis. Infratentorial tumors are predominantly seen in children, and when occurring in adults are most commonly cerebellar metastases of lung and breast cancer. They are largely treated by surgical resection, of which the primary complication is postoperative hematoma (POH). The cerebellar metastasis was resected via craniotomy and the operation proceeded without complications. On the second postoperative day, the patient's condition worsened in the morning presenting with vomiting, hypertension, and headache. An acute CT scan was performed showing a POH, a critical indication for decompressive surgery. The patient was taken for a second surgery immediately wherein the hematoma was evacuated, and an intracranial drain was inserted. The patient's condition stabilized without further complications. The COVID-19 spike protein is known to initiate inflammatory cascades and cross the blood-brain barrier and thus may exacerbate underlying lesions. This presents with increased or worsening clinical symptoms. This case is noteworthy as there are very few reported cases of new-onset neurological symptoms post-vaccination against COVID-19, which reveal neuro-oncological processes on further diagnostic testing. This case illustrates a peculiar confluence of neuro-oncology and COVID-19. The inflammation associated with COVID-19 and its vaccine may reveal underlying lesions, unrelated to the disease process, and must be considered in patients with new-onset neuro-oncological symptoms.

Keywords: Neuro-oncology; COVID-19 vaccine; infratentorial metastasis

# Surgical evacuation of bilateral frontal abscesses followed by 3D-printed PEEK cranioplasty: A case report

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Intracerebral abscess is a collection of pus that develops in response to an infection or brain trauma. It is uncommon, serious, and potentially life-threatening condition. The incidence is quite low – 4.9 per million people. Bilateral frontal abscesses could be a result of contiguous spread from the paranasal sinuses. A 58-year-old female patient presented in the Department of Neurosurgery, after being found unconscious. On admission, she was somnolent, vaguely responsive, with reactive pupils, without motor deficit. Eight months ago the patient was operated on, for a nasal polyp. Due to the symptoms and previous clinical examination, a computed tomography – CT scan of the head was performed, demonstrating bilateral intracerebral lesions. An emergency operation-bilateral frontal craniectomy with evacuation of the abscesses was conducted. A bicoronal skin incision was performed in order to have access to both frontal lesions, and to harvest as much pericranial flap as possible for the anterior cranial fossa reconstruction and as a dural substitute. The dura mater was penetrated, and a huge intracerebral abscess was evacuated from the left frontal lobe, a smaller one from the right lobe. Microbiological cultures were obtained during surgery and they came positive for *Klebsiella oxytoca*. The capsule of the abscess was sent for histopathological verification. A decision was taken not to replace the bone flap due to its infiltration by the purulent process. After 3 months, a 3D-printed Polyetherketone-PEEK cranioplasty based on thin-sliced bone Computed Tomography was performed due to the huge bone defect in the frontal region that lead to cosmetic deformity. Intracerebral brain abscess is a serious emergent condition. Once the blood barrier is overwhelmed by the microorganism, the immune defenses are usually not sufficient to protect the brain from the ongoing infection. After many neurosurgical interventions, there are large skull defects that lead to considerable disfigurement and dissatisfaction of the patient. Custom-made 3D-printed implants might be the best solution to the problem, despite the higher cost.

Keywords: Brain abscesses; Neurosurgery; PEEK; Polyetherketone, 3D-printed Cranioplasty

# Neurofibromatosis Type 1, a case report

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The neurofibromatoses are a heterogeneous group of three genetic disorders that include neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2), and schwannomatosis. NF1 is the most common among them and is also one of the most frequently diagnosed tumor predisposition disorders involving the nervous system, as it affects around 1 in 3,000 live births worldwide. While it primarily affects the nervous system, both central and peripheral, it is also associated with other organ or system involvement. These include some neoplastic or non-neoplastic features such as cutaneous neurofibromas and Cafe-au-lait macules, Lisch Nodules, optic glioma, osseous lesion, and others. Most of them are included in The National Institutes of Health (NIH) Diagnostic Criteria for NF1 which is commonly used even though a significant number of NF1 patients fail to meet the NIH criteria in the first years of life when symptoms usually occur. However, nearly all of them meet the criteria for diagnosis by the age of 8, and almost all of them do so by the age of 20.

In this case report, the patient is a 32-year-old woman, who was diagnosed with NF1 at the age of four when she presented with vision impairment. She underwent her first surgical removal of the occipital meningioma six years later followed by Gamma knife radiosurgery. After C1/C2 Schwannoma surgery at 16, she developed epilepsy due to which she had to take oxcarbazepine, lamotrigine, and methylphenobarbital. At 21, she underwent four occipital and temporal-parietal meningioma ablations in two instances, the second being complicated with pleural effusion. At that time, The Chiari network – fenestrated, net-like embryonic remnants in the right atrium, was discovered. In the remaining years, many more intracranial and peripheral meningiomas and neurofibromas have been removed. In this patient's case, it is visible how NF1 has a big influence on people affected, resulting in reduced life quality but it also shows the need for bringing the awareness of NF1 despite it being a rare diagnosis.

Keywords: Neurofibromatosis type 1; von Recklinghausen, peripheral nerve sheath tumor; optic pathway glioma

# Recurrent hemorrhage: an atypical presentation of cerebral cavernous malformations in an adolescent

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Cerebral cavernous malformations (CCM) are benign vascular lesions of the central nervous system characterized by mulberry-like clusters of vascular sinusoids lined by a thin endothelium, lacking smooth muscle, elastin, or intervening brain tissue. Multiple cavernous malformations are rare and have an annual bleeding incidence of 0.2%. We report one such case of CCM that presented with recurrent intracranial hemorrhage requiring three surgical revisions. A 15-year-old girl presented with two episodes of impaired consciousness and convulsions. She had no significant family history of neurological disease. An MRI scan revealed an intracranial hemorrhage. The considerations for differential diagnosis were a tumor, arteriovenous malformation, aneurysm, and cavernoma. Surgery was initially planned for later date but her condition deteriorated due to raised intracranial pressure and sequelae of anisocoria and herniation. She underwent emergent right craniotomy and hematoma evacuation. Intraoperative macroscopic evaluation revealed no gross vascular anomaly. However, histology confirmed cavernous tissue. She began to exhibit signs of psychoorganic syndrome; with restlessness and aggression. On post-operative day 3, patient exhibited signs of mild left-sided hemiparesis, visual impairment, hypobulia, and disorientation. A slightly progressive hematoma in the resection cavity persisted on Magnetic Resonance Imaging (MRI) and post-operative changes were suspected. However, susceptibility weighted imaging sequences illustrated multiple deposits of supratentorial hemosiderin deposits, a hallmark sign of cavernomatosis. She then underwent a third en-bloc resection. Her surgical recovery was good and without signs of neurodeficiency. Although multiple CCMs are rare, they must be considered in recurrent events of intracranial bleeding, especially in pediatric populations. Del Curling et al. reported symptomatic hemorrhage rates of 0.5% per patient-year and 0.1% per lesion-year. It is crucial to report history of bleeding cavernomas as a significant prognostic factor for future intracranial hemorrhages. The concomitant presence of post-operative changes may impede diagnosis and timely treatment.

Keywords: Cavernous Hemangioma; Intracranial Hemorrhage



# A Case Report of Visual Field Defect due to Unruptured Internal Carotid Artery Aneurysm

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Intracranial aneurysms are possible causes of visual field defects. They are predominantly localized in the anterior part of the circle of Willis. They tend to present with late ocular symptoms such as progressive visual loss with some degree of visual field defect. Unruptured aneurysms have several treatment options, including open surgery and endovascular approaches. However, if untreated, they can lead to subarachnoid hemorrhage with severe consequences. A 50-year-old female patient presented with visual deterioration in her right eye. She reported that progressive loss of vision started 6 months ago and that dull intermittent frontal headaches started 1 year ago. The best corrected visual acuity was 0,9 in the right eye and 1,0 in the left eye. Visual-field examination indicated a complete nasal defect in the right eye and superotemporal scotoma in the left eye. CT (computed tomography) scan of the brain showed 16,5x17x13,5 mm oval hyperdense lesions in the right anterior part of the circle of Willis. DSA (digital subtraction angiography) revealed a 18x20x16 mm right-sided ICA (internal carotid artery) aneurysm on terminal C5 (clinoid)/ C6 (ophthalmic or supraclinoid) medial segment. After considering treatment options with the patient, the initial plan was endovascular treatment with a flow-diverter device (FDD). Due to the wide neck of the aneurysm, FDD was not successfully placed. Therefore, coil embolization endovascular surgery was performed instead. 20 coils were used to occlude the aneurysm. 14 days later control DSA showed stable occlusion of the aneurysm sac with minimal residual filling. Visual symptoms showed no progression. Aneurysms of the ICA distal to the ophthalmic artery usually produce late ocular symptoms. Therefore, this case emphasizes the importance of remembering that visual field defects are potential symptoms of nerve compression caused by intracranial aneurysms. Unruptured aneurysms have multiple promising treatment options if they are recognized in time.

Keywords: Internal Carotid Artery; Intracranial Aneurysm; Visual Field Exam

# Long term medical and physiotherapy approach to treatment of Spina bifida – a literature review

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Spina bifida is a congenital neurological disorder caused by a growth abnormality of the spinal cord during the first month of embryonic development. The consequences depend on the degree and size of the defect and the quality of postnatal surgery and physiotherapy.

The most common and severe consequences of this developmental anomaly are neurogenic bladder, scoliosis, hydrocephalus, and congenital disorders. In addition to various surgical options, there is a wide range of conservative treatments such as the Vojta concept, neuro-modulation, Bobath concept, etc. The aim of this review was to highlight the possibilities of rehabilitation approaches in children and adolescents diagnosed with Spina bifida. For this research, we collected information from books in the Velika Gorica City Library, the National Library, and the University Library in Zagreb and reviewed the literature using the keywords: Spina bifida, rehabilitation, habilitation, physiotherapy, neurological disorders of the spine, myelomeningocele. With current knowledge of rehabilitation of children and adolescents diagnosed with Spina bifida, the goal is to improve quality of life and minimize associated diagnoses. Patients with Spina bifida require an individualized approach, as each case is unique.

Despite rare occurrence of MB in adult patients, surgery should be performed whenever possible to resolve clinical disturbances. The aim of supplementary oncological treatment and further radiological follow-up should be focused on overall survival and better quality of life.

Keywords: Medicine; Neural Tube Defect; Neurology; Spina Bifida

# Recurrent medulloblastoma in an adult patient – a case report

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Medulloblastoma (MB) is a primary malignant brain tumor of chemosensitive nature with a higher frequency of occurrence in children, rarely in adults. It most commonly presents in a mediosagittal axis, less commonly in the surrounding area. A 30 – year – old female patient suffering from nausea, dizziness, and gait disturbance was observed at the outpatient clinic. Previously, the patient has undergone surgery eight years ago at the age of 22. Maximal resection of the tumor was performed via the right-sided suboccipital craniotomy, pathological diagnosis confirmed MB. Postoperatively, the patient underwent oncological treatment; Lomustine, Cisplatin, Vincristine. Radiotherapy of 54 Gy and 36 Gy were applied on posterior cranial fossa and neuroaxis, respectively. Consecutive postoperative magnetic resonance imaging (MRI) of the brain revealed no recurrence of the tumor. An MRI performed in December 2021 confirmed a lesion of the right-sided cerebellar hemisphere with perifocal edema and radiological signs of hypertensive hydrocephalus. The patient underwent surgical re-treatment in a regular microscopic fashion. A right-sided suboccipital re- craniotomy was performed. MB grade 4 was confirmed; a high Ki- 67 positivity and extensive nodularity were noted. Preoperative symptoms regressed one week after surgery, including hydrocephalus. An early postoperative follow-up MRI scan of the brain and the whole spine did not reveal drop metastases at any anatomical level. Oncological treatment is due to be continued. Despite rare occurrence of MB in adult patients, surgery should be performed whenever possible to resolve clinical disturbances. The aim of supplementary oncological treatment and further radiological follow-up should be focused on overall survival and better quality of life.

Keywords: Craniotomy; Medulloblastoma; Magnetic Resonance Imaging; Spine; Radiotherapy

# Vascular dementia and/or depression in hypertensive and obese patient with psychic deterioration

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Hypertension, obesity, and diabetes mellitus (DM) are recognized as risk factors for brain damage that can cause psychic deterioration, memory loss, and cognitive deficits. Assessing patients with comorbidities and multiple symptoms can be a challenge. A 69-year-old female patient consulted her general practitioner (GP) concerned about energy loss and psychic deterioration. She is a former smoker, obese, has hypertension and diabetes, and now has developed chronic complications. Her glucose levels and blood pressure are not controlled. In a GP practice, she was in a good general condition and was worried about her health and her granddaughter whom she takes care of. Physical examination reveals RR 150/80 mmHg, pulse 77 bpm, blood sugar level 17mmol/L, weight 75kg, height 152cm, BMI 32,5 kg/m<sup>2</sup>. Cardiac auscultation reveals a rhythmic heartbeat, normal tones, no murmur over the precordium, murmur over the left carotid, and normal breathing sound. Further examination reveals limbs without edema, warm, with less palpable peripheral pulsations. Lab results reveal increased leukocytes 11,40x10<sup>9</sup>/L, HbA1c 12,1%, 109µmol/L, CDK-EPI 54 ml/min/1,73m<sup>2</sup>, and a trace of protein in the qualitative urine test. Other parameters are in reference intervals.

Given the patients' diagnoses, and considering risk factors, we question two diagnoses – vascular dementia and depression. Several tests were used to distinguish whether it is one of the diagnoses or a combination of both. On the geriatric depression scale test, the patient scores 9/15 which points to minor signs suggestive of depression. A score of 3/5 on the mini-cog questionnaire indicates the need for further medical treatment associated with dementia. On Montreal cognitive assessment (MOCA) screening test the patient scored 21/30 (>26 is normal result). Test results and physical examination indicate the combination of both diagnoses, and further monitoring (appointment with a neurologist, ophthalmologist, and psychiatrist) is suggested.

Keywords: Depression; Diabetes Mellitus; Hypertension; Obesity; Vascular Dementia

# Patient with YY1-related dystonia treated with deep brain stimulation: a case report

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Gabriele-de Vries syndrome is a neurodevelopmental disorder resulting from a YY1 gene mutation inherited in an autosomal dominant manner. It is characterized by intellectual disability, dysmorphic facial features, neurological, behavioral, and other organ system abnormalities.

We present a 32-year-old male patient who underwent DBS evaluation after worsening of dystonia resistant to pharmacological treatment. Pregnancy, perinatal period, speech, and early language development were unremarkable. Patient was diagnosed with Pierre Robin sequence during infancy, showed stunted growth and underwent surgery for craniosynostosis at 4.5 months of age. Speech difficulties were first noted at the age of 8. Six years later, patient developed dyskinetic movements of facial muscles and fingers exacerbated by movement and speech. No chronic diseases or other organ abnormalities described in this syndrome were present. Neurological examination was characterized by oromandibular and hand dystonia with difficult communication due to speech impairment. Brain magnetic resonance imaging (MRI) was unremarkable. Whole exome sequencing revealed a likely pathogenic de-novo YY1 nonsense mutation, c.1123C>T; p.Arg375X (NM\_003403.5), a variant not reported in literature so far. Patient underwent globus pallidus internus (GPi) deep brain stimulation (DBS) with a revision 6 months later due to lead displacement. Dystonia was assessed with a Burke-Fahn-Marsden Dystonia Rating Scale pre- and post-surgery. Motor score (BFMMS) decreased from 100 to 50 and disability score (BFMDS) decreased from 20 to 14 at 6 months follow-up which indicates a positive response to treatment. Movement disorders related to YY1 mutations are not common, with only one patient having a long-term positive response to DBS described to date. This case report affirms that DBS can improve quality of life and should be considered as a treatment option for YY1-related dystonia.

Keywords: Deep Brain Stimulation; Dystonia; Gabriele-de-Vries Syndrome; YY1

# Effect of non-invasive neurostimulation on some aspects of executive function

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Executive functions (EF) of the brain are defined as high-level, complex processes by which individuals optimize their performance according to their goals in a situation that requires the operation of several cognitive processes. As such, cerebral areas involved in EF serve as central hubs which modulate other brain regions to perform and coordinate goal-oriented activity. These functions have been linked with the phylogenetically youngest part of the brain, prefrontal cortex. Specifically, dorsolateral prefrontal cortex (DLPFC) was found to be involved with “on-line” processing of information (e.g. planning, response inhibition, working memory, problem-solving). In studying localization, function, and ways to improve EF, researchers have recently started using a method of non-invasive neuromodulation - transcranial direct current stimulation (tDCS). In tDCS, the cerebral cortex is stimulated by a weak constant electric current that can induce focal changes in cortical excitability that persist after the stimulation period. The aim of this study was to examine the efficacy of anodal tDCS over left DLPFC in improving EF, primarily working memory and inhibition control. This was accomplished by a repeated measures design which included 21 healthy young adults that underwent two sessions separated by a week, one of which included 20-minute anodal stimulation by 1.5mA over DLPFC and the other sham stimulation. In both sessions, participants solved working memory and response inhibition tasks before and after the stimulation. In doing so, efforts are made to identify the potential contribution of tDCS in working memory and inhibition, as well as to verify if DLPFC is associated with these functions.

Keywords: Dorsolateral Prefrontal Cortex; Executive Function; Transcranial Direct Current stimulation; Working Memory

# Third Cranial Nerve Palsy in COVID-19 Patient

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Coronavirus disease (COVID-19) is a highly contagious infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is known to be primarily a viral infection affecting the pulmonary system leading to pneumonia, acute respiratory distress syndrome, and even subcutaneous emphysema in severe cases. Coronavirus disease (COVID-19) can cause various neurological complications among which is also third cranial nerve palsy. The most common causes of third cranial nerve palsy are hypertension and diabetes mellitus, cerebral aneurysms, or tumors. Third cranial nerve palsy has been reported in patients with confirmed COVID-19 disease in only a handful of cases. We describe a case of male patient with acute, painless, and incomplete palsy of the right third cranial nerve as a presenting symptom of COVID-19 infection. A previously healthy 55-year-old male, with no previously recorded risk factors for third cranial nerve palsy (such as arterial hypertension, diabetes mellitus, or hypercoagulable risk factors), presented to the Emergency Department for acute onset of painless right-sided ptosis and diplopia. Patient denied trauma, headache, or any motor or sensory changes. Emergency Department showed no signs of pneumonia. Routine transcription-polymerase chain reaction (RT-PCR) for COVID-19, which specifically detects the presence of viral nucleic acid in clinical samples was done and according to the results -COVID-19 was confirmed positive. Since we were not able to identify the underlying cause of the incomplete third nerve palsy in this patient after clinical, laboratory, and imaging examinations, we suspect that COVID-19 infection is the cause of the incomplete third cranial nerve palsy. Just as in previous case reports, complete recovery of third nerve palsy was noted shortly after the beginning of symptoms. Neurological manifestations of COVID-19 are common. Although a retrospective study with 214 patients infected by COVID-19 suggested that 36.4% had neurological symptoms the mechanism of development of neurologic manifestations remains unclear. This

case report accentuates not only the neurogenic potential of SARS-CoV-2 virus but also the need for further research into mechanisms of neurologic complications of COVID-19.

Keywords: COVID-19; Cranial Nerve Palsy; Infection

# Trigeminal neuralgia associated with solitary pontine/brainstem lesion (SPL-TN) - Case report

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Trigeminal neuralgia (TN) is the most common type of chronic neuropathic facial pain, characterized by intermittent attacks of severe, electric shock-like unilateral pain along the distribution of the trigeminal nerve branches. A well-established and most common etiological factor of essential TN is neurovascular compression (conflict) of the trigeminal nerve at the root entry zone, usually by superior cerebellar artery. Other aetiologies include multiple sclerosis (MS), brainstem infarct, Chiari's malformation, or a mass lesion stretching the nerve root. A dedicated high-resolution scan is needed, as routine brain magnetic resonance imaging (MRI) usually does not reveal the abnormalities. A 74-year-old man presented with recurring right-sided unbearable pain in the innervation area of right mandibular nerve (right lower jaw). Patient could not open his mouth. 7 months prior he underwent trigeminal neurectomy (maxillary and mandibular divisions) and was treated with a combination of carbamazepine and various opioid analgesics but without any improvement. MRI showed right trigeminal nerve atrophy without neurovascular conflict. There was also a 6 mm oval lesion in the right trigeminal nucleus and spinal trigeminal tract area, consistent with a solitary lesion of the pons in trigeminal neuralgia (SPL-TN). SPL-TN is currently considered a rare condition, recently mentioned only a few times in the literature. Tohyama et al. proposed a new clinical syndrome, using a combined clinical and neuroimaging approach - TN associated with solitary pontine lesion (SPL-TN). Abnormal white matter microstructure was found in the lesions uniformly located along the affected trigeminal pontine pathway, without any additional brain lesion. SPL-TN patients have identical clinical features as other TN patients but have a single pontine lesion not consistent with MS and are refractory to standard surgical management. A neuronavigated tractotomy of the pontine trigeminal tract may possibly offer pain relief.

Keywords: Trigeminal Neuralgia; White Matter; Magnetic Resonance Imaging; Differential Diagnosis; Multiple Sclerosis



# Niemann-Pick disease type C- progressive neurological deterioration in a 10-year-old girl – Case report

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Niemann-Pick disease type C (NPC) is a rare autosomal recessive lysosomal disorder associated with an accumulation of sphingomyelin in reticuloendothelial and parenchymal tissues caused by mutations of NPC1 or NPC2 gene. Clinical features include a wide spectrum of visceral and neurological signs and symptoms with onset age ranging from the perinatal period to late. The 'classical' presentation is also referred to as the late-infantile or juvenile form seen in children younger than 5 years of age to adolescence, where learning disabilities, behavioral problems, and progressive motor impairment become evident. The aim of this report is to suggest that the early phases of NPC can be overlooked or misdiagnosed due to the heterogeneous and non-specific nature of the symptoms. An 8-year-old female patient was referred to the pediatric neurologist for multidisciplinary examination of the autism spectrum disorder. The mother indicated normal gross motor milestones: sitting without support at 7 months, walking independently at 15 months, and first words at 16 months. Around the age of 3, the patient underwent an upper lip suturing repair, without sedation. Few months after, her mother noticed a drastic change in behavior and a regression in all aspects of development, which she related to the traumatic event. During neurological examination, the patient was anxious, had poor verbal and non-verbal comprehension and facial dysmorphism. At 10-year-old she developed signs of progressive neurological deterioration with frequent epileptic seizures. Brain MRI showed areas of hypo/dysmyelination in the periventricular occipitoparietal region. The patient was referred for genetic testing where 2 pathological mutations of the NPC1 gene were confirmed. NPC should be suspected in pediatric patients presenting with developmental delay or regression. Diagnostic algorithm includes genetic testing, skin biopsy, and bone marrow examination. NPC can be treated with miglustat, a drug that is associated significantly with the reduction of mortality.

Keywords: Niemann-Pick disease; sphingomyelinase; developmental delay

# Respiratory syncytial virus encephalitis in children – case report

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Respiratory syncytial virus (RSV) is one of the most common pediatric causes of respiratory tract infections worldwide. The disease is usually mild, however, even previously healthy, full-term children can suffer from severe forms of RSV infection and may require hospitalization. Encephalitis consisting of seizures and other neurologic abnormalities such as lethargy, irritability, and abnormal tone has been sporadically reported in infants and children with RSV respiratory infection. It usually develops within 1 to 2 days after the onset of clinical symptoms. The mechanism of RSV encephalitis is not fully understood. A 2-year-old female patient was admitted to the Intensive care unit (ICU) following seizures and loss of consciousness. The patient had prior respiratory symptoms which worsened following the admittance to the ICU and required mechanic ventilation. RSV pneumonia was diagnosed by x-ray and further confirmed microbiologically, which led at the end to severe acute respiratory distress syndrome (ARDS). Due to multiple epileptic seizures and encephalopathy, empiric immunomodulatory and antiseizure therapy was administered. An extensive diagnostic process was carried out, and by exclusion, RSV encephalitis was confirmed as the most likely diagnosis. The patient's status kept on improving and she was discharged after one month with a mild neurological deficit. Encephalitis is a rare complication of respiratory infections caused by RSV. It causes severe symptoms, often with irreversible consequences. Diagnosis is in most cases presumptive, on the basis of clinical finding and exclusion of other causes of encephalitis.

Keywords: Encephalitis; Respiratory Syncytial Viruses; Seizures

# Comparison of Nervous System Agents Utilisation in Croatia in Prepandemic 2019 and Pandemic 2020

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Overall drug utilization in Croatia has a continuous annual rising trend. Accordingly, the increase is seen in the utilization of Nervous system agents (N-category agents in Anatomical Therapeutical Chemical classification system). Concerning changes in the health and lifestyle of the population due to the coronavirus pandemic, we analyzed the consumption of N agents before and during the pandemic. The data was obtained from the Croatian Agency for medical products and medical devices. We observed the overall N agents utilization, as well as that of different N subcategories, in Croatian kuna (HRK) and defined daily doses (DDD/1000/day). Overall N agent utilisation increased by 4,14% (from 885.387.022,00 HRK in 2019 to 923.585.525,00 HRK in 2020). The increase is also applicable to utilization in DDD/1000/day (+3,57%, from 195,46 in 2019 to 202,70 in 2020). The largest increase was seen in utilization of Analgesics (N02, +9,97% financially, +9,06% in DDD/1000/day). Most of that increase is on the account of Antimigraine preparations (N02C, +45,20% financially, +20,93% in DDD/1000/day) and utilisation of Other analgesics and antipyretics (N02B, +9,45% financially, +23,63% in DDD/1000/day). A decrease was noticed only in the utilization of Other nervous system drugs (N07, -5,22% financially, but +0,27% in DDD/1000/day). N07 is a heterogeneous group of agents and it is assumed that there was a price reduction of a drug from this subcategory. Utilization increase higher in HRK than in DDD/1000/day in the N02C subcategory could be explained by the price increase of some agents from the subcategory. As for the increase in DDD/1000/day disproportionate to the financial consumption in the N02B subcategory, it might be caused by greater use of acetylsalicylic acid during the pandemic and reduced price of some agents. Further research is needed to determine the exact cause of obtained results, as well as their relation to the emergence of the pandemic.

Keywords: Central Nervous System Agents; Economics; Health Expenditures

# Atypical neurodegenerative disease presentation with corticobasal degeneration – a case report

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Corticobasal syndrome (CBS) is a heterogenic group of symptoms that may present atypically in the beginning, but with disease progression, it affects the body bilaterally. Myoclonus, limb dystonia, balance and gait disturbances, ideomotor apraxia et cetera may occur in later stages. CBS is an integral part of the clinical picture of corticobasal degeneration (atrophy of brain parenchyma). A 53 – year – the old male patient was admitted to the neurological ward of the Clinical hospital center Osijek for further evaluation due to progressive dementia, visual disturbances (simultanagnosia, optic ataxia, and oculomotor apraxia), myoclonic jerks of limbs, and extrapyramidal symptoms. Via heteroanamnesis it was found that the symptoms first occurred the year prior, coupled with disorientation and difficulty walking. Medical staff has introduced a drug for parkinsonism and myoclonus, to which the patient has responded well. Magnetic resonance imaging (MRI) of the brain showed posterior cortical atrophy predominantly in parietooccipital regions bilaterally. Furthermore, an electroencephalogram (EEG) resulted as mildly diffusely dysrhythmically changed. Neuropsychological testing showed advanced stages of dementia. Acute infections of the central nervous system and changes in regards to demyelinating disease were ruled out via examination of the cerebrospinal fluid (CSF). CSF and blood samples were sent to the Clinical hospital Center in Zagreb for further testing Alzheimer's and Huntington's disease. To summarize, in regards to the anamnesis, clinical picture, disease progression, and diagnostic evaluation, it is most likely that the patient suffers from corticobasal degeneration which resulted in posterior cortical atrophy, and is characterized by dementia, visual disturbances, generalized rigor, hypokinesia, and cortical myoclonus.

Keywords: corticobasal degeneration; dementia; Parkinsonian disorder; lacunar infarct

# Relapsing-remitting multiple sclerosis and response to glatiramer acetate therapy

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Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) characterized by chronic inflammation, demyelination, and neuronal loss. The clinical course of the disease is quite variable, ranging from stable chronic disease to a rapidly evolving and debilitating illness. The aim of this case report is to point out the significance of early recognition of relapsing-remitting MS (RRMS) and the importance of introducing glatiramer acetate into therapy as soon as possible. We present a case of a 57-year-old woman who was admitted to the Neurology department due to general weakness, legs, and buttocks paresthesia, and urinary urgency. During neurological examination, Lhermitte's sign was positive and myotatic leg reflexes were hyperactive. On Expanded Disability Status Scale (EDSS) she showed a score of 2. The patient underwent laboratory and immunological testing, lumbar puncture, brain, and cervical spine MRI. IgG oligoclonal bands were detected in the cerebrospinal fluid and MRI scans showed multiple demyelination lesions. The patient had met the McDonald criteria (dissemination in space and time) for RRMS and received her first glatiramer acetate therapy along with her first dose of pulse corticosteroid therapy. The disease is clinically and radiologically stable. Glatiramer acetate is a drug with beneficial effects on the course of RRMS, reducing both relapse frequency and accumulation of deficit over time. The drug also has beneficial effects on MRI disease activity. Treatment of RRMS is currently easier than before, as the patient can receive therapy as soon as the criteria are set. In conclusion, MS is a lifelong condition that can sometimes cause serious disability and glatiramer acetate is a valuable first-line option in the treatment of RRMS.

Keywords: Demyelination; Multiple sclerosis; Relapse

# OSA in a 14-year old patient with growth hormone deficiency and enuresis – a case report

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Obstructive sleep apnea (OSA) is a condition in which there are partial (hypopneas) or complete (apneas) episodes of the upper respiratory tract obstruction during sleep, followed by blood oxygen desaturation. In the pediatric population, a single apnea/hypopnea episode is considered pathological. Whenever respiratory pauses, snoring, forced mouth breathing, frequent awakenings, daytime irritability/sleepiness, alongside and even growth deterioration and enuresis occur in children, pediatric OSA should be suspected. The whole-night in-laboratory polysomnography (PSG) is the golden standard diagnostic procedure. During a pediatric evaluation, a 14-year-old male patient with growth hormone (GH) deficiency and nocturnal enuresis was referred to the Sleep Medicine Center due to suspected OSA. Patient's complaints entailed occasional snoring, morning headaches, and feeling tired during the day. Tonsillar hypertrophy and deviation of the nasal septum were revealed following ear, nose, and throat (ENT) examination. The PSG recording revealed a relatively preserved sleep architecture with occasional micro-arousals, prolonged sleep latency (133.0 minutes), as well as prolonged rapid eye movement (REM) latency (179.5 minutes). Sleep efficiency was reduced to 74.8%. A total of 54 episodes of respiratory distress were noted in the PSG recording, of which 27 apneas and 27 hypopneas. The apnea-hypopnea index (AHI) was 8.0 events/hour. The average blood oxygen saturation during sleep was 96%, the lowest recorded desaturation was 93%, while the desaturation index was 6.4/h. The majority of respiratory disturbances were observed in the supine sleeping position. Adenotonsillectomy, alongside positional therapy, has been proposed as treatment option. Pediatric OSA management remains challenging, with frequent underestimation of the disease in children. Therefore, all pediatric patients with OSA symptomatology, especially GH deficiency and nocturnal enuresis should be carefully evaluated. Early detection, prompt evaluation, and disease treatment are important to prevent systemic and long-term consequences.

Keywords: obstructive sleep apnea; children, polysomnography; growth hormone; enuresis

# Double seronegative neuromyelitis optica spectrum disorder in a 35-year-old female

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Neuromyelitis optica spectrum disorders (NMOSD) are inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting optic nerves and the spinal cord. The core clinical symptoms of NMOSD include acute attacks of bilateral optic neuritis and acute myelitis with a typically relapsing course. A 35-year-old female presented with spastic paraparesis (1-2/5) of lower limbs and urine retention suspecting longitudinal extensive transversal myelitis. Upper motor neuron lesion of lower limbs was confirmed with EMNG (Electromyoneurography). Urgent MRI (Magnetic Resonance Imaging) revealed T2 extensive hyperintense continuous lesions (Th2-Th10) combined with lesions of optic chiasm. Consequently, NMOSD was suspected, but the patient tested negative for both AQP4-IgG (Aquaporin 4-Immunoglobulin G class antibody) and MOG-IgG (Myelin Oligodendrocyte Glycoprotein-Immunoglobulin G class antibody). As the patient satisfied other diagnostic criteria, a diagnosis of seronegative NMOSD was made. Corticosteroid therapy resulted in significant improvement subjectively (3/5 spastic paraparesis) and objectively with reduced signal of previous hyperintense lesions. She was then discharged with azathioprine, baclofen, and methylprednisolone as maintenance therapy due to residual inflammation confirmed on MRI. A year and four months after patient reported progression of pain in thoracic and lumbosacral spine with propagation in both legs all the way to the knees accompanied by feet hyposensitivity. Due to progression of symptoms and new lesions in the cervical spinal cord patient is preparing to receive biological treatment with rituximab. The patient described in this case report belongs to a minority of patients with NMOSD who are seronegative for both anti-AQP-4 and anti-MOG. The conventional treatment of an acute episode of seronegative NMOSD is intravenous corticosteroids, with or without plasma exchange. Many published papers evaluated biological treatment for seropositive NMOSD and reported significant improvement in clinical outcome, but none of them reported success in double seronegative NMOSD patients. Understanding of pathogenesis of double seronegative NMOSD is challenging and further research is urgently needed.

Keywords: Neuromyelitis optica; demyelination; aquaporin-4; autoantibodies

# Exacerbations of advanced Parkinson's disease after COVID-19 infection in patients treated with invasive therapies – case report

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COVID-19 complicates the clinical course of Parkinson's disease (PD) and poses a risk to patients' functional abilities and quality of life. Patients with advanced PD treated with invasive therapies are especially vulnerable. Herein, post-COVID-19 syndrome manifests as an acute or subacute worsening of a previously stable pre-existing disease symptoms. We present two patients admitted to the Clinic of Neurology Rijeka due to the exacerbation of PD symptoms following a COVID-19 infection. The first is a 66-year-old woman diagnosed with PD in 2013 and treated with deep brain stimulation of the subthalamic nucleus in 2017. She was stable for years, but her symptoms worsened after overcoming COVID-19. She developed fatigue, gait impairment, and leg paresthesia, while increases in rigor and tremor were found during the neurologic examination. Treatment included changes in stimulation parameters and physical therapy, and upon discharge, tremor was absent, while rigidity and bradykinesia were greatly reduced. The second patient is a 70-year-old woman diagnosed with PD in 2008. Invasive therapy with levodopa/carbidopa pump was initiated in 2014. Her post-COVID-19 symptoms included lack of appetite, increased rigor, apathy, insomnia, and freezing of gait. She took extra levodopa doses, which ultimately caused dyskinesia. The neurological examination revealed discrete hypomimia, mild intentional tremor, and bradykinesia, bent gait with apparent dyskinesia. The psychiatric evaluation confirmed a mild depressive episode. Laboratory blood analysis showed abnormalities in kidney function, vitamin D levels, and mild anemia, that could contribute to the worsening. The dosage of levodopa/carbidopa was adjusted, and she was discharged with an improved clinical status. The presented cases suggest that PD patients undergoing invasive therapies may experience worsening motor and non-motor symptoms as a result of the post-acute COVID-19 syndrome. These exacerbations can be successfully managed with careful monitoring and modification of therapeutic parameters.

Keywords: deep brain stimulation; levodopa, Parkinson's disease; post-acute COVID-19 syndrome



# Functional neurological disorder in Parkinson's disease treated with deep brain stimulation: a case report

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Deep brain stimulation (DBS) has been established as a highly effective therapy for advanced Parkinson's disease (PD). Functional neurological disorder (FND), also called conversion disorder, is part of a wide spectrum of functional disorders. The predominant feature is a loss or alteration in physical functioning that suggests a physical disorder but ultimately is without a clear substrate. FND is usually a direct expression of a psychological conflict or need and presents with a wide range of symptoms or false worsening that can affect even advanced PD patients treated with DBS. We present a 54-year-old patient with a history of right-sided tremor and bradykinesia. The diagnosis of Parkinson's disease was given at the age of 46, with levodopa therapy shortly after. Progression of the disease was relatively fast and DBS therapy was indicated at the age of 53. The neurological exam revealed hypophonia, right-hand tremor, bradykinesia, and mild gait impairment despite therapy. Bilateral subthalamic nucleus (STN) DBS was performed in the same year. Initial response to DBS was tremendously positive, with the patient regaining significant work capability. However, the patient reported worsening that often coincided with work or household-related obligations. Several months after implantation, the patient was admitted to the Clinic of Neurology Rijeka due to claimed worsening. During the hospitalization, the levels of stimulation (Table 1.) and levodopa doses were adjusted several times, which reduced bradykinesia and tremor. Initial therapy was levodopa/benserazide in a dose of 125mg and the therapy was adjusted to levodopa/carbidopa in a dose of 250mg/25mg. However, a discrepancy between subjective symptoms and objective findings was seen. Interestingly, the patient reported improvements even in sham DBS parameter changes. This case report signifies the importance of suspecting a functional disorder in patients treated with DBS, as reported worsenings of symptoms can occur with no clear substrate.

Keywords: Conversion disorder; deep brain stimulation; Parkinson's disease

# Migrainous stroke; a myth or a reality? – case report

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Ischemic stroke is a medical emergency caused by an occlusion of one of cerebral arteries resulting in focal brain damage with consequent sudden neurological deficits, while migraines are a very common, usually, non-life-threatening, primary headache disorder. Numerous studies have linked migraines with an increased risk of ischaemic stroke and so does this case report. A 10-year-old girl was admitted to the Emergency department with a stress-induced headache, left-sided hemiparesis, pale skin, shivering, and inarticulate speech. According to her parents, she was feeling upset because of her unwell pet two days prior to admission. She vomited four times one hour prior to arriving to the clinic. She was complaining about dull right-sided temporal headache without aura, 6 out of 10 on a pain scale. Physical exam was normal, but neurological examination revealed left-sided hemiparesis and dysphasia, inability to stand upright, drooping of the left corner of her mouth, inarticulate speech, and dragging of her left leg when walking. Both hematological and metabolic lab examinations did not show any abnormalities. Her CT scan was unremarkable, while the MRI showed an ischemic lesion caused by an occlusion of middle cerebral artery. She was monitored and treated with acetylsalicylic acid of 4 mg/kg/day, and after re-evaluation by neurologist it was concluded that she did not fit the criteria for mechanical thrombectomy and was continued on salicylic acid therapy.

Although migraines do not affect pediatric patients often, and only 10% of them are experienced during elementary school, they can still lead to dangerous conditions such as the ischemic stroke. Therefore, even when there exists the smallest suspicion of it occurring, a detailed medical examination is required.

Keywords: Ischemic stroke; Migraine; Salicylic acid; Thrombectomy

# Neuronal ceroid lipofuscinosis type 2; treatment of an incurable disease- case report



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Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) is a rare autosomal recessive neurodegenerative disorder caused by an enzyme deficiency of tripeptidyl peptidase 1 (TPP1). It usually presents in children aged 2-4 years with seizures and loss of motor and language skills, followed by loss of vision and premature death. Delayed language acquisition frequently precedes the onset of more apparent symptoms, but in most cases remains under-detected. Except for supportive behavioral and symptomatic therapy, including anti-epilepsy medication, the only specific treatment available is an enzyme-replacement therapy, cerliponase alfa (Brineura®). A 3-year-old girl was diagnosed with CLN2 after having been treated for epilepsy for 6 months. The diagnosis of CLN2 was suspected due to additional symptoms such as hand tremor, gait instability, and delayed speech development. Molecular gene testing detected two heterozygous mutations, the c.509-1G>C and the c.614T>A, which confirmed the diagnosis. A significantly decreased enzyme activity of the TPP1 was also detected. 2 months after the diagnosis, the patient was admitted to the hospital and surgically implanted with an Ommaya ventricular reservoir, with the reservoir placed under the scalp and the catheter placed in the cerebral right lateral ventricle for intraventricular infusion of cerliponase alfa, a recombinant form of the deficient enzyme. The patient then started therapy and has been receiving a 300mg dose every two weeks for almost 2 years. After long-term therapy, the psychodiagnostic developmental assessment according to test indicators does not detect a decline in the patient's development. Although on average it takes two years to diagnose CLN2 after the onset of symptoms, due to its nonspecific symptoms, the present case exemplifies how recognizing the disease at an early stage and initiating specific treatment can result in slower decline in motor and language scores.

Keywords: Cerliponase Alfa; Epilepsy; Neuronal Ceroid Lipofuscinoses

## Workshops

# Stress – how it affects our brain and body and how can we deal with it

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Heart beating as crazy, sweaty hands, shallow breathing, headache, chest pain, anxiety? Yes? Your amygdalas hijacked Your body. They activated the HHA axis, sending adrenaline and noradrenalin from hypothalamus and hypophysis to the body; activating cortisol, and voila: now You feel like fighting or fleeing the situation. If Your stress hormones are deprived, then Your body is freezing; Your adrenals are shooting down. Lousy but sometimes also helping You sharpen the mind and improve the ability to remember details about what is happening. This is what happens in acute stress. What about the repeated stressful situation?

Research has shown that stress, especially chronic stress, can produce a wide range of effects on the brain ranging from contributing to mental illnesses such as depression and various emotional disorders to actually shrinking the volume of the brain. Enduring stress can create more myelin-producing cells, but fewer neurons than normal. It literally shrinks our hippocampuses. While stress does not appear to influence the formation of new neurons, it does impact whether or not those cells survive. Chronic stress has a negative impact on spatial memory as well as spatial orientation. High levels of the stress hormone cortisol are connected to short-term memory declines. Stress also impairs memory retrieval. However, if it occurs immediately before learning, memory can actually be enhanced by aiding in memory consolidation. Some people can even become more resilient through stress. It looks like our response to stress is based on the patterning of white matter you get early in life. But – if there is too much stress, it makes it challenging for the future stress, particularly if the next demanding event requires effortful control, emotion regulation, or integrated social processing to overcome it. This is impaired if the stress has affected your prefrontal cortex.

What to do with all the stress? First, we are going to understand the mechanisms behind it, then we will play with our brain and make it more resilient to it. How are we going to do it? Come, see, and experience it. To dare is to do! Welcome!

# Bioinformatic workshop on transcriptomics data analysis – from RNA-seq raw counts to differentially expressed genes

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This bioinformatic workshop is designed to introduce participants to the commonly used tools to analyze gene expression data, focusing on RNA-seq data analysis. We will cover the theoretical background of the main concepts of RNA-seq data analysis, introduce how to use publicly available transcriptomics data repositories, and how to perform differential gene expression and functional enrichment analyses. Practical part of this workshop will be organized via a web-based Galaxy platform and will provide the participants the chance to perform their own RNA-seq analysis, to discuss how to interpret the results and how to visualize them.

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