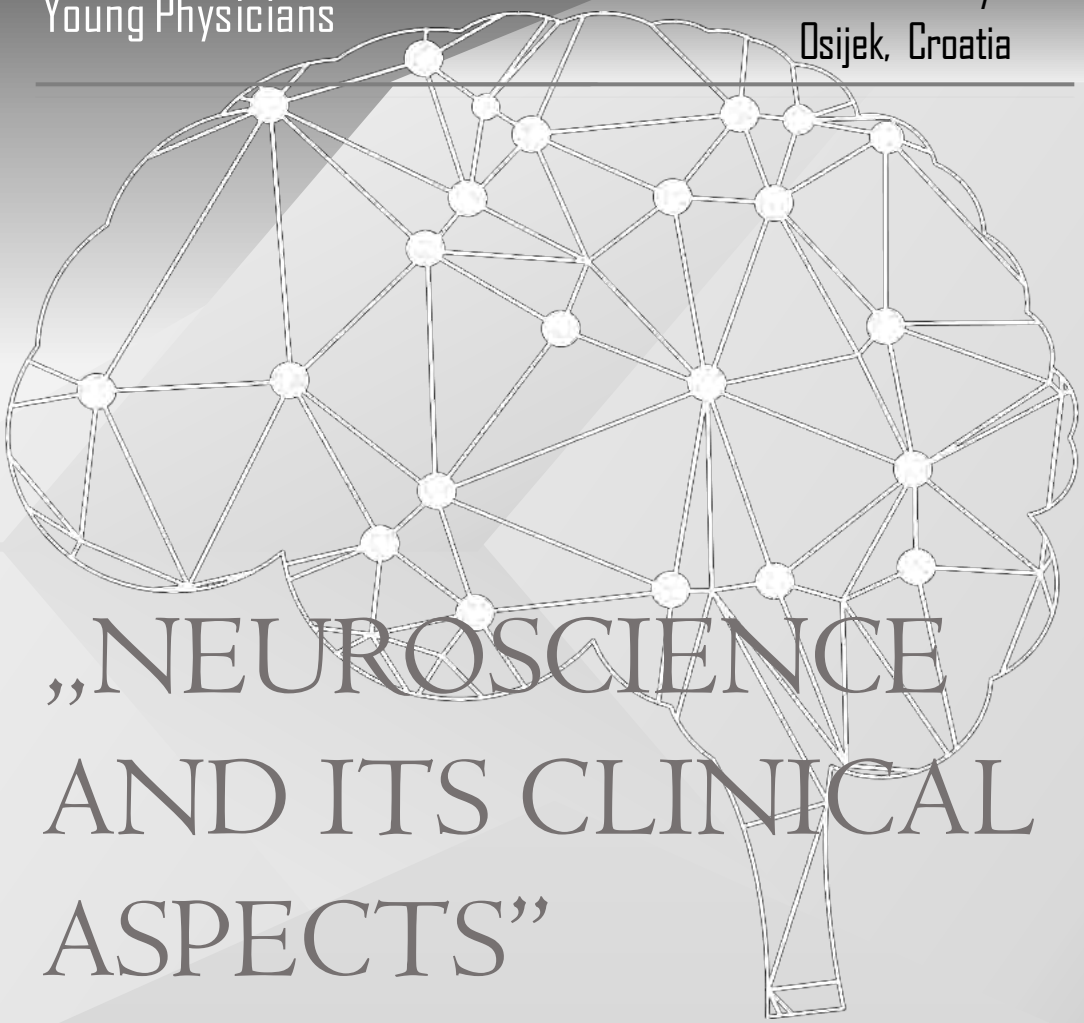
Josip Juraj Strossmayer University of Osijek
Faculty of Medicine

OSCON

1st International TRANSLATIONAL MEDICINE Congress of Students and Young Physicians

7th – 8th February 2019
Osijek, Croatia



„NEUROSCIENCE AND ITS CLINICAL ASPECTS"

University of Osijek
Faculty of Medicine

MF Student Council

OSCON

MF Josip Juraj Strossmayer University of Osijek Faculty of Medicine

1st INTERNATIONAL TRANSLATIONAL MEDICINE CONGRESS OF STUDENTS AND YOUNG PHYSCIANS

ABSTRACT BOOK

7th – 8th February 2019
Osijek, Croatia

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2.SCIENTIFIC COMMITTEE

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Mentor: prof. Marija Heffer MD, PhD

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Lucija Glavaš
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1st INTERNATIONAL TRANSLATIONAL MEDICINE CONGRESS OF STUDENTS AND YOUNG PHYSCIANS

GENERAL INFORMATION

Date: February 7th (Thu) – February 8th (Fri), 2019
Venue: University of Osijek, Faculty of Medicine, Josipa Huttlera 4

Main topic: „NEUROSCIENCE AND ITS CLINICAL ASPECTS"

Guest attendance policy: All registered participants are welcomed to all events and lectures. Wearing official conference badges is obligatory for entering any events.

Official language: English

Social media:

oscon_mefos

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WELCOME MESSAGE FROM THE PRESIDENT OF THE ORGANISING COMMITTEE

Dear colleagues and friends,

It is my great honour and privilege to welcome you in the name of Organising Committee of OSCON 2019. We are very proud to host you this year at the Faculty of Medicine Osijek.

This event has been organised for the first time, but that doesn't mean we haven't put effort into it. In fact, we did our best and tried to begin with this whole project as good as we could, and to make a path for next generations of students who will (hopefully) continue our work and make this event even more pleasurable.

The main motive for organising this kind of event, for the first time in Osijek, was to enable students from our University this kind of professional development in their city.

Last academic year was of great importance for the Faculty of Medicine Osijek. We celebrated 20 years of our Medical Faculty and this event is one of the many that have been held at our faculty in those years, but what makes this event so special? Well, we believe in constant personal and professional growth and OSCON gathers participants, lecturers, students, and speakers from different countries and with different experiences. Such event is an opportunity not only to present your valuable scientific researches, papers or ideas, but also to make new, international contacts, to meet friends, or to renew old acquaintances.

We decided to dedicate this congress to translational medicine because we were intrigued by this relatively new medical area. In my opinion, the future of medicine should hold a holistic approach and that is impossible without basic science and clinical cooperation. We should all strive to give our patients complete care, in the manner that best suits a patient's needs, and translational medicine is the branch of medicine which will help us to do so.

Is there a better way to start then with a nervous system itself? That is why this year's topic is "Neuroscience and its Clinical Aspects". We invited some of the most recognized experts in this field to present you their most recent discoveries.

I am sure that you will learn something new and lose your fears. I hope that you will enjoy this year's OSCON and that you will join us next year as well! We will try to improve as much as possible in order to provide you more each year at OSCON.

Best regards,

Luka Švitek
President of the Organising Committee

WELCOME MESSAGE FROM THE PRESIDENT OF THE SCIENTIFIC COMMITTEE

Dear Colleagues,

It is a great pleasure and honour to welcome you in the name of Scientific Committee of OSCON.

Organizing this kind of project and bringing it to a higher level was a demanding task for us. Our main theme is Translational Medicine which is based on a close collaboration between fundamental and clinical research for faster and more effective implementation of new discoveries in clinical practice.

We decided that "Neuroscience and its Clinical Aspects" is a perfect theme for this year's congress. It is one of the fastest growing areas of international research and the importance of integrating new knowledge in clinical practice is inevitable.

Considering this is our first year, Scientific Committee worked hard to put together a high-quality programme with the latest researches and to enable participants to learn directly from leading experts and young researchers in the field of Neuroscience and Neurology.

OSCON is a great opportunity to hear outstanding scholars and to exchange ideas and share experiences.

Our scientific program is designed to ensure that attendees gain a comprehensive understanding of the latest advances in order to improve their clinical skills.

Hopefully, throughout the years, our meetings will strengthen the relationship between basic and clinical sciences.

We are more than happy to welcome you to our faculty and we hope you will have a pleasant time.

We are looking forward to meeting you at the Congress.

Nora Pušeljić
Head of Scientific Committee of the Congress

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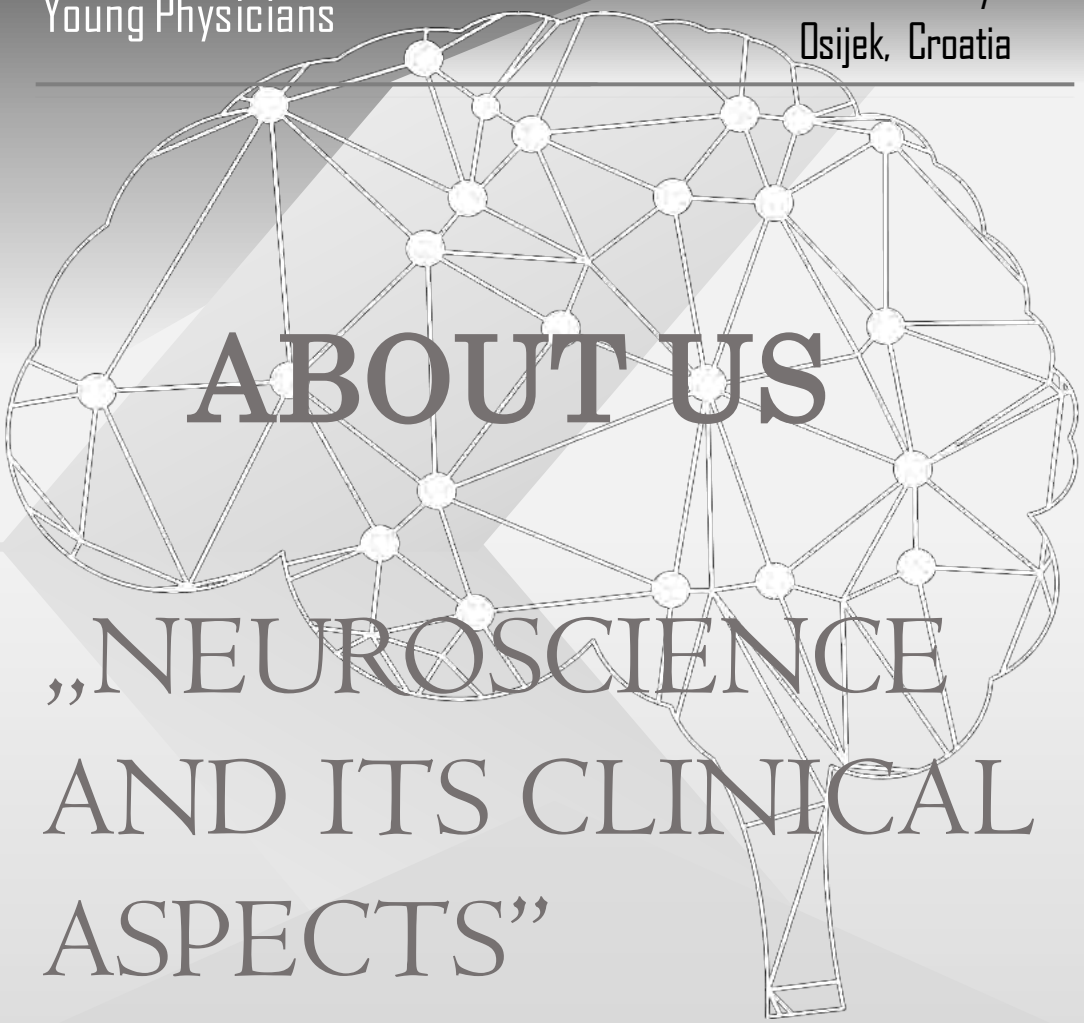

ABOUT US

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ABOUT FACULTY OF MEDICINE

The Faculty of Medicine of University of Osijek is the youngest medical faculty in Croatia. It was officially opened in 1968 as a branch of the School of Medicine in Zagreb, and in 2018 it celebrated 20 years as the independent medical faculty. The largest and main base of the faculty is the University Hospital Centre Osijek. The Faculty of Medicine in Osijek is the only medical faculty in Croatia that shares the same campus with its main teaching base, which is located within the University Hospital Centre complex.

Apart from a three-year undergraduate programme and two-year graduate study programmes (Biomedical-Laboratory Technologies) and a six-year long first degree study programme in Medicine, the Faculty of Medicine offers several postgraduate specialist study programmes and doctoral study programme. The aim is to provide students the highest level of knowledge and training adequate for the professions they are pursuing.

The Faculty of Medicine Osijek has defined main research areas and has been profiled by several interdisciplinary groups that link basic and clinical studies (translational medicine). We would also like to point out that, our two professors emeriti Antun Tucak and Savo Jovanović contributed to the faculty with their work and effort.

ABOUT UNIVERSITY OF OSIJEK

The Josip Juraj Strossmayer University of Osijek is a university located in Osijek, Croatia. It was founded in 1975 and it is organized in 12 faculties, 4 departments and one academy. University is a medium-size in comparison to other European Universities. University of Osijek has been developing into a modern European institution of higher education, and it is becoming a regional centre of knowledge, research and excellence. All efforts are directed towards the constant increase of teaching and studying quality. The University offers a high student standard concerning accommodation, learning facilities and other student services. The city of Osijek is known as the city of students.

ABOUT OSIJEK

Osijek is a modern Central European city with 17 city parks and gardens which make Osijek one of the greenest cities in Croatia. The City of Osijek is also famous for secession (a variation of art nouveau). The promenade along the Drava river is one of the longest walking trails in Croatia. Given the city of Osijek's long history, there's a variety of sights such as Tvrđa, a fortified part of the city from the 18th century.

Some of the most valuable examples of Baroque architecture in Croatia, such as the statue of Holy Trinity and General's-headquarters are located in Tvrđa and printed on 200 kuna bills. The tradition of higher education in Osijek exists since 1707 and today our university with its 17 faculties and departments is one of the most important scientific centres in Croatia. According to the latest official figures, University of Osijek has around 18 000 students enrolled in. Some of the notable people that lived in Osijek are two Nobel laureates in Chemistry. Lavoslav Ružička was awarded in 1939 and Vladimir Prelog in 1975. Both of them finished their secondary education in Osijek.

ABOUT CROATIA

Croatia is a Central European and Mediterranean country, bordering Slovenia in the west, Hungary in the north, Serbia in the east and Bosnia and Herzegovina in the south; the country also has a long maritime border with Italy in the Adriatic Sea. Croatia has an unusual shape (similar to a croissant) that is unlike any other country in the world, which is as a result of five centuries of expansion by the Ottoman (Turkish) empire towards Central Europe. It covers a land area of 56,691 square kilometres and has a population of about 4.29 million people.

The main population centres are Zagreb, the capital, Osijek in the northeast, the ports of Rijeka on the northern part of the coastline, and Split towards the south. Other well known towns include Dubrovnik, Makarska, Poreč, Rovinj, Opatija, Zadar and Šibenik.

On 25th June Croatia declared its independence from Yugoslavia and celebrated 27 years of independence in 2018 and, in that time, it has undergone many transitions – not least coping with the effects of the war in the early 1990s. It is a beautiful country and its unique scenery, culture, sights and beautiful coastline are certainly worth a visit. We've given you just a brief history of the country, but we hope you will experience it for yourself!

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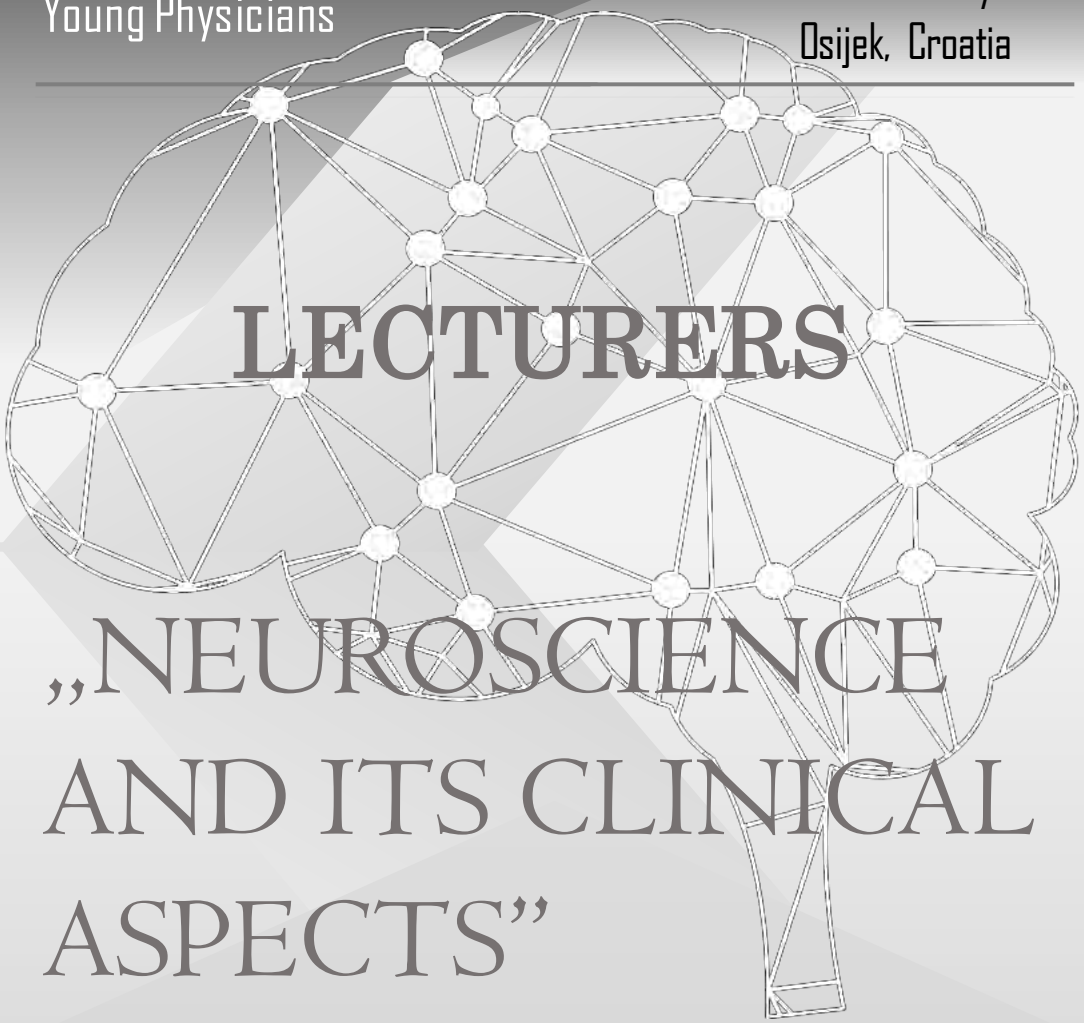

LECTURERS

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CLINICAL NEUROSCIENCE SESSION

Prof. Dunja Degmečić MD, PhD

Schizophrenia and creativity - using creativity in therapy

Prof. Degmečić is employed in KBC Osijek at the psychiatric clinic, as head of the Institute for Integrative Psychiatry and as an associate professor at the Faculty of Medicine of the University of Josip Juraj Strossmayer in Osijek. She is participating in conducting the course Psychiatry, and holds two elective courses in undergraduate and graduate medical studies, and subjects of Mental Health of Women at Postgraduate Study.

She has actively participated in numerous international and domestic congresses where she presented the results of her own research. In addition, one of her focus studies are music as a therapeutic option in psychiatry and the effect of music on the mind. By 2017, Degmečić is the author and co-author of many scientific and professional papers and two university textbooks of Hallucinations (2012) and Mental Health of Women (2014).

The book “Creative Mind”, published in 2017, as well as the previous two books, carries the status of a university textbook and is primarily intended for medical students or students of related disciplines. In chapter Psychopathology and Creativity, the author has devoted most of the lines, and if you want to hear more about the subject, please come to OSCON!

CLINICAL NEUROSCIENCE SESSION

Asst. Prof. Svetlana Tomić, MD,
PhD

Where Parkinson's disease starts - in brain or gut?

Svetlana Tomić graduated from School of Medicine, University of Zagreb in 1998 and received her PhD in 2011 at the Faculty of Medicine, University of J.J. Strossmayer Osijek. She worked as a resident at the Department of Neurology, University Hospital Centre Osijek from 2002 until 2006. Since then she has been working as a neurologist at the same department, specifically working in ambulance for movement disorders, EMNG lab and botulinum toxin ambulance. Regarding her scientific accomplishments, Tomić is serving as an honorary reviewer for Brain Disorders & Therapy and has took part in authoring several research articles and books about dysexecutive syndrome, Parkinson's disease, cefalexine and dystonic reaction. Moreover, she gained valuable experience in many drug clinical trials (mostly phase III) as sub-investigator for indications: multiple sclerosis, Parkinson's disease and Alzheimer's disease. In 2016 Tomić, MD has been appointed as the Head of department for neurodegenerative and neuromusculardiseases. With her broad clinical knowledge and expertise in movement disorders, neurodegenerative diseases and other neuropathologies, you are guaranteed to learn something new and clinically applicable.

TRANSLATIONAL NEUROSCIENCE SESSION

Prof. Marija Heffer MD, PhD

What have we learned from the Mouse Model of Hereditary Spastic Paraplegia?

Prof. Heffer graduated from School of Medicine, University of Zagreb in 1989 and did her postgraduate study in natural sciences. As a part of her scientific training, she studied biochemistry of glycolipids at The Institute for Zoology, Hohenheim University, Stuttgart and at The Institute for Cell Culture Technology, Technical Faculty, University of Bielefeld, Germany. Additionally, prof. Heffer was a guest scientist in the USA at Johns Hopkins School of Medicine and School of Medicine Yale.

Since 2005 she has been appointed as a professor of Cell biology and Neuroscience at Faculty of Medicine, Josip Juraj Strossmayer University of Osijek. Prof. Heffer is a neuroscientist with a very broad research area of interest, such as effects of stress on brain function, distribution of major gangliosides in various brain regions, roles of lipid rafts, dendritic morphology and spine density variations, genetic variations in circadian rhythm genes etc.

Regarding prof. Heffer's tremendous knowledge in many fields, such as biology, chemistry, neuroscience, genetics etc., we assure you that her lecture at OSCON will definitively be worth listening!

TRANSLATIONAL NEUROSCIENCE SESSION

Marta Balog, MSc in Biology

The connection of chronic stress to neurodegeneration

Studied Biology at Department of Biology, University of Osijek where she got bachelor (2008) and master´s degree in biology (2011). During her studies, she took the advantage of the Erasmus exchange program and did master thesis at the Department of Molecular Biosciences, University of Graz, Austria and a training program at the Department of Microbiology, University of Leuven, Belgium. At the moment, she is a PhD student of a Neuroscience program at the School of Medicine, University of Zagreb. Since October 2013 she has been working as a teaching assistant at Department of Medical Biology and Genetics, School of Medicine, University of Osijek. She is currently working at scientific projects ˝The role of gangliosides in the maturation and plasticity of the brain˝ and ˝The role of the stress on cardiovascular function in ovariectomized rats˝.

In 2014 she won the Bohdan Malaniak Cedars Sinai Medical Centre - RECOOP Young Scientist Travel Grant for participation in the Stress related scientific research in Szeged at the Department of Pharmacology under the supervision of prof. Robert Gaspar. In 2016, as a Secretary of Summer School on Stress Organizing Committee she was awarded Medal for Special Achievements of the University of California, Irvine for the excellent organization of the 4th Summer School on Stress, held in Osijek, Croatia.

TRANSLATIONAL NEUROSCIENCE SESSION

Prof. Svjetlana Kalanj-Bognar, MD, PhD

Neuroplastin: A new player in disorders related to memory and cognition

Prof. Svjetlana Kalanj Bognar, MD PhD, a neuroscientist currently appointed as head of Laboratory for Molecular Neurobiology and Neurochemistry at Croatian Institute for Brain Research, and associate editor of scientific journal Translational Neuroscience. Prof. Kalanj Bognar graduated from School of Medicine at the University of Zagreb, Croatia, in 1989, and was awarded a postgraduate doctoral degree in biomedical sciences at the same university in 1998.

Since 2007, prof. Kalanj Bognar was involved in organization and implementation of Doctoral Studies in Neuroscience at the Croatian Institute for Brain Research, and in 2009, she was appointed as associate professor in Biomedicine/Biochemistry and Neuroscience at the School of Medicine. Her research interests include the role of membrane lipids in neurodegeneration, particularly the involvement of sphingolipids in pathogenesis of neurodegenerative processes, and interplay of specific membrane lipids and proteins in synaptic membrane organization.

TRANSLATIONAL NEUROSCIENCE SESSION

The contribution of Western diet to neuropathology

Vedrana Ivić graduated from the Department of Biology and the Department of Chemistry of the J. J. Strossmayer University in Osijek in 2008.

Since 2009 she has been working as a research assistant at the Department of neurobiology at the Faculty of Medicine Osijek. In addition to taking part in the national and international projects of the Laboratory, she participates in the organization of the Department of Medical Biology and Genetics in Medicine, Medical and Laboratory Diagnostics, Dental Medicine and Dental Hygiene. She is also a participant in manifestations of popularization of science such as the Brain Week and the Festival of Science.

In 2010 she enrolled in the University Postgraduate Interdisciplinary Doctoral Study of Molecular Bioscience, the module of Biomedicine. That same year she received a scholarship from the National Science Foundation for six months stay and training at the Department of Neurobiology at the University of Yale Medical School. She is a member of Croatian Society for Neuroscience (HDN), Biology (HDB), Biochemistry and Molecular Biology (HDBMB), Human Genetics (HDHG) and Laboratory Animal Science (CroLASA).

PLENARY SESSION

Prof. Zdravko Petanjek MD, PhD

Neuroarcheology of psychopathology: normal structure but aberrant architecture of cortical network?

Prof. Petanjek graduated from School of Medicine, University of Zagreb in 1991, and was awarded with doctoral degree in biomedical sciences in 1998. His main fields of interests are neurobiology and neuroanatomy, especially development and reorganization of human prefrontal cortex and development of human visual cortex, a project in collaboration with renown neuroscientists such as I. Kostović and Paško Rakić. Moreover, prof. Petanjek is currently the leader of an incentive project for young researchers, called Distribution of associative neurons in human cerebral cortex, and a chief of Laboratory of Neuromorphometry at the Croatian Institute for Brain Research.

As a renown neuroscientist, prof. Petanjek specialized in vast spectrum of disciplines, such as neuroanatomy and neurohystology, neuronal organization of human cerebral cortex, developmental neurobiology and biological psychology, development of human prefrontal cortex and neurobiology of higher cognitive functions and diseases.

If you share our interest in professor Petanjek's work attend his lecture on the development of human cortex and its influences on neuropsychiatric disorders.

ePOSTER PRESENTATIONS

Bardak Ana → Aggression in Schizophrenia – patient case study

Berlančić Terezija → A case of a massive low-grade endometrial stromal sarcoma / Opinions on functional foods among students at the University of Osijek

Čorić Morena → First psychotic episode in perimenopausis

Dimitroska Angela → Tracking development of preeclampsia in 29th week of pregnancy

Földi Mária → Predictive nature and clinical characteristics of pain on admission in acute pancreatitis

Horvat Mario → The bilateral crural ischemic incident in a patient with Marfan's syndrome

Jirouš Maja → Gender and genetic variations as background of placebo analgesia

Jovičić Miloš → Second - language acquisition in adults is linked to changes in neural plasticity and brain structure

Jurić Ivana → Cerebral venous thrombosis as an uncommon cause of headache

Kiss Szabolcs → Predictive biomarkers of pancreatic necrosis in acute pancreatitis

Kurevija Tomislav → Investigation of biofilm production capacity of Pseudomonas aeruginosa clinical isolates

Laslo Dorian → Comorbidity of psychotic and somatic symptoms

Laslo Dorian → From depression to schizophrenia

Lekić Ivan → From tramadol side effects to pituitary macroadenoma

Listeš Ante → Pancoast tumor of right pulmonal lobe with Horner's syndrome: a case report

Lukács Luca → Phagocytic function of monocytes and neutrophil granulocytes before and after surgery in endometriosis

Marinčić Lovro → Neurologic manifestations as a first symptom of lung cancer Case report of the patient with metastatic NSCLC

Matijević Nikola → Socket preservation following tooth extraction using xenogenic bone graft and resorbable membrane: a case report

Olujić Marija → Macular degeneration of a young male patient – case report

Ostojić Luka → Treatment of buccal fenestration associated with periradicular lesion using biphasic calcium phosphate paste and native collagen membrane: a case report

Perić Luka → The transition from intrauterine to a different postnatal diet can affect inflammatory response and non-alcoholic fatty liver disease in male offspring rats

Popović Marina → Substitute therapy in a patient with panhypopituitarism in acute febrile illness with vomiting

Poznić Ema → Two rare monogenic hereditary diseases – Canavan disease and cmt1 neuropathy in one patient

Pušeljić Nika → Congenital hypotonia and epilepsy as main clinical signs of Wolf-Hirschhorn syndrome

Pušeljić Nora → Turner syndrome with haploinsufficiency in Xp22.3 and Xq28 microdeletion

Raguž Petra → Overgowth syndrom - Klippel-Trenaunay-Weber syndrome with cognitive impairment

Romić Dominik → Radiological findings of cerebral vasculitis with ischemic and hemorrhagic stroke associated with Parvovirus B19 in a young boy – case report

Rončević Alen → Review of Sex Differences in Stress Response and Risk of Alzheimer's Disease

Sekulić Antoneta → Herpes zoster in a patient with non-Hodgkin lymphoma: A case report

Stojačić Vlatka → The gut microbiome and multiple sclerosis

Švitek Luka → Ischemic cerebral infarction in the newborn – intrauterine thrombosis of the middle cerebral artery

Tejashwini Reddy Tekula → The prognostic role of neuropeptides proANP and NT pro-BNP levels in hypertensive patients

Tomin Monika → Ectopic pregnancy in a patient with primary infertility

Tóth Boglárka → The anatomy of the sensory and frontal cortico-thalamic pathways

Zubak Hrvoje → Endocrine function of adipose tissue in bone marrow effect structural changes in bone volume and trabecular separation in rats

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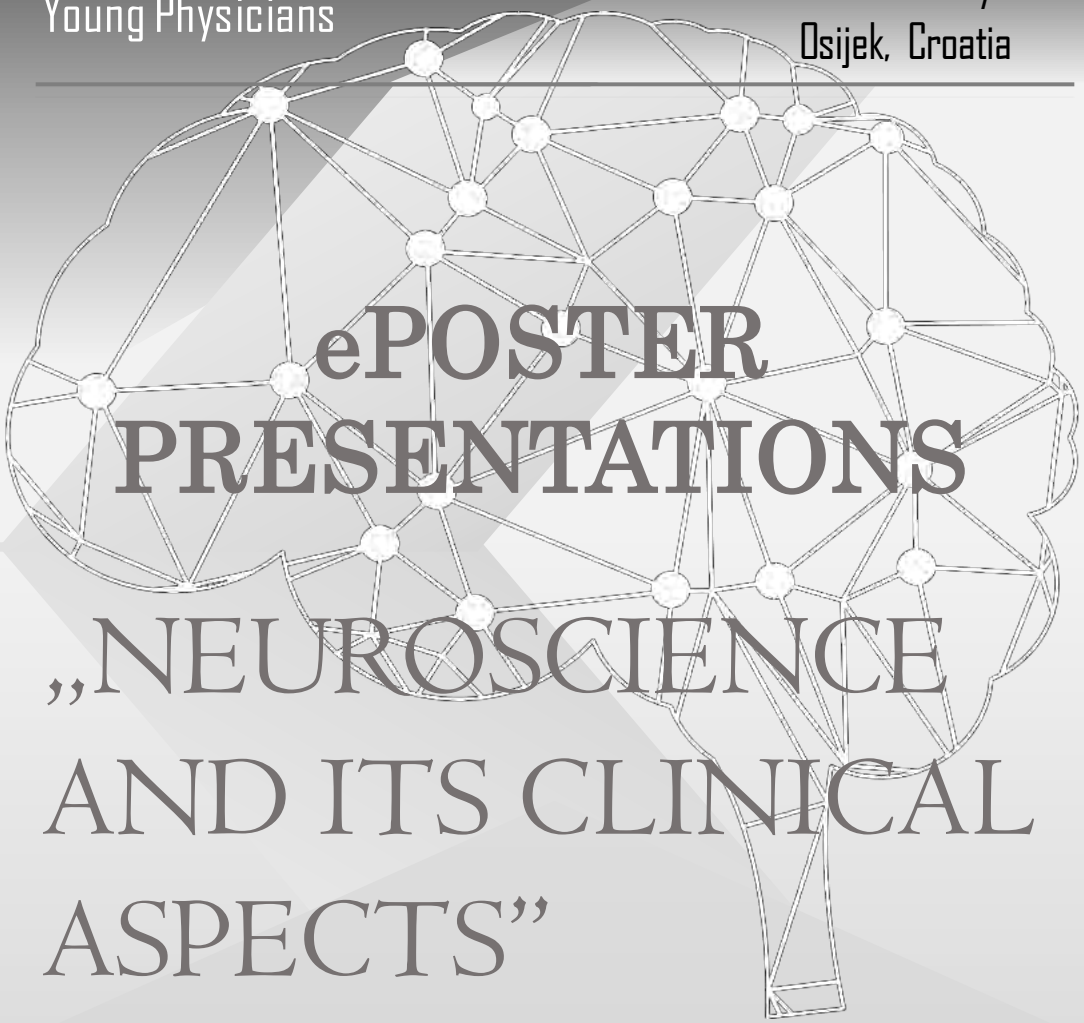

ePOSTER PRESENTATIONS

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Aggression in Schizophrenia – patient case study

Ana Bardak [1]*, Matija Ivančić[1]*, Dunja Degmečić[1,2]

1 - Faculty of Medicine Osijek, J. J. Strossmayer University of Osijek, Osijek, Croatia

2 - University Hospital Center Osijek, University Department of Psychiatry, Osijek, Croatia

* Equally contributing authors

Introduction: Paranoid schizophrenia or schizophrenia with paranoia is the most common example of schizophrenia.Clinical picture is dominated by relatively stable and often persecutory delusions that are usually accompanied by hallucinations, particularly auditory hallucinations. Paranoid schizophrenia is a lifelong, incurable disease, but with proper treatment with antipsychotics person with the illness can attain a higher quality of life.

Case report: Female patient (40) has been treated by a psychiatrist for several years due to an endogenous psychotic process. The patient has been treated under the paranoid schizophrenia diagnosis since 2006, and suffers from autoimmune thyroiditis. Grandfather and uncle had suffered from psychiatric disorders. The patient is divorced, mother of two, unemployed and living alone, and has a bad relationship with her mother, brother and the father of her children who is a drug addict. Delusions of persecution are present. The patient claims she isn't a paranoid schizophrenic and believes she is being followed and that her mother wants to hurt her. On multiple occasions the patient has been treated by a psychiatrist for violent incidents. The patient physically assaulted a shopkeeper and a waiter because, according to her, they were disrespectful towards her. In 2013, the patient tried to commit suicide but denies being suicidal at that moment. The patient is denying her diagnosis but is willing to be hospitalized for the welfare of her children. The patient has undergone treatment at University Hospital Center Osijek and St. Rafael Strmac for a longer period of time.

Conclusion: In this case report it is possible that patients autoimmune thyroiditis affected episodes of higher violence and temper. States like paranoid schizophrenia need to be recognized for the safety of patient and its family, because of many violent outbursts in this disease. Now, with depo therapy by antipsychotics, life quality and stability of this disease is much higher.

Keywords: Paranoid schizophrenia, female patient, autoimmune thyroiditis

A case of a massive low-grade endometrial stromal sarcoma

Terezija Berlančić[1,2], Monika Tomin[1], Zlatko Topolovec[1,3]

1 - Faculty of Medicine Osijek, J.J. Strossmayer University of Osijek Osijek, Croatia

2 - University Hospital Center Osijek, Osijek, Croatia

3 - University Hospital Center Osijek, Department of gynecology and obstetrics, Osijek, Croatia

Introduction: Low-grade endometrial stromal sarcomas (LGESS) are a type of uterine sarcomas which account for less than 0.2% of all uterine malignancies. It usually occurs in premenopausal women age 40-50. The tumor is formed in the endometrial connective tissue, which is between the endometrial cells, with its growth it breaks through the endometrial-myometric border and spreads directly into the muscular part of the uterus. It is usually diagnosed in the first clinical stage of the disease, while it is still limited to the uterus since at this early stage it is manifested by irregular bleeding. Surgical removal is the first-line therapy.

Case report: A 45-year-old patient was hospitalized on October 2018 at Clinic for OB/GYN, KBCO because of an expansive mass in abdomen and pelvis. Her gynecologic history included two full-term pregnancies (normal deliveries). In 2005 she underwent a laparoscopic cystectomy of left ovary, and her PAPA scan from 2012 was negative. Last menstruation cycle was 12 days prior. An enormous tumor filling the entire abdominal cavity from the bladder to the stomach and spleen in the patient did not cause any serious problems and was detected by accident at a regular systematic examination. The patient noted an increase in abdominal volume and attributed it to meteorism. There was no bleeding, although it is common in ESS. Therefore, these tumors are mainly diagnosed by fractionated abrasion. Tumor markers were nonspecifically elevated as a sign of mesothelioma stimulation and are not used in diagnosis of these tumors. The patient did not suffer from polycystic ovary syndrome, nor did she have any hormonal therapy. In this case, unexpectedly, the tumor spread out of the cervix, reached the gigantic scale and the total mass of 7.5 kg, without giving any symptoms. The tumor mass consisted of three separate tumors (15x13 cm, 11x9 cm and 24x17x8 cm) out of which one had a small part of bladder tissue connected to it (3,5x3 cm). Tumor tissue, endometrial origin, showed infiltrative growth in vascular and miometrial tissue and was proved with CD31 staining. Imunohistochemical profile of tumor showed that it was positive for CD10, actin-SMA, WT1, vimentine, and Ki-67 proliferation index was positive in 10% of nuclei in tumor epithelial cells. Pathohistological finding concluded that the tumor was a LGESS.

Conclusion: Such growth and propagation of ESS, according to available data, has so far not been recorded in medical literature. By the decision of oncological counseling, further adjuvant, systemic, hormonal therapy is envisaged in the patient. No residual tumor tissue was found on the first controls performed. Regular routine monitoring will be performed through the Genital Cancer Clinic and it is expected that surgical and hormonal treatment will be sufficient to control the disease

Key words: endometrial stromal sarcoma; immunohistochemistry; low grade; uterine sarcomas

First psychotic episode in perimenopausis

Morena Čorić[1]; Lucija Kljaić[1]; Tatjana Bačun[1,2]; Dunja Degmečić[1,3]

1 - Faculty of Medicine Osijek, J. J. Strossmayer University of Osijek, Osijek, Croatia

2 - Clinical Hospital Centre Osijek, Department of Internal Medicine, Osijek, Croatia

3 - Clinical Hospital Centre Osijek, Department of Psychiatry, Osijek, Croatia

Introduction: At age 40 to 50 years, the menstrual cycle usually becomes irregular, and ovulation often fails to occur. The period during which the cycle ceases and the female sex hormones diminish to almost none is called menopause. The estrogen protection hypothesis says that estrogen has a protective effect in women who are vulnerable to developing mental illness. Perimenopause may lead to an enhanced risk of the first onset of psychoses.

Case report: A 50-year-old woman was admitted to the emergency department after presenting with paranoid interpretations towards her husband, hallucinations and bizarre behavior like talking on foreign language. On admission, her physical examination revealed no abnormalities. Hematologic and biochemical profiles including renal function tests and urine examination were all within normal ranges. EEG showed moderately dysrhythmic irritation. CT scan showed no irregularities. In this patient also premenstrual exacerbation of psychopathological symptoms was observed. Psychological testing has also been done. The treatment has been psychopharmacological paired with sociotherapy.

Conclusion: Authors conclude that in clinical practice it is important to use biopsychosocial approach. In women patients in their reproductive years, it is important to have in mind hormonal background as well as somatic and psychiatric symptoms to choose an adequate therapeutic approach.

Tracking development of preeclampsia in 29th week of pregnancy

Angela Dimitrioska[1]; Kristina Štajdohar[2] ; Mirta Kadivnik[3]

1 - Faculty of Medicine, University of Goce Delčev Štip

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Introduction: Preeclampsia (PE) is a most frequently encountered renal complication of pregnancy and it is characterized by hypertension, proteinuria, and edema, usually by the last trimester of pregnancy. The rate of incidence varies upon the study population but generally ranges from 3% to 7% of all pregnancies. It occurs mainly in the women in their first pregnancies or to those who carry twins. PE when remains untreated, it moves towards more serious condition known as eclampsia and is still one of the leading causes of maternal and neonatal mortality. Hypoperfusion and ischemic conditions evidently show the abnormal placenta. PE is known to be originated from disordered vascular development of the placenta which further widely spreads anti-angiogenic factors into the maternal circulation and causes a systemic endothelial cell dysfunction and microangiopathy. Upon kidneys, these endothelial damages result in glomerular endotheliosis and proteinuria in which the endothelial cells of the glomerulus swell and endothelial fenestrations are lost.

Case report: This case describes a 30-year old female patient, who is in the 29th week of pregnancy. It is her first pregnancy. Patient denies other comorbidities, and in her family medical history, her father had lung cancer. Within the 23rd week of pregnancy patient was diagnosed with preeclampsia, and as a result, prescribed 4x250mg Methyldopa. In the 29th week of pregnancy, the patient was admitted to the intensive care unit because of hypertension (150/100 mmHg). Patient denies a headache, dizziness, blurred vision, pain, hemorrhage, leakage of the amniotic fluid. However, the patient was vomiting once a day, for a couple of days. Movements of the fetus are regular. Also, ECG of the patient is in sinus rhythm, with a frequency of 68 bpm. On admission, albumin was 31,8 g/L, total protein – 58,6 g/L, urea – 5,7 mmol/L, creatinine – 85 μmol/L. Patient's condition got worse, and as a result, she was prescribed 4x500mg Methyldopa and Nifecard. It would be advisable to wait for the delivery until the 30th week of pregnancy, so the development of the baby would not be disturbed. Nevertheless, if the patient's condition continues to be unstable, preterm delivery will be necessary.

Conclusion: Preeclampsia is a systemic disorder characterized by maternal endothelial dysfunction. Adequate screening, monitoring, and routine check-up during and after pregnancy may prevent worsening the maternal and fetus condition. This review summarizes the systemic endothelial dysfunction, risk factors, pathogenesis, pathophysiology and renal effects of PE.

Keywords: preeclampsia, hypertension, pregnancy

Predictive nature and clinical characteristics of pain on admission in acute pancreatitis

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Introduction: Pain is a very common symptom in acute pancreatitis (AP), therefore, understanding its characteristics and predictive role is important. Until now, the detailed characteristics have not been investigated.

Materials and methods: The Hungarian Pancreatic Study Group (HPSG) has prospectively collected multicenter clinical data of 1435 adult patients between 2012 and 2017. The specific pain questionnaire contained data in four categories: intensity (visual analog scale; 1–10, mild (mildP): 1–3, moderate (modP): 4–6, severe (sevP): 7–10), duration of pain prior to admission (hours), localization (upper, middle, and lower abdomen), and type (sharp, dull, or cramping). These data were compared with parameters on admission and with the outcome of AP. Statistical analyses were performed accordingly.

Results: Most of the patients had severe abdominal pain (sevP: 70.29%). The intensity of pain was associated with the severity of AP (mildP: 0% severe AP, modP: 2.81%, sevP: 4.50%; $p<0.01$), higher white blood cell count, elevated lipase and amylase levels, but not with CRP level. Duration of pain was not associated with mortality and severity; however, it markedly influenced the laboratory parameters on admission. Amylase and lipase, RBC, and hemoglobin levels were decreasing, whereas the amount of CRP and thrombocyte was increasing. Localization of pain was not associated with the above-mentioned parameters. Sharp pain was associated with higher mortality, severity, and systemic complication rate vs the other types of pain.

Conclusion: More intensive and sharp pain is associated with worse clinical outcome; therefore, its role should be investigated in clinical trials. The duration of pain prior to admission strongly influences the laboratory parameters on admission. Pain is associated with wide-range of clinical parameters; therefore, it should be incorporated into the scoring systems of AP.

Keywords: pancreatitis, pain

The bilateral crural ischemic incident in a patient with Marfan's syndrome

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Introduction: Marfan's syndrome is a rare hereditary disease caused by mutation of FBN-1 gene which is a gene for fibrillin I. This disorder can cause many anomalies in development of eyes, bones, blood vessels, and connective tissue. Anomalies like dissection of the aorta are common, and they mostly required to be treated urgently.

Case report: This case describes a 31-year-old male patient with the history of an aortic aneurysm treated surgically with surgical procedure according to Tyron-Davis, diagnosed with dissection of the aorta, classified as DeBakey type III dissection, and ischemia of distal parts in both legs. The patient also has severe aortal regurgitation and planned surgery for replacement of the aortal valve. 8 hours before arriving in the Emergency Room (ER), he felt tickling and pain in both legs. He wasn't able to walk and denied any chest pain. Angio-CT of the aorta showed dissection and aneurysmatic dilatation 92 mm in length and 44 mm in width, and the double kinking of infrarenal part of the abdominal aorta, mostly filled with thrombotic masses. Obstruction of the descending aorta caused reduced blood-flow distally, which results with ischemia of both. When arrived in ICU he was awake, communicative, spontaneously sufficiently breathing, SaO_2 100%, RR 170/60 mmHg. He was feeling pain in both legs that were cold and immobile. The therapy was analgesics, sedatives, and antihypertensives. 1 hour after arriving in ER the surgery was performed, and the patient received 3 L of crystalloids and 1 DE. Diuresis was 300 mL and all organs seemed vital during surgery. When arrived in ICU after the surgery, he was hemodynamically stable, spontaneously breathing, awake and communicative, without neurological disorders. His feet were warming up and puls at a. dorsalis pedis was palpable. Blood pressure was controlled with labetalol. Blood image (BI) was normal, with myoglobin at 5742 mg/L and troponin I at 0,123 μg/L. Next day, in the morning, the patient was still unable to move toes, but they had normal color and sensibility. BI was normal, and levels of troponin and myoglobin were decreasing. He was able to move his toes in the evening. The 2nd day, a patient was breathing normally, eucardic, but diuresis was controlled with furosemide (4330mL/d).

Conclusion: Marfan's syndrome is a hereditary disorder, which results with both, severe and mild complications. In this case, an urgent reaction was required to prevent rupture of the aorta and death of the patient, and the preservation of lower extremities. It is important to acknowledge and treat every patient with Marfan's syndrome with caution because of the risk of many deadly complications.

Keywords: Marfan's syndrome, dissection, DeBakey, FBN-1, aneurysm, ischemic

Gender and genetic variations as background of placebo analgesia

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Introduction: The placebo analgesia has been one of the most extensively studied placebo effects since the 19th century. The anegdotal placebo analgesia effect noted in World War II, when saline infusion given to soldiers induced the same pain-relief effect as morphine, triggered further research. Intriguing question is why placebo induces positive response among some people, while for the others it doesn't stimulate any changes or even stimulate negative response - nocebo. Even more fascinating is how gender differences affect the pain response. In the last few decades scientists have conducted brain imaging and genetic studies to uncover the cause of sex-related differences in placebo analgesia. They found that genes and hormones, as well as psychological factors influence pain response.

Materials and Methods: A systematic search strategy was used to identify relevant studies across the online database. Materials are recent findings in MeSH database on PubMed in the field of neurobiology, neuroendocrinology and neurogastroenterology of placebo analgesia response in visceral pain depending on sex and genetic variations.

Results: The placebo interventions effectively reduce pain, both in healthy women and men, but with various mechanisms of responses to pain. The pain is modulated by μ- and κ-opioid, monoamine, GABA and D3/D5 receptors. It was shown that men had higher activation of μ-opioid receptors than women in the thalamus, amygdala and ventral basal ganglia, while women had lower activity in the nucleus accumbens. Estrogens and progesterone seem to be crucial in determining the efficacy of women endogenous inhibitory controls, while women's testosterone levels are positively correlated with the activation of structures implicated in descending inhibitory pathways, such as the rostral ventromedial medulla. The prevailing outcome of sexual hormones and variably receptor distribution are the reason why placebo analgesia in men is more noticeable. Studies about visceral placebo analgesia in IBS patients, in comparison with healthy controls, revealed higher activation in pain-matrix, which includes cingulated cortex, insula, somatosensory cortex and prefrontal cortex. It was also shown that woman and man had comparable results in placebo analgesia in visceral pain, but women have weaker response in descending pain inhibitory mechanism, which involves the insula and dorsolateral prefrontal cortex. Recently, genetic polymorphism screening pointed toward *COMT*, *MAO-A*, *BDNF* and *OPRM1* genes as another reason behind variability in placebo response.

Conclusion: With precise knowledge of all the mechanisms involved in placebo effect, we might discern placebo responders from non-responders, personalize treatments and more efficiently distinguish drug effects from placebo effects.

Keywords: placebo, placebo analgesia, sex hormones, visceral pain

Second - language acquisition in adults is linked to changes in neural plasticity and brain structure

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Introduction: Second - language acquisition has been a burning topic in the science community over the last few decades. Many researchers have attempted to decipher in which way a second language is coded in the brain, as opposed to the mother tongue, carefully considering the changes in neural plasticity and brain structure in the process.

Materials and methods: Using fMRI and DTI during the process of language acquisition, several changes in neural pathways were recorded in the participants. Those with higher language proficiency had stronger connections between the right inferior longitudinal fascicle, right arcuate fascicle, forceps minor of the corpus callosum and the cingulum. Participants with earlier ages of acquisition experienced changes in the left ILF, left arcuate fascicle and stronger connections to the superior temporal gyrus. This suggests the age of acquisition (AoA) and language proficiency as important factors in language learning. Additionally, cortical thickness was measured in monolinguals and bilinguals, revealing greater thickness of the left frontal gyrus in participants who had learned the second language at a later period. Finally, the importance of the left inferior parietal lobule has been noted, having a role in sound mapping, phonological memory and semantics, as well as sentence formation.

Results: These findings point towards changes in neural plasticity as a method of auditory mapping in the cortex. A significant difference has been noted between age-induced plasticity in children, as opposed to experience-induced one in adults. The manner in which the language is acquired has been shown to affect the quantity and quality of neurological changes. For example, the importance of semantic representation in the process of acquiring the phonological code has been demonstrated to improve the performance of the participants. Furthermore, it has been shown that immersive learning had a much greater advantage over the commonly practiced classroom learning. Lastly, a variety of subjective factors have been considered, such as the participants' attention, motivation, environment, and cognitive aging.

Conclusion: Considering these findings, it is clear that the process of second - language acquisition is controlled by a multitude of variables, many of which may be manipulated with the purpose of improving the quality of language learning.

Keywords: language, cortex, plasticity

Cerebral venous thrombosis as an uncommon cause of headache

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Introduction: Cerebral venous thrombosis (CVT) is a rare condition that can present with a variety of symptoms. The incidence of CVT is around 1–1.5/100 000/year. Mortality in untreated cases has been reported from 13.8-48%. Full recovery has 25–30% of patients. It is three times more frequent in a female in reproductive age than in men, especially in those who are pregnant and using oral contraceptives. Established risk factors are thrombophilia, hypercoagulable states, medications, inflammatory bowel disease and collagen vascular disease. Clinical signs can be nonspecific. The most common symptom is a headache with or without other neurological symptoms. Diagnosis is based on clinical findings, neuroimaging (CT, CT venography, MRI and MRV) and laboratory findings. Specific therapy for CVT is based on anticoagulation and symptomatic therapy to prevent complications and death. Prognosis is unpredictable and highly variable and total mortality is around 10%.

Case report: We present a case of CVT in a 32-year-old otherwise healthy woman, currently on the oral contraceptive with complaints of severe right hemicrania for two weeks. Initially, the headache wasn't followed by other symptoms. She went to a primary doctor and got analgesics. The pain was improved from 10/10 severity to 3/10. After two weeks she came to ED with symptoms of worsening headache and fever. Laboratory findings showed mildly elevated CRP and lumbar puncture excluded acute inflammation in CNS. Then she started with focal aware seizures with sensory onset. Physical exam was normal. CT of the head was negative. EEG showed dysrhythmia in the right posterior areas. Laboratory studies showed elevated D-dimers. MRI and MRV were ordered to exclude CVT. MRV confirmed thrombosis of superior sagittal, right transverse and sigmoid sinus and part of the right jugular vein. The patient was placed on LMWH, analgesics, antibiotics and anticonvulsants. Few days after the patient was improved, the headache was 1/10, there was no epileptic seizures and no fever. Laboratory findings discovered gene mutation for PAI-1 (4G/5G), MTHFR (C 677 T mutation), Prothrombin (G20210 A mutation) and Factor V Leiden (G 1691 A mutation). A follow–up MRV three weeks after showed the resorptive dynamic of CVT. The patient was discharged on anticoagulation therapy (warfarin) without neurological deficit. MRI and MRV three months later showed almost total resorption and improved flow of cerebral venous sinuses.

Conclusion: CVT is a rare, but serious condition with a wide spectrum of clinical signs and because of that it can be often underdiagnosed. CVT should be suspected in patients with a headache, other neurological deficits or seizures and with established risk factors. Delay in diagnosis can lead to death.

Keywords: headache, cerebral venous thrombosis

Predictive biomarkers of pancreatic necrosis in acute pancreatitis

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Introduction: Necrosis is one of the major local complications in acute pancreatitis which significantly worsens its outcome. Therefore, understanding pancreatic necrosis and its early prediction is crucially important. The aim of this study was to evaluate clinical characteristics of acute necrotising pancreatitis (ANP) and to identify risk factors for necrosis.

Methods: The Hungarian Pancreatic Study Group has prospectively collected multicentre clinical data of 1435 adult patients between 2012 and 2017. Concerning pancreatic necrosis, 1429 of them provided valuable data, therefore, they were enrolled into the study. 24 parameters were assessed on admission and during the course. Patients were divided into two groups: acute pancreatitis with (ANP) and without necrosis (AP). Statistical analyses were performed accordingly.

Results: 9.31% (n=133) of the patients had ANP. ANP was associated with significantly higher mortality [8.27%, vs 1.93%, (p<0 .0001)], severity (mild/moderate/severe: 0.00% vs 75.69%, 73.68% vs 20.91%, 26.32% vs 3.40%), longer hospitalization [22.95 days vs 10.18 days, (p<0 .0001)], and higher rate of local (pseudocyst, diabetes) and systemic (renal, heart, and respiratory failure) complications. Elevated levels of CRP (100.41 IU/L vs 54.84 IU/L, p=0.029), triglyceride (11.76 mmol/L vs 4.79 mmol/L, p=0.003), cholesterol (8.16 mmol/L vs 5.76 mmol/L, p<0.001) haematocrit (43.59% vs 41.52%, p<0 .001), haemoglobin (150.63 g/L vs 143.38 g/L, p=0.006), glucose (9.72 mmol/L vs 8.14 mmol/L, p<0.001) and white blood cell count (14.68 G/L vs 12.93 G/L, p=0 .001) were associated with ANP. Lower level of albumin (32.55 g/L vs 38.07 g/L, p<0.001) and calcium (2.04 mmol/L vs 2.41 mmol/L, p=0.001) was associated with ANP.

Conclusion: Concerning the parameters measured on admission, several risk factors were identified. Pancreatic necrosis markedly influences the outcome of acute pancreatitis. Increased CRP, triglyceride, cholesterol, haematocrit, haemoglobin, glucose, and white blood cell count and decreased albumin and calcium level are good predictive markers for acute necrotising pancreatitis.

Keywords: pancreas, pancreatitis, necrosis, biomarker

Investigation of biofilm production capacity of Pseudomonas aeruginosa clinical isolates

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Introduction: Production of biofilm is one of the significant bacteria virulence factors that makes it an attractive topic for numerous researches. A plenty of bacterial infections are becoming a serious health problem in chronic infections and implants due to biofilm production. Biofilm is a multicellular structure that protects bacteria from adverse impacts of environment and makes them very resistant to various antibiotics. The aim of this research was to examine the biofilm production capacity of Pseudomonas aeruginosa clinical isolates using Luria-Bertani and Meuller-Hinton broth.

Material and methods: We used 30 strains of P. aeruginosa that we received from clinical samples. After preparing the suspensions of bacteria inoculated on broths, we set them on microtiter plates. Then we measured the biofilm production using the spectrophotometric reader on 550 nm. Obtained results, based on the comparison of optical density of samples and negative control, were classified into four categories: non-producers, low producers, medium and high producers.

Results: Data are presented as the average of triplicate measurement of optical density and includes medians and interquartile ranges for each variable used. It has been found that tested P. aeruginosa strains, successfully and statistically significant, created biofilm both in Luria-Bertani and Mueller-Hinton cultivation media ($p<0.01$, Wilcoxon's Equivalent Pair Test). Nevertheless, there was no statistically significant difference between the biofilm production capacity of isolates regarding in vitro conditions.

Conclusion: On both broths, tested isolates of P. aeruginosa showed a large capacity to produce biofilm, which certainly contributes to their virulence and pathogenicity. This investigation, with a lot of other researches leads to a better understanding of these bacteria in vivo characteristics to cause infections related to biofilm.

Keywords: biofilm, Psudomonas aeruginosa, virulence

Comorbidity of psychotic and somatic symptoms

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Introduction: Acute and transient psychotic disorders are characterised by shorter and transitory psychotic episodes caused by stressful event or traumatic experience. Incoherent speaking and hallucinations could be part of disorder. By the term of stressful event and traumatic experience it is common to think about social stress or trauma. But it is also possible that this type of disorders can be caused by somatic changes such as anaemia, endocrine dysfunction, structural or/and functional brain changes or other somatic changes or dysfunctions.

Case report: We present the case of a 36-year old female patient with psychotic symptoms. The patient came to the psychiatry and expressed paranoid thoughts about her family. There is no known psychiatric heredity in her family. For the last few months before hospitalisation she had sleep problems, loose of appetite and she was oversensitive. The patient reported her parents to the police, claiming that they have abusing her by interfering with her college education. She is student since the year 2000. First she was examined at the emergency psychiatric ambulance and stayed one night in the hospital, but next day she was admitted again to the hospital because of her paranoid and bizarre behaviour (She run into the cafe and said to the waiter that her father wants to rape her). She was hospitalised for two weeks and clinical examinations and tests were performed. CT scan of the head shown calcification in anterior part of falx cerebri. There were no changes in anatomical structures of the brain. The blood test showed very high level of anti-TPO and TSH but low levels of Hb, Htc, MCV, MCH, and Fe. The blood test result is suspect for microcytic and sideropenic anaemia. Ultrasound of thyroid gland shown normal right lobe (RL), but heterogeneous left lobe (LL) filled with nodes. Biopsy sample of nodes from LL was microscopically examined and the result revealed lymphocytic thyroiditis. The conclusion of psychological tests was that the patient is currently psychotic from schizoaffective spectrum (schizoaffective/schizophrenic) with social difficulties, but primary probably average person with signs of cognitive deficit. According to all tests and psychiatric examination the patient's psychiatric condition could be caused by somatic conditions. The patient is diagnosed as acute and transient psychotic disorders unspecified. The pharmacological treatment includes antipsychotics, iron substitutes and anticholinergic medication and replacement of thyroid hormones. The patient is stabilised and can be released for out-treatment.

Conclusion: Shorter psychotic episodes are common sign of acute and transient psychotic disorders. They are usually induced by trauma or stress. It is possible that family problems and colleague difficulties are stress to the patient. On the other hand it is also possible that anaemia and other somatic disorders caused subacute stress to the organism and induced psychotic episodes. We would like to emphasize that both, social problems and somatic disorders, are stress events and both can induce psychotic episodes.

Keywords: psychotic disorders, paranoid behaviour, anaemia, iron-deficiency

From depression to schizophrenia

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Introduction: Schizophrenia is characterised with four groups of symptoms: positive, negative, aggressive and cognitive. Usual positive symptoms are hallucinations, delusions, thought disorder and negative are social withdrawal, motivation loss and self-neglect. Prevalence of schizophrenia in the general population is about 1% and affects equally both sexes.

Case report: We present the case of a 50-year old female patient with symptoms of schizophrenia. The patient is in marriage, mother of two children and lives with the family. There is no known psychiatric heredity in the family. The patient is in long-time psychiatric treatment. She has been hospitalised for the first time in the year 2008 with symptoms of depressive mood disorder and the patient is in psychiatric treatment since then. Before last (fourth) hospitalisation she didn't use pharmacotherapy and her condition got worse. She heard the imperatively characterised voice (imperative hallucinations) which ordered her to hurt herself. She becomes suicidal and overdosed herself by taking too much medication. When the patient was admitted to the hospital she was conscious, well orientated, anxious and contactable, in that time she was neither suicidal nor aggressive and she accepted hospitalisation. This is not the first time that she heard the voice. For the first time when she had hallucinatory experience the voice ordered her to kill herself by cutting blood vessels on the neck (in the year 2008.). During the last (fourth) hospitalisation EEG, blood and urine tests were processed. Pharmacotherapy included risperidon, promazin and alprazolam. EEG result was normal, although the patient did not proceed to photostimulation test. Urine and blood tests were normal, only non-specific LDL cholesterol was increased (LDL_C 5.17 mmol/l). Paliperidone depo was introduced in pharmacotherapy which is continued.

Conclusion: The patient presented negative and positive symptoms (auditory hallucinations are still present). Despite of it, she is not suicidal. The pharmacological treatment is continued and the patient's condition gets better. By taking paliperidone depo and returning the patient in family surroundings improvement of her condition is expected.

Keywords: hallucinations, schizophrenia, antipsychotic agents

From tramadol side effects to pituitary macroadenoma

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Introduction: Tramadol is an opioid analgesic drug used in treating medium to moderately severe pain and has a reduced risk of developing addiction in chronic use. Very common side effects (> 1 out of 10) are nausea, fatigue and drowsiness, while frequent side effects (1-10 in 100) are vomiting, headache, stiffness, dry mouth, sweating and mood swings. The pituitary tumors represent 10% of the central nervous system tumors and are most often dysfunctional. These are mostly adenomas. Due to their size, can exert pressure on healthy pituitary tissue and cause hypopituitarism as well as surrounding structures that can cause vision disorders, appearance of field vision and headache. If cancerous apoplexy occurs, headaches, nausea, fatigue and disorientation can suddenly occur.

Case report: Patient is a 72-year-old male with type 2 diabetes, arterial hypertension, angina pectoris, and vitamin B12 deficiency and that had previously suffered a left knee injury and is therefore occasionally receiving nonsteroidal anti-rheumatics. The day before admission he took a tramadol / paracetamol tablet for planned housework. After a few hours there was general weakness, nausea and headaches, which led to the drug taking. After physical effort, headaches were amplified, he felt weakness, fatigue, vomited several times, and was referred to an internist emergency room. The clinical finding was normal. Since more than 12 hours had past after the drug had been taken, the patients symphtoms remain the same, a neurologist was instructed. Patient noticed loss of eye sight on right eye. An urgent head CT scan was performed, showing hyper-dense tumor formation of 31x20x22 mm, caudally inserted into the sphenoid sinus, cranial to the hypothalamus area, suppressing optical chiasma and partially expanding into the left cavernous sinus, which is pointing to the pituitary adenoma or meningioma. During the endocrinologic examination the patient was adynamic, pale skin and with visible mucous membranes, scarce hairiness, hypotensive and was subfebrile. An urgent MR scan of pituitary gland was performed, patient was diagnosed with pituitary macroadenoma. In emergency laboratory findings there was a decrease in cortisol values (58.6 nmol / l) with a normal value of fT4 and TSH. The next day, in regular findings there were lower values of LH and testosterone with ACTH below normal, indicating secondary hypochorticism and hypogonadism. Patient received the replenishment of hydrocortisone 100 mg four times and adequate hydration, with a gradual dose reduction. Patient was moved to a neurosurgery clinic where he was successfully operated where surgery confirmed the diagnosis of pituitary macroadenoma.

Conclusion: When the patient is treated with tramadol or similar opioid drug in which there are assumptions of side effects, and if they are not receding within the time needed for drugs elimination it needs to be examined for other causes including pituitary adenoma or possible adenoma apoplexy.

Keywords: tramadol, headache, nonfunctioning pituitary adenoma, hypopituitarism, pituitary apoplexy

Pancoast tumor of right pulmonal lobe with Horner's syndrome: a case report

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Introduction: Pancoast tumor representns a tumor of upper pulmonal lobule, and can be characterized by arm and shoulder pain and weakness and ipsilateral Horner syndrome. Horner syndrome is a constellation of neurological findings consisting of ipsilateral ptosis, miosis, and anhidrosis. The rarity and overall poor prognosis of patients with Pancoast tumor has led to few reports detailing pain management strategies with adjunctive therapies.

Case report: This case describes a 48-year old male patient S.B. presenting in Emergency Room with pain in the right shoulder, arm, third to fifth finger of right hand and right hemithorax. He is a smoker, and has mild ptosis of his right upper eyelid from childhood that got worsen in the last two months. During neurogical examination it was discovered that our patient has miosis and ptosis on his right eye that are crucial signs of Horner's syndrome. Also, examination showed weakened muscular strength of right arm. Brain CT and blood tests were normal, while on thorax CT solid mass, 24 in length and 16 mm in width, in upper right pulmonal lobe, was discovered. Mediastinal lymph nodes were swollen in diameter of 16 mm long. Patient was sent to oncologist who diagnosed neoplasma of right apical lobe (Pancoast). Pancoast tumor does pressure on plexus brachialis and sympathetic ganglions that results in neurogical outbreaks such as ptosis, miosis, pain and weakness in his upper limb. Tumor didn't react well to chemotherapy and radiation so S.B. was sent to lobectomy of right superior pulmonal lobe and lymphadenectomia of mediastinal lymph nodes. After his first operation, he developed haematothorax as a postoperative complication. After two operations and regression of haematothorax patient was sent home with therapy that included antibiotics and analgetics. Three months after operation, three new patological formations (one on his right lung, and two on his left lung) were discovered. Oncology counseling decided to do genetic tests on EGFR and ALK, and further therapeutic options are in consideration.

Conclusion: In this case development of Pancoast tumor made pressure on sympathetic ganglions and brachial plexus. As an outcome, patient developed signs of Horner's syndrome, and other neurogical outbreaks such as pain and weakness of his right upper limb and pain in right side of thorax. Because of this non-specific symptoms several months have passed from onset of symptoms to diagnosis. We wanted to emphasize siginficane of neurological exam and adequate radiological tests in obtaining the right diagnosis.

Keywords: Pancoast tumor, Horner's syndrome, ptosis, chemotherapy, Emergency Room

Phagocytic function of monocytes and neutrophil granulocytes before and after surgery in endometriosis

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Introduction: Endometriosis is estimated to affect 10-15% of reproductive-aged women and it's also one of the leading cause of infertility worldwide. The symptoms are significantly worsening the quality of life in the affected population. Pathophysiology of endometriosis is still unclear but immunological disorders became conspicuous recently. Although adaptive immune system is in the focus of research, only few data are available about innate immune system. For this reason, we examined phagocytic function of peripheral leukocytes. Our aim was to investigate whether the phagocytic activity of monocytes and neutrophil granulocytes are affected by the presence and/or removal of the endometriotic lesions.

Material and Methods: We examined peripheral blood samples from patients with endometriosis on the day before surgery (n=26) and on the 7th postoperative day (n=13). We also investigated pre- and postoperative samples (n=14-14) from surgical control group and samples from healthy women (n=23). After separation of monocytes and neutrophil granulocytes, the cells were incubated with opsonized fluorescein isothio-cyanate-labeled zymosan A particles as a target of phagocytosis. We calculated the phagocytic index by using fluorescence microscope. Analysis of variances method was used as statistical analysis.

Results: Preoperative phagocytic indexes of both monocytes and granulocytes derived from patients with endometriosis were significantly lower than phagocytic indexes of these cells from healthy women. Phagocytic function of leukocytes from postoperative patients' samples increased significantly compared to preoperative values and did not differ from the phagocytic indexes of leukocytes from healthy women. In the surgical control group there were no significant difference between preoperative and postoperative values.

Conclusion: Based on our results we assume that endometrial lesions and/or their microenvironment may produce factors which depress the phagocytic function of monocytes and granulocytes. Since postoperative phagocytic index of patients with endometriosis increased significantly we assume that these factors were reduced or eliminated after removal of the lesions. Considering the results of the surgical control group, the surgical intervention has no influence on phagocytic function.

Neurologic manifestations as a first symptom of lung cancer Case report of the patient with metastatic NSCLC

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Introduction: Non–small cell lung carcinoma (NSCLC) is the leading cause of cancer-related death in the world(1).Neurologic manifestations in lung cancers are common and caused by local tumor invasion (16%), metastasis (23%) or paraneoplastic syndromes (PNS) (3%) (2).

Case report: We present a case of 53 years old female patient with NSCLC with multiple metastasis in lymph nodes,bones,brain and the palatine tonsils.The patient was a 30 P/Y smoker.The first symptoms of the disease were general weakness, headache, mandibular paresthesia and ophthalmoplegia.Lately, the patient presented with dysphagia, sore throat, dry cough,dyspnea,pain,night sweats and excessive loss of weight.In the examination,the patient gives the cachectic impression. Temporal,cervical and inguinal lymph nodes were enlarged bilaterally.Oropharyngeal examination revealed enlarged, ulcerated and coated left tonsil.The right eye was edematous and fully closed.Chest X–rays showed a circular shadow 5.5x3.5 cm paratracheal right and mediastinal lymphadenopathy.Head CT scan showed multiple brain secondary lesions, pathological bone remodeling on the right parietal bone and large secundar lesion in left tosil (2,7 cm). Pathohistology of lung biopsy confirmed poorly differentiating carcinoma of squamous cell differentiation. Molecular testing shows EGFR and ALK negative mutations and high expression of PD-L1 (> 95 positive tumor cells).The eye edema responded well to corticosteroid and antiedematous therapy.Other therapeutic measures were symptomatic including whole brain radiation therapy. Symptoms of the disease developed rapidly, and patient died in hospital 2 months after first symptoms appear.

Disscusion and conclusion: In this case, symptoms of NSCLC occurred when carcinoma had already given distal metastasis and progressed rapidly.Among others, patient had symptoms of brain metastasis such as headaches, weakness and loss of coordination, but mandibular parestesia and ophtalmoplegia appear to be PNS (3,4).PNS are related to immunologic mechanisms usually triggered by the neoplastic expression of neuronal proteins and in about 60% of patients occur before the diagnosis is made (5).Metastases to the palatine tonsils are very rare and life span of patients with NSCLC with tonsillar metastases is estimated to be short (6). Recently, therapeutic capabilities of NSCLC with targeted or immunological therapy are much better in patients with positive EGFR, ALK or PD-L1(7).Unfortunately, because of extremely progressive nature of disease, the prognosis was hopeless despite of high expression of PD-L1.

Keywords: non-small cell lung carcinoma (NSCLC), metastases, paraneoplastic syndrome (PNS)

Socket preservation following tooth extraction using xenogenic bone graft and resorbable membrane: a case report

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Introduction: Tooth extraction is an unfortunate outcome in cases such as tooth decay, which may result in significant loss of dental hard tissues, endodontic treatment complication or after dental trauma. Following the tooth extraction, alveolar ridge undergoes bone remodeling and resorption process that results in volume loss and shrinkage of the adjacent bone. If such case occurs in the anterior region, it presents a significant challenge to clinicians in restoring masticatory and aesthetic function using prosthetic crowns on dental implants. The technique of alveolar socket preservation is being used to reduce bone resorption. The bone substitutes in the form of autografts, allografts, xenografts or synthetic materials in combination with resorbable and non-resorbable membranes are used to fill the interalveolar defect.

Case report: Female patient, the age of 48, was referred to oral surgery practice in Community Healthcare Centre in Osijek. Surgical treatment was required because of root fracture of the second left upper incisor, which was assessed by Cone Beam Computed Tomography (CBCT). After the extraction, curettage of inflammatory tissue was performed. The mucoperiosteal buccal and palatal sliding flap was raised. To ensure minimal resorption of the alveolar ridge and to maintain an aesthetic profile of the soft tissues, the defect was filled with xenogenic bone substitute of bovine origin (Cerabone, Botiss GmbH), and covered by resorbable membrane (Jason membrane, Botiss GmbH). Buccal and palatal flaps were used for additional securing of the membrane. Both, the membrane itself, and flaps were secured in place using single 5-0 sutures. Six months after the procedure, control CBCT was done.

Conclusion: Radiographical analysis showed promising results in term of bone tissue preservation, in three-dimensional measurements and bone density. A dental implant was placed in the position of the extracted tooth and temporary crown was provided. The patient still needs to wait for full osseointegration to complete implant-supported prosthetics therapy.

Keywords: socket preservation, resorbable membrane, xenograft, CBCT

Macular degeneration of a young male patient – case report

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Introduction: Macular degeneration is an eye disease that affects the macula, or central portion of the retina. The macula is made up of millions of light-sensing cells that provide sharp, central vision. It is the most sensitive part of the retina, when damaged; field of vision may be blurry, distorted or dark. There are two types of macular degeneration: juvenile and senile. Primary changes could lead to decreased level of visual acuity which are often caused by accumulation of drusen (yellow deposits beneath the retina), hyperpigmentation and depigmentation of the retinal pigmented epithelium (RPE), RPE atrophy, subretinal or sub-RPE choroidal neovascularisation haemorrhages, exudations and forming of the fibrous scar. In order to treat macular degeneration we can use either laser photocoagulation or drugs which are able to block growth of blood vessels. Some studies report a high prevalence of amblyopia (33%) in children with coloboma. Coloboma of the eye is a state when a part of the eye is incomplete or missing. In the presence of decreased visual acuity, ocular pathology must be ruled out before making a diagnosis of amblyopia. The literature also reports a risk of retinal detachment in patients with coloboma of 40%.

Case report: In September 2018, 44-year-old male comes to ophthalmologist due to a checkup. Visual acuity was 0,75 in right eye and 0,1 in left eye. Recorded intraocular pressure in both eyes was 19 mm Hg. During examination, anterior segment of both eyes was unremarkable. Fundus examination revealed optic disc coloboma with pit in both eyes, slightly more prominent on the left eye with macular degenerative changes. Excavation cannot be determined certainly, but the approximate value, with the use of a cup/disc ratio resulted with 0,35. Due to the presence of coloboma and poor visual acuity of the left eye, probably present from early childhood, further examinations will be needed. Therefore, the patient was suggested to come to a checkup 6 months later when optical coherent tomography of the macula and examination of posterior segment of the eye will be performed. The patient was prescribed with dietary supplements based on omega-3 fatty acids and lutein which are beneficial for eye protection.

Conclusion: Juvenile macular degeneration could also be a common cause of irreversible significant deficiency in visual acuity, when it appears along with hereditary states, such as coloboma. Prompt discovery of this state in a young patient could decrease level of losing the sight and result with preservation of current patient's visual acuity.

Keywords: coloboma, macular degeneration, visual acuity

Treatment of buccal fenestration associated with periradicular lesion using biphasic calcium phosphate paste and native collagen membrane: a case report

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Introduction: Despite numerous options in treating the periapical lesion, there are still failures in endodontics, which leads to tooth loss. Augmentation procedures performed prior dental implant placement, ensure the adequate height and width of alveolar bone, which is essential to achieve optimal aesthetics and functional rehabilitation. The aim of this case report is to present alveolar ridge augmentation following extraction of the tooth with the extensive periapical lesion.

Case report A healthy 19-years-old female was referred to an oral surgeon in Community Healthcare Center in Osijek, for tooth extraction due to endodontic treatment failure. An orthopantomogram showed severe bone destruction in the periapical region of tooth 36. The patient was informed about treatment options after tooth extraction and decided to do implant-supported prosthetics at the site of extraction. The site of extraction was exposed via elevation of a mucoperiosteal flap. Elevation of mucoperiosteal flap showed extensive buccal fenestration. Atraumatic tooth extraction was performed and was followed by curettage of the infected tissue in the socket. The socket was filled with biphasic calcium phosphate paste (BCP-paste) (Maxresorb inj., Botiss GmbH) and the whole defect was covered by a resorbable membrane (Collprotect, Botiss GmbH). Primary closure was achieved by using 5/0 single sutures. The healing period was uneventful. Seven days after the surgical procedure, control Cone Beam Computed Tomography (CBCT) showed no dislocation of bone substitute and good volume stability of the bone graft.

Conclusion: This case highlights the use of BCP-paste and native collagen membrane in extensive bone defect due to the periapical lesion. The viscosity of BCP-paste allowed excellent filling of the three-dimensional bone defect and easy handling during a surgical procedure. Follow-up is needed to determine volume stability six months after healing and prior implant placement.

Keywords: biphasic calcium phosphate, augmentation, CBCT, buccal fenestration

The transition from intrauterine to a different postnatal diet can affect inflammatory response and non-alcoholic fatty liver disease in male offspring rats

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Introduction: The aim of this study was to determine how maternal diet and switching male offspring to a different dietary regime after lactation influences rat liver. During pregnancy and lactation maternal diet high in fat can affect metabolic changes that can cause high levels of inflammatory cytokines. The transition from intrauterine to the different postnatal diet affects lipid accumulation in the liver that can cause non-alcoholic fatty liver disease (NAFLD).

Material and methods: Ten highly related female Sprague Dawley rats which were 9 weeks old were randomized in two groups. First group Control Diet (CD) (n=5), were fed with standard laboratory food, and second group High-Fat Diet (HFD) (n=5), were fed with diet mixture that contains large amounts of saturated fatty acids, and then mated with the same male subject. After birth and lactation period, male offspring were divided into four subgroups (n=6), based on their postnatal diet: mother and offspring both on the high-fat diet, mother on the high-fat diet and offspring fed regularly, mother fed regularly and offspring fed with the high-fat diet, and mother and offspring fed with regular diet. At 22 weeks of age, animals were sacrificed and their organs were collected and examined. Also, liver samples were weighted and analyzed for further pathohistological changes.

Results: The most pronounced changes were in the group in which mothers were fed with standard laboratory food and offspring with the high-fat diet. In that group, the liver had the highest percentage of lipid liver accumulation and highest concentrations of inflammatory cytokine TNF-alpha.

Conclusion: The transition from maternal standard laboratory diet during pregnancy and lactation to the high-fat diet in the postnatal period can affect levels of inflammatory cytokines, histological structure of liver parenchyma and lipid accumulation in the liver.

Keywords: Inflammatory cytokines, non-alcoholic, fatty liver disease (NAFLD), TNF-alpha

Substitute therapy in a patient with panhypopituitarism in acute febrile illness with vomiting

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Introduction: Hypopituitarism is a condition of partial or complete secretion absence of one or more pituitary hormone which may be caused by pituitary gland adenoma and other sellar masses, brain injury, surgery, infection, bleeding or it can be idiopathic. Central adrenocortical insufficiency is a life-threatening manifestation. It is determined by measuring basal hormones and stimulation tests. The treatment is based on hormone replacement therapy.

Case report: The patient is a 36-year-old male diagnosed with type I diabetes at the age of 13 and panhypopituitarism at the age of 14. Along with insulin therapy he also takes hormone replacement therapy : 15 mg of hydrocortisone tablets upon waking up and 5mg at 4pm, 100 µg levothyroxine and 50 mg of testosterone gel. He was admitted to the emergency room due to high fever of 38.4°C, general weakness, sore throat, difficulty swallowing and frequent vomiting. The patient was dehydrated, his tonsils were hypertrophic along with hyperemic pharynx. Laboratory findings have shown elevated inflammatory parameters along with hyperglycemia and positive glucose and ketones in the urine. The diagnosis indicated acute tonsillopharyngitis and ketosis. Since the patient was vomiting, the therapy was administered parenterally. He received antibiotics intravenously, then as tablets. Due to ketosis and dehydration, he received 0.9% sodium chloride infusion with short-acting insulin aspart and potassium chloride with metoclopramide ampoules. Once he stopped vomiting, glucose levels were regulated by using insulin aspart subcutaneously with three main meals and insulin degludec at 10 pm. Hydrocortisone was administered parenterally and at an increased dose 50 mg intravenously every 6 hours, subsequent treatment in tablets 20 mg after waking up, 10 mg at 1 pm and 10 mg at 6 pm). After that the dose is gradually reduced to the maintenance dose. With the recommended therapy, the patient felt subjectively better, there was a decrease in inflammatory parameters and satisfactory glycemic, sodium and potassium values were achieved.

Conclusion: In patients with hypopituitarism, dose of hydrocortisone should be increased two to three times in infection, stress and febrile conditions. If the patient is vomiting or has diarrhea, within 24 h the medicine should be applied parenterally. In severe general condition, 100 mg of hydrocortisone should be applied every 6 hours and in acute febrile condition with vomiting or diarrhea, 50 mg every 6 hours. Higher doses of substitution therapy are associated with higher mortality.

Keywords: hypopituitarism, hormone replacement therapy, acute febrile illness, vomiting

Two rare monogenic hereditary diseases − Canavan disease and cmt1 neuropathy in one patient

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Introduction: Canavan disease is a progressive, fatal neurological disorder and it is caused by an inherited genetic abnormality: the lack of an essential enzyme leads to deterioration of the myelin in the brain, thereby preventing the proper transmission of nerve signals. Charcot–Marie–Tooth disease (CMT1) is hereditary motor and sensory neuropathy which is caused by genetic defects that damage the myelin sheath. The disease often is referred to as "demyelinating CMT."

Case report: The essential enzyme in Canavan disease is aspartoacylase (ASPA). ASPA catalyzes the hydrolysis of N-acetylaspartate (NAA) to aspartate and acetate. Its deficiency leads to buildup NAA which interferes with the formation of the myelin sheath. Myelin protein−22 (PMP−22) forms 2−5% of compact myelin of the peripheral nervous system. The duplication of chromosome 17p11.2 in Charcot−Marie−Tooth(CMT1) is increasing copies of PMP22 to overexpress the protein and cause the segmental demyelination. Our patient has a duplication in the PMP22 gene and also two ASPA mutations c.914C>A (p.AIa305GIu) and c.302G>T (p.GIy101VaI). The boy suffers from two rare monogenic hereditary diseases − Canavan disease and CMT1 neuropathy. CIinicaI features presented in this patient are a mild form of symptoms that occur in both diseases. Patient has peroneal walk, discreet intention tremor, and border intellectual abilities difficulties. MRI shows symmetrical hyperintensities in supratentorial areas, the basal ganglia, cerebral peduncles on both sides, on the back side of the pons and also in medial parts of both cerebellar hemispheres.

Conclusion: This case is important to highlight because both diseases are extremely rare even on its own. Also, it is interesting that both diseases usually have pretty severe clinical features but combined they are presented with a mild form of symptoms.

Keywords: Canavan disease, Charcot–Marie–Tooth disease, myelin

Congenital hypotonia and epilepsy as main clinical signs of Wolf-Hirschhorn syndrome

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Introduction: Wolf-Hirschhorn syndrome (WHS, 4p deletion syndrome) is a rare genetic disorder usually caused by de novo deletion of the short arm of chromosome 4. The major characteristics include a distinctive facial feature consisting of "Greek warrior helmet" appearance, delayed growth and development, hypotonia, variable midline defects, and seizures.

Case report: This case represents two children with WHS. First, female child of healthy nonconsanguineous parents, born in a fourth pregnancy (two spontaneous miscarriages and one healthy female child) with intrauterine growth failure. Postnatal presenting with hypotonia and dysmorphic features. Karyotyping confirmed WHS (karyotype: 46, XX, del (4) (p15.32) dn) with most features of the syndrome: typical high-tone crying, microcephaly, hypertelorism, epicanthal folds, blepharophimosis, micrognathia, gothic palate, clinodactyly, camptodactyly, and growth failure. Respiratory infections are extremely common and epilepsy occurs at the age of 7 months. The girl now has 8.5 years, BW 14 kg, epilepsy, immunodeficiency (selective deficiency of IgA) and severe global psychomotor delayed. The second case is a male child of nonconsanguineous parents born in a third pregnancy (healthy brother and sister) which was poorly controlled. The mother has epilepsy from the infant age, high myopia, and border cognitive functioning. Postnatal clinical signs referrers to WHS and karyotype confirmed: 46, XY, del (4) (p15.32) dn. As in the first case, phenotypic features, respiratory infections, and epilepsy at the age of 7 months are present. Differences are a cleft palate, hypospadias with cryptorchism and brain developmental anomaly. At the age of 3.5 years, he acquired severe pneumonia and respiratory insufficiency with multiorgan failure and long mechanical ventilation. As a result of the genetic illness, and acute complications he lost the swallowing reflex, fed it through a nasogastric tube, breathing through the tracheal cannula, and motorically in decerebration rigor. By the end of life, he remains in palliative care and dies at the age of 4 years and 9 months.

Conclusion: It is a rare genetic syndrome characterized by typical phenotype, hypotonia, growth failure, and refractory epilepsy. Most patients die within the first year of life, but this case represents a prolonged survival of up to 9 years of life. For individuals affected by WHS there is no specific treatment, they need multidisciplinary monitoring in the direction of improving the quality of life. The therapeutic measures should be on supporting the parents and also suggest them genetic counseling for next planned pregnancies.

Keywords: Wolf-Hirschhorn syndrome, 4p deletion syndrome, hypotonia, epilepsy

Turner syndrome with haploinsufficiency in Xp22.3 and Xq28 microdeletion

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Introduction: Turner syndrome is a chromosomal disorder that affects sex chromosome of females. These patients have only one X chromosome while other is missing or structurally altered. Most common features of this syndrome are short stature, webbed neck, low hairline at the back of the neck, lymphedema, skeletal abnormalities, early loss of ovarian function and a congenital heart defect. Most of them have normal intelligence but developmental delays and behavioral problems can be presented.

Case report: Patient is a female child in the age of 7,5 years old. She was first sent to the genetic specialist for examination of severe psychomotor development delay and reduced growth. During the inspection patient was presented with reduced growth (112 cm), webbed neck, low hairline at the back of the neck, widely spaced nipples and clinodactyly all of which are listed as characteristics of Turner syndrome. During the examination, the patient seemed severely hyperactive, with occasional stereotypic movements. At the time the patient spoke few basic words without the capability of making sentences. Although cognitive and behavioral problems were not typical for Turner syndrome, phenotype features were strongly suggesting this monosomy so karyotipization was recommended. It showed karyotype 46, X0, after which she was diagnosed with Turner syndrome. After the confirmation, a patient was regularly examined once a year at a genetic specialist. Throughout the years patient developed severe aggression toward herself and mother, continued to express hyperactivity with extremely poor development of higher cognitive functions. Since this difficult and global psychomotor and somatic development delay is not characteristic for Turner syndrome, a genetic specialist recommended a subtelomeric screening. MLPA showed haploinsufficiency in Xp22.3 which according to literature is responsible for neurocognitive deficits in this patient. Screening also showed Xq28 microdeletion which affects the expression of MeCP2 gene. This mutation clinically correlates with Rett like phenotype which is characterized by significant intellectual impairments together with an autistic spectrum disorder.

Conclusion: This case emphasizes the importance of clinical monitoring of such complex patients in order to detect deviations of the classical presentation of syndromes. It also encourages us to rethink about diagnose, if we notice abnormal clinical aspects, even after it was confirmed so that we continue to observe in the purpose of reaching the ultimate cause that can explain the overall clinical picture.

Keywords: Turner syndrome, Rett, Development delay

Overgowth syndrom - Klippel-Trenaunay-Weber syndrome with cognitive impairment

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Introduction: Klippel-Trenaunay-Weber syndrome is a rare condition with wide array of clinical manifestations that has three characteristic features: a red birthmark called a port-wine stain, vein malformations and abnormal overgrowth of soft tissues and bones, which is usually limited to one limb, most often one leg. KTS can be caused by mutations in the *PIK3CA* gene, which provides instructions for subunit of an enzyme called phosphatidylinositol 3-kinase, which plays a role in chemical signaling that is important for many cell activities such as proliferation, migration and cell survival.

Case report: This case represents a male child, now in the age of 11 with KTWS, born in orderly pregnancy as fourth child of young, nonconsanguineous parents. Other children are healthy. Postnatal presenting with macrocephaly (head circumference-41.5cm), hemihypertrophy of the left part of the body, diffuse port-wine stains mostly on the left side. In the area of abdomen and thorax we can find some cutaneous hemangiomas. The child is showing psycho-motor retardation, despite early rehabilitation, and during the first few years of life, he was oftenly hospitalized due to opportunistic respiratory infections. He begun to walk at the age of 3.5 years, and at 8 years he established sphincter-control. By the assesment of a psychologist, he is showing a significant lack in mental development, level harder to hard MR (IQ 20), with elements from an autistic spectre and periodic outbrakes of autoaggression. Until now, he didn't have any tromboembolic incidentes, but at the moment, there is a visible progression of a left leg oedema with a lymphatic drainage dysfunction. At the age of 11, he is showing visible skeletal deformities, dextroscoliosis, finger contracture, difficulty with walking, and is in entirely dependant on the care of another.

Conclusion: It is a rare genetic syndrome characterized by typical phenotype which includes hemihypertrophy, port-wine stains and vein malformations. The treatment for the disease is only symptomatic treatment. Although the mental retardation is only one of the characteristics of the disease, in this case we have the most severe case of mental retardation (IQ 20) which is combined with elements of autism, and that additionaly contributes to complexity of care and therapy for such a patient.

Keywords: KTWS, hemihypertrophy, port-wine stain, hemangioma, MR

Radiological findings of cerebral vasculitis with ischemic and hemorrhagic stroke associated with Parvovirus B19 in a young boy – case report

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Introduction: CNS vasculitis in children may occur as a primary isolated disease or as a secondary manifestation of systemic disease. The diagnosis is based on MR angiography (MRA) findings. This disease is rare, therefore the incidence is not known. Clinically it presents as a headache, also as a wide range of neurological presentation including seizures, motor, and sensory outbursts.

Case report: We present a case of 10 year old boy, otherwise healthy except the atrophy of the left optic nerve without known family heredity. He was admitted to the clinic for acute severe headaches followed by nausea and vomiting. He was subfebrile, neurologically without a deficit. Anamnestically, we learned that Cortexin, a mixture of neuropeptides and amino acids, was parenterally administered a month ago. Head MRI, done in an emergency procedure was normal. Despite extensive analgesia, the feeling of extreme headaches persisted and after 24 hours head MRI was revised and it showed the right occipital zone of hemorrhage with peripheral edge edema with the presence of subarachnoid bleeding on the right. The head MRA verified stenosis at the internal carotid artery, vertebral artery and posterior cerebral artery on the right. Due to the suspicion of intracranial venous thrombosis, CT venography was performed where agenesis of the left sigmoid sinus and the left jugular vein were found. With antiedema, anticonvulsive and analgesic therapy the boy was observed through 72 hours, withdrawal of the symptoms occurred. The symptoms reappeared with photophobia, indicating an emergency head CT control which showed a mild regression of right occipital hematoma and a new ischemic lesion parietally left with diffuse edema. Primary cerebral vasculitis was suspected, pulse corticosteroid and anticoagulant therapy were included. Meanwhile, infection with Parvovirus B19 has been proven. Symptoms of a headache disappeared, control head MRI scan after 3 months showed postischemic parietooccipital encephalomalacia lesion on the left and condition after occipital hemorrhage with a parenchymal defect on the right. The boy is now 11 years old, clinically good without a neurological deficit.

Conclusion: We hypothesized that the CNS vasculitis could be associated with the acute B19 infection. With early recognition and treatment including immunosuppression, anticoagulation and supportive therapy, a good neurological outcome can be achieved. A review of the literature on the association of neurological disorders with B19 infection has described 129 patients, of whom 61% are related to various CNS changes, and rarely with a stroke. The gold standard includes head MRI with angiography.

Keywords: Cerebral vasculitis, stroke, parvovirus B19, children

Review of Sex Differences in Stress Response and Risk of Alzheimer's Disease

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Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder and the most common type of dementia, accounting for 50 – 70 % of dementias. In 2006 it affected more than 25 million people worldwide and that number is expected to increase to more than 100 million by 2050. Although the specific cause of the disease still remains to be discovered, many risk factors have been identified. One of those are female sex and chronic stress with women contributing to about two thirds of patients diagnosed with Alzheimer's disease. The problem of sex disparity still remains controversial with one possible explanation being that women simply outlive men thus more women live to the age when Alzheimer's symptoms start to manifest. However, recent research suggests higher incidence in women with supporting underlying evidence.

Materials and Methods: As a status quo review, materials are recent findings in MeSH database on PubMed in the field of neuroendocrinology and neurobiology of stress response and Alzheimer's disease.

Results: In response to stress many pathways tend to increase their activity, most notably hypothalamus – pituitary – adrenal (HPA) axis. Ultimate result of HPA axis activation is the release of glucocorticoids (GCs), that can cross the blood brain barrier and exert their effects in central nervous system. Even though the complete mechanism of how stress increases AD risk hasn't been discovered, dysregulation of HPA axis has been implicated in both laboratory Alzheimer's models and clinical practice. That dysregulation is manifested by elevated basal concentrations of GCs, which in turn interrupt negative feedback of the axis via glucocorticoid receptors (GRs) in the hypothalamus, hippocampus and adenohypophysis. Moreover, there is correlational evidence between elevated cortisol levels and degree of cognitive decline. Significantly, novel nongenomic pathway of GCs has been discovered, mediated by membrane – associated GRs which promotes Aβ formation. Interestingly, Duma et al. in 2010 discovered sex – specific GR activation in hepatic cells, which in female promoted inflammatory pathways. This finding should be verified in neural tissue because neuroinflammation appears to have significant role in AD pathology.

Conclusion: It is evident that glucocorticoids play an important part in progression of Alzheimer's disease and any sex - specific responses to glucocorticoids may have notable roles. Researchers have already found possible biological causes of different female to male ratio of AD patients and how those could modulate Alzheimer's risk. Consequently, it is extremely important to study the disease in both sexes of laboratory animals.

Keywords: Alzheimer's disease, chronic stress, glucocorticoids

Herpes zoster in a patient with non-Hodgkin lymphoma: A case report

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Introduction: Herpes zoster (HZ) is a sporadic viral disease associated with the reactivation of the varicella zoster virus (VZV) and characterized by painful vesicular skin lesions that are limited to the dermatomal regions. The Non-Hodgkin lymphoma (NHL) is a hematologic malignancy which includes various histological subtypes of lymphoma that develop from the lymphatic system. The reactivation of various viral infections, such as hepatitis B, cytomegalovirus, and VZV, has been described in patients with NHL after immunochemotherapy.

Case report: This case describes a 56-year-old female that arrived to the hospital with complaints of a painful rash on the neck and shoulder that started 3 days ago. In anamnesis: The patient had the NHL (subtype small B-cell lymphocytic lymphoma - SLL) and was treated with immunochemotherapy R-CHOP (6 cycles, last one 5 months ago). The physical exam showed that cervical lymph nodes, tonsils, spleen, and neurological signs were normal, meningeal syndrome negative, liver enlarged 2 cm. The evaluation of vital signs showed that the temperature was 37.3°C, blood pressure 140/90 mm Hg, c/p 110/min, RF 19/min, and SpO2 98%. Blood and urine analyses were performed: WBC 57.5 $x10^9$/L, (differential: Ne 11%, Ly 81.1%, Mo 7.7%, Eo 0.1%, Ba 0.1%), Abs. Ly 46.6 $x10^9$/L, RBC 3.62 $x10^{12}$/L, Hgb 95 g/L, Htc 0.284 L/L, MCV 78.3 fL, PLT 205 $x10^9$/L, CRP 38 mg/L; electrophoresis: total proteins 61 g/L and a lightweight suspicious ribbon was detected in the gamma-globulin fraction; urine analysis: leukocytes 3+, RBC 1+. Based on the case history and clinical findings, a final diagnosis of disseminated HZ was given, the patient was admitted to the hospital department, treatment was performed with acyclovir 800 mg, 5 times per day during 2 weeks, and the basic therapy with the continued follow-up for an acute disease.

Conclusion: The incidence of HZ is associated with compromised immunity and it is higher among patients with malignancies and following cancer-related therapy, and complications are relatively common. Also, the incidence density of HZ is high among the patients that received rituximab added conventional chemotherapy (R-CHOP). The risk factors include female gender, age between 51 and 64, diabetes mellitus, multiple courses of chemotherapy, and a higher accumulated rituximab dose. It has been proven that the majority of HZ episodes occurred within the first two years after the diagnosis of NHL, and the addition of rituximab to the conventional chemotherapy increased the short-term risk of herpes zoster. Our patient was female, age 56, with a HZ episode that occurred within the first year after the diagnosis of NHL and after a treatment with 6 cycles of R-CHOP therapy.

Keywords: Herpes zoster, NHL, diagnosis

The gut microbiome and multiple sclerosis

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Introduction: Microbiome represents an ensemble of microorganisms living in the human body which plays an important role in immune functions and it has been linked to a pathogenesis of different disorders. Multiple sclerosis (MS) is an example of an autoimmune chronic neuroinflammatory demyelinating disease that affects young adults with observed change of intestinal bacteria. Gut microbiota can regulate MS pathogenesis through metabolites, T cells and peripheral tolerance.

In multiple studies, there have been done independent sequencing technologies for finding abundance of prevalent microbiota in MS and wide range of bacteria affecting the gut brain axis. Validating identification is important due selecting the optimal bacteria to monitor in microbial translation studies. Few methods were acompanied - such as gene expression, 16S rRNA sequences, DNA isolation, flow-cytometry analysis, dietary effects on individuals with MS.

Several studies investigated the differential abundance of intestinal bacteria in individuals with MS. For instance, there has been found a relation between MS and chronic low-grade microbial translocation, which was investigated with doses of circulating LPS and its potential induction of interleukins. Also, it has been shown that some bacteria are butyrate-producers affecting anti-inflammatory, anti-tumorigenic effect and even control gene expression.

Conclusion: Increasing evidence shows that the gut microbiota plays a major role in human body and its immune response. In the field of MS, there is a solid scientific evidence pointing that microbiome is involved in the pathogenesis and even in theraphy and prevention.

Keywords: microbiome, bacteria, multiple sclerosis

Ischemic cerebral infarction in the newborn – intrauterine thrombosis of the middle cerebral artery

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Introduction: Cerebrovascular diseases are one of the top 10 leading causes of newborn death. More than a half of survived patients have neurological or cognitive deficits and 5-10% of patients end fatally. Unfortunately, this condition is often unrecognized.

Case report: We are presenting a case of a male full-term newborn from the second pregnancy (first pregnancy was a spontaneous abortion) without known genetical disorders in the family. Patient was born at local hospital with birth weight of 2850 g, Apgar score was 6/7. This patient was also a case of nuchal cord and amniotic fluid was containing meconium. Physicians recognized hypotonia, hyporeflexia and pale skin. Eight hours after birth patient expressed partial convulsions of the right hand with squelch. A patient was transferred to University Hospital Center Osijek. Ultrasound showed hypoxic ischemic encephalopathy with suspicion to thrombosis of the right middle cerebral artery. MR scan indicated multicystic encephalomalacia of the right cerebral hemisphere which was a repercussion of large ischemic insult in the supply area of the right middle cerebral artery. MR angiography was done and the result showed occlusion of a right internal carotid artery in the part of a carotid siphon, the right middle cerebral artery was not visible and cerebral anterior artery was severely hypoplastic. These results were confirmation of ischemic cerebral infarction, probably appeared intrauterine. Pediatric cardiologist excluded congenital heart anomalies, metabolic evaluation was normal. Hematologic and coagulation tests ruled out polycythemia and hyperhomocysteinemia. Protein C and protein S were slightly elevated with high values of D-dimers. Molecular diagnostic tests showed polymorphism on both alleles of plasminogen activator inhibitor type I gene. We also tested mother for coagulation disorders and we have confirmed condition of thrombophilia. Possible metabolic causes for this condition could be mitochondrial disorders, lysosomal storage diseases (Fabry disease, cystinosis), inherited organic acidurias, urea cycle disorders or lipoprotein metabolism disorders. To exclude them we did test for organic acids in urine, amino acids in serum and urine, total carnitine, free carnitine, and biotinidase. Supportive and symptomatic therapy was introduced and most importantly patient participated in intensive rehabilitation program.

Conclusion: With this case, we wanted to point out the importance of considering cerebral infarction in newborns as a valid differential diagnosis. This condition is not as rare as physicians expect it to be. Also, it is important to take into account the metabolic causes of this condition.

Keywords: newborn, infarction, CVI

The prognostic role of neuropeptides proANP and NT pro-BNP levels in hypertensive patients

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Introduction: Despite the existence of sufficient information on the violation of natriuretic peptides, in particular pro-ANP and NT-pro BNP, the impact of these neuropeptides on the structural-functional state of vessels and on neuro-humoral auto-regulatory mechanism leading to development of arterial hypertension is not fully known, leading us to study their plasma content and their co-relation to pulse wave velocity(PWV) and arterial stiffness.

Materials and methods: We examined 76 patients with AH I-III stages (43 men and 33 women average age of 46,9 ± 1,5 years and duration of the disease 9,1 ± 1,4 years). Patients were distributed into groups basing on their degree of hypertension: I stage AH-16 patients, II stage- 43 and 17 patients with III stage AH. The control group consisted of 22 healthy people. The systolic blood pressure(SBP), pulse pressure(PP), diastolic blood pressure(DBP), PWV was measured using the dopplerograph (philips "Envisor" frequency 7,5 MHz) on the left radial artery. Statistical processing of the results was carried out using the Statistica 6.

Results: PWV of control group in the basal state was 8.14 ± 0.26 m/s, and after muscle work(MW) tended to decrease to 7.68 ± 0.19 m / s ($p > 0.05$), which was 5,7%. The autoregulation of blood flow(ABF) in the state of rest Lower Level ABF was 45.7 ± 3.4 mm Hg, significantly decreased after MW to 32.3 ± 1.9 mm Hg. Art. ($p < 0,01$) 29,3%. At the same time, ABFR, in the BS was 49.5 ± 3.4 mm Hg and after MW, increased significantly to 58.2 ± 3.0 mm Hg ($p < 0.01$). The plasma levels of proANP and Nt-proBNP in patients with hypertension was 1598 ± 54 fmol / ml and 445.8 ± 16.9 fmol/ml and 67.9% and 110.7% higher than in the control group (952 ± 51 fmol / ml and 211.6 ± 31.3 fmol / ml, respectively, $p < 0.001$).

Conclusions: A close positive correlation was found between the values of proANP, NT-pro-BNP, and PWV. The violation of forearm ABF, which increased after MW, making the high sensitive peptides a marker of the arterial lesions.

Ectopic pregnancy in a patient with primary infertility

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Introduction: Ectopic pregnancy (EP) is a complication of pregnancy in which the embryo attaches itself outside the uterus. It's more common in pregnancies with in vitro fertilization (IVF) and embryo transfer. In 95% of cases, EP is placed in the fallopian tubes, but it can also be placed in ovaries, abdomen or cervix. Cervical pregnancy, in which embryo is implanted inside the endocervix, is the rarest kind of EP with incidence of only 0,15%. The cervical canal is dilated and has visible parts of the embryo. Cervical pregnancy is presented as incomplete miscarriage, the most important symptom is vaginal bleeding, and it is diagnosed by gynecological examination, transvaginal ultrasound (TVS) and high levels of ßhCG. It usually ends with spontaneous miscarriage, but sometimes it needs to be removed by a surgical procedure or by using medications, mostly methotrexate (MTX).

Case report: A 30-year-old nullipara has been hospitalized at Clinic for gynecology and obstetrics, University hospital center Osijek after treating infertility for 5 years due to observation after IVF which was done 3 weeks earlier. On regular examination, a gestational sac was noticed by TVS on the posterior wall of the cervix, which, combined with the high levels of ßhCG, was a sufficiently specific sign to confirm EP. During hospitalization, after presurgical examination, embryo was removed using MTX; at first, MTX was given systematicaly for 6 days in dosage 1 mg/kg intravenously intermittently with leucovorin. After those six days MTX was also injected directly intraamnioticaly trough the cervical canal with a tuohy needle, 1 mg/kg, under the control of transabdominal ultrasound. Two weeks later, using TVS, only scar tissue was noticed in the place where embryo was implanted and the level of ßhCG has decreased, so the patient was released from hospital. After the procedure, our patient still had functional ovaries and uterus, and one year later she continued with infertility treatment. After two years, the third IVF was successful and the patient gave birth a healthy boy by caesarian section.

Conclusion: Because of the more common use of IVF, a number of EPs is increasing. It's very important to recognize EP, because unrecognized and untreated EP is very dangerous for woman's health and can be lethal. Because of the development of science and clinical research, the number of medications used for EP is increasing, and the most important of them is MTX; because of excellent results and rare complications, MTX, systematic or intraamniotic, is the first choice for treating EP in the first trimester.

Key words: cervical pregnancy, methotrexate, IVF

The anatomy of the sensory and frontal cortico-thalamic pathways

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Introduction: While several studies have investigated the regional differences within the cortex, very little is known about region specific properties of thus cortex's corticothalamic projections. In addition to the ascending subcortical pathways, large territories of the thalamus receive driver inputs from the layer 5 (L5) of the neocortex. In this study, we compared the properties of sensory and frontal L5 inputs to the thalamic relay nuclei and to the major inhibitory interface of the thalamus, the thalamic reticular nucleus (TRN).

Methods: L5 cells of M2 (frontal) and S1 (sensory) cortical regions were selectively labelled in the RBP4-Cre transgenic mice using GFP-labelled conditional viruses. Synaptic bouton size, which correlates with synaptic functional properties, was estimated on confocal z-stack images. Cortico-TRN projection was investigated with fluorescent microscopy. Single labelled TRN neurons was reconstructed in the Neurolucida® software. TRN innervation of relay thalamic nuclei was investigated by retrograde labelling.

Results: L5 axons from the S1 cortex did not innervate TRN and gave large sized boutons (0,89±0,46μm^2) to Po, L5 axons of M2 origin densely innervated TRN and formed small sized boutons (0,47±0,11μm$^{2)}$ in the VM. In addition, we found that the TRN sectors contacted by the frontal L5 terminals innervate thalamic regions which projects back to the frontal cortices.

Discussion: We found significant regional differences between sensory and frontal pathways in the L5-TRN-relay nuclei projection pattern.

Conclusion: We uncovered region specific cortico-thalamic pathways with profound anatomical differences which form parallel closed loops and enable regionally specialized cortical control over the thalamus.

Keywords: thalamus, cortico-thalamic,

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Endocrine function of adipose tissue in bone marrow effect structural changes in bone volume and trabecular separation in rats

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Introduction: A major global issue, obesity, is a cause of many metabolic disorders. Obesity can lead to bone marrow adiposity which increases the release of various cytokines that can lead to bone remodeling. Inflammatory cytokines can cause reduction in trabecular bone volume and trabecular separation.

Materials and methods: Ten Sprague-Dawley female rats, which were highly related, were divided into two groups at nine weeks of age. The first group (n = 5) were fed with a high-fat diet, while the other group (n = 5) were fed with standard laboratory diet for rats, in the period of six weeks. Later, their male offsprings, which we got from mating with the same male subject, were further divided into four subgroups (n = 6) based on their diet regime. In the 22nd week of the offsprings lives, they were weighted and afterward sacrificed. After the sacrifice, bone samples were collected and later analyzed.

Results: Digital photographic images were used for analyzing the fifth lumbar vertebra (n = 24). In addition, TNF-α expression in the bone marrow was measured using immunohistochemistry. The highest immunohistochemical staining response, in the bone marrow, of TNF-α had a group in which the mother was fed with standard laboratory diet and offspring fed with high-fat diet. The highest trabecular separation values and most reduced values of trabecular bone volume were seen in the same group.

Conclusion: We would like to emphasize that the most pathological changes in bone structure are expected in the offspring that were on a different diet than their parents. The changes are most expected if the offspring was on the high-fat diet, while their parent was on standard laboratory diet.

Keywords: Obesity, trabecular separation, TNF-alpha

ORAL PRESENTATIONS

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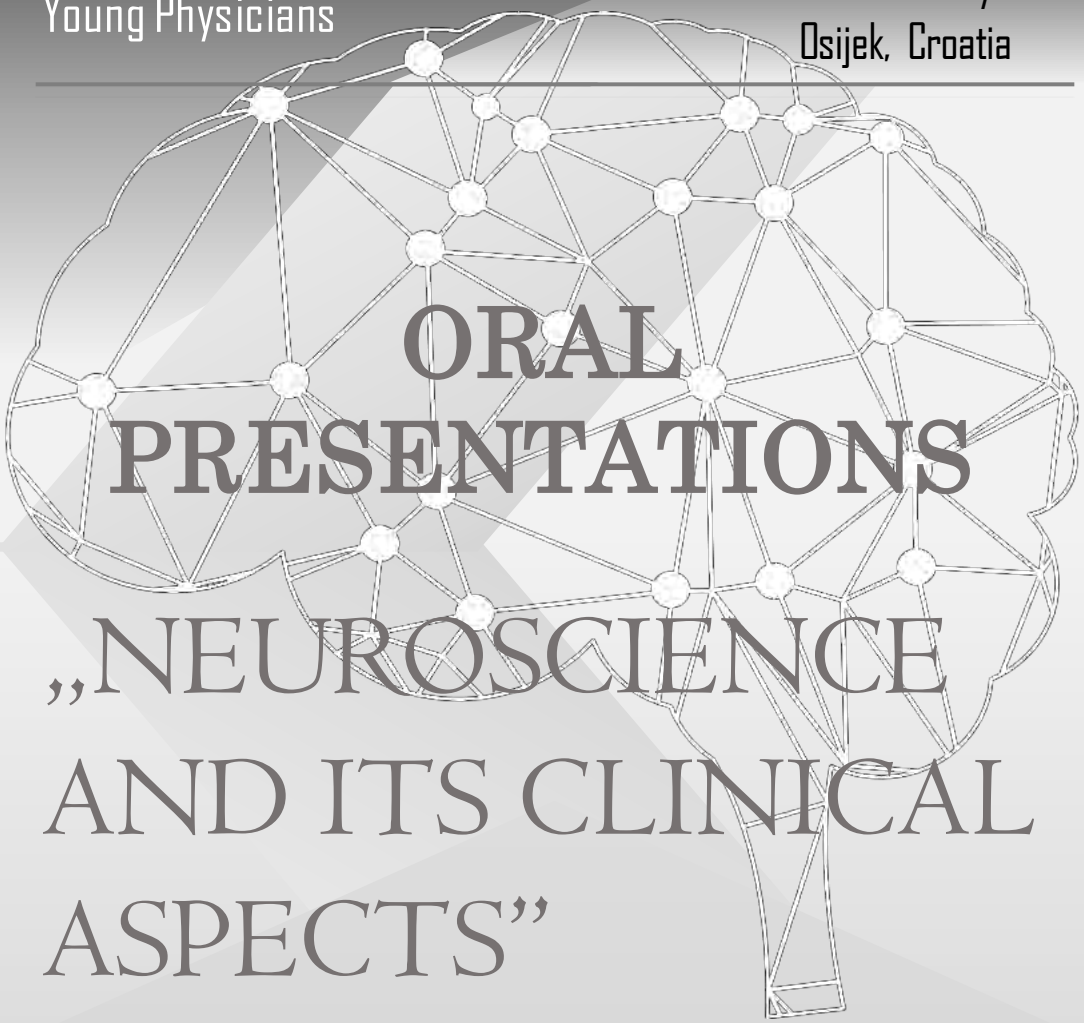

ORAL PRESENTATIONS

„NEUROSCIENCE AND ITS CLINICAL ASPECTS"

University of Osijek
Faculty of Medicine

Student Council

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Josip Juraj Strossmayer University of Osijek
Faculty of Medicine

Our Experiences with the Sorin Perceval S Sutureless Biological Aortic Heart Valve in the Clinical Centre of the University of Debrecen

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Introduction: The primary solution of severe aortic stenosis is the surgical replacement of the heart valve. During an open heart surgery the circulation is maintained by the heart motor. The lenght of the ischemic time (the aortic-cross-clamping time) is really important especially in elderly high risk patients. The usage of sutureless heart valves may decrease the aortic-cross-clamping time which is the most stressful part of the open heart surgeries.

Goals: The aim of our study is to analyse our experiences with the Sorin Perceval S biological aortic valve especially the preoperative measurements, the implantation itself and the postoperative results.

Methods: We performed sutureless Perceval S implantation 33 times between Oktober 2012 and November 2016 in our clinic. The average age of the patients (22 female and 11 male) was 77 ± 4,9 years, their additive Euroscore was 8,7±2,5 while the Euroscore II was 6,16±6,03. We performed an echocardiographic examination and a chest CT to evaluate each patient's suitability to the operation. We checked the function of the prosthetic valve usually on the 6. postoperativ day by echocardiography. We performed isolated valve replacements in 18 cases and combinated operations in 15 cases.

Results: The 30-day mortality was 6,06% (2 patients). In each case the controll echocardiogram showed good valve function, paravalvular leak was not detected. We were able to determine the patient's suitability to the implantation of a sutureless biological valve with the TTE and the CT, too. Since the TTE seemed as precise as the CT, later the CT was left out from the protocol, so we could avoid unnecessary radiation.

Discussion and Conclusions: Sutureless biological aortic valves may decrease the aortic-cross-clamping time and the extracorporal circulation time and reduce the surgical stress, therefore they are useful alternative in the surgical treatment of elderly high risk patients with aortic vitium.

Keywords: aortic stenosis, biological aortic heart valve, sutureless, Perceval S

Ethical Committee or Institutional Animal Care and Use Committee Approval: 2017. 4783-2017 University of Debrecen, Institute of Cardiology and Cardiothoracic Surgery

Results of in-vivo placental volume measurements by ultrasound correlate with sFlt-1/PIGF ratio in preeclampsia

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Introduction: We have designed this prospective study to assess the correlation between in vivo measured placental volume and soluble fms-like tyrosine kinase 1 (sFlt-1)/placental growth factor (PIGF) ratio in preeclampsia (PE) using 3-dimensional (3-D) ultrasonography. sFlt-1 and PIGF have key role in angiogenesis and they have remarkable impact on the placental vasculature, thereby on placental volume too.

Materials and methods: Between January 2017 and September 2017, 73 pregnant women with increased risk for PE were enrolled in our study at the Department of Obstetrics and Gynecology in Szeged, Hungary. We have collected maternal venous blood samples in order to detect sFlt-1/PIGF ratio and measured placental volume in-vivo. These samplings and measurement were performed in parallel, every for weeks between 20th and 36th weeks of gestation.

Results: The mean of measured placental volumes (MPV) and sFlt-1/PIGF ratio are presented below in the following categories: previous pre-eclampsia (PrevPE), chronic hypertension (CHT), gestational hypertension (GHT), pregestational diabetes mellitus (PreDM) and pre-eclampsia (PE).

Conclusion: We have revealed correlation between increased sFlt-1/PIGF ratio and in-vivo measured placental volume in PE. These findings could contribute to the better understanding of pathophysiology of PE and better prediction of adverse outcomes in pregnancy.

Ethical Committee Approval: University of Szeged (No.: SZTE 32/2014) Keywords: placental volume, sFlt-1/PIGF ratio, preeclampsia

Opinions on functional foods among students at the University of Osijek

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Introduction: Functional foods (FF) are fortified, enhanced or enriched foods that provide health benefits beyond the provision of essential nutrients. FF are also known as nutraceuticals and designer foods and usually contain supplements which are intended to improve health. The aim of this study was to investigate the influence of sex, BMI, the field of study and year of study on student's opinions about functional foods. Our hypothesis was that there are differences between students opinion on FF according to a certain sociodemographic characteristic of students.

Materials and methods: This on-line, anonymous, cross-sectional questionnaire study was done during April 2018 by the use of specially designed questionnaire which contained demographic data questions and questions about functional foods regarding its quality, price, expected benefit and popularity. Questions regarding opinions about FF were ranked using Linkert scale 1-5 where 1 meant "I completely disagree" and 5 "I completely agree". There were a total of 227 students that participated in this study.

Results: There were 41 (18.1%) males and 186 (81.9%) females. Age median was 22 (range 19-33) years. According to the field of study, there were 13 (12.8%) of students within humanities, 91 (40.1%) within social science, 14 (6.2%) within technical field, 71 (31.3%) within biomedicine and health science and 22 (9.7%) attending biotechnical field. There was statistically significant difference among males and females concerning statement which express believe in food that promises to improve their health ($p=0.030$).There was statistically significant difference among students belonging to different BMI categories concerning statement which express believe in food that promises to improve their health ($p=0.030$). Female students and those with higher BMI were more likely to believe in food that can improve their health. On the other hand, female students were also more likely to consider FF as a trend that will eventually disappear ($p=0.034$).

Conclusion: Female students and those with higher BMI do believe in foods that can improve their health but female students are also of an opinion that FF is just a new trend that will eventually disappear.

Keywords: functional foods, university students, questionnaire study, opinions, Croatia

Two-photon fluorescence and second harmonic generation imaging of classic and vascular type Ehlers–Danlos syndrome affected skin

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Introduction: Ehlers–Danlos syndrome (EDS) is the name for a heterogenous group of rare genetic connective tissue disorders with an overall incidence of 1 in 5000. The accurate determination of the diagnosis of the EDS subtype is of utmost importance, as it provides essential information for counseling; it helps to assess the inheritance pattern, prognosis and management options. The histological characteristics of EDS have been previously described in detail in the late 1970s and early 1980s. Since that time, the classification of EDS has undergone significant changes, yet the description of the histological features of collagen morphology in different EDS subtypes has endured the test of time.

Methods: Nonlinear microscopy techniques can be utilized for non-invasive in vivo label-free imaging of the skin. Among these techniques, two-photon absorption fluorescence (TPF) microscopy can visualize endogenous fluorophores, such as elastin, while the morphology of collagen fibers can be assessed by second-harmonic generation (SHG) microscopy. In our present work, we performed the clinical assessment and molecular genetic testing of one patient with classical EDS and two patients with vascular EDS. We carried out TPF and SHG microscopy imaging on skin biopsy samples of these patients among with two healthy controls

Results: We detected irregular, loosely dispersed collagen fibers in a non-parallel arrangement in the dermis of the EDS patients, while as expected, there was no noticeable impairment in the elastin content. We validated these results with standard histological stains including haematoxylin and eosin, Van Gieson's and Weigert's elastic stain.

Discussion: Based on our study, in vivo nonlinear microscopic imaging could be utilized for the non-invasive diagnostic testing of EDS and the assessment of the skin status of EDS patients in the future.

Conclusion: Besides, as there is a niche in the objective diagnostic approaches of EDS, a novel non-invasive diagnostic tool would be of great value.

Keywords: Ehlersd-Danlos syndrome, Nonlinear microscopy

Ethical Committee or Institutional Animal Care and Use Committee Approval:SE TUKEB:266/2015. Date of approval:25th February, 2016. Semmelweis University Regional and Institutional Committee of Science and Research Ethics.

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Reduction in number of hippocampal calretinin- and parvalbumin-immunoreactive interneurons in cuprizone-induced demyelination in mice

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Introduction: Inhibitory interneurons play prominent roles in the function of the cerebral cortex. They are involved in modulation and plasticity of the cortical micro-columns. Changes in phenotype of interneurons have been observed in schizophrenia, seizures, autism and many other neurodevelopmental disorders. Our hypothesis is that disturbance of plasticity through demyelination results in a change of phenotype of hippocampal interneurons.

Materials and methods: The study was conducted on six C57BL/6 mice, 3 of which were fed on chow containing 0.2% cuprizone in order to induce demyelination, and 3 were fed on standard chow. The mice were anesthetized with isoflurane, and perfused with 4% paraformaldehyde in phosphate buffer saline (pH = 7.4). Brains were isolated, perfused, cryoprotected using 30% saccharose, and stored at -80 °C. The specimens were cut on cryostat (Leica CM3050S) in 35 microns thick slices, and immunohistochemistry for parvalbumin (PV) and calretinin (CR) was conducted. The following hippocampal regions of interest were identified: dentate gyrus (DG), cornu Ammonis 1 (CA1) and cornu Ammonis 3 (CA3). Slices were photographed on Zeiss Axioskop 2 MOT microscope, and an intensity threshold was applied on each micrograph based on the intensity measured on negative controls. A number of neuronal somata per area unit was counted in respective hippocampal regions in both hemispheres using ImageJ (version 1.52i). The extent of demyelination was determined in a previous study.

Results: A statistically significant reduction in number of CR-interneuronal somata per μm^2 was observed in DG of animals fed on cuprizone ($p = 0.009$). The count of PV-interneuronal somata per μm^2 was also lesser in mice fed on cuprizone compared to the control, in DG ($p = 0.015$) and in CA1 ($p = 0.02$).

Conclusion: Our results suggest that a reduction in number of CR- and PV-immunoreactive interneurons takes place in hippocampi in the cuprizone model of demyelination. However, more interneuronal markers are to be included in future studies for more elusive conclusions.

Keywords: Interneurons, Hippocampus, Parvalbumins, Calbindin 2

Authentication of a cell lines by determination of a short tandem repeats-STR profile

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Introduction: Continuous cell lines are well-recognized models for the study of medical conditions, particularly for cancer. However, there are cautions to be aware of when using continuous cell lines, including the possibility of contamination which has far-reaching consequences on the results of the research. This is the reason why there are a lot of tests designed to help authentication of the cell line, which actually means finding out whether a certain cell line is "free" from another cell line and/or microorganism or not. These kinds of tests are called authentication tests. The most frequently used one also called "gold standard", is a short tandem repeat profiling (STR) test.

Objective: The aim of this study was to authenticate 6 cell lines grown in vitro using short tandem repeat (STR) profiling, as well as to define match percentage between electropherograms and ATCC- database.

Materials and methods: 6 cell lines were used in this research (HeLa, SW620, CCRF-CEM, K-562, HT-29, Caco-2) and were analyzed on 15 loci + amelogenin. The steps of the analysis were: DNA isolation, determination of DNA concentration, PCR duplication, and electrophoresis. GeneMapper software for electropherograms was used for the analysis of the results.

Results: Electropherograms obtained were compared to standard reference STR database which made it possible to determine if cell lines were authentic and the percentage match between them. 4 cell lines, HeLa, SW620, CCRF-CEM, and HT-29, were verified as authentic at 100 %, CaCo-2 cell line authentic at 75 %, while K-562 STR profile was not determined.

Conclusion: Short tandem repeat profiling (STR) test established the authenticity for HeLa, SW620, HT-29, and CCRF-CEM cell lines, while further analysis should be conducted with Caco-2 cell line in order to make a final conclusion about its authenticity. Furthermore, an analytical procedure for K-562 cell line should be repeated.

Keywords: cell line, contamination, authentication, STR profile.

Molecular biological changes in the background of Olaparib treatment on HeLa cells

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Introduction: Olaparib is a member of poly (ADP-ribose) polymerase (PARP) family, which is involved in several cellular processes, including programmed cell death and DNA damage repair. Olaparib is an applied agent in the treatment of metastatic breast and prostate cancers. Irradiation, as a therapy, affects 3.5 million people in a year, and it is an essential treatment in lung, brain, and cervix cancer. Previously, our research group investigated the effect of Olaparib on cervix carcinoma cell line. It is known, that Olaparib increases the radiosensitivity of breast and ovarian carcinoma cell lines, through the decreased expression of JNK and Akt pathways as well. Therefore, in the present study we investigated known elements of pro- and antiapoptotic pathways after Olaparib treatment and irradiation.

Methods: First, we investigated the viability of cells after 2Gy irradiation and Olaparib treatments, and the combined effects of them in different concentrations (8uM, 4uM, 2uM, 1uM, and 500nM) on MTT tests after 24, 48, and 72h. After, we applied "Human Phospho-Kinase Antibody Array Kit" to detect the expression of several pro-and antiapoptotic factors (elements of Akt, JNK, GSK, RSK). Later the expression of these factors was investigated with Western blot technique as well.

Results: We detected that the viability of cell lines decreased significantly ($p<0.05$) after 8uM, 4uM and 2uM Olaparib treatments on MTT tests. We detected the most efficient changes after 72h treatment, therefore later we applied this pretreatment time. The irradiation effected decreased ($p<0.05$) cell viability as well. The expression of Akt1/2/3 significantly decreased after irradiation, 72h Olaparib treatment and the after the combined treatment. Similarly, the expression of c-JUN, JNK1/2/3, RSK, and GSK decreased after 2Gy irradiation, PARP inhibitor and the combination of them. These results were affirmed by Western blot results.

Conclusion: Olaparib treatment decreased the expression of JNK1/2/3, Akt1/2/3, RSK, and GSK, these factors are targets of different approved oncological treatment protocols. Based on our results Olaparib ameliorated the effectiveness of irradiation on cervix carcinoma cell lines.

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Keywords: PARP inhibitor, JNK, Akt, HeLa, irradiation

Socket preservation using guided bone regeneration technique with xenograft material: study plan and preliminary histological findings

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Introduction: Bone defects in the alveolar ridge are atrophic tissue areas of lower bone density or volume. Epidemiology of bone defects may vary from trauma, congenital malformation and most frequently resorption after oral surgery or infection of the periodontium.Patients demand for restoration of masticatory function and dental aesthetics through implantology after tooth loss is permanently growing. Implant placement requires sufficient bone volume and healthy trabecular architecture. To augment bony defects we use various materials as substitutes to match aesthetic and functional requirements for implant placement. We can choose among autografts, allografts, xenografts and synthetic grafting materials. Despite autografts being the gold standard at the moment, xenografts are primarily used for augmentation in dentistry worldwide. Xenografts are materials from equine, bovine or porcine sources that are deproteinized and contains no organic substance and is risk free of disease transmission. The material itself consists of particles with crystal structures that closely resembles human cancelous bone. In this research our aim is to histologicaly asees newly formed bone after guided bone regeneration as a method of alveolar socket preservation following tooth extraction.

Materials and methods: Twenty healthy patients with indications for tooth extraction will be included in this research. Excluding criteria are systemic conditions like diabetes mellitus, uncontrolled hypertensive disease and such others that can cause complications. After the extraction alveolar socket will be filled with xenogenic bone substitute material (Cerabone, Botiss Dental GmbH) and covered with a native collagen membrane (Jason membrane, Botiss Dental GmbH) to prevent ingrowth of gingival tissue and epithelium in the defect. Six months after, during the implant site preparation bone samples will be harvested and analyzed. Samples will be histologically analyzed to determine percentage of the new bone formation, a percentage of the residual biomaterial and a percentage of the soft tissue.

Preliminary results: Concerning the fact that this research is ongoing at the present moment this presentation offers insight in the preliminary results. Histological analysis shows formation of the new bone at the margins of bone defect along with elevated activity of multinuclear cells who carries out important role in absorption of material following new bone formation.

Conclusion: Descriptive histological methods used for analysis of the samples showed osteoconductive properties of Cerabone. In following research these properties should be analyzed more thoroughly to determine histological and radiological evidence of osteoconductivity.

Keywords: guided bone regeneration, Cerabone, histology, oral surgery

Spiral-shaped piezoelectric MEMS Cantilever Array forFully Implantable Cochlear Implants

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Introduction: The habilitation or rehabilitation of deafness due to cochlear lesions is available for the past decades with cochlear implantion. However, the recent devices are not fully implantable resulting in a series of disadvantages. A fully implantable cochlear implant could significantly increase the quality of life of the patients suffering from severe sensorineural hearing loss or deafness. In this work we demonstrate a fully implantantable low volume, piezoelectric micro-electromechanical system array which could be mounted on one of the ossicles in the middle ear.

Materials and Methods: To mimic the tonotopy of the cochlea is to apply an array of micro-electromechanical system cantilevers having varying length thus varying natural resonance frequency. The test array consisting of 16 cantilevers has been fabricated by standard bulk micromachining using a Si-on-Insulator wafer and aluminium-nitride as a biocompatible piezoelectric material. Archimedean spiral geometry ensures the reduced device footprint. The output voltage signals were collected for each cantilever at continuous sweep of the sinusoidal excitation in the frequency range of 20 Hz-1.2 kHz.

Results: The test arrays showed clear frequency selectivity in the 281-672 Hz range which corresponds to the lowest part of the voice frequency range. By applying a shorter cantilever it can be easily extended even up 20 kHz at the same or at a smaller device footprint. The obtained output voltage signals (3-10 mV) are sufficient to excite hearing nerves through an implantable amplifier using a similar system.

Conclusion: The manufactured 2 mm × 2 mm cantilevers can satisfy the size constraint for middle ear implants and can provide a new generation of implantable hearing aids. Moreover, a multi-contact, Fermat-spiral-shaped cantilever array are under construction which may open the way to collect more than one ambient frequency with a single cantilever.

The effects of PARP inhibitor Olaparib on cervix carcinoma cells

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Introduction: In Hungary cervical carcinoma claims 500 lives annually and affects hundreds of women. Therefore, therapeutic modalities need to develop to increase the effectiveness of the therapy. Poly (ADP-ribose) polymerase (PARP) family of proteins is involved in numerous cellular processes, including DNA damage repair and programmed cell death, therefore the inhibition of this proteins is an applied strategy in oncological practice. In present study we investigated the separated antiproliferative effects of the PARP inhibitor Olaparib in different concentrations and the combined effects of this PARP inhibitor and irradiation on HeLa (ATCC), a cervical adenocarcinoma cell line.

Methods: We investigated the viability of cells after Olaparib treatment in different concentrations (8uM, 4uM, 2uM, 1uM, and 500nM). More than half of cervical cancer patients receive radiotherapy, therefore we examined how Olaparib pretreatment can influence the effectiveness of radiation. We measured cell viability with MTT test and applied radiation in dosages of 1Gy; 2Gy respectively. The effects of Olaparib treatment, the response to radiation, and the combined treatment of both were tested first on colony formation assays, than we performed "Annexin V dead cell assay kit" and "Cell cycle assay kit" of Merck to detect different forms of apoptosis.

Results: We detected that the viability of cell lines decreased significantly ($p<0.05$) after 8uM, 4uM and 2uM Olaparib treatments on MTT tests. Also, the pretreatment with Olaparib resulted more effective radiation on MTT tests. We observed a significant cell number reduction with colony formation assays. The presence of living cells decreased significantly and the early and late apoptotic forms of cells increased after Olaparib treatment significantly.

Discussion: Olaparib is an FDA- approved targeted therapy for ovarian and metastatic breast cancers, accordingly to test its effect on other cell lines is necessary.

Conclusion: Olaparib pretreatment strengthened the antiproliferative effect of radiation on cervical adenocarcinoma cells *in vitro*. The molecular biological background of the above-mentioned results should be the subject of further examinations.

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Keywords: Olaparib, cervix carcinoma, radiosensitivity, PARP inhibitor

Alterations in motor neuronal calcium homeostasis after long-term treatment with blood serum from patients diagnosed with sporadic amyotrophic lateral sclerosis

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Introduction: Different pathological processes contribute to motor neuronal degeneration in the sporadic form of amyotrophic lateral sclerosis (sALS). Our aim was to understand the effect of chronic treatment with blood serum that contains anti-motoneuronal antibodies of sALS patients on the intracellular calcium level, neuronal survival and motor function.

Materials and methods: Balb/c mice were injected intraperitoneally for 75 days with blood serum from healthy individuals (n=3) and patients diagnosed with sALS (n=6). Isometric muscle strength of their limbs was measured during the passive transfer. Number of motor neurons in the spinal cord was measured with the disector method. Intracellular calcium level was quantified with geometrical statistics in the spinal cord and in the axon terminals of their *musculus interosseus* samples.

Results: Isometric muscle strength significantly decreased after long-term inoculation of blood serum from sALS patients. The number of motor neurons were also significantly decreased in the cervical ($p<0.001$) and lumbar ($p<0.001$) spinal cord. Significant increase of intracellular calcium could be documented in the cervical ($p<0.001$) and lumbar ($p<0.001$) regions of the spinal cord and in the axon terminals of their forelimb ($p<0.001$) and hindlimb ($p<0.01$). Ultrastructural alterations of perikarya and neuromuscular synapses were observed.

Conclusion: Functional regression, motor neuronal loss and elevated intracellular calcium level confirm the motor neuronal degeneration in this model. Such long-term treatment provides a feasible representation of sALS, as no genetic mutations were observed in the patients. However, it is reconcilable with the transgenic animal models widely used in pharmacotherapeutic tests. Therefore this model could be give us further understanding of motor neuronal degeneration in ALS.

Keywords: ALS; motor neuron; calcium homeostasis; stereology; electron microscopy

Guided Bone Regeneration using biphasic calcium phosphate paste: study plan and preliminary histological findings

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Introduction: Human bone has great potential for regeneration. Bone remodeling is a balance of two processes: bone resorption by osteoclast and bone healing by osteoblast. The purpose of augmentation procedures in implant dentistry is to promote bone regeneration by using different biomaterials. Autogenous bone, allografts, xenografts, and alloplastic materials in combination with resorbable or non-resorbable membranes are used in Guided Bone Regeneration (GBR), which is one of the most frequently used techniques in implant dentistry, with a predictable clinical outcome. In the present study, we want to assess and describe bone histology 6 months after GBR.

Materials and methods: The study will include twenty healthy patients with at least one or two wall intrabony defects after tooth extraction. The intrabony defects are filled with biphasic calcium phosphate paste (Maxresorb inject, Botiss Dental GmbH) and covered with a native collagen membrane (Jason membrane, Botiss Dental GmbH), to ensure the isolation of the bone defect against gingival connective tissue and epithelium. Six months after healing, simultaneously with dental implant placement, bone biopsies for histological analysis will be harvested. Following parameters will be determined: percentage of new bone formation, percentage of the residual biomaterial and percentage of the soft tissue.

Preliminary results: This report presents preliminary histological findings of the osteoconductive properties of Maxresorb inject. The histological examination of the specimen showed new bone formation at the peripheral border of the bone defect. The granules of Maxresorb inject are incorporated into bone tissue and there are no histological signs of inflammation.

Conclusion: In the present study, we evaluated the regenerated bone by descriptive histological examination. Maxresorb injects shows osteoconductive potential for bone regeneration. Further work is needed to complete histological, radiological and clinical evidence of osteoconductive properties of Maxresorb inject.

Keywords: guided bone regeneration, implant dentistry, Maxresorb inject, histology

Effect of a grape polyphenols on a cell cycle of a tumor cell lines *in vitro*

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Introduction: Polyphenols are secondary plant metabolites that have shown numerous bioactivity features in many researches, such as antioxidant, antimicrobial, antiproliferative activity and protection from UV radiation. They are phytochemicals and formed as phenylalanine derivatives with an aromatic ring or a hydroxyl group. According to the most recent classification system, polyphenols are divided into two main groups: flavonoids and non-flavonoids (phenolic acids, stilbenes, and lignans). Polyphenols inhibit tumor proliferation, induce apoptosis, prevent angiogenesis, and have antioxidant properties that prevent DNA oxidation and reduce the risk of cancer.

Objective: The aim of this study is to explore the effect that polyphenols isolated from grapes have on the in vitro cell cycle and to determine the extent to which the efficiency of polyphenolic components changes after the treatment of microorganisms that stimulate the degradation of grape pomace. Materials and Methods: In the research, the following materials were used: an extract of pure polyphenolic components and extracts of polyphenols formed after the treatment of microorganisms (Phanerochaete chrysosporium (PC) and Trametes gibossa (TG) in the adequate concentrations corresponding to the IC50 values on the human tumor cell line and CaCo-2. The cells were cultivated under standard cultivation conditions (37°C / 5% CO2) in DMEM without the usage of antibiotics. After 48 hours of exposure to the extracts, the method of flow cytometry for cell cycle analysis was applied.

Results: Of the three analyzed polyphenolic extracts, the best results in terms of efficiency in stopping the cell cycle of CaCo-2 and SW620 cells were traced in a PP extract that affected all three phases of the cell cycle; G1 and S phase reduction cycle with G2 / M increase. The effect of TG and PC extracts on the cell cycle are lesser than that of the PP extract. The TG extract resulted in an increase in G1 cell portion and G2 / M phase followed by S phase reduction in SW620 cells. PC extraction caused an increase in the G1 phase and the reduction of S phase on the same cell line. The effect on the cell cycle of CaCo-2 cells of these two extracts is lower than that of the PP extract.

Conclusion: Polyphenolic components cause changes in the cell cycle of SW620 and CaCo-2 tumor cells by stopping it in the G2 / M phase and reducing the S phase proportion. The effect on the G1 phase is different, possibly depending on the composition of polyphenols and cell types.

Keywords: polyphenols, cell cycle, antiproliferative effect, tumor cells

Complex Reactiometer Drenovac: A Novel Tool for Mild Cognitive Impairment Assessment in Cancer Patients

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Introduction: Mild cognitive impairment (MCI) is the clinically noticeable cognitive dysfunction between the expected cognitive decline of normal aging and dementia. It can involve problems with memory, language, thinking and judgment that are significantly more common and pronounced in comparison to usual age-related changes, associated with impaired overall quality of life. Incidence of MCI is higher in patients with comorbidities (cancer, anemia, diabetes etc.). The aim of this study was to assess and compare cognitive function in cancer patients initially and after the treatment of anemia. We therefore hypothesize that treatment of anemia can reverse cognitive impairment in cancer patients.

Participants and methods: Overall, the study included 400 newly diagnosed, therapy naive hemato-oncologic patients. Furthermore, patients were categorized in equally distributed (n=100) groups, based on malignant disease and anemia in clinical status (group 1: malignancy and anemia ; group 2: malignancy in absence of anemia ; group 3: anemia in absence of malignancy ; group 4: healthy participants). Cognitive function was assessed in latter groups using Complex Reactiometer Drenovac (CRD) – Croatian product designed for performing series of computational tests (convergent thinking, spatial visualization, visual orientation, learning and memory, operative thinking, reaction on sound, reaction on light). Data were analyzed using Microsoft Excel (Microsoft Office) and Statistica v10.0 (StatSoft Inc., Tulsa, Oklahoma, United States). Criterion for statistical significance was estimated on $p<0.05$.

Results: An increase in hemoglobin level was associated with decrease in time necessary to complete convergent inductive thinking - CRD11 test ($\beta=-0.458$, $p<0.001$) among group 1, after adjusting for plausible confounders. Time necessary to complete CRD11 test significantly decreased ($p<0.05$) after anemia treatment (336.05±153.14 vs 263.12±113.80 s) in the latter group.

Conclusion: Hemoglobin level is significantly positively correlated with cognitive function in cancer patients. Hence, early assessment of MCI and well-managed treatment of comorbid anemia are cornerstones of cognitive impairment progression prevention and supportive care in cancer. CRD is clinically useful tool for cognitive function assessment due to overall time demands and absence of age, education and language limits.

Keywords: Anemia; Cognition Disorders; Mental Status and Dementia Tests; Neuropsychological Tests

Synthesis of new 7-hydroxycoumarin derivatives and their biological effects on the growth of human cells in vitro

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Background: Intense environmental pollution, aging world population and changes in diet have resulted in an increase in the occurrence of tumors, which have become one of the leading causes of death in the world.

Aim: The aims of this work were to synthesize and characterize novel molecules which in their structure contain 7-hydroxycoumarin core and to examine the influence of derivatives of 7-hydroxycoumarin on the growth of normal and tumor cells in vitro.

Methods: New 7-hydroxycoumarin derivatives were synthesized by nitration reactions, condensation and esterified. Confirmation of purity and identification of the obtained compounds was performed by thin layer chromatography, elemental analysis, IR spectroscopy and by 1H NMR spectrometry. Cytotoxicity testing were performed on six human tumor cell lines: cervical carcinoma cells (HeLa); colon adenocarcinoma (CaCo2); larynx carcinoma cells (HEp-2); pancreatic adenocarcinoma cells (MiaPaCa-2); lung adenocarcinoma (NCI-H358); breast adenocarcinoma (MCF-7) and two normal cell lines: human fibroblasts (BJ) and epithelial canine kidney cells (MDCK).

Results: Citotoxicity of investigated compounds depended on the cells and applied concentrations. Morphological changes suggest apoptosis as a mechanism of death.

Conclusion: Further examination of mechanism of action of examined compounds should be performed.

Keywords: 7-hydroxycoumarin, citotoxicity, cell growth

Pituitary hormones in breast milk

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Introduction: Human milk provides the building blocks of postnatal development with its nutritional and regulatory compounds. After birth breastfeeding is the exclusive hormonal connection between the mother and the infant. Several examinations revealed the rich hormone content of human milk, the limitation of these studies was the shortness of the examination period. In the present work we investigated the concentration of FSH, TSH, and PRL in breast milk during the first 6 months of lactation.

Methods: We involved 9 mothers who gave birth to term infants at the Department of Obstetrics and Gynecology. Milk samples were collected monthly from mid-day breastfeeding during the first 6 month of lactation. FSH and PRL concentration of breast milk samples was detected with chemiluminescent microparticle immunoassay technology. TSH level was measured with immunoluminometric assay at the Department of Laboratory Medicine.

Results: During the examination period we did not detect monthly fluctuation in the FSH concentration (0.150±0.007 U/l). The level of TSH was significantly higher (p=0.036) in the first month of lactation 0.031±0.0042 mU/l) compared to the average of the 2nd through 6th month (0.021±0.0025 mU/l). The concentration of PRL showed similar pattern to TSH, the level of it in the first month (31.570± 13.956 ng/ml) was significantly (p=0.019) higher compared the other months of the examination period (11.684±1.614 ng/ml). We analyzed the total protein level of breast milk samples, which was significantly higher (p=0.028) in the first month.

Conclusion: Breast milk contains hormones produced by the pituitary gland in the first 6 months of lactation. Since the half-life of these hormones are hours, from the gastrointestinal tract through absorption they are able to exert their effect on the developing human.

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Effect of insulin on the transient receptor potential vanilloid 1 (TRPV1) nociceptive ion channel in the rat dura mater

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Introduction: TRPV1 receptor (TRPV1-R) expressing chemosensitive primary sensory neurons have dual function. They transmit the nociceptive information to the central nervous system and upon activation they also release neuropeptides from their peripheral terminals that provoke tissue reactions. Fifty % of primary sensory neurons express insulin receptor (IR). Activation of IR may affect also the function of TRPV1-Rs via intracellular signaling mechanisms. The aim of our research is to investigate the functional interaction of insulin and TRPV1-R in dura mater preparations of rats.

Materials and methods: We used *ex vivo* dura mater preparations of adult male Wistar rats to study the effect of IR activation on the release of calcitonin gene-related peptide (CGRP) from chemosensitive afferents. CGRP content of the samples was measured with enzyme-linked immunosorbent assay (ELISA) method. In *in vivo* experiments laser Doppler flowmetry was used to examine the effect of insulin on meningeal blood flow changes. Immunohistochemical staining was performed to observe the colocalization of IR and TRPV1-R in the trigeminal ganglion.

Results: In *ex vivo* dura mater preparations the application of insulin at 1 and 10 μM concentrations resulted in a dose-dependent increase in CGRP release (20.1 ± 9.6 and 85.3 ± 35.3 % compared to the basal release). Pretreatment of the dura mater with insulin increased also the capsaicin-induced CGRP release. Pretreatment with an IR antagonist (BMS-754807) or a TRPV1-R antagonist (capsazepine) decreased the insulin-triggered CGRP release. The results of our *in vivo* experiments confirmed that insulin enhanced the meningeal blood flow increasing effect of capsaicin. Immunohistochemical double staining indicated the colocalization of IR and TRPV1-R in the trigeminal ganglion neurons.

Conclusion: According to our results insulin may influence the meningeal nociceptive reactions by activating or sensitizing the TRPV1-R.

Keywords: insulin, TRPV1, nociception, dura mater, trigeminal ganglion

Effect of region selection method on the quantitative evaluation of dopamine receptor SPECT studies

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Introduction: By the integrated processing of SPECT and MRI images, we investigated how various spatial registration methods influenced the radiopharmaceutical uptake, characterizing dopamine receptor distribution in the sub-regions of the striatum. To do this, we used three methods for defining volumes of interest (VOIs) on SPECT-MRI image pairs: an atlas-based automatic procedure after elastic or general linear (affine) transformation, and manual VOI drawing. Then we performed statistical analysis of the radiopharmaceutical uptake parameters.

Materials and methods: Image processing was performed in MatLab R2015a framework. First, we spatially registered and visually checked the patient's SPECT and MRI images. The next step was to register the patient's MRI after removing the skull to the reference image of the atlas. After both linear and elastic transformation, the 12 sub-regions (VOIs) of the striatum were automatically transferred from the atlas to the patient's SPECT image. As a final step, I drew manual VOIs.

Results: VOIs created on MRI images well matched the putamen and the caudate on the SPECT images by visual inspection. From among the 12 VOIs, only one gave significantly different values between the elastic and general linear transformation, in the dorsal part of the right posterior putamen ($p = 0.006$). When comparing the manual VOIs to those based on the elastic transformation used as reference, the right ($p = 0.003$) and the left ($p = 0.001$) posterior putamen and the right caudate ($p = 0.022$) showed significant difference. There were 3 significant ($p<0.05$) differences between the VOI data obtained by linear transformation and manually. On the more abnormal side, there was a difference in the posterior putamen / caudate ratios between the three VOI definition methods ($p = 0.002$), while there was no significant difference on the less pathological side.

Conclusion: The differences indicate that it is difficult to manually delineate the posterior borders of the striatum, this being the region where the radiopharmaceutical uptake is first affected by the pathological processes. Applying an automated atlas-based quantification method can better establish the early diagnosis of Parkinson's disease. Our results are just preliminary since we had only six pairs of DatScan and MRI studies with adequate quality.

Keywords: dopamine, SPECT, Parkinson's disease

PAIN-net: Molecule to man pain network
Painful and painless SFN: genetics, morphometric and expression studies in skin nociceptors

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Neuropathic pain affects 5% of the general population and the pathogenesis of pain in most patients is unknown, therefore no biomarkers are available yet. A striking example is diabetic neuropathy, whose prevalence is estimated to double over the next two decades following the epidemics of diabetes, thus increasing from current 371 million of individuals affected to 552 million by the year 2030. Among these patients, about 21% (116 million) will develop a painful neuropathy that is known to be unrelated to age, diabetes duration, metabolic control, or severity of neuropathy. The reason why some patients develop the painful form of diabetic neuropathy is unknown. Neuropathic pain is recognized to play a key role also in the pathophysiology of cancer pain, with a prevalence of about 50% at the time of the diagnosis and early in the course of the disease, to 75% at advanced stages. Overall, not all individuals develop pain and it is currently not possible to predict who is more or less susceptible among those with similar risk exposure. Such variability remains unexplained yet. Over the past years, novel variants in sodium channel genes partially explaining pain variability in patients have been identified.

When it comes to diagnostic methods, skin biopsy has been recognized as golden standard in small fiber neuropathy assessment, regardless etiology. Nerve fibers innervating the epidermis and the superficial layer of the dermis act as terminal nociceptors in mammals. The complex environment includes non-neuronal cells and structures that might be involved in the chronification of neuropathic pain and, possibly, in the diverse susceptibility among individuals also in terms of response to drugs. Therefore, skin biopsy will be performed to patients suffering from diabetic, cancer and immune mediated neuropathy clustered in several groups according to persistence of pain (painful and painless) and suggestive genetic background (carriers of genetic variations in pain related ion channels).

This project is focused on investigating the expression of pain-related ion channels (e.g. sodium, potassium, calcium, chloride, Transient Receptor Potential) and their changes in the different groups of patients by different techniques (e.g. immunohistochemistry; indirect immunofluorescence; bright-field, confocal and correlative microscopy). Moreover, we are investigating the correlation between the expression of ion channels and nodal/paranodal proteins (e.g. Caspr, Contactin, Gliomedin, Ankyrin G), and the changes in resident cells and connective matrix.

The PAIN-Net programme has been designed to meet the innovation needed in neuropathic pain through the integration of clinical, advanced genetics and basic science research at academic and non-academic level with aim of translating scientific findings in the complex field of pain into solutions which will be able to provide clues for a better management of neuropathic pain patients in clinical practice, with direct and indirect benefits to the society and the healthcare systems.

Keywords: neuropathic pain, voltage gated ion channels

"This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 721841"

WORKSHOPS

ALS

Workshop leader: Nenad Nešković

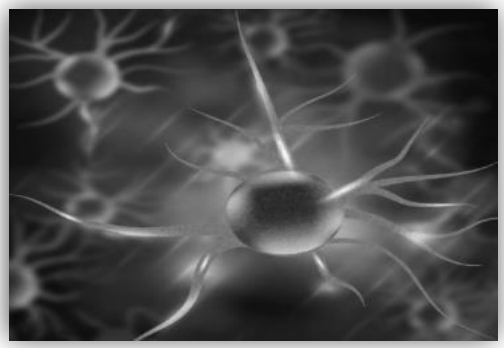
One-third of people who get myocardial infarction die before they get to the hospital, partly due to inadequate and late onset of cardiopulmonary resuscitation. Each doctor will meet a patient who is in cardiopulmonary arrest at least once during his or her work, and much often will meet a patient who is deteriorating and or at risk of cardiopulmonary arrest. The duty of every doctor is to provide advanced measures of cardiopulmonary resuscitation. The skills that will be taught during the various courses of cardiopulmonary resuscitation will enable him or her to promptly and properly help the patient. Skills such as defibrillation, effective chest compressions, ability to ventilate, recognition of the underlying cardiac arrest rhythm, which are all important components of a successful resuscitation, are usually referred to as technical skills. At this workshop, students of the final years will be given a chance to gain some technical skills and to learn the methods of advanced adult life support (ALS) and the ALS algorithm of European Society of Resuscitation. The workshop is organized as a simulation of the cardiorespiratory arrest on the resuscitation dummy and the student will practice the skills necessary for correct cardiopulmonary resuscitation.

SURGICAL SUTURING WORKSHOP

Workshop leader: Clinic of surgery Osijek

In this workshop, attendees will have the opportunity either to improve their already developed skills in surgical suturing, or to learn the very basics and try to sew their first surgical sutures on an animal model. The workshop will be carried out under a supervision of a surgeon, and it will encompass theoretical, as well as practical knowledge on wound care, including surgical needle selection, basic surgical knots, performing a simple interrupted and a continuous suture, as well as knowing how and when should sutures be removed.

VISUALIZATION OF STRUCTURES IN THE NEURAL TISSUE



Workshop leader: Milorad Zjalić
Workshop duration: 45 min
Materials & methods:
Murine brain slices mounted on glass slides
Nissl staining histological dye
Solution for silver-impregnation quick staining
Alcohol solution gradient
Xylene substitute from orange etheric oil
Histomount – mounting solution for tissue slides
Latex gloves
Cover slips
Light microscopes
Preprepared immunohistochemically stained tissue samples

Workshop description:
In the workshop, attendees will firsthand conduct neurobiological tissue staining protocols (Nissl and silver impregnation). The workshop will also encompass identification of several murine brain regions, overview of structural specificities of cellular layers of the cortex and its implications in neurodegeneration. The brain's most abundant glial cells, microglia and astrocytes, will be shown on the immunohistochemically pre-stained samples.

WORKSHOPS

Workshop leader: MLDSA

DIFFERENTIAL BLOOD COUNT

1.)Theoretical part: Differential blood count gives relative percentage of each type of white blood cell and also helps reveal abnormal white blood cell populations (eg, blasts, immature granulocytes, or circulating lymphoma cells in the peripheral blood). Differential blood count is also used along with leukocyte count (WBC) to generate an absolute value for each type of white blood cells (eg, absolute neutrophil count, absolute lymphocyte count, or absolute eosinophil count), which usually gives more meaningful information than the percentage of each, since relative percentage can be misleading. Differential blood count is not a part of complete blood count (CBC) but is interpreted together with CBC to help support or exclude a suspected diagnosis. For example, the presence of anemia along with thrombocytopenia with a low or high white blood cell count may suggest bone marrow involvement by leukemia.
2.)Practical part: At the workshop it will be shown how to make and paint blood smear, microscope it and differentiate the white blood cells.

VENIPUNCTURE

Venipuncture:
1.)Theoretical part: Venipuncture is the collection of blood from a vein which is usually done for laboratory testing. Venipuncture reduces the total amount of blood in the bloodstream and shortens venereal and capillary passage and later arterial blood pressure.
2.) Practical part: (Practical part is supervised and provided by professional medical staff) Exercise of venipuncture on the artificial hand. Exercise of venipuncture on the human hand (interconnection of venipuncture).The first step in drawing blood correctly is to identify the appropriate veins to puncture.
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PARTNERS

AIMS MEETING

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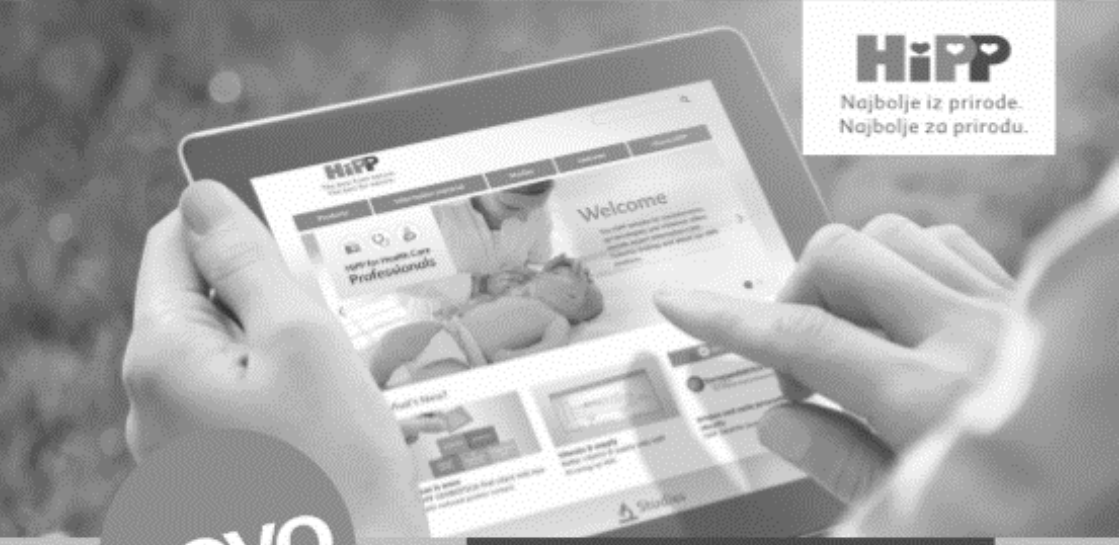

NOVO

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Što smo Vam pripremili?

- Nedavno objavljene studije: bitne i sažete informacije:
  Pročitajte zanimljive članke iz područja pedijatrije i nutricionizma
- Pogledajte i poslušajte stručna predavanja putem web-seminara s raznih simpozija
- Informacije o proizvodima posebno namijenjene zdravstvenim djelatnicima
- Saznajte više o HiPP proizvodima, prehrani dojenčadi, njezi kože te proizvodima namjenjenim za posebne medicinske potrebe

PRESENTING AUTHORS INDEX

THANK YOU VOLUNTEERS!

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