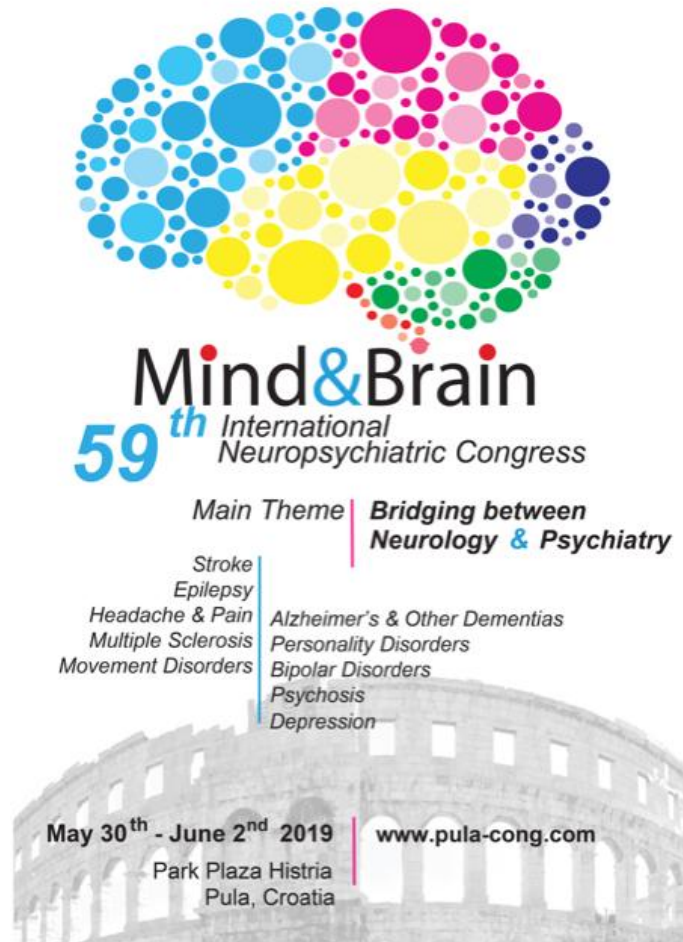


# ABSTRACT BOOK 2019



## MIND & BRAIN

## 59<sup>th</sup> INTERNATIONAL NEUROPSYCHIATRIC CONGRESS

Pula, Croatia

MAY 30<sup>th</sup> – JUNE 2<sup>nd</sup>, 2019.

ISSN 2469-5748

[www.pula-cong.com/abstract-book-2019](http://www.pula-cong.com/abstract-book-2019)

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**[www.pula-cong.com/abstract-book-2019](http://www.pula-cong.com/abstract-book-2019)**

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**Publisher**

International Institute for Brain Health

Ulica grada Vukovara 271/4  
Zagreb, Croatia

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**Design & Layout**

International Institute for Brain Health

Printing was completed in May 2019. © International Institute for Brain Health, Zagreb, 2019.  
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**ISSN 2469-5748**

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

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

**mizmo.ibrain@gmail.com**

**www.pula-cong.com**

## CONTENTS

### MIND & BRAIN – 59<sup>th</sup> INTERNATIONAL NEUROPSYCHIATRIC CONGRESS

PROGRAM .....	17
MAIN THEMES LECTURES .....	25
Franz Fazekas (Graz, Austria): The contribution of MRI to the management of MS treatment .....	25
Norbert Müller: THE ROLE OF INFLAMMATION IN ALZHEIMER’S DISEASE.....	26
Martin Brüne: SOCIAL COGNITION IN HEALTH AND DISEASE – INSIGHTS FROM NEUROIMAGING AND GENETICS.....	27
Vida Demarin: THERE IS NO HEALTH, WITHOUT BRAIN HEALTH .....	28
Ervina Bilić: IVIG IN TREATMENT OF NEUROMUSCULAR DISEASES WITH FOCUS ON CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY .....	29
Milan Latas: PHOBIC VERTIGO - DOES IT REALLY EXIST?.....	30
Milija Mijajlovic (Belgrade, Serbia): Patent foramen ovale: to close or not? .....	31
Boris Tsygankov Boris, Galina Ivanova, Galina Mamedova: SUPPOSED MECHANISMS OF INFLUENCE OF THE HEPATITIS C VIRUS ON THE DEVELOPMENT OF NEUROPSYCHOLOGICAL DISORDERS.....	32
LECTURES PULA'S WORLD MS DAY SYMPOSIUM - MULTIDISCIPLINARY APPROACH TO PERSONS WITH MULTIPLE SCLEROSIS .....	33
Senka Rendulić Slivar, Robert Rendulić: HEALTH-RELATED QUALITY OF LIFE BY MULTIPLE SCLEROSIS PATIENTS – IMPORTANCE OF NEUROPHYSIOTHERAPY INTERVENTION .....	33
Robert Rendulić, Senka Rendulić Slivar: THE ROLE OF DINAMIC NEUROMUSCULAR STABILISATION IN THE COR STABILITY .....	34
Jagoda Kragujević, Vlasta Pekić, Ivana Kampić, Silva Butković Soldo: MULTIPLE SCLEROSIS AND FATIGUE .....	35
Vlasta Pekić, Tanja Lazarević, Ksenija Pandža, Natalija Sikora, Silva Butković Soldo: MULTIPLE SCLEROSIS AND NUTRITION .....	36
Dunjica Karniš: ART THERAPY AS AN AID IN THE TREATMENT OF MULTIPLE SCLEROSIS PATIENTS .....	37
Sanja Tomasović: NEUROIMMUNOLOGY- PARANEOPLASTIC SYNDROMES .....	38
MULTIPLE SCLEROSIS SYMPOSIUM – HOT TOPICS IN MS TREATMENT .....	39
Tanja Hojs Fabjan: FIRST LINE THERAPY IN MULTIPLE SCLEROSIS .....	39
Vanja Bašić Kes: HOW TO TREAT NON-RESPONDENT MS PATIENTS?.....	40
Uroš Rot: TREATMENT OPTIONS IN PROGRESSIVE MULTIPLE SCLEROSIS.....	41
GRAZ NEUROLOGY SYMPOSIUM - HISTORICAL DEVELOPMENT, PRESENT STATUS AND FUTURE ASPECTS OF DIAGNOSIS AND TREATMENT .....	42
Tadeja Urbanic-Purkart, Franz Payer: FUTURE ASPECTS IN NEURO-ONCOLOGY.....	42
PSYCHOPATHOLOGY SUMMER SCHOOL.....	43
Gonzalo Forno, Christina Josefa Herold, Jorge Calderon, Johannes Schröder, Pablo Toro: NEUROLOGICAL SOFT SIGNS (NSS) AND COGNITIVE DEFICITS IN HIV ASSOCIATED NEUROCOGNITIVE DISORDER .....	43
Martin Brüne: IS SCHIZOPHRENIA THE PHENOTYPIC CORRELATE OF PARASITIC BEHAVIOUR MANIPULATION? .....	44

Arjen L. Sutterland, Anne Kuin, Bouke Kuiper, Tom van Gool, Marion Leboyer, Guillaume Fond, Lieuwe de Haan: DRIVING US MAD: THE ASSOCIATION OF TOXOPLASMA GONDII WITH SUICIDE ATTEMPTS AND TRAFFIC ACCIDENTS - A SYSTEMATIC REVIEW AND META-ANALYSIS .....	45
Margherita Bechi: AUTISTIC TRAITS NEGATIVELY INFLUENCE THEORY OF MIND AND TRAINING EFFICACY IN PATIENTS WITH SCHIZOPHRENIA.....	46
Nikola Ilanković, Andrej Ilanković: SCHIZOPHRENIAS ARE FREQUENTLY NOT PRIMARY CEREBRAL DISORDERS .....	47
PSYCHIATRY SYMPOSIUM- NEW INSIGHTS IN NEUROINFLAMMATORY AND AUTOIMMUNE DYSREGULATION IN PSYCHIATRIC DISORDERS: IT THERE A ROLE FOR HERPES VIRUSES? .....	48
E. Marion Schneider, Stella Steinhauser, Karl Bechter (Ulm, Germany): METABOLISM AND MITOCHONDRIAL DYSREGULATION – ROLE OF PRO- AND ANTI-OXIDANT PATHWAYS IN PSYCHIATRY .....	48
Hans C. Klein, H. Knegeter, Karl Bechter : PSYCHOSIS AS A NON-CLEARING INFLAMMATORY RESPONSE TO A LATENT HERPES VIRUS IN THE LIMBIC SYSTEM .....	49
Christian Scheiber, Hans C. Klein, E. Marion Schneider: HERPES VIRAL AND INFLAMMATORY MARKERS IN PATIENTS WITH SEVERE MENTAL DISORDERS. NEW DATA FROM CSF. ....	50
PSYCHIATRY SYMPOSIUM: FROM NEUROBIOLOGY TO PSYCHOTHERAPY.....	51
Darko Marčinko: PERSONALITY AND PSYCHOSOMATIC REACTION .....	51
Martina Rojnić Kuzman: TREATMENT OF FIRST EPISODE PSYCHOSIS: BIOLOGICAL THERAPY OR/AND PSYCHOTHERAPY? .....	52
Bjanka Vuksan-Ćusa, Marina Šagud: BIPOLAR DISORDER -PHARMACOTHERAPY OR/AND PSYCHOTHERAPY.....	53
5 <sup>TH</sup> PULA NEUROSCIENCE SYMPOSIUM Jasna Kriz: INNATE IMMUNE RESPONSE FOLLOWING BRAIN INJURIES: LOST IN TRANSLATION .....	54
Mathias Hoehn, Claudia Green, Dirk Wiedermann: FUNCTIONAL NEURONAL NETWORKS IN HEALTH AND DISEASE .....	55
Srećko Gajović, Dunja Gorup, Marina Radmilovic Dobrivojević, Siniša Škokić, Anton Glasnović, Paula Josić, Jasna Kriz: MULTIMODAL APPROACHES TO EVALUATE MOUSE BRAIN REPAIR AFTER ISCHEMIC LESION.....	56
Vedrana Ivić , Milorad Zjalić, Irena Labak, Srećko Gajović, Robert Gaspar, Sandor G. Vari, Marija Heffer: METFORMIN AND LIRAGLUTIDE DIFFERENTLY AFFECT CENTRAL INSULIN RESISTANCE IN THE RAT MODEL OF PREDIABETES.....	57
Jelena M Kezic, Paul G McMenamin: SYSTEMIC EXPOSURE TO TOLL-LIKE RECEPTOR 9 LIGAND CPG-ODN ELICITS LOW-GRADE INFLAMMATION IN THE RETINA THAT IS UNALTERED IN DIABETIC MICE.....	58
Anja Barešić, Alexander Jolyon Nash, Tarik Dahoun, Oliver Howes, Boris Lenhard (London, UK): SCHIZOPHRENIA GWAS INTERPRETATION: LESSONS FROM FUNCTIONAL AND COMPARATIVE GENOMICS .....	59
Dunja Gorup, Siniša Škokić, Jasna Kriz, Srećko Gajović (Zagreb, Croatia): CAGED-LUCIFERIN BIOLUMINESCENCE IMAGING IN EVALUATING MOUSE BRAIN ISCHEMIC LESION.....	60
Barbara Hausott, Letizia Marvaldi, Sitthisak Thongrong, Jong-Whi Park, Lars Klimaschewski: IMPROVING BRAIN DISORDERS BY TARGETING THE ENDOGENOUS ERK INHIBITOR SPROUTY2 .....	61



Antonio Šarolić: ELECTROSTIMULATION WAVEFORM AND FREQUENCY EFFECT ON NERVE EXCITABILITY.....	62
Marina Dobrivojevic Radmilovic, Sinisa Skokic, Dunja Gorup, Anton Glasnovic, Helena Justic, Paula Josic, Anja Baric, Srecko Gajovic: LONGITUDINAL MRI ANALYSIS OF ISCHEMIC LESION IN TOLL-LIKE RECEPTOR 2-DEFICIENT MOUSE.....	63
Rozi Andretić Waldowski, Ana Filošević, Franka Rigo: NEUROGENETIC APPROACH IN THE STUDY OF ADDICTION USING INVERTEBRATE MODEL ORGANISM University of Rijeka, Department of Biotechnology, Rijeka, Croatia.....	64
Milan Kopecek: MULTIMODAL MOLECULAR IMAGING IN (PRE) CLINICAL RESEARCH.....	65
Dirk Wiedermann, Mathias Hoehn, Claudia Green, Anuka Minassian: MRI APPLICATIONS IN PRECLINICAL BRAIN RESEARCH .....	66
Emanuele Buratti, Francesca Paron, Ursa Susjnar, Sara Cappelli, Cristiana Stuani, Maurizio Romano (Trieste, Italy): IMPORTANCE OF TDP-43 EFFECTS ON RNA METABOLISM IN NEURODEGENERATIVE AND MUSCULAR DISEASES .....	67
Andrea Markovinovic, Nikolina Prtenjaca, Marin Dominovic, Ivana Munitic: OPTINEURIN DYSFUNCTION IN NEURODEGENERATION .....	68
Kristina Pilipović, Tamara Janković, Jelena Rajič Bumber, Petra Dolenc, Jasna Križ, Gordana Župan (Rijeka, Croatia & Quebec, Canada): TDP-43 MISLOCALIZATION FOLLOWING A SINGLE AND REPETITIVE TRAUMATIC BRAIN INJURY IN THE MOUSE CORTEX.....	69
Nicholas J. Bradshaw: CHRONIC MENTAL ILLNESSES AS DISORDERS OF PROTEIN AGGREGATION....	70
Anton Glasnović, Dunja Gorup, Ivan Alić, Siniša Škokić, Dinko Mitrečić: STROKE IN MICE CAN BE MODIFIED BY BLOCKAGE OF RANKL AXIS WITH DENOSUMAB.....	71
Valentina Hribljan, Damir Lisjak, Dinko Mitrečić: TRANSPLANTATION OF NEURAL STEM CELLS AFTER ISCHEMIC BRAIN STROKE INFLUENCES EXPRESSION OF GENES INVOLVED IN THE PROGRAMMED CELL DEATH.....	72
JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY AND WFN APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF CARE.....	73
SYMPOSIUM ON RECENT APPROACHES IN MANAGEMENT ON HEADACHE .....	73
Marjan Zaletel, Ljiljana Krager Zaletel, Bojana Žvan: THE IMPACT OF HEADACHE ON PUBLIC HEALTH IN SLOVENIA .....	73
Bojana Žvan (Ljubljana, Slovenia): NEW EMERGING THERAPIES IN MIGRAINE – CGRP ANTAGONISTS AND NEW EHF GUIDELINES .....	74
ALZHEIMER'S DISEASE SYMPOSIUM.....	75
Ninoslav Mimica: DEPRESSION, DEMENTIA AND DELIRIUM - CONTINUUM OR COMORBIDITY .....	75
Marina Šagud, Bjanka Vuksan Ćusa, Suzan Kudlek-Mikulić, Alma Mihaljević Peleš: DEMENTIA OR DEPRESSION: HOW TO KNOW AND WHAT TO DO? .....	76
Natasa Klepac, Maja Relja (Zagreb, Croatia): EARLY DETECTION OF DEMENTIA.....	77
Marija Kušan Jukić, Ninoslav Mimica: PATHOPHYSIOLOGY, CLINICAL PICTURE AND TREATMENT OF DELIRIOUS STATE IN PERSONS WITH DEMENTIA.....	78

JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY AND WFN APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF CARE.....	79
NEUROPSYCHIATRIC MANIFESTATIONS OF NEUROLOGICAL DISORDERS.....	79
Osman Sinanović: NEUROPSYCHIATRIC MANIFESTATIONS OF STROKE.....	79
Vladimira Vuletic (Rijeka, Croatia): NON-MOTOR SYMPTOMS IN PARKINSON’S DISEASE – UPDATES...	80
Uroš Rot: NEUROPSYCHIATRIC MANIFESTATIONS OF MULTIPLE SCLEROSIS .....	81
JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY AND WFN APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF CARE.....	82
CEESS STROKE SYMPOSIUM – ENDORSED BY WORLD STROKE ORGANIZATION.....	82
David Bonifačić, Vladimira Vuletić, Natalia Kučić: SERUM PROGNOSTIC BIOMARKERS OF ISCHEMIC STROKE .....	82
Dijana Zdravec: RADIOLOGICAL DIAGNOSTICS AND ENDOVASCULAR TREATMENT OF STROKE ...	83
Bartłomiej Piechowski-Jozwiak: CLOT MORPHOLOGY IN ISCHEMIC STROKE.....	84
Senta Frol: INTRAVENOUS THROMBOLYSIS IN PATIENTS ON DIRECT ORAL ANTICOAGULANTS .....	85
Hrvoje Budincevic: HOW TO IMPROVE STROKE CARE? .....	86
Vesna Đermanović Dobrota: COGNITIVE IMPAIRMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS .....	87
1 <sup>ST</sup> HISPA HR SYMPOSIUM – HYPERTENSION INFARCTION STROKE PREVENTION ASSOCIATION - CROATIA .....	88
Hrvoje Budincevic: ANTICOAGULANT THERAPY IN SECONDARY STROKE PREVENTION.....	88
SHORT PRESENTATIONS .....	89
Oleg Zaitsev: SIDE OF PREDOMINANT BRAIN DAMAGE AND PSYCHOPATHOLOGY OF SEVERE TRAUMATIC BRAIN INJURY .....	89
Svetlana Kuzmina, Naida Mollaeva: OCCUPATIONAL RISK FACTORS OF CHEMICAL INDUSTRY FOR WORKER’S MENTAL HEALTH .....	90
David Jutrić, Domagoj Đikić, Dragan Jurić, Elena Marić, Diana Odeh, Nada Oršolić, Irena Landeka: EFFECTS OF THE ANTIEPILEPTIC VALPROATE AND OF THE FLAVONONE NARINGENIN ON THE ANTIOXIDATIVE DEFENCE SYSTEM IN THE BRAIN OF C57BL6 MOUSE .....	91
Natalia Ustinova, Tatyana Borovik, Tatyana Bushueva: STRATEGIC PLANNING: HOW TO IMPROVE HEALTH CARE SERVICES FOR CHILDREN WITH AUTISM IN RUSSIA? .....	92
Emina Horvat Velić (Zagreb, Croatia): STUDENTS' SYMPOSIUM IN BIOLOGY AND LIFE SCIENCES – SISB .....	93
Nataliya Ustinova, Mikhail Zobin (Kotor, Montenegro): KETAMIN IN THERAPY OF PHARMACORESISTANT DEPRESSION – A NATURALISTIC STUDY .....	94
Lene Marie Groenlund, Carsten Kock-Jensen: INTRATHECAL BACLOFEN AS TREATMENT FOR MYOCLONUS AND CATABOLISM AS PART OF HYPOXIC BRAIN DAMAGE - A NEW TREATMENT? A CASE REPORT .....	95

Galina Ivanova, Boris Tsygankov, Yulia Dobrovolskaya, Ummuraisat Gadzhieva (Moscow, Russian Federation): THE POSSIBILITY OF PSYCHOTHERAPY OF ANXIOUS AND DEPRESSIVE DISORDERS IN PATIENTS AT DISTANT STAGES OF BRAIN INJURY .....	96
Valentino Racki: EFFECTS OF IN-VITRO ANTIPSYCHOTIC ADMINISTRATION ON IMMUNOMETABOLIC PROPERTIES OF BV-2 MICROGLIAL CELLS. ....	97
YOUNG INVESTIGATORS' CORNER .....	98
Eliša Papić, Valentino Rački, David Bonifačić, Vladimira Vuletić, Natalia Kučić: BRAIN ENTRAINMENT: EFFECTS OF BINAURAL BEATS ON CEREBRAL FUNCTION .....	98
Alen Juginović, Ivan Aranza, Miro Vuković: IMPORTANCE OF DIAGNOSIS AND TREATMENT OF SLEEP APNEA IN ADULTS .....	99
Miro Vuković, Ivan Aranza, Alen Juginović: IS MUSIC THERAPY AN EFFECTIVE TREATMENT OPTION IN ALZHEIMER'S DISEASE? .....	100
Ivan Franin: PATHOHISTOLOGICAL CLASSIFICATION OF CNS TUMORS THROUGHOUT HISTORY: A REVIEW .....	101
Alen Juginović, Miro Vuković, Ivan Aranza: COGNITIVE EFFECTS OF ANTIEPILEPTIC DRUGS IN THE PEDIATRIC POPULATION: A LITERATURE REVIEW .....	102
WORKSHOPS.....	103
WORKSHOP HOW TO READ AND WRITE A SCIENTIFIC PAPER?.....	103
Anton Glasnović: NORMAL DISTRIBUTION AND RELATED TOPICS .....	103
Anton Glasnović: STUDY TYPES .....	104
Srećko Gajović: NEW WAYS TO CONCEPTUALISE THE BIOMEDICAL KNOWLEDGE .....	105
WORKSHOP - CHILD AND ADOLESCENT PSYCHIATRY.....	106
Aldo Špelić: PSYCHOANALYTIC APPROACH IN PSYCHOTHERAPY OF AUTISM .....	106
Aleksandra Mindoljević Drakulić: SOCIAL NEUROSCIENCE OF ATTACHMENT-BASED TEACHING IN THE CLASSROOM .....	107
POSTERS PSYCHIATRY.....	108
1. "THAT LAWYER IS A SHARK BECAUSE HE HAS TEETH": DISENTANGLING METAPHOR INTERPRETATION IN PATIENTS AFFECTED BY SCHIZOPHRENIA. Giulia Agostoni.....	108
2. CLINICAL ASPECTS OF SCHIZOPHRENIA COMORBID TO TYPE 2 DIABETES. Marina Artemieva, Tatiana Varnakova, Roman Suleymanov, Anastasia Lazukova .....	108
3. MAIN PSYCHOGENIC CAUSES OF NON-PSYCHOTIC NEUROPSYCHIATRIC DISORDERS IN RESIDENTS OF MOSCOW. Marina Artemieva, Roman Suleymanov Ivan Danilin, Anastasia Lazukova .....	109
4. PSYCHOSOMATIC ASPECTS OF GASTRIC ULCER DISEASE AND HYPOTHYROIDISM. Marina Artemieva, Vladimir Kuznetsov, Ivan Manyakin, Elena Basova, Sergey Safaryan .....	109
5. THE QUALITY OF LIFE OF PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE. Marina Artemieva, Vladimir Kuznetsov, Ivan Manyakin, Elena Basova, Sergey Safaryan .....	110
6. AN ANALYSIS OF HIGH RANGE IQ EXAMINATIONS. Sriram Balasubramanian.....	110
7. ONTOLOGICAL VALIDITY OF DEPRESSIVE REALISM EVIDENCED FROM PHILOSOPHY AND NATURE OF DEPRESSION DIAGNOSIS. Sriram Balasubramanian.....	111
8. "HYSTERICAL CHARACTER STRUCTURE" IN PATIENT WITH BIPOLAR AFFECTIVE DISORDER – A CASE REPORT. Sarah Bjedov, Ivana Picek, Darko Marčinko.....	111

9. AGGRESSION INCIDENCE, TYPE AND SEVERITY AMONG INVOLUNTARILY HOSPITALIZED PSYCHIATRIC PATIENTS. Andreja Celofiga, Jure Koprivsek .....	112
10. COMPARISON OF INCIDENCE AND DURATION OF COERCIVE MEASURES AMONG VOLUNTARILY AND INVOLUNTARILY HOSPITALIZED PSYCHIATRIC PATIENTS. Andreja Celofiga, Jure Koprivsek, Ilonka Vucko Miklavcic .....	112
11. EYES OPEN – THE ORGANICITY OF DIAGNOSIS IN A CASE OF VISUAL HALLUCINATIONS: A CASE REPORT. Zenn Chua, Ambrose Cheng .....	113
12. NEUROPSYCHOANALYSIS - BRAIN/BODY AND MIND. Mirko Čorlukić.....	114
13. NEUROSENANCE AND PSYCHODINAMICS IN CONTEMPORARY PHENOMENOLOGY. Neda Esapović-Greš, Ljubomir Radovančević .....	114
14. FORENSIC PSYCHIATRIC ASPECTS OF PERSONALITY DISORDER. Viktor V. Gorinov, Elena S. Shekhovtsova .....	115
15. HOW TO TREAT TREATMENT-RESISTANT DEPRESSION – A CASE REPORT. Alen Greš, Marina Šagud.....	115
16. ANHEDONIA AND THE SEVERITY OF DEPRESSION IN TWO PSYCHIATRIC DISORDERS. Dejana Jezernik, Lucija Šimunić, Marina Šagud, Lucija Tudor, Zoran Madžarac, Ivana Stefanović, Ivona Šimunović Filipčić, Bjanka Vuksan-Ćusa, Biljana Kosanović Rajačić, Alma Mihaljević Peleš, Suzan Kudlek Mikulić, Nela Pivac .....	116
17. FEATURES OF PARENT-CHILD RELATIONSHIPS IN FAMILIES OF MOTHERS WITH SCHIZOPHRENIA. Liubov Karnitskaya.....	116
18. DIFFERENTIAL DIAGNOSIS OF STUPOR IN THE ACUTE PSYCHIATRY - A CASE REPORT. Marin Kirigin, Miro Jakovljević .....	117
19. PERSON-CENTERED CARE AND ACCESS TO DRUGS IN THE DIGITAL ENVIRONMENT: TO CURE OR TO SELL. Vanja Kopilaš, Srećko Gajović .....	117
20. THE CONNECTION OF THE NITROSATIVE AND OXIDATIVE STRESS WITH THE DEPRESSIVE DISORDER. Ivana Kostić-Petrović, Olivera Žikić, Ivana Stojanović .....	118
21. CONCENTRATION OF THE BRAIN-DERIVED NEUROTROPHIC FACTOR IN DRUG FREE SCHIZOPHRENIC PATIENTS FOLLOWING ACUTE ANTIPSYCHOTIC TREATMENT WITH OLANZAPINE. Suzan Kudlek Mikulić, Alma Mihaljević Peleš, Maja Bajs Janović, Marina Šagud, Bjanka Vuksan Ćusa, Saša Jevtović, Špiro Janović.....	118
22. EMOTIONS AND MOTIVATIONS IN CHILDREN AFTER SPINAL TRAUMA AT EARLY REHABILITATION. Ekaterina A. Lvova, Yuliya G. Sidneva .....	119
23. THE NEED FOR A MULTIDISCIPLINARY APPROACH AND INDIVIDUAL SCOPE IN FOCUS. Jasminka Matic, Azijada Srkalovic-Imsiragic, Anto Kreso.....	119
24. CHILDREN WITH MENTAL HEALTH DISORDERS IN EDUCATION SYSTEM. Filip Mustač, Vera Musil .....	120
25. DEPRESSION, LOWER URINARY TRACT SYMPTOMS AND SEXUAL DYSFUNCTION IN CROATIAN OBESE PATIENTS. Filip Mustač, Katarina Ivana Tudor, Martina Matovinović, Nenad Jakšić, Andrej Kovačević, Zrinka Vuksan-Ćusa, Ervina Bilić, Bjanka Vuksan-Ćusa, Marina Šagud .....	121
26. MENTAL HEALTH PROBLEMS IN MEDICAL STUDENTS. Filip Mustač, Marjeta Majer, Roberto Mužić, Vesna Jureša, Vera Musil .....	121
27. OMNIPOTENCE AND HELPLESSNESS OF NARCISSISTIC CULTURE. Filip Mustač, Hana Karlica, Sarah Bjedov, Darko Marčinko .....	122

28. PROBIOTIC SUPPLEMENTATION IN REDUCING SYMPTOMS OF PTSD – FUTURE POSSIBILITIES. Filip Mustač, Dunja Leskovar, Ana Klarica, Sara Zadro, Donatella Verbanac .....	122
29. THE UNBEARABLE SYMBIOSIS IN NARCISSISTIC/BORDERLINE INTERACTION. Filip Mustač, Sarah Bjedov, Ivana Picek, Darko Marčinko.....	123
30. DEPRESSIVE DISORDERS IN PATIENTS WITH PRIMARY HYPOTHYROIDISM. Olena Pityk .....	123
31. A TUNNEL BETWEEN DEPRESSION AND DEMENTIA – FOLIC ACID , VITAMIN B12 AND HOMOCYSTEINE – A CASE REPORT. Iva Radoš, Marina Šagud, Biljana Kosanović - Rajačić.....	124
32. SLEEP AND RELATED HABITS IN PTSD PATIENTS. Hrvoje Raos, Hana Đogaš, Marijana Vučković, Dora Kirigin, Neda Pleić, Dolores Britvić.....	124
33. QUANTIFICATION OF PSYCHOSTIMULANT SELF-ADMINISTRATION IN DROSOPHILA MELANOGASTER. Franka Rigo, Ana Filošević, Rozi Andretić Waldowski .....	125
34. AN AUDIT OF SODIUM VALPROATE PRESCRIBING TO FEMALES OF CHILD BEARING AGE WHO ATTEND AN INTELLECTUAL DISABILITY SERVICE. Thomas Ryle, Anita Ambikapathy, Niamh Mulryan, Martin Mc Laughlin, Jean Lane, Meghan Mc Nicholas, Kristen Maunder .....	125
35. DE NOVO ARTERIAL HYPERTENSION IN PATIENTS WITH POST TRAUMATIC STRESS DISORDER. Alejandra Salgar, Luisa Aristizabal, Catalina Moreno, Mansiel Buitrago, Danny Gonzalez, Alejandra Guatibonza.....	126
36. THE EMOTIONAL DISTURBANCES IN PATIENTS WITH THYROTROPINOMA. Yuliya Sidneva, Ludmila Astafyeva, Pavel Kalinin, Boris Kadashev, Maksim Kutin.....	126
37. THE NEUROPSYCHIATRIST IN THE MULTIDISCIPLINARY TEAM IN REHABILITATION AFTER BRAIN INJURY IN CHILDREN. Yuliya Sidneva, Svetlana Valiullina, Zhanna Semenova.....	127
38. THE INTERACTION BETWEEN AGE AT ONSET AND CATECHOL-O-METHYLTRANSFERASE POLYMORPHISM (COMT) ON COGNITIVE FUNCTIONING IN SCHIZOPHRENIA: A 10 YEARS STUDY. Maria Paola Silvestri.....	128
39. ANHEDONIA AND SUICIDE ATTEMPTS IN DEPRESSION AND SCHIZOPHRENIA: IS THERE A LINK? Lucija Šimunić, Dejana Jezernik, Marina Šagud, Lucija Tudor, Zoran Madžarac, Ivana Stefanović, Ivona Šimunović Filipčić, Bjanka Vuksan-Ćusa, Biljana Kosanović Rajačić, Alma Mihaljević Peleš, Suzan Kudlek Mikulić, Nela Pivac.....	128
40. ARIPIRAZOLE INDUCED PATHOLOGICAL GAMBLING IN PATIENT WITH ALCOHOL INDUCED PSYCHOSIS. Azijada Srkalović Imširagić, Jasminka Matić-Jogunica, Ante Krešo.....	129
41. SEVERE HEADACHE IN A PATIENT WITH BORDERLINE PERSONALITY DISORDER. Ozren Veselić, Javor Vouk Kamenski, Maja Vincek, Duje Krstulović-Jelić .....	129
42. COMPLEX VISUAL HALLUCINATIONS EMBEDDED IN DELUSIONAL CONTEXT FOLLOWING OCCIPITAL LOBE INFARCTION: A CASE REPORT. Javor Vouk-Kamenski, Ozren Veselić, Duje Krstulović-Jelić, Draženka Topolnjak-Pavišić, Maja Vincek.....	130
43. DEMOGRAPHIC CHARACTERISTICS OF CROATIAN WAR VETERANS WITH PTSD AND COMPLEX-PTSD. Marijana Vučković, Hana Đogaš, Hrvoje Raos, Dora Kirigin, Neda Pleić, Dolores Britvić	130
44. PSYCHOPHARMACOLOGICAL TREATMENT OF BEHAVIOUR AND PSYCHOLOGICAL SYMPTOMS IN ALZHEIMER'S DISEASE - A CASE REPORT. Mirna Zagrajski Brkic, Mirjana Grubic Markovic, Mladen Tomas, Aljosa Ugrin .....	131
POSTERS NEUROLOGY .....	132
45. ARTERY OF PERCHERON INFARCTION – A CASE REPORT. Terezija Berlančić, Silva Soldo – Butković .....	132

46. LIGHT POLLUTION AND COMMUNITY NOISE AS PREDICTORS OF SLEEP QUALITY AMONG UNIVERSITY STUDENTS. Terezija Berlančić, Dorian Laslo, Maja Miškulin, Ivan Miškulin .....	132
47. ETIOLOGY OF STROKES IN YOUNGER PATIENTS. David Bonifačić, Vladimira Vuletić, Kristina Kampić .....	133
48. REFRACTORY STATUS EPILEPTICUS COMPLICATED BY SEPSIS – A CASE REPORT. Mateja Boskovic, Vanja Basic Kes.....	133
49. STUDY OF THE MENTAL ACTIVITY OF CHILDREN AFTER SEVERE NEUROTRAUMA (EARLY STAGE OF REHABILITATION). Margarita Bratkova, Alla Zakrepina, Yuliya Sidneva.....	133
50. COULD RADIOLOGICAL IMAGING TECHNIQUES GIVE US THE RIGHT ANSWER? Petra Cukon, Nataša Biondić, Matija Pajić, Dolores Janko-Labinac, Frederic-Ivan Silconi, Vinka Kos, Igor Grgorinić. ....	134
51. QUALITY OF LIFE IN DIABETIC PATIENTS WITH PAINLESS DIABETIC POLYNEUROPATHY - THE RESULTS OF 8 – YEARS FOLLOW-UP STUDY. Vesna Đermanović Dobrota, Pero Hrabač, Savko Dobrota, Vesna Lukinović- Škudar, Dario Rahelić, Kristijan Peroš. Ingrid Prkačin, Vanja Bašić Kes, Silva Butković Soldo.....	135
52. CEREBELLAR STROKE AND WALENBERG’S SYNDROME – A CASE REPORT. Jasna Hanižjar-Berlančić, Dorian Laslo.....	135
53. ATYPICAL CLINICAL PRESENTATION OF MULTIPLE SCLEROSIS: A CASE REPORT. Vera Horvat, Emina Horvat Velić.....	136
54. POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME AS A COMPLICATION OF MULTIPLE SCLEROSIS: A CASE REPORT. Ivana Hustić, Vanja Bašić-Kes .....	136
55. PSYCHOTIC PRESENTATION OF SPORADIC HEMIPLEGIC MIGRAINE- A CASE REPORT. Ana Kalazić, Suzan Kudlek Mikulić, Sara Medved, Marina Šagud, Bjanka Vuksan Ćusa.....	137
56. NEW MATERIAL IN MEDICINE AS A PROTECTOR OR POSSIBLE CAUSE OF STROKE – A CASE REPORT. Kristina Kampić, Vladimira Vuletić, David Bonifačić .....	137
57. A DURAL ARTERIOVENOUS FISTULA OF CEREBELLOPONTINE ANGLE AS A CAUSE OF TRIGEMINAL NEURALGIA IN A PATIENT WITH HYPERINTENSIVE LESIONS OF CNS OF UNDETERMINATED ETIOLOGY - A CASE REPORT. Ivana Kobasic, Vanja Basic Kes .....	138
58. TAU PROTEIN SPREADING AFTER INJECTION OF TAU OLIGOMERS INTO THE RAT ENTORHINAL CORTEX. Lea Langer Horvat, Mirjana Babić Leko, Ena Španić, Emma Štampar, Goran Šimić .....	138
59. BASAL GANGLIA MATTERS IN THE PRIMARY BURNING MOUTH SYNDROME-TRANSCRANIAL SONOGRAPHY STUDY. Milija Mijajlović, Jasna Zidverc Trajković, Nadežda Šternić.....	139
60. LAMINAR SHIFTS OF SOX2 EXPRESSION PATTERN IN THE HUMAN FRONTAL CORTEX DURING MIDGESTATION. Terezija Miškić, Višnja Majić Zidarić, Janja Kopic, Ana Bosak, Ivica Kostović, Željka Krsnik .....	140
61. LOWER URINARY TRACT SYMPTOMS IN PATIENTS WITH OBESITY. Filip Mustač, Katarina Ivana Tudor, Martina Matovinović, Andrej Kovačević, Ervina Bilić .....	140
62. SEXUAL DYSFUNCTION IN PATIENTS WITH OBESITY. Filip Mustač, Katarina Ivana Tudor, Martina Matovinović, Andrej Kovačević, Ervina Bilić.....	141
63. SLEEP DISORDERS AND LOWER URINARY TRACT SYMPTOMS IN OBESE PATIENTS. Filip Mustač, Katarina Ivana Tudor, Martina Matovinović, Barbara Barun, Andrej Kovačević, Ervina Bilić .....	141
64. THE IMPORTANCE OF AN INTERDISCIPLINARY APPROACH TO RETT SYNDROME THERAPY - A CASE REPORT. Eliša Papić, David Bonifačić, Vladimira Vuletić.....	142

65. SEXUAL DYSFUNCTION AND DEPRESSION IN MULTIPLE SCLEROSIS. Hanna Pašić, Katarina Ivana Tudor, Sandra Nađ Škegro, Filip Mustač, Fabijan Rajič, Marija Bošnjak Pašić .....	142
66. VALUE OF HEAD CT SCAN IN THE EMERGENCY DEPARTMENT IN PATIENTS WITH VERTIGO WITHOUT FOCAL NEUROLOGICAL ABNORMALITIES. Tomislav Pavlović, Sanja Trtica, Marina Milošević, Hrvoje Budinčević .....	143
67. RAMSAY HUNT SYNDROME - A CASE REPORT. Dobrinka Petković, Borislav Vuković, Ivana Vuković, Albert Thur .....	143
68. CLEVELAND CLINIC ABU DHABI STROKE REGISTRY (CCADSR) METHODOLOGY. Bartłomiej Piechowski-Jozwiak, Ann O’Sullivan, Syed I Hussain, Seby John, Ramon Navarro, Khalil Zahra, Stephen Samples, Victoria Mifsud .....	144
69. EFFECTIVE CORTICOSTEROID THERAPY IN MELAS – A CASE REPORT. Valentino Racki, Mira Bucuk, Iva Gasparovic, Slavica Kovacic, Barbara Zadkovic, Anja Babic, Vladimira Vuletic .....	144
70. ADVANCED 3D MODELING FOR PREDICTION AND QUANTIFICATION OF THE PERIHEMATOMAL BRAIN EDEMA FORMATION AFTER INTRACEREBRAL HEMORRHAGE: IMPLICATIONS OF BIOCHEMICAL, RADIOLOGICAL AND CLINICAL VARIABLES. Vladimir Rendevski, Boris Aleksovski, Ana Mihajlovska Rendevska .....	145
71. ANTI-GQ1B ANTIBODY SYNDROME: A CASE REPORT. Gordana Sičaja, Marija Sedlić, Hrvoje Budinčević .....	145
72. CRYOGLOBULINEMIA AND SENSORIMOTOR POLYNEUROPATHY: A CASE REPORT. Gordana Sičaja, Marija Sedlić, Hrvoje Budinčević .....	146
73. EPILEPTIC SEIZURES IN PATIENTS WITH LARGE AND GIANT PROLACTINOMAS. Yuliya Sidneva, Ludmila Astafieva, Pavel Kalinin, Maxim Kutin, Boris Kadashev .....	147
74. PATIENT WITH NEWLY DIAGNOSED MESENCEPHALIC GLIOMA AND TREMOR – A CASE REPORT. Ivana Šimić, Marija Olujić, Darko Kotromanović, Zoran Čavajda, Marko Kovačević, Svetlana Tomić .....	147
75. STROKE AND ULCERATIVE COLITIS – A CASE REPORT. Ivana Šimić, Darko Kotromanović, Jasna Hanižjar- Berlančić .....	148
76. HOW TO LABEL SOMEONE TREATED FOR EPILEPSY? Ana Sruck, Latica Friedrich, Ivan Bielen.....	148
77. DISTRIBUTION OF DEMYELINATING LESIONS WITHIN THE CEREBRAL WHITE MATTER SEGMENTS AND THEIR CORRELATION WITH NEUROLOGICAL DISABILITY IN PATIENTS WITH MULTIPLE SCLEROSIS. Sarah Stančić-Rokotov, Milan Radoš, Anton Vladić .....	149
78. THE PREVALENCE OF MCI IN RURAL CHILE. PabloToro, Claudia Bambs, Catterina Ferreccio, Johannes Schröder.....	150
79. PRELIMINARY EVALUATION OF CROATIAN VERSION OF THE NON-MOTOR SYMPTOMS SCALE IN PARKINSON’S DISEASE. Zvonimir Uzarevic, Anamarija Soldo Koruga Ivana Kampic, Zeljka Popijac, Silva Butkovic Soldo .....	150
80. CLINICAL CHARACTERISTICS, DIAGNOSTIC PROCEDURES AND THERAPY OF CEREBRAL VENOUS AND SINUS THROMBOSIS – A CASE REPORT. Ivana Vuković, Borislav Vuković, Dobrinka Petković .....	151
81. RESTORATION OF THE MENTAL HEALTH OF CHILDREN WITH STBI: PEDAGOGICAL MEANS IN REHABILITATION. Alla Zakrepina, Yuliya Sidneva .....	151
82. THE STUDY ON MANIFESTATION OF MENTAL ACTIVITY IN PRESCHOOL CHILDREN WITH SEVERE CRANIOCEREBRAL TRAUMA. Alla Zakrepina, Yuliya Sidneva, Elena Strebeleva .....	152

USEFUL INFORMATIONS.....	153
SPONSORS AND SUPPORTERS.....	156
PARTNER EVENTS.....	157



**PROGRAM**

**THURSDAY, May 30<sup>th</sup>, 2019.**

**14:30-17:30 PULA'S WORLD MS DAY SYMPOSIUM**

**Bianca MULTIDISCIPLINARNI PRISTUP OSOBAMA S MULTIPLOM SKLEROZOM**

**Istriana Hall** Chairperson: S. Butković Soldo (Osijek, Croatia)

S. Butković Soldo (Osijek, Croatia): Uvod

S. Rendulić Slivar (Lipik, Croatia): Kvaliteta života oboljelih od MS – važnost neurofizijatrijske intervencije

D. Janko Labinac (Pula, Croatia): Važnost vitamina D kod multiple skleroze

R. Rendulić (Lipik, Croatia): Uloga dinamičke neuromuskularne stabilizacije u stabilizaciji trupa

J. Kragujević (Osijek, Croatia): Multipla skleroza i umor

T. Lazarević (Osijek, Croatia): Multipla skleroza i prehrana

Ž. Vukšić & A. Soldo Koruga (Osijek, Croatia): Odnos liječnik – pacijent: „Razgovaramo li dovoljno s bolesnikom?“

D. Karniš (Lipik, Croatia)– Art terapija kao pomoć u liječenju pacijenata s multiplom sklerozom

S. Tomasović (Zagreb, Croatia): Diferencijalna dijagnoza multiple skleroze i paraneoplastičkog sindroma

**17:30-18:30 MULTIPLE SCLEROSIS SYMPOSIUM – HOT TOPICS IN MS TREATMENT**

**Bianca** Chairpersons: U. Rot (Ljubljana, Slovenia) & V. Bašić Kes (Zagreb, Croatia)

**Istriana Hall**

T. Hojs Fabjan (Maribor, Slovenia): First line therapy in multiple sclerosis

V. Bašić Kes (Zagreb, Croatia): How to treat non-respondent MS patients

U. Rot (Ljubljana, Slovenia): Treatment options in progressive multiple sclerosis

**18:30-19:15 MERCK SIMPOZIJ:**

**Bianca GODINU DANA ISKUSTVA U LIJEČENJU VISOKO AKTIVNE MS LIJEKOM**

**Istriana Hall MAVENCLAD®**

V. Bašić Kes (Zagreb, Croatia)

FRIDAY, May 31<sup>st</sup>, 2019

**08:30-09:00 OPENING CEREMONY**

**Ulika Hall**

**09:00-11:00 MAIN THEME**

**Ulika Hall**

Chairpersons: F. Fazekas (Graz, Austria) & M. Brüne (Bochum, Germany)

F. Fazekas (Graz, Austria): The contribution of MRI to the management of MS treatment

N. Müller (Munich, Germany): The role of inflammation in Alzheimer's disease

M. Brüne (Bochum, Germany): Social cognition in health and disease: Some insights from neuroimaging and genetics

S. Bašić (Zagreb, Croatia): Managing drug-resistant epilepsy

**11:00-12:30 GRAZ NEUROLOGY SYMPOSIUM - HISTORICAL DEVELOPMENT, PRESENT**

**Ulika Hall**

**STATUS AND FUTURE ASPECTS OF DIAGNOSIS AND TREATMENT**

Chairpersons: G.E. Klein (Graz, Austria) & K. Niederkorn (Graz, Austria)

Stroke

K. Niederkorn (Graz, Austria) & T. Gatteringer (Graz, Austria)

Multiple Sclerosis

S. Fuchs (Graz, Austria) & C. Enzinger (Graz, Austria)

Neurooncology

F. Payer (Graz, Austria) & T. Urbanic-Purkart (Graz, Austria)

**11:00-13:30 SHORT COMMUNICATIONS**

**Bianca**

Chairpersons: B. Tsygankov (Moscow, Russian Federation) & I. Šain (Pula, Croatia)

**Istrian Hall**

N. Ustinova (Kotor, Montenegro): Ketamin in therapy of pharmacoresistant depression - A naturalistic study

S. Kuzmina (Moscow, Russian Federation): Occupational risk factors of chemical industry for worker's mental health

O. Zaitsev (Moscow, Russian Federation): Side of predominant brain damage and psychopathology of severe traumatic brain injury

G. Ivanova (Moscow, Russian Federation): The possibility of psychotherapy of anxious and depressive disorders in patients at distant stages of brain injury

D. Jutrić (Zagreb, Croatia): Effects of the antiepileptic valproate and of the flavonone naringenin on the antioxidative defence system in the brain of C57Bl6 mouse

V. Rački (Rijeka, Croatia): Effects of in-vitro antipsychotic administration on immunometabolic properties of BV-2 microglial cells.

L.M. Groenlund (Esbjerg, Denmark): Intrathecal baclofen as treatment for myoclonus and catabolism as part of hypoxic brain damage - a new treatment?

E. Horvat Velić (Zagreb, Croatia): Students' Symposium in Biology and Life Sciences – SiSB

**12:30-13:15 SANOFI SATELLITE SYMPOSIUM:**

Program

**Ulika Hall TERIFLUNOMIDE IN TODAY'S MS LANDSCAPE**

V. Bašić Kes (Zagreb, Croatia) & M. Bošnjak Pašić (Zagreb, Croatia)

**12:30-13:30 TAKEDA SPONZORIRANI SIMPOZIJ:**

**Belica Hall KOGNITIVNI POREMEĆAJI KOD GAUCHEROVE BOLESTI**

V. Vuletić (Rijeka, Croatia)

**13:00-14:30 LUNCH**

**14:30-16:00 ALZHEIMER'S DISEASE SYMPOSIUM**

**Ulika Hall** Chairperson: N. Mimica (Zagreb, Croatia)

N. Mimica (Zagreb, Croatia): Depression, dementia and delirium - continuum or comorbidity

M. Šagud (Zagreb, Croatia): Dementia or depression: how to know and what to do?

N. Klepac (Zagreb, Croatia): Early detection of dementia

M. Kušan Jukić (Zagreb, Croatia): Pathophysiology, clinical picture and treatment of delirious state in persons with dementia

**14:30-16:00 1ST HISPA HR SYMPOSIUM - HYPERTENSION INFARCTION STROKE**

**Belica Hall PREVENTION ASSOCIATION - CROATIA**

Chairpersons: N. Tasić (Beograd, Serbia) & S. Morović (Zagreb, Croatia)

N. Tasić (Beograd, Serbia): Vision And Mission Of HISPA International

V. Demarin (Zagreb, Croatia): Croatian Preventive Strategy - What have we done?

S. Morović (Zagreb, Croatia): Croatian Preventive Strategy - Where are we going?

H. Budinčević (Zagreb, Croatia): Anticoagulant therapy in secondary stroke prevention

Roundtable: Implementation of HISPA Programme In the Region - from wishes to fulfillment

**14:30-16:30 PSYCHOPATHOLOGY SUMMER SCHOOL**

**Bianca** Chairpersons: M. Brüne (Bochum, Germany) & J. Schroder (Heidelberg, Germany)

**Istrian Hall**

K-J. Bär (Jena, Germany): Autonomic nervous system processing in schizophrenia

J. Schröder (Heidelberg, Germany): Neurological soft signs (NSS) and cognitive deficits in HIV associated neurocognitive disorder

M. Brüne (Bochum, Germany): Is schizophrenia the phenotypic correlate of parasitic behaviour manipulation?

A. Sutterland (Amsterdam, The Netherlands): Driving us mad: the association of *Toxoplasma gondii* with suicide attempts and traffic accidents - a systematic review and meta-analysis

M. Bechi (Milan, Italy): Autistic traits negatively influence Theory of Mind and training efficacy in patients with schizophrenia

N. Ilanković (Beograd, Serbia): Schizophrenias are frequently not primary cerebral disorders

**16:00-17:30 NEUROPSYCHIATRIC MANIFESTATIONS OF NEUROLOGICAL DISORDERS**

**Belica Hall** Chairpersons: O. Sinanović (Tuzla, BIH) & V. Vuletić (Rijeka, Croatia)

O. Sinanović (Tuzla, BIH): Neuropsychiatric manifestations of stroke

Program

V. Vuletić (Rijeka, Croatia): Non-motor symptoms in Parkinson's Disease –updates

U. Rot (Ljubljana, Slovenia): Neuropsychiatric manifestations of multiple sclerosis

D. Vidović (Zagreb, Croatia): Sleep deprivation and cognitive functioning

**16:30-17:45 PSYCHIATRY SYMPOSIUM- NEW INSIGHTS IN NEUROINFLAMMATORY AND AUTOIMMUNE DYSREGULATION IN PSYCHIATRIC DISORDERS: IT THERE A ROLE FOR HERPES VIRUSES?**

**Bianca Istriana Hall**

Chairperson: H. Klein (Groningen, The Netherlands)

M. Schneider (Ulm, Germany): Metabolism and mitochondrial dysregulation – role of pro- and anti-oxidant pathways in psychiatry

H. Klein (Groningen, The Netherlands): Psychosis as a non-clearing inflammatory response to a latent herpes virus in the limbic system

C. Scheiber (Ulm, Germany): Herpes viral and inflammatory markers in patients with severe mental disorders. New data from CSF.

**16:30-17:30 5TH PULA NEUROSCIENCE SYMPOSIUM - SESSION 1. - PLENARY SESSION**

**Ulika Hall**

Chairpersons: S. Gajović (Zagreb, Croatia) & I. Munitić (Rijeka, Croatia)

V. Demarin (Zagreb, Croatia): Mind and Brain Congress and Neuroscience Symposia

J Kriz (Quebec, Canada): Innate immune response following brain injuries: Lost in translation

M. Hoehn (Cologne, Germany): Functional neuronal networks in health and disease

**18:00-20:00 POSTER SESSION**

**Ulika Hall**

Chairpersons: M. Brüne, F. Benedetti, K. Niederkorn, O. Sinanović, M. Latas, S. Gajović, I. Šain, V. Vuletić, S. Morović, H. Budinčević

**SATURDAY June 1<sup>st</sup>, 2019**

**09:00-12:30 MAIN THEME – PLENARY SESSION**

**Ulika Hall**

Chairpersons: V. Demarin (Zagreb, Croatia) & A. Korczyn (Tel Aviv, Israel)

V. Demarin (Zagreb, Croatia): There is no Health without Brain Health

A. Korczyn (Tel Aviv, Israel): Non epileptic seizures, are they psychogenic?

M. Latas (Beograd, Serbia): Phobic vertigo - does it really exist?

F. Benedetti (Milan, Italy): Neuroinflammation and white matter damage in the neuroprogression of mood disorders

E. Bilić (Zagreb, Croatia): IVIG in treatment of neuromuscular diseases with focus on chronic inflammatory demyelinating polyneuropathy

M. Mijajlović (Beograd, Serbia): Patent foramen ovale: to close or not ?

B. Tsygankov (Moscow, Russian Federation): Supposed mechanism of influence the hepatitis C virus on the development of neuropsychological disorders

**08:30-10:30 5<sup>TH</sup> PULA NEUROSCIENCE SYMPOSIUM - SESSION 2.**

**Bianca Istriana Hall**

Chairpersons: M. Heffer (Osijek, Croatia) & Dinko Mitrečić (Zagreb, Croatia)

Program

- S. Gajović (Zagreb, Croatia): Multimodal approaches to evaluate mouse brain repair after ischemic lesion
- M. Heffer (Osijek, Croatia): Metformin and liraglutide differently affect central insulin resistance in the rat model of prediabetes
- J. Kežić (Zagreb, Croatia): Systemic exposure to toll-like receptor 9 ligand CpG-ODN elicits low-grade inflammation in the retina that is unaltered in diabetic mice
- M. Mladinić (Rijeka, Croatia): Exploring the basis of neuroregeneration: identification of key molecules with proteomics and functional assays in the mammalian spinal cord
- A. Barešić (Zagreb, Croatia): Schizophrenia GWAS interpretation: lessons from functional and comparative genomics
- D. Gorup (Zagreb, Croatia): Caged-luciferin bioluminescence imaging in evaluating mouse brain ischemic lesion

**11:00-13:00 5<sup>TH</sup> PULA NEUROSCIENCE SYMPOSIUM - SESSION 3.**

**Bianca Istriana Hall** Chairpersons: K. Pilipović (Rijeka, Croatia) & L. Klimaschewski (Innsbruck, Austria)

- L. Klimaschewski (Innsbruck, Austria): Improving brain disorders by targeting the endogenous ERK inhibitor Sprouty2
- A. Šarolić (Split, Croatia): Electrostimulation waveform and frequency effect on nerve excitability
- M. Dobrivojević Radmilović (Zagreb, Croatia): Longitudinal MRI analysis of ischemic lesion in Tlr2-deficient mouse
- R. Andretić Waldowski (Rijeka, Croatia): Neurogenetic approach in the study of addiction using invertebrate model organism
- Technical Forum
- M Kopecek (Amsterdam, the Netherlands): Multimodal molecular imaging in (pre)clinical research
- D. Wiedermann (Cologne, Germany): MRI applications in preclinical brain research

**12:00-13:30 WORKSHOP - CHILD AND ADOLESCENT PSYCHIATRY**

**Belica Hall** Chairperson: I. Šain (Pula, Croatia)

- A. Špelić (Pula, Croatia): Psychoanalytic approach in psychotherapy of autism
- A. Mindoljević Drakulić (Zagreb, Croatia): Social neuroscience of attachment-based teaching in the classroom
- N. Ustinova (Moscow, Russian Federation): Strategic planning: how to improve health care services for children with autism in Russia?

**13:00-14:30 LUNCH**

**14:30-17:00 PSYCHIATRY SYMPOSIUM: FROM NEUROBIOLOGY TO PSYCHOTHERAPY**

**Ulika Hall** Chairpersons: M. Jakovljević (Zagreb, Croatia) & D. Marčinko (Zagreb, Croatia)

- M. Jakovljević (Zagreb, Croatia): The concept of staging
- D. Marčinko (Zagreb, Croatia): Personality and psychosomatic reaction

Program

M. Rojnić Kuzman (Zagreb, Croatia): Treatment of first episode psychosis: Biological therapy or/and Psychotherapy?

A. Savić (Zagreb, Croatia): Neuroimaging and personality - challenging dichotomy between biology and psychology

T. Franić (Split, Croatia): Mental illness: Why help starts at a milestone birthday

B. Aukst-Margetić, D. Karlović (Zagreb, Croatia): Personality and schizophrenia

B. Vuksan Ćusa (Zagreb, Croatia): Bipolar disorder - pharmacotherapy or/and psychotherapy?

S. Drmić (Zagreb, Croatia): Tobacco harm reduction-experiences from Great Britain-nonconventional strategies in "old" fight against smoking

**14:30-15:45 JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND WFN  
Bianca APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF  
Istrian Hall CARE**



**SYMPOSIUM ON RECENT APPROACHES IN THE MANAGEMENT ON  
HEADACHE**

Chairpersons: V. Demarin (Zagreb, Croatia & B. Žvan (Ljubljana, Slovenia)

M. Zaletel (Ljubljana, Slovenia): Impact of migraine on public health in Slovenia

K. Bačić Baronica (Zagreb, Croatia): Current treatment modalities in migraine

B. Žvan (Ljubljana, Slovenia): New emerging therapies in migraine – CGRP antagonists and new EHF guidelines

**15:45-16:30 NOVARTIS SATELLITE SYMPOSIUM:  
Bianca AIMOVIG® (ERENUMAB) - THE FIRST SPECIFIC TREATMENT FOR  
Istrian Hall PROPHYLAXIS OF MIGRAINE**

V. Vuletić (Rijeka, Croatia): Aimovig (erenumab) – efficacy and safety profile in patients with episodic and chronic migraine

Z. Tomić (Rijeka, Croatia): Our the first experiences – “The diary of a migraine”

K. Bačić Baronica (Zagreb, Croatia): The efficacy of Aimovig (erenumab) in patients with medication overuse

**14:30-17:00 5<sup>TH</sup> PULA NEUROSCIENCE SYMPOSIUM - SESSION 4.**

**Belica Hall** Chairpersons: M. Dobrivojević Radmilović (Zagreb, Croatia), E. Buratti (Trieste, Italy)  
E. Buratti (Trieste, Italy): Importance of TDP-43 effects on RNA metabolism in neurodegenerative and muscular diseases

I. Munitić (Rijeka, Croatia): Optineurin dysfunction in neurodegeneration

K. Pilipović (Rijeka, Croatia): TDP-43 mislocalization following a single and repetitive traumatic brain injury in the mouse cortex

N. Bradshaw (Rijeka, Croatia): Chronic mental illnesses as disorders of protein aggregation

A. Glasnović (Zagreb, Croatia): Stroke in mice can be modified by blockage of RANKL axis with denosumab

D. Mitrečić (Zagreb, Croatia): Transplantation of neural stem cells after ischemic brain stroke influences expression of genes involved in the programmed cell death

Final Remarks



S. Gajović (Zagreb, Croatia)

**17:00-18:30 YOUNG PSYCHIATRISTS SYMPOSIUM: PSYCHODYNAMIC COACHING IN Ulika Hall CROATIA**

Chairpersons: D.Marčinko (Zagreb, Croatia), V. Bilić (Zagreb, Croatia), A.Bagarić (Zagreb, Croatia)

Promocija knjige: “Psihodinamika poslovnih odnosa”

autor: D. Marčinko, recenzenti: A. Bagarić i V. Bilić

Okrugli stol: Psihodinamski coaching - primjena psihodinamike u poslovnom svijetu

Moderatori: V. Bilić, A. Bagarić, M. Jakovljević, D. Marčinko

**16:30-18:30 CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY SYMPOSIUM Bianca ENDORSED BY WORLD STROKE ORGANIZATION**

**Istriana Hall** Chairpersons: K. Niederkorn (Graz, Austria) & V. Demarin (Zagreb, Croatia)

D. Bonifačić (Rijeka, Croatia): Serum prognostic biomarkers of ischemic stroke

D. Zadavec (Zagreb, Croatia): Radiological diagnostics and endovascular treatment of stroke

B. Piechowski-Jozwiak (Abu Dabi, UAE): Clot morphology in ischemic stroke

S. Frol (Ljubljana, Slovenia): Intravenous thrombolysis in patients on direct oral anticoagulants

H. Budinčević (Zagreb, Croatia): How to improve stroke care?

V. Đermanović Dobrota (Zagreb, Croatia): Cognitive impairment in patients with type 2 diabetes mellitus

**17:00-19:00 YOUNG INVESTIGATORS' CORNER**

**Belica Hall** Chairpersons: F. Đerke (Zagreb, Croatia) & L. Filipović Grčić (Zagreb, Croatia)

F. Đerke (Zagreb, Croatia): Better follow-up of patients with neurological diseases through mobile applications - our experiences

K. Stemberger (Zagreb, Croatia): Artificial intelligence and neuroradiology

L. Filipović-Grčić (Zagreb, Croatia): Novelties in Interventional neuroradiology

E. Papić (Rijeka, Croatia): Brain entrainment: Effects of binaural beats on cerebral function

A. Juginović (Split, Croatia) : Importance of diagnosis and treatment of sleep apnea in adults

M. Vuković (Split, Croatia): Is music therapy an effective treatment option in Alzheimer's disease?

I. Franin (Rijeka, Croatia): Pathohistological classification of CNS tumors throughout history: A review

A. Juginović (Split, Croatia): Cognitive effects of antiepileptic drugs in the pediatric population: a literature review

**17:30-18:30 WORKSHOP: HOW TO READ AND WRITE A SCIENTIFIC PAPER?**

**Bianchera Hall**A. Glasnović (Zagreb, Croatia): Normal distribution and related topics

A. Glasnović (Zagreb, Croatia): Study types

S. Gajović (Zagreb, Croatia): New ways to conceptualise the biomedical knowledge

**SUNDAY, June 2<sup>nd</sup>, 2019**

Program

**09:00-11:00 BEST POSTERS AWARDS PRESENTATIONS**

**Bianca** Chairpersons: V. Demarin (Zagreb, Croatia) & F. Benedetti (Milan, Italy)  
**Istriana Hall**

**11:00-12:00 CLOSING CEREMONY**

**Bianca**  
**Istriana Hall**



**MAIN THEMES LECTURES****Franz Fazekas (Graz, Austria): The contribution of MRI to the management of MS treatment**

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

Magnetic Resonance Imaging (MRI) provides valuable insights both at the beginning of and during the treatment of patients with Multiple Sclerosis (MS). Before considering any long-term treatment the diagnosis of MS has to be secured by confirming dissemination of CNS lesions in time and space and ruling out other differentials. This can be achieved quite fast and efficiently with the help of MRI according to the recently updated McDonald criteria although a careful clinical evaluation remains the mainstay of differential diagnosis and has to include laboratory and other diagnostic assessments as needed. MRI findings compatible with a diagnosis of MS also do not automatically imply the initiation of long term treatment. During treatment MRI can help to identify ongoing disease activity by showing contrast enhancing lesions or the accumulation of T2 lesions over time. While there exists no absolute threshold of active / new lesions a close to full suppression of MRI disease activity should be aimed for at least in patients with a mild to moderate disease course. MRI thereby strongly supports clinical findings such as continuing relapses or disability progression in the decision for treatment modification. When using MRI to monitor treatment response a strict and identical protocol should be followed using the same field strength and ideally the same scanner. Automated volumetric analyses have not yet been shown to be helpful. With specific long-term treatments MRI is also used for the early detection / ruling out of significant cerebral side effects such as progressive multiple leukoencephalopathy (PML). If this is done at short intervals a reduced MRI protocol without contrast material should be considered.

**Norbert Müller: THE ROLE OF INFLAMMATION IN ALZHEIMER'S DISEASE**

Marion von Tessin Memory-Zentrum and Ludwig-Maximilians-University München. Department of Psychiatry and Psychotherapy, München, Germany

The pathogenetic mechanisms of Alzheimer's disease (AD) are up to now only partly understood. There is no doubt that 'immunosenescence', the aging of the (healthy) immune system, leads to impaired immune function and that aging is the main risk factor for AD. Also, beyond doubt is that neuroinflammation plays a key role in the pathophysiology of the disease. However, whether inflammation is an underlying cause or a resulting condition in AD remains unresolved. At higher ages, communication in the peripheral and CNS immune systems, including both the initiation of the immune process and the down-regulation of inflammation, are impaired; this impaired communication might be one of the main factors contributing to the immune pathology of AD. The innate and adaptive immune systems (T- and B-cells) have been shown to be upregulated in aging and AD. Mounting evidence indicates that microglia activation contributes to neuronal damage in neurodegenerative diseases, but beneficial aspects of microglia activation have also been identified. The purpose of this lecture is to highlight new insights into the detrimental and beneficial role of neuroinflammation in AD. In this regard, we discuss the limitations and advantages of the protective effects of non-steroidal anti-inflammatory drugs (NSAIDs) and anti-inflammatory treatment options and identify possible future implications for AD therapy that might result from this underlying neuroinflammation.

**Martin Brüne: SOCIAL COGNITION IN HEALTH AND DISEASE – INSIGHTS FROM NEUROIMAGING AND GENETICS**

LWL University Hospital Bochum, Department of Psychiatry, Bochum Germany

The ways we relate to and interact with others critically depend on our understanding of other people's mental life in terms of their feelings, desires, thoughts and intentions. Empathic perspective-taking enables us to comprehend what is happening in our social environment at a given time, but also to predict future actions of others. In the last 25 years or so, neuroscientists have started to explore the manifold facets of social cognition that are involved in social behavior, from relatively simple emotional contagion to higher cognitive perspective-taking, that is, inferring thought and intentions of others, understanding what is morally right or wrong etc. using a bunch of technological tools, including EEG, brain stimulation, neuroimaging, and genetics. Social cognition is associated with the activation of a distinct neural network of the brain involving both phylogenetically older limbic structures, as well as more recently evolved brain regions of the neocortex. Together, our sophisticated social cognitive abilities give us enormous freedom of action and help us navigate our everyday lives, resolve conflicts, negotiate compromises and feel compassionate about friends and family. All this critically depends on gene-environment-interaction, whereby some genetic variants confer plasticity in regard of expressing empathic concern for others.

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In summary, neuroimaging and genetics provide us with powerful tools to study social cognitive processes in health and disease.

**Vida Demarin: THERE IS NO HEALTH, WITHOUT BRAIN HEALTH**

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

The idea about the importance of healthy life for brain health is present centuries ago, from Juvenalis' *Mens sana in corpore sano*, along with Ramon y Cajal's that Every man can, if he so desires, become a sculptor of his own brain, to the recent motto of the World Federation of Neurology: There is no health, without brain health.

Today, we have scientific proofs for these ideas. Neuroscience research, especially intensive during Decade of the Brain at the end of 20th century, especially by use of neuroimaging techniques, have clearly shown what is happening in the brain during physical exercise, during acute or chronic stress, during so called „brain fitness“, as well as the importance of healthy nutrition to preserve brain health, the importance of sleep and social inclusion. We obviously have the keys to healthy brain in our hands.

Epidemiological and prospective studies have shown that regular physical activity improves cognitive functions, fights depression and protects from neurodegenerative diseases. Extensive research is going on to prove biological mechanisms that underlie such beneficial effects. Multi domain interventions could improve or maintain cognitive functions in at-risk elderly people (FINGER study, 2015.). Prevention is the key. Greater gray matter volume, measured by MRI, was found with higher aerobic activity, pointing out that it might be neuroprotective.

Results of PREDIMED study showed the value of Mediterranean diet not only for prevention of stroke, but for prevention of cognitive decline as well.

Chronic stress is an important risk factor for brain decline, killing neurons and preventing the creation of new ones. That is why strategies for coping with stress, should be incorporated in our everyday life, as well as “brain fitness” programs with wide range of possible items.

But the most important is our attitude to life, if it is full of energy and positive vibrations, then our life would be filled with health and wealth and anti-aging process would be active and successful.

**Ervina Bilić: IVIG IN TREATMENT OF NEUROMUSCULAR DISEASES WITH FOCUS ON CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY**

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

When we talk about chronic autoimmune neuropathies, we may say that the most important task in clinical work is to distinguish the dominant motor forms of chronic neuropathies, because this finding has a significant influence on the choice of therapeutic approach. An additional challenge is the fact that only 51% of patients with chronic inflammatory demyelinating neuropathy (CIDP) have so-called "a classic form of disease".

CIDP is acquired, autoimmune, most commonly demyelinating and most commonly sensorymotor, but sometimes insufficiently recognized and treated disease. The reasons for possible underestimation of this most frequent treatable neuropathy may lie in the fact that CIDP may overlap with other forms and types of polyneuropathy. Even more, CIDP is nine times more common in diabetics. CIDP can also be found as a secondary neuropathy in patients with inherited demyelinating polyneuropathies. Even though CIDP is dominantly large fiber neuropathy, small sensory or/and autonomic fibers also can be affected.

Fortunately, a large number of CIDP patients can be successfully treated with immunomodulatory and immunosuppressive therapeutic approach. This is a neuromuscular disease in which we can witness a rapid recovery of severe motor deficits and monitor the overall recovery of patients to our mutual satisfaction. However, motor deficiency is not the only nor most important clinical manifestation of this disease. Even though we are more aware of the fact that significant autonomic dysfunction occurs in acute neuroimmunopathy, it can also occur in CIDP, which may be an important determinant of the patient's prognosis and the success of the treatment.

**Milan Latas: PHOBIC VERTIGO - DOES IT REALLY EXIST?**

Belgrade University School of Medicine, Department of Psychiatry, Belgrade, Serbia

**Introduction/Objectives:** Patients that are suffering from dizziness due to vertigo are usually directed in the department of otolaryngology. When various clinical examinations do not reveal any medical conditions, then the patients are referred to the department of neurology or psychiatry. In many cases, the diagnosis is psychological dizziness or phobic postural vertigo. Phobic postural vertigo is a term used to define a population of patients with dizziness and avoidance behavior often as a consequence of a vestibular disorder.

**Participants, Materials/Methods:** Phobic postural vertigo manifests with one or more symptoms of dizziness, unsteadiness, or non-spinning vertigo and it may be precipitated by conditions that disrupt balance or cause vertigo, unsteadiness, or dizziness, including peripheral or central vestibular disorders, other medical illnesses, or psychological distress. It is chronic functional vestibular disorder.

**Results:** Rates of psychiatric comorbidity in patients with structural vestibular syndromes are much higher with nearly 50%. Symptoms of anxiety disorders are frequent among patients with vestibular disorders.

**Conclusions:** Treatment plans should include patient education, vestibular rehabilitation, cognitive and behavioral therapies, and medications substantially reduce morbidity and offer the potential for sustained remission when applied systematically. Cognitive-behavioral therapy is an effective treatment for anxiety disorders, and vestibular rehabilitation exercises are effective for vestibular disorders.

**Milija Mijajlovic (Belgrade, Serbia): Patent foramen ovale: to close or not?**

Neurology Clinic Clinical Center of Serbia and School of Medicine University of Belgrade, Belgrade, Serbia

Patent foramen ovale (PFO) occurs when the septum primum and secundum fail to fuse after birth. A quarter of adults have this defect, which is usually an incidental finding with no clinical repercussions. However, the presence of PFO has been associated with a range of clinical conditions such as cryptogenic stroke (CS), migraine, platypnea-orthodeoxia syndrome, and decompression illness. PFO has been shown to be highly prevalent in CSs. The efficacy of PFO closure for CS has been controversial. A paradoxical embolism that is produced through a PFO is hypothesized to be a leading cause of CS, especially in younger patients with low risk factors for stroke. It remains controversial as to which anticoagulation therapy or antiplatelet therapy, is better for patients with CS and a PFO. In addition, surgical and transcatheter closure of a PFO has been proposed for the secondary prevention of stroke in patients with CS with PFO. Several randomized controlled trials have been conducted in recent years to test whether a PFO closure gives a significant benefit in the management of CS. Three earlier randomized controlled trials failed to show a statistically significant benefit for a PFO closure; thus, many investigators believed that a PFO was an incidental bystander in patients with CS. However, meta-analyses and more recent specific trials have eliminated several confounding factors and possible biases and have also emphasized the use of a shunt closure over medical therapy in patients with CS. Therefore, these latest studies (the CLOSE and REDUCE trials) can possibly change the treatment paradigm in the near future.

**Boris Tsygankov Boris, Galina Ivanova, Galina Mamedova: SUPPOSED MECHANISMS OF INFLUENCE OF THE HEPATITIS C VIRUS ON THE DEVELOPMENT OF NEUROPSYCHOLOGICAL DISORDERS**

A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Department of Psychiatry-Narcology and Psychotherapy, Moscow, Russian Federation

**Introduction/Objectives:** Hepatitis C virus (HCV) infection produces a chronic systemic disease that induces chronic hepatitis, cirrhosis and hepatocellular carcinoma. In addition to its effects on liver, patients with chronic HCV infection may present with a range of extrahepatic symptoms including neuropsychiatric disorders. These extrahepatic manifestations are independent of severity of the underlying chronic liver disease and hepatic encephalopathy. The presence of HCV-associated neuropsychological disorders has a significant impact on the quality of life and wellbeing of patients with HCV. The aims of this review are to summarize recent literature looking at the associations between psychosocial and neurocognitive factors and HCV, identify the most common neuropsychological disorders and consider the probable mechanisms of mental and cognitive impairment in patients with HCV.

**Participants, Materials/Methods:** PubMed/Medline was systematically searched for psychosocial and neurocognitive factors associated with hepatitis C and patient wellbeing. In this review 83 valid articles were analyzed from 1994 to 2018.

**Results:** According to the literature review in the group of HCV-positive patients were found a significant decrease in higher cognitive functions: memory impairment, concentration and listening. These manifestations of cognitive dysfunction are supposed to be similar to the early symptoms of Alzheimer's disease. An increased risk of developing dementia (including Alzheimer's disease) has also been noted. The most frequently diagnosed symptoms were fatigue and sleep disturbances, associated with mood disorders diagnosed in 19,2 % of cases. Several mechanisms have been considered to explain the pathogenesis of neuropsychiatric disorders observed in chronic HCV infection: 1) the concept of the direct neuroinvasion of HCV; 2) derangement of metabolic pathways (including alterations in neurotransmitter circuits); 3) cerebral or systemic inflammation.

**Conclusions:** HCV's impact on quality of life and wellbeing has serious clinical and social consequences. Considering the serious extrahepatic implications for individuals, it is imperative that healthcare professionals pay close attention to neurocognitive factors, especially since early manifestations of neuropsychological disorders are similar to early symptoms of Alzheimer's disease and the risk of dementia in this group of patients is significantly higher. To date, the mechanisms of various mental and neurological disorders in patients with chronic HCV infection have been partially identified, but the long-term effect of these changes requires further study. Further research in this area may provide a potential opportunity to create targeted therapy that could significantly improve the quality of life of patients with HCV.



**LECTURES****PULA'S WORLD MS DAY SYMPOSIUM - MULTIDISCIPLINARY APPROACH TO PERSONS WITH MULTIPLE SCLEROSIS****Senka Rendulić Slivar, Robert Rendulić: HEALTH-RELATED QUALITY OF LIFE BY MULTIPLE SCLEROSIS PATIENTS – IMPORTANCE OF NEUROPHYSIOTHERAPY INTERVENTION**

Specialized hospital for medical rehabilitation Lipik, Lipik Spa, Lipik, Croatia; Department of Neurology, Faculty of Medicine at the J. J. Strossmayer University Osijek, Osijek, Croatia

**Introduction/Objectives:** Multiple sclerosis (MS) is one of the most common neurologic diseases of unknown etiology. People with MS have a highly degraded health-related quality of life due to the many symptoms that manifest themselves in these diseases. Health-related quality of life refers to the value one places on current abilities and limitations, including the effects of illness and treatment upon physical, and emotional, and social wellbeing. The research conducted in 2017 on 844 MS patients in Croatia confirmed that 51% of respondents have a significantly deteriorated quality of life. During 2017, a total number of MS patients who underwent rehabilitation in the Lipik Spa was 364 with a rise in 2018 on 372 patients. The goal of the research was to examine the quality of life of MS patients and the impact of neurorehabilitation at the spa on pain and mobility.

**Participants, Materials/Methods:** The research was performed on 50 subjects affected by relapsing-remitting MS (RRMS), EDSS<6. The patients underwent rehabilitation in the Lipik Spa during the time from March 1st, 2017 to September 30th, 2017. The neurorehabilitation lasted for two weeks. The quality of life was evaluated with Functional Assessment of Multiple Sclerosis (FAMS) questionnaire. The impact of neurophysiotherapy intervention on pain and mobility was evaluated with Visual Analog Scale (VAS) and Time and up go test (TUG/s). A dependent t-test was used initially and finally for the comparison of the results.

**Results:** There were 42 (84%) women and 8 (16%) men; their average age was 51,4 (28-67) years and the average duration of the disease was 11,3 (0,4-28) years. A statistically significant increase in the overall quality of life occurred after the neurorehabilitation, along with the clinical reduction of pain and greater overall mobility: FAMS 118.06 in. vs. 126.44 fin; VAS 4.31 vs 2.22; TUG 12.87s vs. 9.66s. Results of the ANOVA procedure suggest that even just the experimental treatment made significant impact on positive variable changes in the FAMS questionnaire subcategory for mobility, symptoms and fatigue (part. eta sq. VAS 0,774; TUG 0,401; FAMS 0,775).

**Conclusions:** There is a need to capture the multidimensional impact of MS on physical functioning, social functioning, and emotional well-being. Physiotherapy treatments are considered a symptomatic therapy for those affected by MS and neurorehabilitation is a factor that modifies the course of the disease. Neurorehabilitation at a spa improves the quality of life of MS patients.

**Robert Rendulić, Senka Rendulić Slivar: THE ROLE OF DINAMIC NEUROMUSCULAR STABILISATION IN THE COR STABILITY**

Specialized hospital for medical rehabilitation Lipik, Lipik Spa, Lipik, Croatia; Department of Neurology, Faculty of Medicine at the J. J. Strossmayer Univerersity Osijek, Osijek, Croatia

**Introduction/Objectives:** Based on the predominant problems rehabilitation by multiple sclerosis (MS) patients focuses in particular on spasticity, muscle strenght, decreased coordination and consequences of ataxia. Whit a mild and moderate degree of involvement (EDSS<6), the patient's main problem is their overall decrease in performance and fatigue, motor deficits, spasticity and ataxia. The mobility deficits disrupt daily activities and a further decrease in gait quality. In a majority of patients with movement deficits, characteristic deviations in the stabilizing muscle function is observed. The concept of dynamic neuromuscular stabilization (DNS) has been shown beneficial for cor stability. DNS is based on a neurodevelopmental kinesiology. Postural muscle function must be examined via tests that assess the quality of muscle engagement and must also consider muscle function during stabilization. Postural stabilization is understood to be an active muscular holding of body segments against the activity of external forces controlled by the CNS. This muscle activity holds body segments against the action of external forces (especially gravitational force). During static conditions a relative tightness of joints is achieved via muscular activity, which is coordinated by the activity of agonists and antagonists (co-activation activity). Without coordinated muscle activity our sceleton would collapse – hence postural stabilisation. Postural stabilisation does not only act against gravity, but it participates in all movements, even movements involving only the lower or upper extremities. During stabilisation of the spine and trunk, spinal extensors are always involved. At first, the deep extensors are engaged and the superficial muscles only become engaged during greater force demands. Their function is balanced by a flexor synergy which is formed by deep neck flexors, and an interplay between diaphragm, the abdominal musculature and the pelvic floor muscle. During stabilisation of the spine, the diaphragm is contracted, its contour is flattend. Therapeutic exercises by multiple sclerosis patients include also an active type therapy in an open and closed kinetic chain with the aim of improving the strength, power and endurance of the upper and lower extremities and the body. Therapeutic exercises have been included to improve balance and coordination by using unstable substrates in the standing position.

**Conclusions:** The foundation of a rehabilitation program for patients with MS consist of neurophysiology-based methods, especially for patients whit a mild and moderate neurological involvement. Neurophysiological approaches utilize CNS plasticity and contribute to the adaptation and reorganization of CNS function.

**Jagoda Kragujević, Vlasta Pekić, Ivana Kampić, Silva Butković Soldo: MULTIPLE SCLEROSIS AND FATIGUE**

University Hospital Center Osijek, Department of Neurology, Osijek, Croatia

**Introduction/Objectives:** Tiredness, or rather fatigue, is described in literature as a reduced ability to work with mental or psychological activity. However, the very term patients describe with a much wider range of symptoms such as tiredness and need for rest, drowsiness, weakness and is often considered as worsening of the disease symptoms. Fatigue is a multifactorial phenomenon in MS that can be present to a greater or lesser extent in a patient. Research /Objective: Examine the presence of fatigue in patients with multiple sclerosis.

**Participants, Materials/Methods:** The general questionnaire consisted of demographic questions and patient self-reported quality of life. The study was conducted at KBC Osijek at the Neurology Clinic for Multiple Sclerosis. As a Modified Fatigue Impact Scale (MFIS) study tool for assessment of fatigue. Sleep quality was evaluated using the Pittsburgh Sleep Quality Inventory (PSQI) and Functional Assessment of Chronic Illness Therapy (FACS).

**Results:** Out of a total of 81 respondents, slightly more than half were females (57). The mean age of respondents was 42.2 years ( $\neq$  12.4) and the average duration of MS was 9.9 years ( $\neq$  7.9). Most of the respondents were employed (30, 37%). Out of the total number of respondents, 56 (69.1%) receive some therapy. There are no significant differences in sleepiness and therapy ( $p = 0.507$ ), nor in the presence of fatigue in relation to the use or non-therapy ( $p = 0.270$ ). Fatigue is more pronounced in subjects older than 40 ( $p = 0.001$ ), in women ( $p = 0.039$ ) and in on-working ( $p = 0.001$ ). Fatigue is less pronounced than patients with MS suffer shortly.

**Conclusions:** Regardless of the level of fatigue and the range of symptoms of the disease, fatigue has been shown to be more or less presenting a large number of patients suffering from MS. Through the study, it was confirmed that fatigue affects the functional condition of the patient, ie the fatigue is less pronounced as the functional condition of the patient is better.

**Vlasta Pekić, Tanja Lazarević, Ksenija Pandža, Natalija Sikora, Silva Butković Soldo: MULTIPLE SCLEROSIS AND NUTRITION**

University Hospital Center Osijek, Department of Neurology, Osijek, Croatia

**Introduction/Objectives:** Today, more and more research deals with nutrition. The impact of eating habits on the development of Multiple Sclerosis is all the more commonly discussed. Good nutrition is important for everyone. In MS patients, the role of a healthy diet is multiple: from helping to deal with the disease, adapting to the new state, reducing disease symptoms to a lower level, and reducing the progression of the disease. Objective: To test the usefulness of the Nutrition Risk Screening 2002 test in assessing nutritional status in hospitalized patients with Multiple Sclerosis.

**Participants, Materials/Methods:** The research was conducted at the Clinic for Neurology KBC Osijek for a period of one year. "Modified Swallowing Assessment" (MSA) was used for the evaluation of swallowing, and "Nutrition Risk Screening" (NRS) for the evaluation of the nutritional status.

**Results:** The survey covered 42 respondents who were hospitalized under the diagnosis of Multiple Sclerosis in the investigated period. The average life expectancy of the subjects is 49.3 years ( $\neq$  11.6) in the range of 20 to 79 years. Majority of respondents, 32 (76.2%), were hospitalized five or more times. 36 of them (85.7%) have high school education. The results show that on the first estimate 14.3%, and on the second, 19.1% of the respondents are in nutritive risk. Respondents who are dependent on the assistance of another person have a significantly worse nutritive score ( $p = 0.033$ ) on the first estimate.

**Conclusions:** Although data indicate that a certain number of respondents are in nutritive risk, a wider research should be undertaken to seriously assess and include more specific scales for assessing the nutritional status of patients with Multiple Sclerosis. Regardless of the results, good nutrition and nutritional status monitoring certainly contribute to a better quality of life for people with disabilities.

**Dunjica Karniš: ART THERAPY AS AN AID IN THE TREATMENT OF MULTIPLE SCLEROSIS PATIENTS**

Specialized hospital for medical rehabilitation Lipik, Lipik Spa, Department of physical and rehabilitation medicine, Lipik, Croatia

Art therapy was developed in the west in the beginning of the 20th century, in Croatia it is still in its infancy. Benefits of art therapy are well studied and confirmed; they include general health improvement, faster individual recovery, emotional awareness, strengthening of personal creativity which encourages good mood (increases secretion of the happy hormones), decrease of blood pressure. It is important to note that in rehabilitation, unlike in psychoanalysis, art therapy is focused on the production phase of the creativity process and there is no analysis of the final work. Some of art therapy activities can be used in patients regardless of the stage of motor impairment. Artistry helps in maintaining fine motor skills of the arm. In SB Lipik, art therapy activities used are: dance evenings (through movement and dance), poetic evenings, gardening; hospital has on a display various art works done by MS patients, who donated them to the hospital.

**Sanja Tomasović: NEUROIMMUNOLOGY- PARANEOPLASTIC SYNDROMES**

Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia; J. J. Strossmayer University of Osijek, Faculty of Medicine, Osijek, Croatia

Paraneoplastic neurologic syndromes (PNS) result from immune cross-reactivity between tumor cells and components of the nervous system. In response to a developing cancer, a patient produces tumor-directed antibodies known as *onconeural antibodies*. Because of antigenic similarity, these onconeural antibodies and associated onconeural antigen-specific T lymphocytes inadvertently attack components of the nervous system as well. PNS are detected before cancer is diagnosed in 80% of case. Because tumor cells themselves do not directly produce the causative agents of PNS, and because onconeural antibodies may cause permanent damage, successful cancer treatment does not necessarily result in neurologic improvement. The diagnosis of PNS may incorporate imaging, serologies, electroencephalography, nerve conduction studies, electromyography, and cerebrospinal fluid (CSF) analysis for signs of inflammation. Onconeural antibodies, which are usually detectable in the serum and rarely require CSF testing, may lack sensitivity and specificity. Depending on the affected nervous system compartment, PNS symptoms may include cognitive and personality changes, ataxia, cranial nerve deficits, weakness, or numbness. Paraneoplastic neurologic syndromes can affect the central nervous system (eg, limbic encephalitis and paraneoplastic cerebellar degeneration), the neuromuscular junction (eg, Lambert-Eaton myasthenia syndrome [LEMS] and myasthenia gravis), or the peripheral nervous system (eg, autonomic neuropathy and subacute sensory neuropathy). The diagnosis of PNS may incorporate imaging, serologies, electroencephalography, nerve conduction studies, electromyography, and cerebrospinal fluid (CSF) analysis for signs of inflammation. Onconeural antibodies, which are usually detectable in the serum and rarely require CSF testing, may lack sensitivity and specificity. Approximately 30% of patients with presumed PNS do not have detectable antibodies in either serum or CSF. Conversely, some well-defined onconeural antibodies may be detected in individuals with no neurologic illness. Given the overlapping clinical features with nonparaneoplastic disorders and the limitations of serologic testing, new diagnostic criteria have been proposed. These include the presence of cancer, the definition of classical syndromes, and the presence of onconeural antibodies. On the basis of these criteria, PNS have been classified as “definite” and “possible. Even in patients with detectable onconeural antibodies, it has been suggested that a diagnosis of PNS be made only after other possible causes of a particular neurologic syndrome have been excluded. Beyond treatment of the underlying tumor, immune modulation is a key component of PNS therapy. Specific modalities include corticosteroids, corticosteroid-sparing agents (eg, azathioprine, cyclophosphamide), the anti-CD20 monoclonal antibody rituximab, IV immunoglobulin (IVIG), and plasmapheresis (plasma exchange).

**MULTIPLE SCLEROSIS SYMPOSIUM – HOT TOPICS IN MS TREATMENT****Tanja Hojs Fabjan: FIRST LINE THERAPY IN MULTIPLE SCLEROSIS**

University Medical Centre Maribor and Faculty of Medicine Maribor, Department of Neurology, Maribor, Slovenia

Multiple sclerosis (MS) is an inflammatory and degenerative disease of the central nervous system and is the leading cause of neurologic disability in young adults. Disease-modifying drugs (DMD) have been available for more than two decades. With currently available immunomodulatory and immunosuppressive drugs we can reduce the clinical and radiological activity of the disease and slow down the progression of disability by improving the quality of life. Because treatment influences the inflammatory process, the treatment is most efficient at the beginning of the disease. The currently approved first line immunomodulatory therapy is proportionally safe, moderately effective and some medications are injectable, and inconvenient and painful for the patients. New oral drugs are much more convenient and patient friendly. Interferon (IFN) b-1a and b-1b and glatiramer acetate (GA) administered by subcutaneous (SC) or intramuscular (IM) injection are the established first-line therapies for clinically isolated syndrome (CIS), relapsing remitting MS (RRMS) and secondary progressive MS with relapses. Oral drugs such as teriflunomide and dimethyl fumarate (DMF) are other first line options and are indicated for RR MS. The first line therapies are often used in treatment of naïve patients or those with mild to moderate MS. Injection–site reactions and flu like symptoms are the most common adverse events. Lymphopenia, a risk factor for rare cases of progressive multifocal leukoencephalopathy with DMF, and elevation of liver enzymes and gastrointestinal disturbances with teriflunomide are the common safety concerns. The primary aim of treatment is to reduce clinical and radiological disease activity. Treatment sequencing is often necessary to maintain disease control. For INF beta recipients specifically the Rio score estimated after 1 year of treatment is prognostic for ongoing disease activity in the ensuing 3 years. Lateral sequencing between IFN beta, glatiramer acetate, DMF and teriflunomide therapies is sometimes considered to address concerns of route of administration, family planning, tolerability, adherence and/or safety profile, but not for inadequate treatment response. When planning a treatment program a benefit-risk assessment must consider the activity of the disease, DMD safety efficacy/profile and patient related factors. A treatment escalation approach is based on starting with relatively safer drug and active switches due to the breakthrough disease. Optimizing treatment early in MS may prevent accumulation of irreversible neurological damage and reduce the risk of disease progression.

**Vanja Bašić Kes: HOW TO TREAT NON-RESPONDENT MS PATIENTS?**

Clinical Hospital centre Setsre Milosrdnice, Department of Neurology, Zagreb, Croatia

Multiple Sclerosis (MS) is a major disabling neurologic disease of young adults and represents the most common immune-mediated inflammatory and demyelinating disorder of the central nervous system. The disability that MS produces is underscored by nearly 50% of patients who will require ambulatory aids within 15 years after disease onset. Therapy is targeted at changing the short-term natural history of MS to decrease relapse rates and to postpone long-term disability. Number of disease – modifying treatments are currently available for the treatment of RRMS and their aim is to decrease the relapse rate and the inflammation within the central nervous system . The challenges raised by the protracted course of the disease, the presence of neurodegeneration in all MS stages and the pathological burden (demyelination and axonal loss) inflicted over time by both inflammation and neurodegeneration raise challenges that are not yet completely tackled by the current therapies. New treatment strategies involving remyelination and neuroprotection are under study. It is likely that the next decade brings substantial changes in the understanding and ways of approaching the treatment in MS.

Although the number of disease-modifying treatments (DMTs) for relapsing-remitting multiple sclerosis (RRMS) has considerably increased over the past 20 years, some patients suffer from persistent disease activity despite highly active immunosuppressive DMT. In such patients, therapeutic strategies are limited and frequently associated with important side effects.



**Uroš Rot: TREATMENT OPTIONS IN PROGRESSIVE MULTIPLE SCLEROSIS**

University Medical Centre, Department: Department of Neurology, Ljubljana, Slovenia

A substantial proportion of multiple sclerosis (MS) patients have progressive MS. There are many disease modifying agents available for relapsing-remitting (RR) MS but clinical studies for progressive MS were mainly negative. Specific pathological processes in progressive stages such as compartmentalized inflammation and neurodegeneration are much more difficult to tackle than high inflammatory activity with demyelination of RRMS. However, some promising results were observed recently. Ocrelizumab, an anti-CD 20 agent was found to reduce disability progression in patients with primary progressive (PPMS). Many patients with early and active PPMS are now treated with the drug. Furthermore, siponimod, sphingosine-1-phosphate modulator reduced disability progression in patients with secondary progressive (SP) MS and was approved by FDA for patients with active SPMS couple of months ago. Disease modifying treatment for progressive MS is only moderately effective but it will enhance earlier and correct recognition of both progressive subtypes of the disease and foster novel clinical trials in progressive MS.

**GRAZ NEUROLOGY SYMPOSIUM - HISTORICAL DEVELOPMENT, PRESENT STATUS AND FUTURE ASPECTS OF DIAGNOSIS AND TREATMENT****Tadeja Urbanic-Purkart, Franz Payer: FUTURE ASPECTS IN NEURO-ONCOLOGY**

Medizinische Universität Graz, Univ. Klinik für Neurologie, Klinische Abteilung für allgemeine Neurologie und Klinische Abteilung für Neuroradiologie, vaskuläre und interventionelle Radiologie, Graz, Austria.

Chemoradiation with temozolomide after surgery has been the standard of care for patients with glioblastoma since 2005, whereas the other cancer fields have been zooming fast forward. With the new WHO classification of CNS tumors in 2016, a new era in Neuro-Oncology based on molecular genetics has begun. Molecular markers such as MGMT (O-6-methylguanine-DNA methyltransferase), IDH (isocitrate dehydrogenase), 1p19q codeletion led to a redefinition of tumor entities and can be used to tailor tumor-specific treatments. Marker-based classification nowadays allows a *à priori* estimation of treatment response and prognostic stratification. Patients with unfavorable molecular profile should therefore be strongly encouraged to participate in clinical trials with new investigational drugs.

Discoveries in basic and translational research contributed essentially to changes in treatment algorithms. New targeted therapies such as antiangiogenic treatment with antivascular endothelial growth factor antibodies (bevacizumab), antibody-drug-conjugates (depatuxizumab), as well as combinations of well-known chemotherapeutic agents such as temozolomide plus lomustine/CCNU for the methylated subgroup of glioblastoma patients (CeTeG, NOA-09 trial) are all parts of modern treatment regimens in selected cases. In 2017, a portable electrical field medical device was added to the treatment armamentarium.

Immunotherapies and immunology-based approaches are still under investigation and not yet a standard of care. 5-ALA mediated fluorescence-guided resection in high grade gliomas and tailored awake surgery in low grade gliomas have become essential techniques in the surgical treatment. Furthermore, refinement of conventional photon-based radiotherapy techniques and the use of proton-beam techniques all aim at providing maximal net-clinical benefit and minimizing detrimental effects, especially cognitive deficits.

The characterization of molecular pathways involved in glioma development led not only to a better understanding of glioma driver mutations, but also to the development of advanced imaging techniques visualizing these pathways. The Response Assessment in Neuro-Oncology (RANO) working group has developed criteria for the assessment of treatment responses to new therapies.

Moreover, the use of amino acid PET imaging for brain tumor management has recently been proposed as adjunct imaging technique in unclear cases.

All these approaches allow a, on a case-by-case basis, personalized treatment plan, a future hope for all our patients still suffering from a deadly disease.

**PSYCHOPATHOLOGY SUMMER SCHOOL****Gonzalo Forno, Christina Josefa Herold, Jorge Calderon, Johannes Schröder, Pablo Toro: NEUROLOGICAL SOFT SIGNS (NSS) AND COGNITIVE DEFICITS IN HIV ASSOCIATED NEUROCOGNITIVE DISORDER**

University of Heidelberg, Section of Geriatric Psychiatry, Heidelberg, Germany

**Introduction/Objectives:** Neurological soft signs (NSS) – or subtle motor and sensory deficits – are frequently found in severe mental disorders, such as Alzheimer’s disease, schizophrenia or patients with HIV associated neurocognitive disorder (HAND) which includes asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV-associated dementia. To further characterize NSS in patients with HIV we sought to examine them with respect to neuropsychological deficits typically found in the disorder.

**Participants, Materials/Methods:** 67 HIV+ patients without a history of head trauma, opportunistic infections, severe psychiatric disorders or acute confounding comorbidities of the CNS were recruited. NSS and neuropsychological deficits were examined on the Heidelberg scale and the Cambridge Neuropsychological Test Automated Battery (CANTAB), respectively. Semantic and phonematic verbal fluency were established additionally.

**Results:** According to NIMH and NINDS criteria, 18 patients were diagnosed with ANI and 21 with MND, while 28 did not show cognitive deficits. NSS total scores were significantly ( $p < 0.05$ ) correlated with episodic memory, spatial working memory, reaction time, problem solving, but not verbal fluency. Similar patterns of significant correlations applied for the NSS subscales motor coordination, right/left and spatial orientation, and complex motor tasks. These correlation were confirmed when motor performance was entered as a covariate.

**Conclusions:** According to our findings, NSS in HIV positive patients are significantly correlated with deficits in a broad range of neuropsychological domains, in particular episodic memory and executive functions. Interestingly, similar findings were reported in schizophrenia. These findings underline the transdiagnostic character of NSS and facilitate the use of NSS in screening HIV patients for HAND.

**Martin Brüne: IS SCHIZOPHRENIA THE PHENOTYPIC CORRELATE OF PARASITIC BEHAVIOUR MANIPULATION?**

LWL University Hospital Bochum, Department of Psychiatry, Bochum Germany

The conviction of being manipulated by some unknown agent, is a prominent, so-called “first-rank”, symptom of schizophrenia. Clinicians call this “delusion of alien control”, suggesting that this peculiar subjective impression has no match in reality. But what if there is a kernel of truth in this belief? Can the manipulation actually be real?

The present talk seeks to explore how signs and symptoms of schizophrenia and its neurobiology can be understood as phenotypic manifestation of host-parasite interaction caused by *Toxoplasma gondii* infection. Specifically, it is suggested that *T. gondii* actively manipulates its host’s behavior for its own reproductive benefit, and as such, schizophrenia is the phenotypic correlate of parasitic manipulation ultimately promoting social exclusion. This proposition is also in line with the influence of *T. gondii* on dopamine and glutamate turnover, with the intracellular alterations caused by *T. gondii* infection, and with immunological correlates of schizophrenia, including genetics.

**Arjen L. Sutterland, Anne Kuin, Bouke Kuiper, Tom van Gool, Marion Leboyer, Guillaume Fond, Lieuwe de Haan: DRIVING US MAD: THE ASSOCIATION OF TOXOPLASMA GONDII WITH SUICIDE ATTEMPTS AND TRAFFIC ACCIDENTS - A SYSTEMATIC REVIEW AND META-ANALYSIS**

Amsterdam UMC, Department of Psychiatry, University of Amsterdam, The Netherlands.

**Introduction/Objectives:** Unnatural causes of death due to traffic accidents (TA) and suicide attempts (SA) constitute a major burden on global health, which remained stable in the last decade despite widespread efforts of prevention. Recently, latent infection with *Toxoplasma gondii* (*T. gondii*) has been suggested to be a biological risk factor for both TA and SA.

**Participants, Materials/Methods:** A systematic search concerning the relationship of *T. gondii* infection with TA and/or SA according to PRISMA guidelines in Medline, Pubmed and PsychInfo was conducted collecting papers up to 11 February 2019 (PROSPERO #CRD42018090206). The random-effect model was applied and sensitivity analyses were subsequently performed. Lastly, the population attributable fraction (PAF) was calculated.

**Results:** We found a significant association for antibodies against *T. gondii* with TA [odds ratio (OR) = 1.69; 95% confidence interval (CI) 1.20-2.38,  $p = 0.003$ ] and SA (OR = 1.39; 95% CI 1.10-1.76,  $p = 0.006$ ). Indication of publication bias was found for TA, but statistical adjustment for this bias did not change the OR. Heterogeneity between studies on SA was partly explained by type of control population used (OR<sub>healthy controls</sub> = 1.9,  $p < 0.001$  v. OR<sub>psychiatric controls</sub> = 1.06,  $p = 0.87$ ) and whether subjects with schizophrenia only were analysed (OR<sub>schizophrenia</sub> = 0.87,  $p = 0.62$  v. OR<sub>various</sub> = 1.8,  $p < 0.001$ ). The association was significantly stronger with higher antibody titres in TA and in studies that did not focus on schizophrenia subjects concerning SA. PAF of a *T. gondii* infection was 17% for TA and 10% for SA.

**Conclusions:** This indicates that preventing *T. gondii* infection may play a role in the prevention of TA or SA, although uncertainty remains whether infection and outcome are truly causally related.

**Margherita Bechi: AUTISTIC TRAITS NEGATIVELY INFLUENCE THEORY OF MIND AND TRAINING EFFICACY IN PATIENTS WITH SCHIZOPHRENIA**

IRCCS San Raffaele Scientific Institute; Department: Department of Clinical Neurosciences, Milan, Italy

**Introduction/Objectives:** Literature has recently identified a discrete subgroup of patients affected by schizophrenia that also present autistic traits (ATs), showing a peculiar cognitive, clinical and functional profile. Theory of Mind (ToM) represents a core, impaired feature in both schizophrenia and Autism Spectrum Disorder (ASD), however no one has already investigate ToM in patients with schizophrenia and ATs. Thus, this study aims, on the one hand, to assess differences among patients with and without ATs on clinical, cognitive and ToM abilities as well as in daily functioning; on the other hand, to compare the efficacy of a specific ToM training in these two groups.

**Participants, Materials/Methods:** Ninety-six patients affected by schizophrenia were enrolled and underwent a broad cognitive, social-cognitive and functional assessment before and after the ToM training.

**Results:** Patients with schizophrenia and ATs are more impaired in cognition, ToM, in premorbid and daily functioning as well as in clinical features, as compared to patients without ATs. This latter group also showed a general improvement in mentalizing abilities after ToM training, while patients with schizophrenia and ATs did not.

**Conclusions:** These data shed new light on the relation among schizophrenia and ATs, highlighting that patients with these traits are highly impaired in ToM abilities. Thus, ATs seem to limit the effectiveness of ToM training, having implications in clinical and rehabilitative practice.

**Nikola Ilanković, Andrej Ilanković: SCHIZOPHRENIAS ARE FREQUENTLY NOT PRIMARY CEREBRAL DISORDERS**

MEDIGROUP General Hospital, Department of Neuropsychiatry, Belgrade, Serbia

**Introduction/Objectives:** Introduction In the last decade the simplification in clinical medicine and the unethiological, general approach is very frequent (the “medicine of consequences”, N. Ilankovic). Because the syndromological diagnoses and (relative) effective symptomatic therapy, in clinical psychiatry in most cases the targets recently are only the phenomenology of behavioral disorders and the hypothesized neurochemical consequences, without precise etiopathogenetic or/and psychodynamic approach. Objectives Researchers have found that both medical and psychiatric comorbidity is common in patients with psychiatric disorders, particularly in children, adolescents and in old age. This nonethiological approach push the mental illnesses and the mental ill patients back in the darkness of unscientific era of middle century. Aims To show how many psychotic disorders has real and detectable etiology.

**Participants, Materials/Methods:** Methods Clinical and etiological analysis of 100 patients with psychotic disorders with data of all clinical laboratory and neuroimaging investigations.

**Results:** Results In most of patient (29%) the cause of psychotic episode was the substance abuse, in 25% focal and systemic infection (inflammation), in 16% endocrin-metabolic disorders, in 11% brain damage, in 7% cerebrovascular disorders, and in 7% neurodevelopmental disorders.

**Conclusions:** Conclusion The real etiological approach in clinical psychiatry open the door to most targeted etiological therapy of psychotic and other mental disorders.

**PSYCHIATRY SYMPOSIUM- NEW INSIGHTS IN NEUROINFLAMMATORY AND AUTOIMMUNE DYSREGULATION IN PSYCHIATRIC DISORDERS: IT THERE A ROLE FOR HERPES VIRUSES?****E. Marion Schneider, Stella Steinhauser, Karl Bechter (Ulm, Germany): METABOLISM AND MITOCHONDRIAL DYSREGULATION – ROLE OF PRO- AND ANTI-OXIDANT PATHWAYS IN PSYCHIATRY**

University of Ulm, Division of Experimental Anaesthesiology, Department of Anaesthesiology, Ulm, Germany

**Introduction/Objectives:** To identify the trigger of inflammation in psychiatric diseases, we here concentrated on phenotypes of patients with major depression. Using flow cytometry, leukocyte subpopulations can be analyzed for their activation phenotype by testing the surface expression of CD45, a phosphatase involved in lymphocyte, monocyte and granulocyte activation. Moreover, CD64 on granulocytes can be used to identify contact to bacterial pathogens. Cytoplasmic expression of the interferon response factor 7 (IRF-7) is noteworthy as a sensor for nucleic acids which may trigger inflammation against chronic virus infections as well as mitochondrial and genomic DNA. The latter may result from immune mediated cell damage as well as mitochondrial dysfunction which would also explain symptoms of fatigue. As an indicator of immune suppression, we also included Siglec3, detected by CD33, a marker for myeloid derived suppressor cells.

**Participants, Materials/Methods:** A selection of patients with psychiatric disorders (affective and schizophrenic) were included and results were compared with healthy volunteers from volunteer colleagues. Standardized flow cytometry was applied to distinguish leukocyte marker expression and a standardized semi-automated ELISA (Immulite 1000®) was applied for the quantification of pro- and anti-inflammatory cytokines. Sybr dye dependent fluorescence measurement (Quantus, promega.com) were used to quantify circulating DNA. Transelectron microscopy (TEM) serves for the detection of virus particles in leukocytes from cerebrospinal fluid (Jeol microscope at 1400 at 120 keV)

**Results:** The most impressive finding was that a majority of patients with both bipolar disorders as well as schizophrenia presented with an autoimmune phenotype. Some showed evidence for increased responsiveness to nucleic acids and an interferon type I based immune activation. The distribution of increased CD64 expression in granulocytes was only marginally different from the pattern observed in healthy controls. In SZ patients the most remarkable finding resided in increased CD33 expressing monocytes which characterizes severe immune suppression by myeloid derived suppressor cells. A similar phenotype has been previously described in patients with early onset of Alzheimer's disease.

**Conclusions:** Immune phenotypes and patterns of immune activation in patients with depression, bipolar and schizophrenia provide evidence for a type I interferon guided inflammation, which is either related to tissue destruction, autoimmune activation. And/or chronic virus infections. A highly remarkable feature was detected in schizophrenic patients by highly increased immunosuppressive CD33.



**Hans C. Klein, H. Knegtering, Karl Bechter : PSYCHOSIS AS A NON-CLEARING INFLAMMATORY RESPONSE TO A LATENT HERPES VIRUS IN THE LIMBIC SYSTEM**

Lentis Research/VNN Addiction Care/Rob Giel Research Centre Groningen/Gunzburg Bezirkskrankenhaus, FACT Leek and Oostersingel Groningen, Leek, The Netherlands

**Introduction/Objectives:** The etiopathogenesis of most psychotic disorders is unknown. Increasing evidence supports the mild encephalitis/ auto-immune hypothesis and a potential viral trigger (Borna Virus, Human Herpes Viruses). Recent research indicates that an (antiviral?) immune response with anti-brain antibodies may cause (chronic) psychosis and immune therapy may offer curative treatment options. These new insights may remodel the field of schizophrenia research in the future, more towards inflammatory and viral aetiology, pathogenesis and treatments. The important role of the limbic system in psychosis is often suggested. Inflammatory changes in schizophrenia in the hippocampus may explain memory deficits. In psychosis due to anti-NMDA antibodies, the hippocampus is also involved.

**Participants, Materials/Methods:** The herpes simplex virus can trigger limbic inflammation (and has like borna virus a specific affinity for this system, especially the hippocampus). Herpes simplex 1 (HSV-1) is the causative agent of fever blisters. HSV-2 is mainly responsible for genital herpes. HSV-1 probably transmits from the oral infection site directly to the trigeminal ganglion and nucleus and next to midbrain (monoaminergic) neurons to end its route higher level limbic regions (amygdala/hippocampus/insula) where it sometimes post mortem is found in human.

**Results:** We will present a summary on what is known about how a latent (not replicating) herpes simplex and what its possible role in the aetiopathogenesis of psychotic disorders (currently represented in the container diagnosis “schizophrenia”) can be. Further research directions will be suggested on (herpes simplex) virus related psychoses. Should herpes simplex psychosis have a place in the differential diagnosis of schizophrenia?

**Conclusions:** This presentation addresses core clinical features of (schizophrenia-like) herpes simplex psychosis that may indicate a viral etiopathology, such as catatonia, acute onset with changes in attentional functioning, EEG rhythm changes, as well as findings from MRI and PET scans. Then, the specific functional changes in the brain are addressed and its possible link to a disseminating (but low grade or not replicating) herpes simplex virus in the limbic systems is discussed. Last, results from very recently completed PET imaging research and ongoing research for biomarkers of herpes infection in CSF from research groups in Gunzburg, Ulm and Groningen are discussed.

**Christian Scheiber, Hans C. Klein, E. Marion Schneider: HERPES VIRAL AND INFLAMMATORY MARKERS IN PATIENTS WITH SEVERE MENTAL DISORDERS. NEW DATA FROM CSF.**

University Hospital Ulm, Department of Experimental Anaesthesiology, Ulm, Germany

**Introduction/Objectives:** Psychiatric mood disorders, including unipolar depression, bipolar disorder or schizophrenia present with yet unexplained pro-inflammatory phenotypes. Nonetheless, current treatment is mostly based on psychotropic drugs addressing serotonin, dopamine and noradrenaline. New molecular biomarkers may contribute to better insights into pathology and offer new therapeutic approaches. This study deals with microRNAs (miRNAs) in cerebrospinal fluid (CSF) related to infectious agents as a cause of chronic inflammation. We here focused on the detection of miRNA species related to innate immune responses as well as to Herpes simplex virus 1 (HSV-1). HSV-1 reactivation has been long proposed to be linked to the manifestation of schizophrenia.

**Participants, Materials/Methods:** CSF was available from psychiatric patients (including both, depressive and schizophrenic individuals). Control CSF was obtained from patients with subarachnoidal hemorrhage (SAH) or hydrocephalus as negative controls. In addition, a second (positive) control group was used, made up of HSV-1-positive individuals' CSF. Extracellular vesicles (EVs) in CSF were enriched by ultracentrifugation, followed by miRNA isolation and cDNA synthesis of their specific content. Using reverse transcription (RT-) qPCR, relative expression levels of miRNAs hsa-miR-21 and -146a, related to NF- $\kappa$ B-signaling pathways, were determined. In addition, HSV-1-derived latency-associated miRNAs were screened.

**Results:** In EVs isolated from cell-free CSF of patients with psychiatric diseases we found more HSV1-derived hsv1-miR-H2 when compared with CSF from patients with SAH. Moreover, we found higher hsa-miR-21 and -146a expression levels in EVs from psychiatric patients' CSF compared to SAH patients. Accordingly, inflammatory- and hypoxia-regulated hsa-miR-21 as well as inflammatory pathway regulating hsa-miR-146a and some evidence for the involvement of herpes virus infections is likely to play a role in psychiatric patients.

**Conclusions:** We found elevated levels of both host and viral miRNAs in psychiatric patients compared to controls. Upregulation of hsa-miR-21 and -146a may reflect hypoxia and Toll-like-receptor-mediated inflammation, respectively. Further, upregulation of hsv1-miR-H2 suggests that chronic exposure to HSV-1 has a role in psychiatric patients' inflammatory response. Future investigation of other host- as well as viral-derived miRNAs will extend the knowledge of host-viral-interactions and their contribution to the manifestation of psychiatric diseases.

**PSYCHIATRY SYMPOSIUM: FROM NEUROBIOLOGY TO PSYCHOTHERAPY**

**Darko Marčinko: PERSONALITY AND PSYCHOSOMATIC REACTION**

Clinical Hospital Center Zagreb, Department for Psychiatry, Zagreb, Croatia

Personality factors which affect vulnerability to specific diseases has been widely promoted in contemporary medicine. Some personality patterns have been extensively studied, such as alexithymia, type A personality, type D personality, also temperament and character parameters. The term ‘psychosomatic’ is now in common use although its definition is still less than clear. Definition of psychosomatic conditions emphasizes the role of emotional influences as a significant part in genesis, recurrence or expression of disease. This certainly does not exclude the possible co-existence of many other factors that contribute to the development of a particular illness (genetic, physical, environmental, etc.). In my presentation, I will present contemporary psychodynamic theories of the psychosomatic concept with some original investigations conducted by my team (psychiatric department at the Clinical Hospital Center Zagreb).

**Martina Rojnić Kuzman: TREATMENT OF FIRST EPISODE PSYCHOSIS: BIOLOGICAL THERAPY OR/AND PSYCHOTHERAPY?**

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

Antipsychotic medication has for a long time been the core the treatment of the schizophrenia, including of the first episode psychosis. However, in the last twenty years, specialized services for the treatment of first episode psychosis emerged, showing their superiority in comparison to treatment as usual in achieving functional recovery of the patients. These services for first episode psychosis usually include a multimodal treatment approach combining individualized pharmacotherapy and a variety of psychosocial and psychotherapeutic approaches, including life style modifications, such as regular exercise. No individual pharmacological, psychosocial or psychotherapeutical approach stand out as better than the other for the general treatment of psychosis, but rather specialized approaches for selected features of psychosis are proposed, in example cognitive remediation for cognitive symptoms. In addition, some of the novel approaches combining psychotherapy/ psychosocial approaches with modern information technology further decreasing the boundaries in treatment approaches: for example, the Avatar therapy is proposed for treatment of symptoms that were traditionally considered as targets of antipsychotics, such as hallucinations.

In line with these findings, our results, which will be presented here, also showed that addition of psychosocial treatment, as well as appropriate medication are crucial for restoring patients' level of functioning assessed after 18 months after the first episode psychosis.

**Bjanka Vuksan-Ćusa, Marina Šagud: BIPOLAR DISORDER -PHARMACOTHERAPY OR/AND PSYCHOTHERAPY**

University Hospital Centre Zagreb, Department of Psychiatry, Zagreb, Croatia

**Introduction/Objectives:** Bipolar disorder is characterized by a high degree of psychosocial impairment, low rates of medication adherence, interpersonal dysfunction and cognitive impairment, particularly when bipolar disorder is comorbid with the presence of borderline personality disorder. Although pharmacotherapy is the mainstay of treatment for bipolar disorder, medication offers only partial relief for patients. Gradually, the field moved from conceptualizing bipolar disorder as a disorder requiring only medication to an illness that, like many chronic disorders, is best treated using a combination of pharmacotherapy and psychotherapy .

**Participants, Materials/Methods:** We searched the available data on psychotherapy for adults with bipolar disorder investigating the efficacy and effectiveness of individual psychoeducation, group psychoeducation, individual cognitive-behavioral therapy, group cognitive-behavioral therapy, family therapy, interpersonal and social rhythm therapy, and integrated care management.

**Results:** The evidence demonstrates that bipolar disorder-specific psychotherapies, when added to medication for the treatment of bipolar disorder, consistently show advantages over medication alone on measures of symptom burden and risk of relapse.

**Conclusions:** Psychotherapeutic strategies common to most bipolar disorder-specific interventions utilize more directive and symptom-focused strategies such as encouragement of medication adherence, provision of psychoeducation, involvement of family members, development of strategies for relapse prevention, exploration of the reciprocal relationship between mood and either cognitions or interpersonal relationships, and establishment of regular sleep-wake cycles.

**5<sup>TH</sup> PULA NEUROSCIENCE SYMPOSIUM****Jasna Kriz: INNATE IMMUNE RESPONSE FOLLOWING BRAIN INJURIES: LOST IN TRANSLATION**

CERVO Brain Research Centre, Laval University, Department of Psychiatry and Neuroscience, Quebec City, Canada

**Introduction/Objectives:** Experimentally and clinically, brain injuries including stroke are associated with the acute and more chronic inflammatory responses characterized by the activation of resident glial cells, production of inflammatory cytokines and leukocyte infiltration in the brain, events that may contribute to ischemic brain injury including. Microglia are the principal immune cells of the brain. Once activated, in injured and/or diseased brain, microglia can acquire a wide repertoire of the context-dependent immune profiles. However, at present, the molecular mechanisms involved in the control of microglia polarization profiles remain elusive.

**Participants, Materials/Methods:** We recently created novel transgenic model/in vivo model-system for analysis of the dynamic translational state of microglial ribosomes with mRNAs as input and newly synthesized peptides as an output. We analyzed in parallel in vivo transcriptome and proteome of activated microglia.

**Results:** We found a marked dissociation of microglia mRNA and protein molecular signatures following an acute innate immune challenge. The results revealed that highly up-regulated and ribosome-associated mRNAs were not translated resulting in creation of two distinct microglia molecular signatures: i) a highly specialized pro-inflammatory mRNA and ii) immunomodulatory/homeostatic protein signature. The most striking divergence was observed in the key immune NF- $\kappa$ B network where we found that the cluster of highly up-regulated LPS-induced and polysome-associated transcripts are not translated. As mechanism, we discovered a selective 3'UTR-mediated translational suppression of highly expressed mRNAs. Moreover, we identified a novel and previously unknown role for RNA binding protein SRSF3 as a master suppressor/regulator of innate immune genes translation.

**Conclusions:** Our study provide important in vivo evidence of ribosome based translational check point mechanism of innate immune response in microglia. Furthermore, our results demonstrate that, by blocking translation of the highly regulated LPS genes, SRSF3 serves as a master regulator of innate immune response in resident microglia. This discovery suggests avenues for therapeutic modulation of innate immune response in resident microglia.

**Mathias Hoehn, Claudia Green, Dirk Wiedermann: FUNCTIONAL NEURONAL NETWORKS IN HEALTH AND DISEASE**

Max Planck Institute for Metabolism Research, Department: In-vivo-NMR Laboratory, Cologne, Germany

**Introduction/Objectives:** Cognitive performance is often assessed using task-based functional MRI (fMRI). However, this approach probes only a particular brain representation area but does not allow further far-range interactions with other brain networks. Furthermore, for preclinical studies of functional deficits and recovery, animals need to be anesthetized thus limiting options for responses to external stimuli. Resting state fMRI (rsfMRI), instead, assesses the brain without task processing due to stimuli. With this technique, the whole brain-wide neuronal networks are measured and the connectivity strength between far range network nodes is recorded. In this contribution, the broad range of applications of rsfMRI in mouse models of Alzheimer's disease (AD), stroke, and stem cell based brain regeneration will be discussed. Also, age dependence of the functional neuronal networks and influence of the gut-brain axis on the networks are presented.

**Participants, Materials/Methods:** Mouse models of AD and stroke are used. IN AD mice, conditional expression of human tau is followed. In ischemic animals, human neural stem cells are implanted two days after stroke induction. Resting state fMRI is recorded at a dedicated animal MRI scanner at 9.4 T, employing a cryo-cooled detector for sensitivity enhancement. Animals are anesthetized with an isoflurane/medetomidine protocol and physiological conditions are constantly monitored throughout the MRI session. Animals are repetitively recorded for up to three months. Stem cell vitality is controlled with bioluminescence imaging.

**Results:** AD studies demonstrated that already an increase in soluble tau in the mouse brain, even before tau aggregation, leads to substantial degradation of the neuronal networks. Switch-off of human tau results in normalization of the connectivity strength. After stroke, the networks show a persistent reduction for three months, extending into the contralateral hemisphere. Implantation of stem cells completely stabilizes the neuronal networks, indistinguishable from pre-stroke normal condition. Upon loss of stem cell vitality this stabilization is lost and the connectivity strength quickly approximates the ischemic condition.

**Conclusions:** Using rsfMRI, the functional networks condition can sensitively be probed, providing a complex picture of the whole brain-wide situation, and discriminating the effect of the diseases on individual neuronal networks such as e.g. the sensorimotor network or the default mode network. With this innovative technique, a door is opened to unravel functional deficits and functional improvement mechanisms during the course of cerebral diseases or lesions.

**Srećko Gajović, Dunja Gorup, Marina Radmilovic Dobrivojević, Siniša Škokić, Anton Glasnović, Paula Josić, Jasna Križ: MULTIMODAL APPROACHES TO EVALUATE MOUSE BRAIN REPAIR AFTER ISCHEMIC LESION**

University of Zagreb School of Medicine, Croatian Institute for Brain Research, Zagreb, Croatia; Laval University Faculty of Medicine, Department of Psychiatry and Neuroscience, Quebec, Canada

**Introduction/Objectives:** The stroke represents a major health problem, and besides the acute interventions aimed on restauration of the blood supply, there is no causal neuroporetictive nor neurorestorative therapies. Subsequently, the preclinical evaluation of medical interventions after stroke represent a major medical challenge. The objective of this study was to longitudinally monitor the molecular events after ischemic mouse lesion and indicate critical elements either to design medical inteventions or to evaluate their effects.

**Participants, Materials/Methods:** The mouse were monitored by multimodal in vivo imaging. This included magnetic resonance imaging (MRI) with 7T preclinical scanner (Bruker) to characterise the morphology of the ischemic lesion, and bioluminescence imaging (BLI) to get insight in gene activity in the living mouse brain using luciferase as reporter by optical imager (IVIS Spectrum, Perkin Elmer). Ischemic lesion was introduced by middle cerebral aretery occlusion (MCAO) for 60 minutes, following by filament removal and reperfusion. The affected animals were followed during 28 days by multiple imgaing sessions, functional evaluation by neurological scoring and subsequent brain analysis at the end of the experiment.

**Results:** The evolution of the ischemic lesion was characterised by manual delineation on T2-weighted and T2-map MRI recordings. The molecular activity monitored by BLI included neuroinflammaton by Tlr2 gene, neurorepair by Gap43 gene and apoptosis by innovative approach developed in our laboratory using caged luciferin, DEVD-luciferin (VivoGlo, Promega). The analysis of Tlr2-deficient mice indicated that modified neuroinflammation could enhance the neurorepair, but was accompanied by increase in apoptosis, in particular in the chronic phase of the stroke.

**Conclusions:** The in vivo imaging allowed to follow animals through the time, and evaluate both morphology and molecular aspects of the lesioned brain. The modified inflammation in our model had controversial effects by enhancing neurorepair but as well the apoptosis.

**Acknowledgments:** The study was supported by EU European Regional Development Fund, Operational Programme Competitiveness and Cohesion, grant agreement No.KK.01.1.1.01.0007, CoRE – Neuro, and Croatian Science Foundation project RepairStroke (IP-06-2016-1892). The work of doctoral student Paula Josić has been fully supported by the “Young researchers' career development project – training of doctoral students” of the Croatian Science Foundation funded by the European Union from the European Social Fund. Multimodal imaging was done at Laboratory for Regenerative Neuroscience - GlowLab, University of Zagreb School of Medicine.



**Vedrana Ivić , Milorad Zjalić, Irena Labak, Srećko Gajović, Robert Gaspar, Sandor G. Vari, Marija Heffer:  
METFORMIN AND LIRAGLUTIDE DIFFERENTLY AFFECT CENTRAL INSULIN RESISTANCE IN  
THE RAT MODEL OF PREDIABETES**

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**Introduction/Objectives:** In the last three decades obesity became the leading health problem Worldwide. Obesity is the major risk factor for development of adult-onset Type 2 diabetes and a potential risk for Alzheimer's disease (AD). Drugs directed toward prominent pathophysiological markers of AD failed in clinical phase probably due to late pharmacological intervention. Metformin and Victoza (liraglutide) are used for treating type 2 diabetes. In patients who were newly diagnosed with type 2 diabetes (T2DM), liraglutide combined with metformin led to remission and the combined therapy is potentially effective treatment for central insulin resistance.

**Participants, Materials/Methods:** Males and females of 44 weeks old Sprague-Dawley rats were divided in four groups (8 animals in each). The first group was left on standard diet (SD) while in the following 3 groups obesity was induced by high fat high sugar diet (HFHSD). After 5 weeks of induction, one of HFHSD groups started treatment with metformin (HFHSD-M) and another one with liraglutide (HFHSD-L). Animals were sacrificed after 15 weeks of treatment. Brain and liver tissue were subjected to biochemical, histological and immunohistochemical analysis.

**Results:** HFHSD induced animals developed liver steatosis. Metformin was less effective than liraglutide in decreasing steatosis, particularly in males. Quantification of receptors for insulin (IR), insulin like growth factor (IGF-1R) and leptin (ObR) in satiety centres (arcuate, paraventricular nucleus and lateral hypothalamus) showed upregulation of all receptors in males and downregulation in females under HFHSD. Male groups treated with either metformin or liraglutide expressed high concentrations of all receptors, while female groups reacted equally just in the case of metformin. The inflammation markers (glial fibrillary acidic protein and microglial marker Iba1) decreased under HFHSD and increased after metformin treatment. Liraglutide upregulated just microglial marker of inflammation.

**Conclusions:** Both treatments alleviate liver steatosis caused by HFHSD, but only metformin increases sensitivity of satiety centres to insulin and leptin. The response to liraglutide treatments is sex specific – females developed insulin and leptin resistance of satiety centres. Central inflammation is upregulated in the case of both antidiabetic treatments, but in the case of liraglutide administration -microglia was the major driver of inflammation. While moderate inflammation encourages plasticity, in the case of liraglutide it was maladaptive.

**Funding:** The study has been funded by RECOOP HST grant, and in part by the Croatian Science Foundation under project number IP-09-2014-2324. Acknowledgement: This study was supported by the Association for Regional Cooperation in the Fields of Health, Science and Technology (RECOOP HST Association) and the participating Cedars – Sinai Medical Center - RECOOP Research Centers (CRRC). Ethical Committee Approval: Hungarian Ethical Committee for Animal Research: registration number IV/3796/2015.

**Jelena M Kezic, Paul G McMenamin: SYSTEMIC EXPOSURE TO TOLL-LIKE RECEPTOR 9 LIGAND CPG-ODN ELICITS LOW-GRADE INFLAMMATION IN THE RETINA THAT IS UNALTERED IN DIABETIC MICE.**

University of Zagreb, Department of Histology and Embryology, Zagreb, Croatia, Monash University Anatomy and Developmental Biology, Melbourne, Australia

**Introduction/Objectives:** Studies suggest that peripheral inflammation may adversely influence the progression of neurodegenerative disorders, with the chronic activation of microglia being a potential contributing factor. Further, data have emerged linking low-grade systemic inflammation with the development of diabetes and interestingly, this disease has been associated with an increased susceptibility to a number of infections, as well as a greater risk of CNS conditions including stroke. Here we investigated the inflammatory response following exposure to the toll-like receptor 9 ligand CpG-ODN in the retina and explored whether inflammation was altered in diabetes.

**Participants, Materials/Methods:** Male non-diabetic Cx3cr1+/gfp and diabetic Cx3cr1+/gfp Ins2Akita mice were injected intraperitoneally with 40 µg CpG-ODN. Ins2Akita mice develop hyperglycaemia by 4 weeks of age. Cx3cr1+/gfp mice allow for microscopic visualization of Cx3cr1+ microglia and macrophages. Mice were clinically examined (Micron III camera) 1 week after exposure to CpG-ODN. Immunofluorescence staining was performed on retinal wholemounts to assess expression of MHC Class II and glial fibrillary acidic protein (GFAP). Morphological changes to microglia and changes in cell density of retinal macrophages were compared in non-diabetic and diabetic mice.

**Results:** No overt changes to the retinal fundus or vasculature were observed by clinical evaluation 1 week after CpG-ODN treatment. Assessment of retinal wholemounts revealed upregulated expression of GFAP on Müller cells and MHC Class II on retinal vessels. Additionally, there was an increased accumulation of subretinal macrophages and characteristic morphological changes to microglia indicative of an activated phenotype. Interestingly, the inflammatory changes in response to systemic CpG-ODN were not enhanced in diabetic mice.

**Conclusions:** Systemic exposure to CpG-ODN elicits low-grade inflammation in the retina that is unaltered in hyperglycaemic conditions. Examining inflammatory responses in the eye may provide insight into potential changes in the brain following systemic inflammation in the context of neurodegeneration.

**Anja Barešić, Alexander Jolyon Nash, Tarik Dahoun, Oliver Howes, Boris Lenhard (London, UK):  
SCHIZOPHRENIA GWAS INTERPRETATION: LESSONS FROM FUNCTIONAL AND COMPARATIVE  
GENOMICS**

MRC London Institute of Medical Sciences, London, UK; Institute of Clinical Sciences, Faculty of Medicine, Imperial College London, London, UK; Sars International Centre for Marine Molecular Biology, University of Bergen, Bergen, Norway; Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, UK; Ruder Bošković Institute, Zagreb, Croatia

With ever more information gathering on the disease-associated variants, and 95% of the variations located in the non-coding part of the human genome, the question of determining the most likely causative gene(s) through which a variant exerts its effect is becoming one of the last unsolved problems.

The aim is to present how to utilise extreme non-coding conservation of vertebrate genomes to address this issue: the genomic regulatory block (GRB) model predicts transcription of which genes are under long-range regulation by the elements distant in genomic space, and coming into proximity by chromatin three-dimensional structure. The analysis on the schizophrenia GWAS dataset exemplifies how the GRB model can be used to prioritise target genes, from genomic neighbourhood of GWAS-significant SNPs, creating a list of enhancer-gene pairs most likely to contribute to the disease aetiology. The same approach is easily expanded to other (neuro)developmental GWAS datasets, providing testable biological hypotheses of disease/trait emergence.

**Dunja Gorup, Siniša Škokić, Jasna Kriz, Srećko Gajović (Zagreb, Croatia): CAGED-LUCIFERIN BIOLUMINESCENCE IMAGING IN EVALUATING MOUSE BRAIN ISCHEMIC LESION**

Croatian Institute for Brain Research, University of Zagreb School of Medicine, Zagreb, Croatia; Department of Psychiatry and Neuroscience, Faculty of Medicine Laval University, CERVO Brain Research Center, Québec, Canada

**Introduction/Objectives:** Our goal was to determine the critical relation between the caged-luciferin bioluminescence (cBLI) approach and classical direct luciferin BLI, accompanied by complementary magnetic resonance imaging (MRI) that could provide necessary normalisation parameters for intrinsic variability of the brain ischemic lesion (IL) size in a transient Medial Cerebral Artery Occlusion (tMCAO) model. Since the evolution of the IL is substantially influenced by the chief player of the aseptic inflammation Toll Like Receptor 2 (TLR2), we focused to monitor remodelling in TLR2 deficient mice (Tlr2<sup>-/-</sup>) and their wild type controls (WT) by *in vivo* cBLI showing activation of cleaved Caspase 3 (cCASP3) coupled with the Growth Associated Protein 43 (*Gap43*) expression, which, respectively, represent apoptosis, pruning and sprouting. Complementary MRI was used to determine the IL's size and, together with protein quantities assessed by Western Blot, was correlated with the BLI signal in order to co-validate the two imaging modalities.

**Participants, Materials/Methods:** In the experiment we compared 12-16 weeks male Tlr2<sup>-/-</sup> mice with their WT counterparts after 60 minutes of tMCAO in a one month follow-up. Both mouse lines were also *Gap43* transgenics on an albino B6 background which enabled bioluminescent imaging indicating expression of *Gap43*. The bioluminescence imaging was performed at the baseline and subsequently at 2, 7, 14 and 28 days. Two reagents applied intraperitoneally were VivoGlo (VivoGlo Caspase 3/7 Substrate; Z-DEVD-Aminoluciferin Sodium Salt, Promega, Madison, WI, USA) and luciferin (XenoLight D-Luciferin - K<sup>+</sup> Salt Bioluminescent Substrate, PerkinElmer, Waltham, MA, USA), with the latter applied 24 hours after VivoGlo. VivoGlo represents a luciferase prosubstrate that provides photons only if the cCASP3 or cCASP7 are present in the same cell with an active luciferase. This approach represented double logical test requiring both, expression of luciferase driven by *Gap43* promotor and activity of cCASP3/7 that produced the final signal. MRI imaging was performed at the baseline and subsequently at 3, 14 and 28 days after tMCAO. In parallel, mice were assessed using battery of behavioural test (neurological deficit scoring of 56 points, accelerating rotarod, Y-maze, bilateral tactile stimulation test and Schallert's cylinder test) which were introduced to mice 2 weeks prior to tMCAO. Furthermore, stroke areas of ipsilateral hemisphere were isolated from comparable batch of mice undergoing tMCAO for Western Blot measurements of  $\beta$ 3-Tubulin as a loading control, Disc Large Homologue 4 (DLG4), GAP43, synaptophysin clone SY38 and cCASP3.

**Results:** Major outcome of this study was establishing a powerful congruency of the cBLI, BLI photon flux and MRI-determined IL size obtained at the same time point, which provided correction factors for the high variability of the IL size inherent with in the tMCAO model.

cBLI/BLI signals were normalised according to the IL size, and the longitudinal time curves were clearly distinguishable for each genotype group. *Gap43* expression normalised to IL size was significantly higher at 3 and 14 days in Tlr2<sup>-/-</sup>, while at 7 days being on the border of statistical significance. Respectively, cCASP3/7 activity in *Gap43*-expressing cells was higher in Tlr2<sup>-/-</sup> at 14 and 28 days post tMCAO. This was accompanied by enhanced levels of synaptic plasticity markers DLG4 and synaptophysin in Tlr2<sup>-/-</sup> compared to WT mice.

**Conclusions:** cBLI is a useful method for determining the enzymatic activity of cleaving enzymes, but only when accompanied with the critical integration of multimodal imaging. This increased the power of our longitudinal study of measured markers reducing the number of used animals. It allowed us to conclude that in the acute phase of IL, Tlr2<sup>-/-</sup> mice seem protected from early deleterious IL-consequences and have lower mortality rate than their WT controls. Altered inflammation in Tlr2-deficient mice was accompanied by enhanced elements of post-stroke repair, in particular during the chronic phase of recovery, but also with delayed consolidation of the stabile brain lesion. In summary, multimodal imaging offers a realistic possibility for the assessment of complex post-stroke events, with the potential for the evaluation of novel medical interventions (drugs, patient rehabilitation and stem cells).

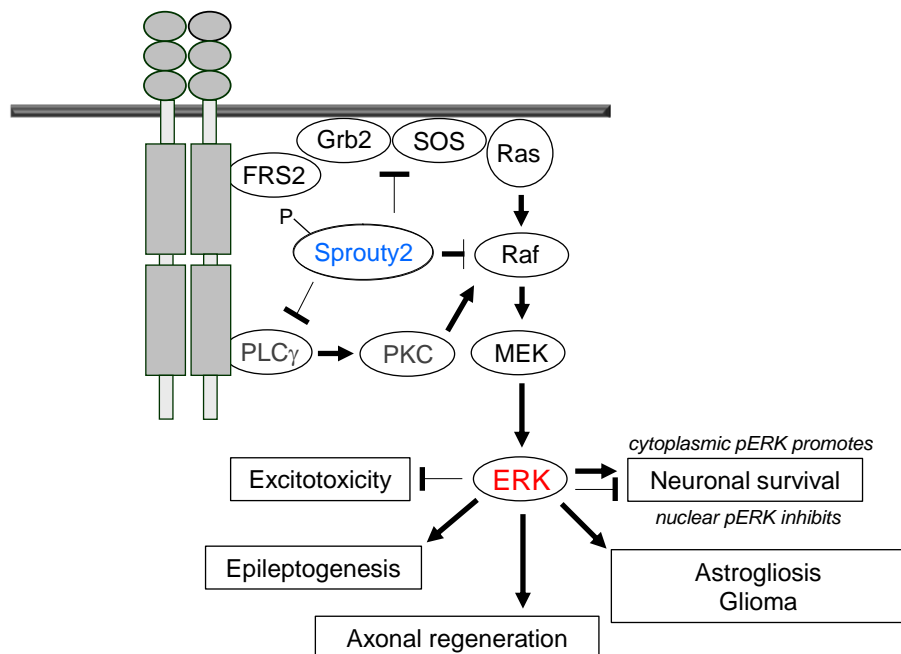
**Acknowledgement:** This work was fully supported by EU FP7 grant GlowBrain (REGPOT-2012-CT2012-316120), EU European Regional Development Fund, Operational Programme Competitiveness and Cohesion, grant agreement No.KK.01.1.1.01.0007, CoRE – Neuro, and by Croatian Science Foundation project IP-06-2016-1892. The *in vivo* imaging (MRI and BLI) were done at GlowLab multimodal imaging facility, University of Zagreb School of Medicine, Zagreb, Croatia.

**Barbara Hausott, Letizia Marvaldi, Sitthisak Thongrong, Jong-Whi Park, Lars Klimaschewski: IMPROVING BRAIN DISORDERS BY TARGETING THE ENDOGENOUS ERK INHIBITOR SPROUTY2**

Medical University of Innsbruck, Division of Neuroanatomy, Department of Anatomy and Histology, Innsbruck, Austria

Intracellular negative feedback inhibitors of receptor tyrosine kinase signaling, such as the Sprouty (Spry) proteins, play a key role in development and maintenance of the nervous system. Sprouties function as growth factor antagonists by specific interference with processes upstream of extra-cellular regulated kinases (see figure). Applying three different in-vivo lesion models, we demonstrate that reduction of Spry2 and -4 in neurons and glial cells promotes neuronal survival and axonal regeneration in the central and peripheral nervous system. Injection of Spry2/4 siRNAs into the rodent brain reduces the lesion size in response to endothelin-induced vasoconstriction (a model for stroke) three weeks after the injury. In kainate-induced epileptogenesis, secondary brain damage is decreased as well. Heterozygous Spry2/4 knockout mice exhibit reduced neuronal loss three weeks after kainate injection into the hippocampus, which is accompanied by increased astrogliosis and reduced neuronal migration (dispersion of granule cells). In brain tumors, however, the down-regulation of Spry2 causes excessive ERK activation and sensitizes glioblastoma cells to DNA damage that eventually leads to decreased proliferation and reduced tumorigenic capacity. In the peripheral nervous system, primary sensory neurons dissociated from Spry2 knock-out ganglia reveal stronger ERK activation and enhanced axon outgrowth. Following sciatic nerve crush, significantly more myelinated axons regenerate in Spry2<sup>+/-</sup> mice which is accompanied by faster recovery of sensomotor performance and increased expression of GAP-43. Taken together, our results suggest a role for Spry2 as a potential target for pharmacological inhibition to accelerate long-distance regeneration in peripheral nerves and to promote long-term neuronal survival in neurological disease.

Supported by the Austrian Science Fund (FWF).



**Antonio Šarolić: ELECTROSTIMULATION WAVEFORM AND FREQUENCY EFFECT ON NERVE EXCITABILITY**

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**Introduction/Objectives:** The response of the neuron membrane to an electrical stimulus is the basis for understanding the interaction of nerves with electromagnetic stimuli of various origins, either in biomedical applications (e.g. neuromodulation) or in electromagnetic field (EMF) exposure studies. The wide range of potential electrostimulation sources motivates us to research the nerve excitability in general, in terms of the neuron membrane response to a specific selection of electrostimulation parameters, such as waveform (the signal shape in time domain) and frequency.

**Participants, Materials/Methods:** The pure response of the neuron membrane is best studied on a single neuron: either a computer model (in silico), or an isolated single neuron in vitro, or a single axon animal model. Studies in humans or any animal models with nerve bundles result with the response which is more difficult to analyze, as it contains a compound action of a number of neurons, which is stochastic in nature. Accordingly, we performed a series of experiments to observe the responses of a single neuron membrane to a selection of waveforms and frequencies. We used the Spatially Extended Nonlinear Node (SENN) nerve model for several in silico studies, analyzing the neuron excitability as a response to various stimulation protocols: monophasic single and repetitive signals; biphasic single cycle and repetitive signals; pseudomonophasic (charge-balanced) signals. The waveform was varied over rectangular, sinusoidal and triangular shapes, with varying frequencies and phase durations. In vitro patch-clamp study was performed on cultured Sprague Dawley rat dorsal root ganglions, analyzing their excitability as a response to rectangular monophasic single pulses with varying phase duration, and to sinusoidal biphasic signals with varying frequency. In vivo studies were performed on *Lumbricus terrestris*. The excitability of its median giant fiber was analyzed, as a response to rectangular monophasic single pulses with varying phase duration, and to sinusoidal biphasic signals with varying frequency.

**Results:** The results were conveniently analyzed as either strength-duration and strength-frequency curves. The results for simple waveforms were in line with the expectations, as these were previously very well-analyzed. For the biological samples (in vitro and in vivo), a variation between specimens was very notable in terms of absolute values, but the results converged when analyzed in relative terms (i.e. thresholds normalized to the rheobase, and time parameters normalized to the membrane time constant). Several sets of experiments with repetitive and pseudomonophasic waveforms, less analyzed in literature, yielded interesting and illustrative results, especially for the short phase durations that were well below the membrane time constant.

**Conclusions:** The novel paradigms in neural electrostimulation require further research of nerve excitability. Our studies showed the effects of electrostimulation waveforms and frequency not thoroughly addressed or analyzed in the existing literature, however potentially relevant either for innovative biomedical applications or for human exposure to EMF.



**Marina Dobrivojevic Radmilovic, Sinisa Skokic, Dunja Gorup, Anton Glasnovic, Helena Justic, Paula Josic, Anja Baric, Srecko Gajovic: LONGITUDINAL MRI ANALYSIS OF ISCHEMIC LESION IN TOLL-LIKE RECEPTOR 2-DEFICIENT MOUSE**

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

**Introduction/Objectives:** Toll-like receptors play an important role in the induction of inflammatory response after stroke. Previous studies of Tlr2 loss of function assessed Tlr2 function in ischemic brain injury, reporting a possible dual role, an initial neuroprotection followed by delayed exacerbation. However, there are no conclusive answers regarding its specific effects on lesion progression. The aim of the current study was to use longitudinal *in vivo* MRI to follow up the evolution of the ischemic lesion in Tlr2-deficient mice and to clarify the role of TLR2 signaling in the ischemic brain injury.

**Participants, Materials/Methods:** Tlr2-deficient (Tlr2<sup>-/-</sup>) and C57Bl6 (WT) mice underwent a 60 minutes middle cerebral artery occlusion (MCAO) followed by reperfusion. The animals were scored for neurological deficit 7 days prior to MCAO and 1, 2, 3, 7, 14 and 28 days after. At the same time points the animals were imaged by a 7T BioSpec MRI system. At the end of this period the brains were processed for histological analysis. Histological and MRI volumetric segmentation was performed by manual delineation of ipsilateral hemisphere, contralateral and ischemic lesion in ImageJ.

**Results:** The survival analysis showed lower mortality for Tlr2<sup>-/-</sup>, despite showing significantly higher neurological deficit in the first three days after MCAO. The Tlr2<sup>-/-</sup> group had significantly bigger ischemic lesion volume two days after MCAO. Both groups showed a marked reduction of the ipsilateral cortical and striatal tissue at 14 days after MCAO, progressing over time, more prominently for Tlr2<sup>-/-</sup>. *Ex vivo* segmentation showed different volumetric results for the ipsilateral hemisphere compared to MRI, revealing that the fixation and dehydration processes affected differently the damaged and the healthy hemisphere.

**Conclusion:** Tlr2 deficiency can be correlated with better survival after stroke, regardless the initial higher neurological deficit and lesion volume shown by longitudinal MRI volumetric assessment. Histological tissue processing affects differently the damaged tissue compared to healthy tissue, resulting in an inherent fixation-induced bias when doing *ex vivo* volumetric analysis.

**Acknowledgments:** EU European Regional Development Fund, Operational Programme Competitiveness and Cohesion, grant agreement No.KK.01.1.1.01.0007, CoRE – Neuro; Croatian Science Foundation projects RepairStroke (IP-06-2016-1892), and BRADISCHEMIA (UIP-2017-05-8082). The work of doctoral students Anja Barić and Paula Josić has been fully supported by the “Young researchers' career development project – training of doctoral students” of the Croatian Science Foundation funded by the European Union from the European Social Fund. Multimodal imaging was done at Laboratory for Regenerative Neuroscience - GlowLab, University of Zagreb School of Medicine.

**Rozi Andretić Waldowski, Ana Filošević, Franka Rigo: NEUROGENETIC APPROACH IN THE STUDY OF ADDICTION USING INVERTEBRATE MODEL ORGANISM**

University of Rijeka, Department of Biotechnology, Rijeka, Croatia

**Introduction/Objectives:** Fruit fly, *Drosophila melanogaster*, has been used for years as a invertebrate laboratory model organism in translational biomedicine based on the significant genetic homology to humans with similar organisation and function of different organs. Different endophenotypes relating to addiction have been successfully modelled in *Drosophila*, such as behavioural sensitization to volatilized cocaine (COC). Strength of *Drosophila* research is in application of forward genetic approach (genetic screens) used for the identification of genes involved in the addictive drug-induced neuromodulation of the central neuronal system. The progress is limited due to the lack of an adequate high-throughput test for objectively measuring cocaine-induced behavioural changes in *Drosophila*.

**Participants, Materials/Methods:** We have developed a new high-throughput test named FlyBong for quantification of drug-induced locomotor activity. FlyBong allows for precise delivery (duration and concentration) of volatilized psychostimulants, COC or methamphetamine (METH), to individual flies whose locomotor activity is monitored using infrared sensors.

**Results:** Flies respond to acute dose of volatilized COC or METH with transient increase in locomotor activity compared to their baseline activity, and after second dose given 6 to 10 hours later, with further increase in locomotor response, indicating development of locomotor sensitization (LS). As in mammals, there is an individual difference in sensitivity to COC or METH administration, and only a subset of sensitive flies develops locomotor sensitization. Using FlyBong we have confirmed that development of LS is under control of several circadian genes (period, Clock and cycle) and shown association of LS with molecules which perturb redox (reduction-oxidation) balance. COC or METH administrations change the activity of antioxidant enzymes catalase and superoxid dismutase as consequence of drug induced reactive oxygen species production, and this change differs in circadian mutants that do not develop LS.

**Conclusions:** The high-throughput nature of FlyBong combined with quantification of locomotion of individual flies represents a significant advancement over previously used methods. It allows for application of genetic screen and selective breeding, which are instrumental for identification of new genes and elucidation of their roles in the neuromodulation that leads to addictive behaviors.



**Milan Kopecek: MULTIMODAL MOLECULAR IMAGING IN (PRE) CLINICAL RESEARCH**

FUJIFILM Visualsonics, Department of Preclinical Imaging Amsterdam, the Netherlands.

**Introduction/Objectives:** Photoacoustic (PA) imaging is a hybrid imaging modality, for non-invasive detection of tissue structural and functional anomalies.

**Participants, Materials/Methods:** The approach is based on optical absorption, which uses pulsed laser-induced ultrasound from specific endogenous tissue chromophores (e.g., melanin or hemoglobin) to map their distribution. The technique combines the advantageous properties of optical and ultrasound imaging.

**Results:** In contrast to purely optical imaging, PA imaging retains good spatial resolutions at higher imaging depths since ultrasound waves are not scattered as highly as photons inside biological tissue. So the PA imaging has a potential for identifying both the anatomical features and functional activity of tissues at higher depths.

**Conclusions:** Spectroscopic PA imaging can provide information of tumor oxygenation, and can serve as a tool for diagnosing malignancy. Some important applications of this technique include breast cancer detection, skin cancer visualization and small animal imaging.

**Dirk Wiedermann, Mathias Hoehn, Claudia Green, Anuka Minassian: MRI APPLICATIONS IN PRECLINICAL BRAIN RESEARCH**

Max Planck Institute for Metabolism Research, Department: in-vivo NMR, Cologne, Germany

**Introduction/Objectives:** MRI in preclinical brain research has different challenges compared to clinical MRI (e.g. smaller voxel sizes and thus reduced SNR, mandatory anesthesia,...) but offers also possibilities and research aspects that cannot easily be investigated in humans. Some key aspects here are: - the possibility to use contrast mechanisms or -agents that are not available for use in humans (e.g. MEMRI, smart contrast agents, fluorine labels) - specifically engineered cells, drugs or animal models (e.g. DREADD applications) - the combination with potentially more invasive methods (e.g. optogenetics, simultaneous Ca imaging)

**Participants, Materials/Methods:** This talk is intended as a coarse overview over the possibilities and varieties of MRI methods available for imaging anatomy, vascular properties, functional activation and functional / structural connectivities in rodents.

**Results:** Anatomical imaging is the most straightforward application of MRI in brain research. Major differences to standard clinical imaging are the altered relaxation times at the higher field strengths used in preclinical MRI. Anatomical images are valuable for phenotyping and with disease models to visualize pathological changes. They are also commonly recorded as a reference for functional data and can be used during post processing for a coregistration to a brain atlas which enables e.g. automated ROI evaluation. The vasculature can be imaged by TOF Angiography (large to medium sized vessels) while the microvasculature can be assessed by vessel density and vessel size imaging by employing T2 and T2\* images w/o and w/ an intravascular T2\* contrast agents. Functional imaging (fMRI) relies on the BOLD effect which is eventually a marker of neuronal activity. For a more precise evaluation the acquisition of the BOLD data can be done with an Arterial Spin Labeling (ASL) technique which then gives rise to the CBF simultaneously. An additional scan with an intravascular T2 contrast agent visualizes the changes in CBV, the delta-CMRO2 and OEF might be calculated and the circulatory reserve can be challenged by breathing CO2. Functional imaging can be stimulated by many kinds of triggered sensational inputs or by exogenous events like optogenetic or DREADD (de-) activation of selected cell populations. Finally, neuronal network und connectivity analysis can be done functionally by resting state fMRI and anatomically by diffusion imaging based tractography (DTI, Q-Ball, DSI, ...) or based on the directed transport of a contrast agent (MEMRI)

**Conclusions:** The main advantage of MRI is its non-invasiveness combined with its versatility, allowing longitudinal follow up studies. This enables us to depict and account for the biological or methodological variability with a great potential to reduce the number of animals needed and used.

**Emanuele Buratti, Francesca Paron, Ursa Susjnar, Sara Cappelli, Cristiana Stuani, Maurizio Romano (Trieste, Italy): IMPORTANCE OF TDP-43 EFFECTS ON RNA METABOLISM IN NEURODEGENERATIVE AND MUSCULAR DISEASES**

International Centre for Genetic Engineering and Biotechnology, Department of molecular pathology, Trieste, Italy

**Introduction/Objectives:** TAR DNA-Binding Protein 43 kDa (TDP-43) is a ubiquitously expressed and highly conserved protein of 414 aa belonging to the Heterogeneous Nuclear Ribonucleoprotein (hnRNP) family. TDP-43 is a general regulator of RNA metabolism, playing many cellular functions. These functions can be modulated by the interaction of TDP-43 with other members of hnRNP family and by the local cellular context. Interestingly, abnormal cellular distribution and post-translational modifications of TDP-43 are present in many disorders which are now generally referred as TDP-43 proteinopathies. In particular, Amyotrophic Lateral Sclerosis (ALS), Niemann-Pick Type C (NPC), and Inclusion Body Myositis are three examples of distinct TDP-43 cellular dysfunctions that have been described to occur in neuronal and muscle tissues. In our laboratory, our aim in recent years has been to characterise the functional role of TDP-43 in these tissues with the aim of trying to understand the pathological pathways involved in these diseases.

**Participants, Materials/Methods:** To do this, we have extensively used several human and mouse cellular models of disease to perform RNAseq analysis. The major aim has been to identify potentially important mRNA targets that become dysregulated in these diseases. As a result, our studies have provided a general overview of TDP-43 functions in all these systems.

**Results:** With regards to ALS, our studies have been focused at uncovering hnRNPs involvement in controlling TDP-43 functions whilst with regards to NPC our analyses have highlighted the importance of TDP-43 related pathways in metabolic disorders with visceral and neurological symptoms. Finally, in muscle we have identified a novel TDP-43 target, Tbc1d1, which gives rise to different isoforms in these two tissues and could therefore represent an important alteration in disease. As downregulation of Tbc1d1 protein was reported to result in disturbed glucose uptake, we are currently investigating this phenomenon by performing basic metabolic measurements in TDP-43 silenced C2C12 and NSC34 cells.

**Conclusions:** Our future directions with regards to ALS will be the investigation of the synaptic plasticity/death-signalling pathways after depletion/overexpression of selected transcripts that can be modified by TDP-43 and by disease modifier hnRNPs in cell models of disease. In addition, concerning NPC and IBM disease we are also going to validate the most misregulated and TDP-43 related genes in order to identify possible therapeutic markers.

**Andrea Markovinovic, Nikolina Prtenjaca, Marin Dominovic, Ivana Munitic: OPTINEURIN DYSFUNCTION IN NEURODEGENERATION**

University of Rijeka, Department of Biotechnology, Laboratory for Molecular Immunology, Rijeka, Croatia

**Introduction/Objectives:** Mutations of optineurin have been found in patients with three neurodegenerative diseases: amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD) and glaucoma. Optineurin is a ubiquitously expressed multifunctional ubiquitin-binding adaptor protein shown to regulate numerous cellular processes including inflammatory signaling, autophagy, vesicular trafficking and cell death. Disruptions in all of these processes have been found in neurodegenerative diseases, but the mechanistic link between optineurin mutations and the disease pathogenesis is still unclear. Interestingly, ALS and FTD have been linked to optineurin loss-of-function mutations whereas glaucoma has been linked to gain-of-function mutations.

**Participants, Materials/Methods:** To assess the protective role of optineurin in ALS and FTD we constructed an optineurin insufficiency mouse model with C-terminal truncation of ubiquitin binding region (Optn<sup>470T</sup>), which mimics loss-of-function mutations found in patients. We primarily focused on the role of optineurin in neuroinflammation, the major hallmark of all neurodegenerative diseases.

**Results:** We found that in contrast to previous reports in various cell lines, optineurin function is dispensable for inflammatory NF- $\kappa$ B activation upon LPS stimulation in primary innate immune cells including microglia and macrophages. However, treatment with LPS or poly (I:C) lead to diminished Tank-binding kinase 1 (TBK1) activation and production of IFN- $\beta$  in Optn<sup>470T</sup> in both cell types. This was consistent with the proposed role of optineurin as a scaffold for TBK1 activation. Expression of several IFN- $\beta$ -regulated genes, including both pro- and anti-inflammatory factors IRF7, NOS2, IL-10 and CXCL1 was diminished, whereas expression of CXCL10 was increased. The balance of pro- and anti-inflammatory factors was successfully restored upon IFN- $\beta$  supplementation, arguing that optineurin function is necessary for balanced inflammatory responses. Diminished IFN- $\beta$  signaling was also found in Optn<sup>470T</sup> primary neurons. Given that unmanipulated aged Optn<sup>470T</sup> mice did not show signs of microgliosis and neurodegeneration, we applied short-term systemic LPS stimulation to try to uncover the differences between the genotypes. Optn<sup>470T</sup> mice showed increased production of granulocyte and monocyte chemoattractants such as CXCL1, G-CSF, LIX and MIP- $\gamma$ . However, such short-term inflammatory stimulation did not reveal differences in microgliosis between WT and Optn<sup>470T</sup> mice.

**Conclusions:** We conclude that optineurin is necessary for optimal immunomodulatory IFN- $\beta$  production in various primary cells in the brain. Given that that does not by itself trigger neurodegeneration, we speculate that additional stimuli (infectious or other) are needed for disease manifestation in optineurin loss-of-function models.

**Kristina Pilipović, Tamara Janković, Jelena Rajič Bumber, Petra Dolenc, Jasna Križ, Gordana Župan (Rijeka, Croatia & Quebec, Canada): TDP-43 MISLOCALIZATION FOLLOWING A SINGLE AND REPETITIVE TRAUMATIC BRAIN INJURY IN THE MOUSE CORTEX**

Department of Pharmacology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia, Department of Psychiatry and Neuroscience, Faculty of Medicine, University Laval, Quebec, Canada

The 43 kDa transactive response (TAR) DNA binding protein (TDP-43) is expressed in multiple tissues, including the brain, and it is suggested to be involved in different pathways which control specific nuclear pre-mRNA splicing and all steps of mRNA life cycle as well the regulation of non-coding RNAs, but all its physiological roles are not known and have to be determined. Moreover, TDP-43 dysregulation has been identified in frontotemporal lobar degeneration, amyotrophic lateral sclerosis and in a number of other neurodegenerative disorders. Recent data indicate that TDP-43 could also be included in pathophysiological processes initiated by traumatic brain injury (TBI) but its role remains unclear. TBI is a major public health problem. Single brain trauma is usually caused by traffic accidents and falls while the repetitive form of the injury is frequently the consequence of the sports, recreational and military accidents and violence. Therefore, in this study the effects of a single and repetitive TBI on the TDP-43 cytoplasmic and nuclear expressions in the mouse cortex were examined.

Experiments were performed on adult male C57BL/6J mice. Single moderate lateral fluid percussion injury was performed over the left parietal cortex (McIntosh et al., 1989). Repetitive mild TBI was induced during five consecutive days, twice daily, with 6 h intervals, according to the weight drop method (Kane et al., 2012). Control, sham-injured animals went through the corresponding procedures without receiving head impacts. Mice were sacrificed at different time points after the trauma or sham procedures and their brains were prepared for immunohistological analyses. Brain slices were double-stained with TDP-43 antibody together with antibodies against specific neuronal, astrocytic or microglial markers.

TDP-43 nuclear expression was detected in all mentioned cell types of investigated brain structure in the injured animals and also in the mice of the control groups. In the animals with TBI, TDP-43 cytoplasmic localization was found in the cortical neurons and the microglia at different time points after the brain trauma.

In conclusion, a single as well as repetitive TBI induces translocation of TDP-43 from the nucleus to the cytoplasm of the neurons and microglia in the mouse cortex.

This research was supported by grants awarded to G.Ž. by the Croatian Science Foundation (IP-2016-06-4602) and to K.P. by the University of Rijeka (uniri-biomed-18-199).

**Nicholas J. Bradshaw: CHRONIC MENTAL ILLNESSES AS DISORDERS OF PROTEIN AGGREGATION**

University of Rijeka, Department of Biotechnology, Rijeka, Croatia

**Introduction/Objectives:** In spite of their devastating effect both on individual patients and society as a whole, the biology of major mental illnesses such as schizophrenia, bipolar disorder and major depressive disorder remain poorly understood. Genome wide association approaches have been successful in identifying many risk genes, however the effect size of any individual variant remains small. We have therefore proposed the study of proteins involved in these conditions, as a complementary approach to probing their underlying biology. Specifically, we have taken inspiration from the formation of protein insoluble aggregates in many neurodegenerative conditions, and hypothesised that similar, perhaps more subtle, defects in protein homeostasis may also occur in the brains of patients with chronic instances of major mental illness.

**Participants, Materials/Methods:** Initial identification of putative aggregating proteins was made in brain samples from patients with schizophrenia, bipolar disorder and/or major depression, plus control individuals. The insoluble protein fractions of these tissue were purified biochemically, and then probed for protein content. This involved either Western blotting for products of known mental illness risk genes, or else using proteomic-based approaches to identify novel proteins. Following these initial identifications, further characterisation of the proteins has occurred in both cell and rodent models of the conditions.

**Results:** To date, five proteins have been identified which seem to form insoluble aggregates specifically in the brains of patients. Three of these, DISC1, dysbindin-1B and NPAS3, are products of previously studied risk genes, while the remaining two, CRMP1 and TRIOBP-1, were identified through hypothesis free proteomics approaches. These are all brain-expressed proteins containing stretches of disordered secondary structure. Functionally, they are each involved in either synaptic function, cytoskeletal regulation or both. In many instances, one isoform or variant of the protein readily forms aggregates in cell culture and/or animal models, while others do not. For several of the proteins, specific regions of the protein have been shown to be essential for aggregation. Further characterisation of the aggregation propensity of these proteins is ongoing.

**Conclusions:** While still in its infancy as a field, the study of major mental illnesses as proteinopathies is showing promise, with multiple candidate proteins implicated as potentially aggregating specifically in the brains of patients. Studies in larger brain collections, as well as further biochemical characterisation of the proteins, is now required to determine their ultimate relevance for diagnosis and/or treatment of chronic mental illness.

**Anton Glasnović, Dunja Gorup, Ivan Alić, Siniša Škokić, Dinko Mitrečić: STROKE IN MICE CAN BE MODIFIED BY BLOCKAGE OF RANKL AXIS WITH DENOSUMAB**

Zagreb University School of Medicine, Department of Histology and Embriology, Zagreb, Croatia

**Introduction/Objectives:** In this pilot study, our aim was to get insight if RANKL (receptor activator of nuclear factor kappa B ligand) axis has an effect on stroke size in mice.

**Participants, Materials/Methods:** We used 16 WT (wild type) and 16 TKO (toll-like receptor knocked-out) mice. After initial MRI scan before the procedures, mice were scanned 24 hours and 4 days after the MCAO (middle carotid artery occlusion) procedure. On the first day, examined group was given IV (intraventricular) denosumab (RANKL inhibitor) injection on the side of brain affected by stroke. Meanwhile, sham groups of both MCAO and IV denosumab injection were performed thus concluding with 8 groups of mice and every group, each consisted of 4 mice. Stroke size was calculated manually with two independent examiners for every mouse.

**Results:** There were no significant differences between the groups. However, we noticed a tendency of bigger stroke size in those receiving denosumab in both WT and TKO groups, and also lower effect of denosumab in TKO mice.

**Conclusions:** Although no significant differences were shown, our pilot study indicates a tendency towards increase of stroke size when blocking RANKL response in brain. The possible mechanism could be less RANK signalling on microglial/macrophageal lineage in the brain which enhances ischaemic cascade and consequent brain tissue damage.

**Valentina Hribljan, Damir Lisjak, Dinko Mitrečić: TRANSPLANTATION OF NEURAL STEM CELLS AFTER ISCHEMIC BRAIN STROKE INFLUENCES EXPRESSION OF GENES INVOLVED IN THE PROGRAMMED CELL DEATH**

Croatian Institute for Brain Research, University of Zagreb School of Medicine, Department: Neurogenetics, Medical Genetics and Regenerative Neuroscience, Zagreb, Croatia

**Introduction/Objectives:** Destructive nature of necrosis following stroke is combined with different types of programmed cell death, including necroptosis, with effects which are not only detrimental, but also needed for functional restoration. The aim of the study was to analyse how transplantation of neural stem cells in the brain affected by stroke influences expression of genes involved in the programmed cell death.

**Participants, Materials/Methods:** After inducing stroke by occlusion of the middle cerebral artery in mouse, animals were 24 hours after induction of ischemia transplanted either by neural stem cells or medium enriched by growth factors. Neural stem cells were isolated from the telencephalic wall of 14.5 days old mouse embryos, obtained from the B6.Cg-Tg(Thy1-YFP)16Jrs/J transgenic mice strain. Fourteen days after transplantation, 5 groups of animals have been sacrificed: animals affected by stroke, animals affected by stroke and treated by medium, animals affected by stroke and treated by stem cells, healthy animals and healthy animals treated by stem cells. RNA has been isolated separately from affected and non-affected hemisphere followed by RT-PCR based on Taqman standardized probes and assessment of gene expression.

**Results:** Here we show that transplantation of neural stem cells in the mouse brain affected by stroke significantly increased expression of genes with well-known protective effects on hypoxic damage, like *Iduna*, while their antagonists, damage-supportive genes *Casp8* and *Aif* were significantly downregulated. In addition, we distinguished between effects obtained by stem cells (*Iduna*, *Aif*, *Nmdar1*, *Mif*, *Ripk1*, *Ripk3*, *Mlkl*) and those ones as well obtained by supporting tissue with enriched medium (*Casp8*, *Gfap*). We also report a significant downregulation of *Ripk1*, the major trigger of necroptotic cell death, but upregulation of *Ripk3* and *Mlkl*, other elements of this pathway, which suggests a complex role of necroptosis in both tissue damage and recovery.

**Conclusions:** Transplantation of NSC into the brain affected by stroke significantly influences expression of genes involved in the programmed cell death. The most striking effects include a strong upregulation of genes which counteract hypoxic damage, like *Iduna* or a strong downregulation of genes involved in necroptotic cell damage, like *Ripk1*. Moreover, response of stem cells transplanted in the brain affected by stroke points towards desired levels of expression of the certain gene in the certain time point.



**JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY AND WFN APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF CARE****SYMPOSIUM ON RECENT APPROACHES IN MANAGEMENT ON HEADACHE****Marjan Zaletel, Ljiljana Krager Zaletel, Bojana Žvan: THE IMPACT OF HEADACHE ON PUBLIC HEALTH IN SLOVENIA**

University Clinical Center of Ljubljana; Department: Department of Vascular Neurology, Ljubljana, Slovenia.

**Introduction/Objectives:** For more than ten years, the World Health Organization (WHO) has ranked headaches in the very top of major public health problems. A systematic review of the 2010 literature, which was carried out as an introduction to the Eurolight project. In Slovenia, data on the prevalence of headache are very scarce. The first as much in-depth information about the prevalence of headache among the population of Slovenia was obtained on the basis of a more complex analysis of the available data.

**Participants, Materials/Methods:** The data for the survey were collected under the program of continuous monitoring of behavioral factors for non-communicable diseases in Slovenia according to the CINDI Health Monitor methodology. The analysis included data for 2012. In total, the analysis included 9498 adult population of Slovenia aged 25-74 years. In the multivariate logistic regression model, a headache was observed in the last month before the survey, while the explanatory factors selected behavioral, demographic and socioeconomic factors were observed.

**Results:** The prevalence of headache in the last month before the study was 38.1%. The results of the multivariate analysis showed that the most significant results with the observed outcome are the following: risky stress behavior (RO<sub>da: no</sub> = 2.04,  $p < 0.001$ ), sleep habits (RO<sub>6-7 hours:  $\geq 8$  hours</sub> = 1.25,  $p$  RO<sub>1 cup: zero</sub> = 1.30,  $p = 0.003$ ; RO<sub>> 1 cup: zero</sub> = 1.63,  $p < 0.001$ ; RO<sub><6 hours:  $\geq 8$  hours</sub> = 1.45,  $p$ . (ROs: no = 0.79,  $p \neq 0.0001$ ), sex (RO<sub>men: men</sub> = 1.96,  $p \neq 0.0001$ ), age (RO<sub>25-29: 70-74</sub> = 5.67,  $p \neq 0.0001$ , RO<sub>30-39: 70-74</sub> = 3.60,  $p < 0.0001$ , RO<sub>40-49: 70-74</sub> = 2.76,  $p \leq 0.0001$ , RO<sub>50-59: 70-74</sub> = 1.76,  $p = 0.001$ , RO<sub>60-69: 70-74</sub> = 1.41,  $p = 0.015$ ), persons under 18 years of age in the household (RO<sub>da: no</sub> = 1.14,  $p = 0.039$ ), type of work (RO<sub>statement / administrative: retired</sub> = 1, 29,  $p = 0,040$ , RO<sub>intellectual / managerial: retired</sub> = 1,47,  $p = 0,006$ , RO<sub>nezaposlen: retired</sub> = 1,38,  $p = 0,022$ ) and social layer (RO<sub>chost lower: higher middle / upper</sub> = 1,38,  $p = 0,003$ , RO<sub>working: higher mean / upper</sub> = 1,25,  $p = 0,042$ ).

**Conclusions:** The research showed where there are potential holdings of headache management at the population level as well as at the level of individuals at risk, and suggests the need to develop appropriate policies in the field of managing this major public health problem.

**Bojana Žvan (Ljubljana, Slovenia): NEW EMERGING THERAPIES IN MIGRAINE – CGRP ANTAGONISTS AND NEW EHF GUIDELINES**

University Medical Centre Ljubljana, Neurology Clinic, Centre TeleKap, Ljubljana, Slovenia

Migraine is a common, chronic neurovascular disorder of the brain with cranial autonomic findings. It is characterized by recurrent, severe attacks of headaches often associated with other symptoms and much disability, as well as personal, familial and societal impact. Recently, preventive treatments of migraine have been limited worldwide. They often were ineffective and caused adverse events leading to low retention rates. Better therapies are badly needed.

The monoclonal antibodies (mAbs) acting on the calcitonin gene-related peptide (CGRP) are now available. These medications have specificity, as they were designed for primary migraine prevention. They work across a group of wide therapeutic targets, episodic migraine, chronic migraine, medication-overuse headache, and episodic cluster headache. CGRP-mAbs to the ligand and receptor display at least, if not greater, comparable efficacy to the currently available oral therapies, with better safety data and adherence and can be recommended for migraine prevention. Four mAbs have been developed: one targeting the calcitonin gene-related peptide receptor (erenumab) and three targeting the calcitonin gene-related peptide (eptinezumab, fremanezumab, and galcanezumab). They separate from placebo within 1 week, and often show clinical effects within a month or less. They have tolerability similar to placebo. There has been no significant or worrisome safety signal thus far in their use. They manifest unprecedented responder rates at  $\geq 75\%$  and even 100%. They lower all acute medication use and can convert patients from chronic migraine to episodic migraine and from acute medication overuse to non-overuse. They work in patients who have already had lack of success with at least 2-4 previous preventive medications.

The aim of this shortened version of the document by the European Headache Federation (EHF) is to provide an evidence-based and expert-based guideline on the use of the CGRP-mAbs for migraine prevention.

Real-world data will be very important to support efficacy and safety of those drugs particularly in the long-term.

**ALZHEIMER'S DISEASE SYMPOSIUM**

**Ninoslav Mimica: DEPRESSION, DEMENTIA AND DELIRIUM - CONTINUUM OR COMORBIDITY**

University Psychiatric Hospital Vrapče, School of Medicine, Department: Department for Biological Psychiatry and Psychogeriatrics, Zagreb, Croatia

The World population is becoming older and proportion of people older than 65 years is growing significantly. In some developed countries, till year 2050, almost 1/3 of people will be among elderly, what will change the morbidity. Although depression usually occur earlier in life span it will also be present among older people, together with dementia which will (often) be complicated with delirium superimposed on dementia. Depression and dementia are both recognised by World Health organisation as a public health priorities due to the impact on whole society. Depression starts usually in younger population, is pretty common, more affecting women, mostly recoverable disorder, but usually recurrent, and not rare in elderly. Dementia, is more common as people are older, more manifest in women, mostly not treatable, progressive. Delirium is present in many cases of dementia and lead to hospitalisation, low quality of life and may be fatal. Although depression, dementia and delirium as separate disorders may not be connected and be comorbid, in many occasions it is obvious that depression proceed dementia and delirium appears after, so this “3D continuum” may be observed.

**Marina Šagud, Bjanka Vuksan Ćusa, Suzan Kudlek-Mikulić, Alma Mihaljević Peleš: DEMENTIA OR DEPRESSION: HOW TO KNOW AND WHAT TO DO?**

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

**Introduction/Objectives:** Depression and dementia are prevalent in elderly people. While the symptoms of both disorders are overlapping, their relationship is complex and incompletely understood. Symptoms of depression might resemble dementia and vice versa. Mild impairment in multiple cognitive domains is common in depression and incipient dementia.

**Participants, Materials/Methods:** The aim of the present report was to summarize the current knowledge on recognition and treatment of depression in elderly individuals.

**Results:** According to longitudinal studies, depression earlier in life might increase the risk for developing dementia, and it is still unknown if effective treatment might reduce this risk. There is also a shared neurobiology, such as elevated cortisol levels. There might be a biological difference between early- and late-onset depression, given that late-life depression might be more likely to share cerebral pathology with dementia. Prevention, early recognition and effective treatment of depression in elderly individuals is of utmost importance. Despite the high prevalence of depression in individuals with dementia, only few appropriately designed and powered studies of antidepressants have been carried out in this population. At the moment, no specific antidepressant can be recommended as a first-line treatment for depression in dementia. There is evidence of the efficacy of cognitive-behavior therapy and music therapy.

**Conclusions:** Given the current lack of evidence for specific antidepressants in dementia, the treatment choice should be highly individual. It should consider comorbidities, potential drug interactions, and target specific symptoms, along with the psychosocial treatment. The best results might be obtained with multidisciplinary team.

**Natasa Klepac, Maja Relja (Zagreb, Croatia): EARLY DETECTION OF DEMENTIA**

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

Dementia is an undeniable concern for modern societies. A survey carried out by YouGov in 2011 revealed that dementia is people's biggest fear in later life – ahead of cancer and any other illnesses (ARUK 2011). Dementia is an overall term that describes a group of symptoms associated with a decline in memory or other thinking skills severe enough to reduce a person's ability to perform everyday activities. Alzheimer's disease (AD) accounts for the majority of cases of dementia; many of the remaining cases of dementia are caused by vascular disease and Lewy body disease. However population studies have established that people over 80 years (that is, most of those with dementia) have a mixture of pathologies in their brains. Moreover the clinical features that, when seen together, make up the diagnostic criteria are all continuous and affected by many other factors. Cognitive performance is affected by education, conditions such as depression, delirium, and proximity to death, and the ability to live independently is affected by physical conditions as well as social expectations. Therefore other markers of incipient dementia, such as brain atrophy, and levels of amyloid beta and tau in cerebrospinal fluid there are present early in the course of the disease, and not only cognitive deficits are also important. An approach that combines cognitive and non-cognitive preclinical markers is needed to improve our ability to detect people in the early phase of dementia. Detecting dementia as early as possible is essential for improving the success rates of different health care interventions, increasing the quality of life of older adults and their relatives, and reducing the societal costs of dementia. According to ADI's World Alzheimer Report 2011 there are several advantages of earlier diagnosis; 1. Earlier diagnosis allows people to plan ahead and make decisions about their future care; 2. People with dementia must have a diagnosis in order to receive pharmaceutical and non-pharmaceutical therapies that may improve their condition and quality of life; 3. Earlier diagnosis also provides an opportunity for people with dementia to participate in research, should they choose. Despite all these advantages there is a myth as underlined in the same report by Alzheimer International „that there is no point in early diagnosis, since nothing can be done“. Although no method of curing AD is currently available, as potentially useful and proven treatments become available, early diagnosis of dementia will become increasingly important.

**Marija Kušan Jukić, Ninoslav Mimica: PATHOPHYSIOLOGY, CLINICAL PICTURE AND TREATMENT OF DELIRIOUS STATE IN PERSONS WITH DEMENTIA**

Andrija Štampar Teaching Institute of Public Health, Department for mental health and prevention of dependence, Zagreb, Croatia; University Psychiatric Hospital “Vrapče, Zagreb, Croatia

The delirium appears in the overlapping grounds of somatic medicine, neurology and psychiatry. It is a phenomenon occurring abruptly, in dramatic clinical picture, and commits us to quick reaction, recognition and treatment mostly at the hospital ward. Delirium is a syndrome occurring in all age groups, but it is most important in older age patients with Alzheimer's and other types of dementia. So, we will focus on diagnosis and treatment of delirium within geriatric psychiatric patients suffering from dementia. The lecture brings the review of the recent literature about delirium superimposed to dementia, including current knowledge about pathophysiology, clinical picture and treatment of delirious state in persons with dementia. We will also discuss the current guidelines that are used in diagnosing and treatment as well as the methods of prevention.

**JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY AND WFN APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF CARE****NEUROPSYCHIATRIC MANIFESTATIONS OF NEUROLOGICAL DISORDERS****Osman Sinanović: NEUROPSYCHIATRIC MANIFESTATIONS OF STROKE**

University of Tuzla, Tuzla, Bosnia and Herzegovina

Psychiatric disorders (PDs) in neurology are more frequent than it is verified in routine exam, not only in the less developed but also in large and very developed neurological departments. Furthermore, psychiatric symptoms (PSs) in neurological diseases (NDs) among primary health care physicians and other specialties are often neglected. Anxiety and depression are most common, but hallucinations, delusions, obsessive-compulsive disorder, delirium or confusional state and cognitive disturbances are also frequent comorbidity in many neurological conditions such as stroke, epilepsy, multiple sclerosis (MS), Parkinson disease (PD), Huntington disease.

Psychiatric syndromes associated with stroke lead to significant psychological distress, functional impairments, poor rehabilitation outcomes, and excess mortality. There are different reports on frequency of delirium in acute stroke, from 24 to 48%, and it is more frequent in hemorrhagic than ischemic stroke. Cognitive impairment are part of clinical picture of many stroke patients. A variety of classifications, diagnostic criteria, and descriptive syndromes are used to define post-stroke cognitive impairment (PSCI), but a widely accepted and harmonized terminology is still missing. Post-stroke dementia (PSD) is a frequent condition after stroke and its prevalence ranges from 6 to 32%. However, not all cognitive impairment cases following a stroke are enough severe to fit the criteria for dementia, and many patients after a stroke develop mild cognitive impairment that in some cases can progress to PSD. Post stroke depression (PSD) and anxiety is also very frequent consequences on the stroke, and the prevalence of PSD has ranged from 5 to 63% of patients in several cross-sectional studies, peaking three to six months after a stroke. It is one of the more frequent complications of stroke, and has significant negative consequences on the recovery of motor and cognitive deficits, as well as the mortality risks associated with stroke, and has negative consequences on the recovery of motor and cognitive deficits, as well as the mortality risks associated with stroke.

Language disorders (aphasia, alexia, agraphia and acalculia), unilateral neglect, anosognosia (deficit disorders), delirium and mood disorders (productive disorders) in urgent neurology, first of all in acute phase of stroke are also very frequent neuropsychiatric manifestations in this disease. Language disorders are common consequence of left hemispheric lesion and most common neuropsychological consequence of stroke, with prevalence of one third of all stroke patients in acute phase although exist reports on greater frequency. Unilateral neglect is a disorder that mostly affects the patient after the lesion of the right hemisphere (infarct or haemorrhage affecting a large area – up to two thirds of the right hemisphere). Reports on the incidence of visual neglect vary and they range from 13 to 85%. Anosognosia is on the second place as neuropsychological syndrome of stroke in right hemisphere, characterized by the denial of the motor, visual or cognitive deficit. This syndrome, defined as denial of hemiparesis or hemianopsia, is a common disorder verified in 17-28% of all patients with acute brain stroke.

**Vladimira Vuletic (Rijeka, Croatia): NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE – UPDATES**

UHC Rijeka, Clinical Department of Neurology, Rijeka, Croatia

**Introduction/Objectives:** Although we usually think on motor symptoms when treat Parkinson's disease (PD), the non-motor symptoms (NMS) are more important for quality of life and often neglected and under-recognized. A modern approach to PD is holistic and include individual treatment of motor and non-motor symptoms. It is basic of personalized medicine tailored by symptoms. We know today how act some medications and invasive methods on some NMS. We will show in this lecture an overview and updates on NMS and effects of medications and invasive methods. Also we will present our results with observation of effects of deep brain stimulation (DBS) and continuous infusion of levodopa-carbidopa intestinal gel (LCIG) on nonmotor symptoms in advanced Parkinson's disease (APD).

**Participants, Materials/Methods:** We tested 50 patients before and 3 months after DBS and 15 patients before and 3 months after LCIG that came to our Center. The investigation was conducted with anamnesis and treatments' data, Non-motor Symptom Scale (NMSS), Non Motor Symptoms Questionnaire (NMSQ), Visual Analogue Scale (VAS), McGill questionnaire and Hospital Anxiety and Depression Scale (HADS), Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE), Parkinson's disease sleep scale (PDSS), Unified Parkinson's Disease Rating Scale- part II (activities of daily living-ADL), part III (motor examination -ME), Hospital Anxiety and Depression scale (HAD), Parkinson's Disease Questionnaire- 39 (PDQ-39) and levodopa dosage.

**Results:** Mean age was  $70.09 \pm 0.9$  (man 57%; women 43%). Mean disease duration was  $14.3 \pm 0.6$ . We found statistically significant improvement in nonmotor symptoms (NMSS total score and NMSQ), motor symptoms and PDQ-39 in both methods. Considering subdomains, we found significant beneficial effect on sleep, gastrointestinal, cardiovascular and urological symptoms in both methods, but better improvement in pain and sexual function in DBS and mood and apathy section in LCIG patients.

**Conclusions:** We found beneficial effects after 3 months with both invasive methods (DBS and LCIG) on nonmotor symptoms and quality of life. The most consistent improvements are seen concerning sleep, cardiovascular, gastrointestinal and urological symptoms. This can help us to decide on advanced therapy for individual patients.



**Uroš Rot: NEUROPSYCHIATRIC MANIFESTATIONS OF MULTIPLE SCLEROSIS**

University Medical Centre, Department of Neurology, Ljubljana, Slovenia

Clinical spectrum of multiple sclerosis (MS) is broad and includes neuropsychiatric manifestations. Some of them such as depression and cognitive decline are very common. Up to 50% of MS patients have depression, Depression highly affects quality of life of people with MS but the condition is often overlooked and undertreated. Furthermore, depression is associated with high suicide rate in patients with MS. Cognitive deficits are observed in approximately 60% of people with MS and significantly affect daily life, for example employment, activities of daily living and social functions. Cognitive impairment often includes information processing speed, episodic memory, long-term memory retrieval, executive functioning and visual perceptual skills. Cognitive deficits are sometimes found in early stages of the disease such as clinically isolated syndrome, but they are more pronounced in secondary progressive MS. They are associated with burden of T2 MRI lesions and also measures of global, cortical and regional brain atrophy. Disease-modifying treatment may have beneficial effects in prevention of cognitive decline.

**JOINT MEETING WITH ALPS-ADRIA NEUROSCIENCE SECTION AND CENTRAL AND EASTERN EUROPEAN STROKE SOCIETY AND WFN APPLIED RESEARCH GROUP ON THE ORGANIZATION AND DELIVERY OF CARE**

**CEESS STROKE SYMPOSIUM – ENDORSED BY WORLD STROKE ORGANIZATION**

**David Bonifačić, Vladimira Vuletić, Natalia Kučić: SERUM PROGNOSTIC BIOMARKERS OF ISCHEMIC STROKE**

Clinical Hospital Center Rijeka, Department of neurology, Rijeka, Croatia; Faculty of Medicine, University of Rijeka, Rijeka

Suitable biomarkers that have prognostic values are one of the key points of interest in ischemic stroke. The prognostic value of a biomarker is based on the association between inflammatory markers in the acute stroke phase. For ethical reasons, serum biomarkers are more suitable for analysis, especially in the case of ischemic stroke with an mild and moderate deficit. Based on research data, it was shown that the initial NIHSS score is not a reliable prognostic indicator for patients with IMU. For the purpose of finding an earlier prognostic biomarker of the clinical status of stroke patients, immunological events were analyzed during the early phase after the onset of IMU. Focal brain injury, including ischemic stroke, is characterized by adverse events such as resident microglial activation and neutrophils and monocyte / macrophage arriving from systemic circulation in the injured brain area. Monocytes (and to a lesser extent T cells and NK cells) are accumulate in the area of the injured tissue between the third and sixth day after the injury and in the case of ischemic brain injury, monocytes infiltrate at least 72 hours after injury and to the peak of the seventh day after the injury.

**Dijana Zadavec: RADIOLOGICAL DIAGNOSTICS AND ENDOVASCULAR TREATMENT OF STROKE**

University Hospital Center Sestre Milosrdnice, Department of Diagnostic and Interventional Radiology, Zagreb, Croatia

**Introduction/Objectives:** Mechanical thrombectomy is the newest interventional radiology accomplishment in acute ischemic stroke treatment, which should be performed within twenty-four hours of symptoms onset. Main imaging techniques used in radiological diagnostic algorithm are non-contrast-enhanced multislice computed tomography (MSCT), MSCT angiography (MSCTA) and MSCT perfusion (MSCTP). Magnetic resonance imaging can exceptionally be used with wake-up strokes and posterior circulation ischemia symptoms. MSCT determines localization and extent of brain ischemic changes using Alberta Stroke Program Early CT Score (ASPECTS). Minimally invasive MSCTA gives information about obstruction localization, thrombi or emboli length and status of intracranial collateral and extracranial circulation. MSCTP enables differentiation between irreversible and reversible brain tissue changes, i.e. between the infarct core and the penumbra. Patients with small infarct core, bigger penumbra and good collateral circulation are the best mechanical thrombectomy candidates.

**Participants, Materials/Methods:** Around 160 mechanical thrombectomies have been made in University Hospital Centre Sestre milosrdnice. Brain MSCT and MSCTA, along with prior neurological examination, select the mechanical thrombectomy candidates. For ASPECTS, middle cerebral artery (MCA) territory is divided into 10 regions and radiologic signs of ischemia subtract 1 point from the total of 10 points. Patients with high ASPECTS (8-10) are ideal candidates for mechanical thrombectomy. The procedure is performed in general anesthesia with blood pressure monitoring and systemic heparinization. After the thrombus aspiration, control digital subtraction angiography is performed.

**Results:** Our patients can be divided into 3 categories. A few patients' neurological status fully recovered with no imaging signs of ischemia. Around 50% of patients showed neurologic improvement compared to before treatment, but with remaining smaller neurological deficits and smaller ischemic areas on brain MSCT. Finally, less than 50% of patients had severe neurological deficits and bigger ischemic lesions on brain MSCT. Rare cases had postprocedural complications or fatal outcome.

**Conclusions:** Our current results confirm the progress of acute ischemic stroke treatment due to interventional neuroradiology progressive development. Mechanical thrombectomy is performed in three centers in Croatia at the moment. Experiences in Croatia and some other European countries show that organising a national network for acute ischemic stroke management is needed.

**Bartłomiej Piechowski-Jozwiak: CLOT MORPHOLOGY IN ISCHEMIC STROKE**

Cleveland Clinic Abu Dhabi, Department of Neurology, Abu Dhabi, United Arab Emirates

Stroke is a leading cause of death and disability worldwide. Up to 50% or more stroke cases are related to occlusion of pre-cerebral and/or intracranial artery. Most of these strokes are related to proximal large artery disease and cardiac source of emboli, however up to 30-40% of cases depending on the age group will be of undetermined etiology. The main focus of this talk is on the morphology of the clot causing acute occlusion of intracranial artery. The classical view on the pathology of the clots is that arterial ones would have more fibrin/platelet (F/P) structure and venous ones would contain more red blood cells (RBC). In a case series of patients consisting of those with in situ cardiac clots undergoing left atrial appendage closure and those with peripheral arterial emboli undergoing embolectomy the authors found that cardiac clots had more F/P and the embolized ones more RBCs. In a small case series in stroke patients undergoing embolectomy for acute stroke the authors did not find any particular pattern related to the etiology of the clot and its morphology. Only in the most recent study the authors found that arterial emboli would consist mostly of RBCs, followed by F/P and white blood cells (WBC) and this pattern would be similar in other determined causes of embolism. In case of cardiac clots the proportion would be F/P more than RBC and more than WBC, and this pattern would be similar in cryptogenic emboli. We believe that addition of clot morphology into stroke classification may add to understanding etiology of stroke. Further research is needed to sub-classify ischemic stroke with addition of clot morphology results.

**Senta Frol: INTRAVENOUS THROMBOLYSIS IN PATIENTS ON DIRECT ORAL ANTICOAGULANTS**

University Clinical Centre Ljubljana, Department of vascular neurology, Ljubljana, Slovenia

**Introduction/Objectives:** Intravenous thrombolysis (IVT) with rt-PA is well established and the recommended therapy for acute ischemic stroke according to guidelines. The administration of rt-PA in ischemic stroke requires absence of effective anticoagulation proven by appropriate laboratory tests. In updated EHRA guidelines in year 2018 there is a clear algorithm about direct NOAC antidote usage in patients with acute ischemic stroke. Rapid inactivation of dabigatran by its specific inhibitor idarucizumab allows IVT in patients suffering ischemic stroke while being treated with dabigatran.

**Participants, Materials/Methods:** Retrospective analysis of all stroke patients treated with idarucizumab and IVT (n = 15) in the period from July 2016 to March 2019 from Slovenian region were analyzed.

**Results:** Median age of the patients was 74 years. Eight patients were male. In only 3 patients dabigatran was initiated in secondary stroke prevention. Nine patients were treated with a lower dosage. 6 out of 15 cases were classified as severe ischemic strokes (National Institutes of Health Stroke Scale; NIHSS  $\geq$  10). At admission, prolonged activated partial thromboplastin time was present in 13 patients indicating therapeutic anticoagulation activity. The average door-to-needle time was 156 minutes. Thirteen out of 15 patients benefited significantly from IVT with a mRS score  $\leq$  2 at discharge. Two patients died due to symptomatic intracranial hemorrhage (sICH); 1 due to spontaneous sICH, and the other due to a large ischemic stroke with hemorrhagic transformation. In all 13 patients, who survived, anticoagulation therapy was restarted. No thrombotic complications were observed.

**Conclusions:** Our data show that administration of rt-PA after reversing dabigatran activity with idarucizumab in cases of acute ischemic stroke is feasible, easy to manage, effective, and appears to be safe.

**Hrvoje Budincevic: HOW TO IMPROVE STROKE CARE?**

Sveti Duh University Hospital, Department of Neurology, Stroke and Intensive Care Unit, Zagreb, Croatia; J.J. Strossmayer University of Osijek, Faculty of Medicine, Osijek, Croatia.

Stroke is among leading causes of disability and death worldwide. Despite there are advances regarding prevention, therapy and rehabilitation are present, more improvements are needed to reduce global burden of stroke. Disparities between and within European countries in stroke care are present and reported. Nevertheless, in following 20 years the number of strokes is expected to rise by 34%, mostly due to an aging population and better acute stroke care. The Stroke Action Plan for Europe is a document with clear targets to be reached by 2030. These targets are divided in several domains: 1. Primary prevention, 2. Organization of stroke care, 3. Acute stroke care, 4. Secondary prevention, 5. Rehabilitation, 6. Evaluation of outcomes, and 7. Life after stroke. To improve stroke care all parts in the stroke pathway should be involved (population, patients, physicians, stroke societies, health authorities, health insurance companies, etc). Education and training with stroke awareness campaigns directed to population and health professionals should improve the identification, protocols, and treatment practices. The methods for stroke care improvement will be discussed.

**Vesna Đermanović Dobrota: COGNITIVE IMPAIRMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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

Diabetes (DM) is one of the most common chronic non-infectious diseases and one of the leading public health problems of the modern society. Furthermore, most of the diabetic patients, especially in developing countries, are likely to arise from the working population. Consequently, the number of micro vascular and macro vascular diabetic complications increases with the main risk factors being aging and the duration of illness. This in turn increases healthcare expenses and decreases the quality of life for patients. Prevention and control of complications in diabetic patients is one of the most important mechanisms in any public health system. Recent studies have demonstrated diabetic patients show a higher risk for developing Alzheimer's disease (AD), vascular dementia (VaD), mixed-type dementia (AD plus cerebrovascular disease) and comorbidity. Cerebrovascular disease, hypertension, hypercholesterolemia have been shown to greatly increase the risk. The precise mechanisms involved in the development of cognitive impairment are not yet fully understood. Whole-brain analysis has revealed a consistent link between DM and brain atrophy which is often more pronounced within the hippocampus. The degree of hippocampal atrophy in T2 DM is directly comparable to the degree of total brain atrophy. Brain atrophy in T2DM is associated with poor cognition, predominantly attention and executive function, paired with poorer information-processing speed and memory. T2DM is clearly associated with occurrence of lacunas. MRI studies have consistently shown that chronic hyperglycemia is associated with brain atrophy and cerebrovascular lesions, which are hallmarks of attention deficits and impaired executive functioning. Although it is sometimes termed, „type 3 diabetes“, what it actually represents is a brain related metabolic syndrome associated with metabolic stress and neuroinflammation in the brain. ACCORD-MIND study conducted on 3000 individuals with DM demonstrated that tight glycemic control significantly reduced the rate of brain atrophy over a period of 20-40 months with the standard glucose treatment. Current guidelines for treatment of individuals with DM include extensive life style changes, changes in diet, more pronounced physical activity, smoking cessation, and routine medical follow-up. Population studies have shown that among people with DM, lower cognitive function was associated with worse efficiency of treatment indices such as glucose control.

**1<sup>ST</sup> HISPA HR SYMPOSIUM – HYPERTENSION INFARCTION STROKE PREVENTION ASSOCIATION  
- CROATIA**

**Hrvoje Budincevic: ANTICOAGULANT THERAPY IN SECONDARY STROKE PREVENTION**

Sveti Duh University Hospital, Department of Neurology, Stroke and Intensive Care Unit, Zagreb, Croatia; J.J. Strossmayer University of Osijek, Faculty of Medicine, Osijek, Croatia.

Atrial fibrillation is well known risk factor for ischemic stroke. The oral anticoagulant therapy with vitamin K antagonists have been a gold standard for secondary prevention of cardioembolic stroke. Development and presence of direct oral anticoagulants (direct thrombin inhibitors and direct inhibitors of factor Xa) with at least similar efficacy and better safety profile included them into guidelines. Aspirin is the gold standard of prevention of non-cardioembolic stroke, but it seems lost the role in primary stroke prevention, as well as in patients with non-valvular atrial fibrillation. The current dilemmas regarding usage of oral anticoagulant therapy will be discussed.



**SHORT PRESENTATIONS****Oleg Zaitsev: SIDE OF PREDOMINANT BRAIN DAMAGE AND PSYCHOPATHOLOGY OF SEVERE TRAUMATIC BRAIN INJURY**

Burdenko National Medical Research Center of Neurosurgery, Psychiatric Research Group, Moscow, Russian Federation

**Introduction/Objectives:** Objectives: to reveal correlations between the side of the predominant brain damage and psychopathological picture in patients with severe traumatic brain injuries (TBI).

**Participants, Materials/Methods:** 183 patients with severe TBI were studied. 99 patients had predominant damage to the right hemisphere and 84 patients - to the left one. All patients were examined clinically with a total registration of psychopathological symptoms from the acute phase to follow-up.

**Results:** Differences between groups with predominant right and left hemisphere damage were evident from the moment of contact with the patient. In the group with predominant right hemisphere damage compared to the left one, the most frequent clinical features were: 1) amnesic type of confusion (including “the shift in the past”); 2) confabulations and false recognition; 3) memory loss for current events, disturbed perception of time and space (including left-sided type of unilateral neglect); 4) low level of insight; In the group with the predominant left hemisphere damage compared to the right one more frequent signs were as follows: 1) confusion with speech and motor disintegration; 2) false conclusions, paraphasias and perseverations; 3) cognitive disorders related on speech processes (including disorders of verbal memory); 4) anxiety. Cause of nonobservance of revealed regularities were sinistrality and developing of intracranial infections complications and hydrocephalus. There were no marked differences in social assessment of outcomes between groups, but after right hemisphere damage there were more frequently long-term (> 1 month) period covered by the post-traumatic amnesia. Because of differences in psychopathology it was necessary to modify rehabilitation approaches, including psychopharmacology.

**Conclusions:** The side of predominant brain damage must be taken into consideration not only for assessing clinical condition, but also developing special programme for mental recovery after TBI.

**Svetlana Kuzmina, Naida Mollaeva: OCCUPATIONAL RISK FACTORS OF CHEMICAL INDUSTRY FOR WORKER'S MENTAL HEALTH**

Kazan State Medical University, Department of Psychiatry, Kazan, Russian Federation

**Introduction/Objectives:** Industrial factors is included in the definition of «environmental health» and could play the important role in mental health (MH) of workers. Follow to evidence base data, evaluation of MH during preventive medical examination of workers does not show sufficient effectiveness in assessing the prognosis of the development of MH problems. Aim. Determining the relationship of risk factors in chemical industry with the quality of MH of employees.

**Participants, Materials/Methods:** Hygienic assessment of the main occupational factors - chemical, physical, the severity and intensity of the work processes, especially risk for fire and explosion at the working place. MH examination was carried out during periodical medical examination for 742 workers and employees of the plant «Organic synthesis» and 128 pyroxylin production workers, Powder Plant. Experience in the profession, psycho-hygienic assessment of occupational factors and personality features of workers were especially take into consideration.

**Results:** Most of the studied working conditions on the Organic Synthesis and in the manufacture of gunpowder are characterized as fire hazardous and explosive. Influence of combination of occupational physical and volatile solvents of organic solutions, constant emotional stress into workers physical and MH were studied. Among chemical industry workers, the prevalence of unstable adaptation and maladaptation of the anxious-neurotic spectrum ( $p \leq 0.005$ ) was revealed: the symptoms on the scale of neurotic depressive symptoms are 27%, with a conversion type of response to the situation 21%, obsessive-phobic disorders 21% which corresponds to the response options among persons exposed to extreme conditions that pose a threat to life. The terms of their formation and the clinical features of their manifestations turned out to be closely related to the professional experience of the subjects, with the psycho-hygienic characteristics of production factors, as well as with the individual-personal characteristics of those working in these conditions. With the exception of the anxious tension characteristic of borderline mental disorders, severe anxiety and fear were not observed. This was the main difference between non-pathological manifestations and initial and erased neurotic disorders in the nosological forms that characterize the borderline mental illnesses proper.

**Conclusions:** The survey showed a high prevalence among workers in the chemical production of psychophysical, socio-psychological, behavioral manifestations characteristic of mental disadaptation syndromes that do not reach the level of clinical diagnosis. Among the workers with neurosis-like and organically determined borderline mental disorders, a group of people with mental disorders was identified, to date who have not found their place in the systematics of mental illness.

**David Jutrić, Domagoj Đikić, Dragan Jurić, Elena Marić, Diana Odeh, Nada Oršolić, Irena Landeka:  
EFFECTS OF THE ANTIPILEPTIC VALPROATE AND OF THE FLAVONONE NARINGENIN ON THE  
ANTIOXIDATIVE DEFENCE SYSTEM IN THE BRAIN OF C57BL6 MOUSE**

Faculty of Science, University of Zagreb, Department of Animal Physiology and Toxicology, Zagreb, Croatia

**Introduction/Objectives:** Valproate is a widely used antiepileptic drug. It is considered generally safe, but adverse effects, mainly in lipid metabolism are known to occur among patients. Similarly, adverse effects caused by valproate in the antioxidative defence system, in various tissues, including the brain, are known from in vivo and in vitro experimental systems. Our aim was to investigate, whether the use of polyphenylene naringenine, a known antioxidant and antilipidemic agent, together with valproate, affects the redox balance, and whether the synergistic application of naringenine and valproate, can reduce the potential negative effects in C57Bl6 mice.

**Participants, Materials/Methods:** Lipid peroxidation, the concentration of total glutathione and the antioxidant activity of superoxide dismutase were measured in the prefrontal and central cortex, and in the cerebellum, after 15 days of exposure to PBS (control), Valproate 400 mg/kg bw, naringenin (25 mg/kg be) and joint valproate+naringenine treatment (in the same doses as individual groups).

**Results:** Our results showed, that the treatment with valproate and naringenine, and their combinations, caused increased lipid peroxidation in both males and females, in all three measured brain regions. The activity of the superoxide dismutase, and of the reduced glutathione in the brain, has been differentially activated dependent on the treatment.

**Conclusions:** The protective effect of the polyphenolic naringenine molecule, has not been demonstrated as expected.

**Natalia Ustinova, Tatyana Borovik, Tatyana Bushueva: STRATEGIC PLANNING: HOW TO IMPROVE HEALTH CARE SERVICES FOR CHILDREN WITH AUTISM IN RUSSIA?**

National Medical Research Center for Children's Health, Laboratory of social paediatrics and quality of life  
Moscow, Russian Federation

**Introduction/Objectives:** Autism is a worldwide multifaceted problem. According to official statistics only 1 in 1000 children has an ASD in Russia. It means that too many children missed proper health care. In 2019, National Medical Research Center for Children's Health (laboratory of social paediatrics) received the approval of the Ministry of Health to conduct a project “The Model of multidisciplinary medical support for children with ASD in paediatric centers”. Understanding of the main problems in development of health care system for children with ASD is one of the tasks of this project.

**Participants, Materials/Methods:** One day strategic session «Autism: step by step» was held on 8 April 2019 in Moscow. It was organized by the support of non-profit organization “Center for Autism Problems”, parents societies (RPO"Contact”) and SAP company (CIS). There were created 8 groups, each one included representatives from parents of children with ASD, doctors (psychiatrists, neurologists, pediatricians), psychologists and teachers.

**Results:** There were indicated numerous problems associated with ASD care in Russia: 1) there is no early detection system, pediatricians are not familiar with autism signs, no referrals with psychiatrists; 2) medical staff (non-psychiatric) has small knowledge of the signs of medical comorbidities in autism as well as the autism behavioral signs, are not trained to conduct medical procedures for children with ASD; 3) separation of psychiatric service in Russia from other medical care, leading to the fact that medical comorbidities (neurological, gastroenterological, allergic and so on) are not detected, no cooperation between neurologists and psychiatrists; 4) psychiatric care are associated with unreasonable widespread use of antipsychotic drugs and unreasonable hospitalization, which leads to the additional stigmatization of psychiatry; 5) psychiatrists are not familiar with somatic comorbidity in autism, consider some signs (for example selectivity in food, constipation, aggressive behavior) only as a psychopathology. All parents-participants didn't want to have a psychiatrist as a “case manager”, they preferred neurologist. Parents perceive contacts with psychiatric services as an extreme step and as a stigma.

**Conclusions:** Strategic planning. Development of the Model of multidisciplinary medical support for children with ASD in paediatric centers. As a first step to destigmatization of psychiatry is including of psychiatrist in multidisciplinary team in pediatric center. Development a special trainings about ASD issues for pediatricians, special trainings for other specialists (neurologists, gastroenterologists, dietologists, immunologists, medical staff). Development a guideline for parents about early signs of ASD and how to receive health care support.

**Emina Horvat Velić (Zagreb, Croatia): STUDENTS' SYMPOSIUM IN BIOLOGY AND LIFE SCIENCES – SISB**

University of Zagreb, Faculty of Science, Department of Biology, Zagreb, Croatia

The Students' Symposium in Biology and Life Sciences (SiSB) was founded by a group of enthusiastic biology students who saw the need for students to present their scientific work and develop valuable business connections. It was founded in 2015 and has since been taking place annually in late May or early June. The aim of the symposium is to create a platform targeted mainly at Bachelor's and Master's students where they can present their laboratory work to their colleagues, discuss their work, and form potential partnerships. All of this is meant to help students in furthering their careers and aid them in bettering themselves as scientists and professionals. Our target group are not only students of the Department of Biology at the University of Zagreb and other universities, but students of other biology-related fields, such as medicine, pharmacy, biotechnology, agriculture, biochemistry, biophysics, and forestry. Students from neighbouring countries (Bosnia and Herzegovina, Slovenia, Serbia) are participants as well. The symposium itself is divided into two main students' sections – oral presentations are reserved for students who have received or have been nominated for the Rector's award or have published an article in a prestigious journal. They should not only explain their work but advise fellow students on how to find suitable mentors, apply, and/or publish their work. In the poster section, students present their laboratory, internship, and student exchange projects. Also, every year, a plenary lecturer gives a lecture just after the opening ceremony. Despite being a rather young event, SiSB has proved itself to be a very important part of students' scientific life, because it's often the first step they take when starting their careers. The importance of SiSB lies in the interdisciplinary approach to biology as well, which proved to be the right theme for our symposium, since we have been having an increasing number of participants each year. We will continue to improve our event and motivate students even more in the upcoming years, hopefully with even bigger support.

**Nataliya Ustinova, Mikhail Zobin (Kotor, Montenegro): KETAMIN IN THERAPY OF PHARMACORESISTANT DEPRESSION – A NATURALISTIC STUDY**

Center of Transformational Therapy, Kotor, Montenegro

**Introduction/Objectives:** Pharmacotherapy of depression based on a monoaminergic model in many cases is not effective enough. In this regard the ketamine treatment outcome of pharmacoresistant depression by subanesthetic doses, including the patients with double diagnosis is of interest.

**Participants, Materials/Methods:** In an open label naturalistic non-randomized trial, 12 patients with non-psychotic treatment-resistant depression (10 of whom had concomitant addictive disorder), 6 sessions of ketamine therapy (0.5 - 0.75 mg/kg intravenously) were undertaken. Clinical and psychometric (Beck scale, visual analogue scale and scale of general clinical impression) assessment were used. Statistical processing - general linear model and nonparametric criterion.

**Results:** The effectiveness of therapy was noted in 11 of 12 respondents, and in 7 ones the improvement was qualified as significant. The total scores of the scales applied corresponded to 50% reduction of depressive symptoms ( $p < 0.05$ ).

**Conclusions:** Ketamine proved to be an effective and safe method of the fast achieving therapeutic effect in patients with therapeutically-resistant depression. However, insufficiently representative sample, the lack of a control group and the mechanism of randomization and the open nature of the study limit the wide extrapolation of the results.

**Lene Marie Groenlund, Carsten Kock-Jensen: INTRATHECAL BACLOFEN AS TREATMENT FOR MYOCLONUS AND CATABOLISM AS PART OF HYPOXIC BRAIN DAMAGE - A NEW TREATMENT? A CASE REPORT**

Hospital South West Jutland, Department of Neurology, Esbjerg, Denmark

**Introduction/Objectives:** In June 2017 a man aged 27 suffered cardiac arrest, and was successfully resuscitated after 12 minutes. Hypoxic brain damage followed, and EEG showed myoclonic status epilepticus for two weeks. He was diagnosed with Lance Adams syndrome, a rare complication to successful resuscitation often complicated with action myoclonus. He was severely bothered by spontaneous myoclonic jerks provoked by touching, intention to move, movement, speech and anxiety. Due to this he suffered from severe muscle catabolism, lost about 20 kg, and his body mass index (BMI) was reduced from 20 to 14. Myoglobin levels increased as a sign of nitrogen loss. Attempts at rehabilitation were impossible because of both the myoclonus itself and low muscle mass, he was bound to bed and not self-handling activities of daily living (ADL).

**Participants, Materials/Methods:** Several anti epileptic drugs were tried, even four types simultaneously, without significant relief. After three months with no improvement, a three- day test with intrathecal baclofen was initiated. He received daily lumbar punctures with injections of baclofen, 75 µg the first day, 150 µg the second day and 300 µg the third day. He experienced significant relief of myoclonus during this. Two days later a baclofen pump was implanted. Start dose was 350 µg/day, and it was gradually increased up to 1200 µg/ day.

**Results:** His myoclonus progressively became more resistant to the provocations. He also started to gain muscle mass and weight. Myoglobin levels quickly decreased to normal. Now, sixteen months after implantation of the pump, the dose of intrathecal baclofen has been gradually reduced by 20% each time, to a minimum dose of 12 µg/day without increasing myoclonus. His walking skills, ADL and overall rehabilitation is significantly improved. His BMI has increased to 24. The pump will be explanted soon.

**Conclusions:** Myoclonus caused by hypoxic brain damage is often associated with loss of nitrogen, muscle mass and thereby motor skills. This condition can even be life-threatening, especially if the weight loss is more than 20%. Rehabilitation can be impossible. We recommend initiating treatment at an early stage to improve outcome. Intrathecal baclofen test trial with increasing dosages given by repeated lumbar punctures should be considered, and can be done easily and safely while the patient is still in the ICU.

**Galina Ivanova, Boris Tsygankov, Yulia Dobrovolskaya, Ummuraisat Gadzhieva (Moscow, Russian Federation): THE POSSIBILITY OF PSYCHOTHERAPY OF ANXIOUS AND DEPRESSIVE DISORDERS IN PATIENTS AT DISTANT STAGES OF BRAIN INJURY**

A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Department of Psychiatry- Narcology and Psychotherapy, Moscow, Russian Federation

**Introduction/Objectives:** Patients with exogenous organic pathology of the brain have an increased vulnerability to psychotrauma and exogenous hazards in combination with the asthenic syndrome. This requires a special approach in the treatment of such patients. It was intended to study the possibilities of using psychotherapy in complex therapy of neurotic disorders that developed at remote stages of exogenous organic pathology of the brain.

**Participants, Materials/Methods:** A. Beck's depression scale, A. Beck's anxiety scale, SCL-90-R psychopathology scale, Wayne vegetative disturbance questionnaire, the scale of self-evaluation "State of health. Activity. Mood" were used for diagnosis. Two groups of patients were examined: a control group (65 people), in which only standard psychopharmacotherapy was performed, and the main group (49 people), in which standard therapy was combined with complex psychotherapy. A specially developed program of psychotherapeutic correction was based on methods of cognitive-behavioral therapy, relaxation techniques, and was conducted in a group format.

**Results:** In the main group, 87.8% of patients showed a decrease in anxiety and vegetative disorders after treatment, in contrast to the control group. Also depressive symptoms and explosiveness reducing, subjectively assessed well-being improving, activity increasing were noted. When examining patients after 1.5 years, the stable effect of the proposed therapeutic model was noted in 52.4% of cases in the main group and only in 38.2% of cases in the control group.

**Conclusions:** The proposed combination of psychopharmacotherapy and psychotherapy was effective for relieving anxiety, depressive symptoms and vegetative disorders in patients with exogenous organic pathology of the brain.



**Valentino Racki: EFFECTS OF IN-VITRO ANTIPSYCHOTIC ADMINISTRATION ON IMMUNOMETABOLIC PROPERTIES OF BV-2 MICROGLIAL CELLS.**

Clinical Hospital Centre Rijeka, Department: Clinic of Neurology, Rijeka, Croatia

**Introduction/Objectives:** Microglia cells are resident cells of innate immunity in the brain. They perform key functions such as promoting development, maintaining synaptic and neuronal homeostasis. Novel research increasingly implicates microglial activation in the pathogenesis of numerous neurologic diseases and psychiatric disorders such as schizophrenia, a psychiatric disease treated by antipsychotics. However, there is a lack of evidence as to how antipsychotics affect microglia on a cellular level. The aim of these experiments was to assess the effects of in-vitro administration of antipsychotics on the immunometabolic phenotype of BV-2 microglial cells.

**Participants, Materials/Methods:** The experiments were performed on the immortalized BV-2 microglial cell line, a proven replacement for the primary microglia. Cell viability was assessed using the trypan blue method and an automated cell counter. Immunofluorescent microscopy was used to study morphology and expression of cell phenotype markers (CD206, iNOS and Arginase-1), while cell surface markers CD86 and CD16/32 were assessed using flow cytometry. mTOR signaling pathway activation was assessed using the activity of p70s6k on Western blot. Real-time metabolic status of the cells was studied using the Seahorse method. Cellular activation was induced with IFN-gamma. The antipsychotics used were haloperidol, risperidone and aripiprazole, each belonging to a different generation of antipsychotics.

**Results:** Cell viability for experiments in effective doses was  $\geq 95\%$  for risperidone and aripiprazole, while for haloperidol it was  $\geq 85\%$ . Cell morphology compared to control was altered only with haloperidol. Expression of iNOS was lower than control in all tested drugs, most effectively reduced using risperidone and aripiprazole, while the expression of CD206 was not affected by the treatment. Expression of Arginase-1 was increased only by aripiprazole compared to control. Activity of p70s6k was increased in aripiprazole and haloperidol treated cells, while the cell surface markers were unchanged by treatment. Hypermetabolic state induced by IFN-gamma stimulation has been effectively amended by all drugs.

**Conclusions:** Antipsychotics significantly alter only the metabolic phenotype of microglial cells to a less activated state, while the immune phenotype was not changed by treatment. There are significant differences between the three generations of antipsychotics in the degree of effectiveness and toxicity, with aripiprazole showing the most beneficial effect.

**YOUNG INVESTIGATORS' CORNER****Eliša Papić, Valentino Rački, David Bonifačić, Vladimira Vuletić, Natalia Kučić: BRAIN ENTRAINMENT: EFFECTS OF BINAURAL BEATS ON CEREBRAL FUNCTION**

Clinical hospital Centre Rijeka, Clinic of Neurology, Rijeka, Croatia

**Introduction/Objectives:** Brain entrainment, also known as brainwave entrainment, is the hypothesized ability of the brain to synchronize its brainwave frequencies with the rhythm of external stimuli (auditory, visual, tactile). Binaural beats refer to the phenomena occurring when two pure-tone sine waves, with a difference of less than 40 Hz, are delivered binaurally (one through each ear). There is evidence that specific regions of the cerebral cortex can be activated this way. It has been previously shown that sound has an effect on various neural cells. In our study we used microglia to test this.

**Participants, Materials/Methods:** We performed experiments in an in-vitro environment, on the immortalized BV-2 microglial cell line. Cell viability was assessed using the trypan blue method and an automated cell counter. Cells were cultivated in 10% FCS DMEM. We exposed microglial cells to binaural beats through a period of 24 hours, using a Bluetooth speaker isolated next to them. Two different conditions were used. First involved cells exposed directly to sound emanating from a speaker placed next to them, while the second condition was delivering sound indirectly through a stereo system placed outside the incubation chamber. We observed microglial morphology changes through light microscopy after that period. The beats were developed through an audio production software (FL studio 11), and presented with a difference of 8 Hz and 12 Hz.

**Results:** Placing the speaker next to the cells in the incubator induced changes in microglial phenotype, which moved to an M2-ramified state and multiplied more quickly than the control culture. Delivering sound waves from a stereo system outside the chamber did not induce significant changes in morphology or growth of the cells after a 24h period.

**Conclusions:** The results indicate that there is an effect of binaural beats on cellular microglial cultures in-vitro. Further research is required to reveal the significance of these changes and whether there is a change in cellular function as well. Our further goal would be to use binaural beats in a clinical setting, determining their effects through brain function monitoring. Overall, brainwave entrainment is an emerging research that could prove beneficial in modifying brainwave activity and maybe even cellular function.

**Alen Juginović, Ivan Aranza, Miro Vuković: IMPORTANCE OF DIAGNOSIS AND TREATMENT OF SLEEP APNEA IN ADULTS**

University of Split School of Medicine, Šoltanska 2, 21 000 Split, Croatia

**Introduction:** Sleep apnea (SA) is one of the most common sleep disorders. It is defined by the absolute absence of breathing during sleep that lasts for at least 10 seconds together with blood desaturation of 3% or more. Symptoms that accompany SA are snoring, absence of breathing, suffocating sensation, daily tiredness, low enthusiasm and concentration levels, morning headaches and others. The gold standard for diagnosing SA is full-night polysomnography. The most acclaimed treatment option is CPAP (Continuous Positive Air Pressure). Taking into consideration the high prevalence of up to 38% in the general population, serious health problems can occur if SA is left untreated. Thus, the importance of early diagnosis and optimal treatment is obvious.

**Materials and methods:** This literature review included PubMed (MEDLINE) available case reports, original articles, and data gathered from registered clinical trials that reported effects of untreated apnea on the incidence of several diseases. Reviewed studies also included data on patients who showed improvement after starting some type of therapy, usually CPAP. Search terms used were: sleep apnea, CPAP, cardiovascular disease, diabetes.

**Results:** Undiagnosed, untreated or improperly treated SA can have several major health impacts on adults. Chronic and repetitious episodes of micro-awakenings during the night as a result of untreated SA lead to long-lasting fatigue, sleepiness, drowsiness, and distraction during the day. In professional drivers, this increases the risk of road traffic accidents up to 5 times. Another major systemic effect of untreated SA is increased risk for cardiovascular diseases such as arterial hypertension, myocardial infarction, and atrial fibrillation. Patients who had already been diagnosed with arterial hypertension showed an even more amplified sympathetic response to apneic events. Furthermore, an increase in insulin resistance due to elevated sympathetic activity together with repeated hypoxia and sleep deprivation leads to diabetes mellitus type 2. Untreated SA also increases the risk of stroke, metabolic syndrome, and non-alcoholic fatty liver disease. Recent studies showed a correlation between neurocognitive disorders and SA in adolescent patients. In elderly patients with breathing problems during sleep, the use of CPAP has shown a positive effect on preventing early appearance of mild cognitive impairment which can lead to Alzheimer's disease. Change of lifestyle, timely diagnosis, and proper treatment can significantly reduce the risk of the onset of these diseases.

**Conclusion:** Sleep apnea, as the most common sleep breathing disorder, should be taken seriously due to the connection with many cardiovascular, metabolic and other diseases if left untreated. The importance of early diagnosis alongside timely CPAP treatment is crucial in preventing future illnesses that can dramatically deteriorate the health, as well as the general quality of a patient's life. Therefore, sleep apnea symptoms should not be underestimated during patient check-ups for the long term improvement in the quality of life.

**Miro Vuković, Ivan Aranza, Alen Juginović: IS MUSIC THERAPY AN EFFECTIVE TREATMENT OPTION IN ALZHEIMER'S DISEASE?**

University of Split School of Medicine, Šoltanska 2, 21 000 Split, Croatia

**Introduction:** Music therapy is the clinical and evidence-based use of music interventions for addressing the physical, emotional, cognitive, and social needs of individuals. Music therapy has been proved beneficial in patients with stroke, dementia, acute and chronic pain, autism spectrum disorders, insomnia, depression, Parkinson's disease, and others. The aim of this review is to determine if music therapy can improve cognitive abilities and emotional function and thus improve the quality of life (QOL) in patients with Alzheimer's disease (AD) since there is still no known cure.

**Materials and methods:** This literature review included PubMed (MEDLINE) available case reports, pilot studies, original articles, meta-analysis and data gathered from randomized trials that analyzed various effects of music therapy in AD patients. Search terms used were: Alzheimer's disease, music therapy, cognition, quality of life.

**Results:** Many studies have researched the effects of various types and forms of music therapy in improving symptoms of AD. Improvements can be seen in memory, orientation, depression, and anxiety in both moderate, and mild cases. Furthermore, reduction in symptoms of delirium, hallucinations, agitation, irritability and language disorders in moderate cases has also been observed. The effect on cognitive measures was appreciable after only 4 music therapy sessions. When combining video and music therapy, positive effects on QOL can also be seen, but only in patients with questionable, mild and moderate neurocognitive impairment. Patients with severe deterioration did not report any change in QOL. When adding music therapy to the treatment protocol for patients suffering from AD, cortisol levels tend to decrease along with levels of anxiety and depression. Furthermore, music therapy combined with classic pharmacotherapy used for AD is more effective than pharmacotherapy alone in improving the psycho-behavioral profile of AD patients. However, there has been no noted positive change in language and verbal communication when combining music therapy with standard pharmacotherapy in patients with moderate AD. Music therapy has been proved to be the safest intervention in comparison to physical therapy and computerized cognitive training with the efficacy less than that of physical therapy but higher than computerized cognitive training. Music therapy can also help patients decrease the use of antipsychotic and anxiolytic medications and reduce behavioral problems.

**Conclusion:** Most of the reviewed literature evaluates music therapy as an effective and valuable asset to add to standard therapy protocols for patients suffering from AD. It can improve various negative symptoms and signs of AD such as depression, anxiety, stress levels, behavioral problems, etc. However, the severity of the disease should be taken into consideration because music therapy can produce specific positive effects only in milder forms of the disease. More research is needed to affirm these findings and to explore other potential indications and positive effects of music therapy, not only in AD but also in other neurodegenerative diseases.

**Ivan Franin: PATHOHISTOLOGICAL CLASSIFICATION OF CNS TUMORS THROUGHOUT HISTORY: A REVIEW**

University of Rijeka, Faculty of Medicine, Rijeka, Croatia

An intensive search for the correct pathohistological classification of the central nervous system tumors has been going on for almost the entire century and is constantly evolving. Baily and Cushing introduced the histogenic classification of CNS tumors in 1926, whose basic concept has remained largely unchanged, regardless of the development of methods applied in modern diagnostics. Tumors were classified according to their similarity to cells of the central nervous system, such as astrocytes, oligodendrocytes and ependymal cells, and were further divided according to the differentiation level determined on the basis of morphological irregularities compared to their normal appearance.

In 1979, the first edition of the “World Health Organization Classification of Tumours of the Central Nervous System” was published, which has covered findings in this area and revolutionized the neurooncologic pathology. It was based mostly on histological microscopic findings. The most recent WHO classification from 2016. has largely adopted a molecular approach to diagnosis and classification of CNS tumors. A large number of molecular tests and methods are being used in clinical practice, and as time goes by, an ever-expanding range of specific tests will be launched. So far, four issues of the “World Health Organization Classification of Tumours of the Central Nervous System” have been published and each has brought revisions that reflect changes in the CNS tumor field, some fundamental, as well as less or subtle changes. In general, they represent very significant changes. This is largely a result of the more researched histological variants of tumors and the application of new technologies (electronic microscopy and its variants, immunohistochemistry, in situ hybridization and molecular genetic methods), but it also reflects the balance between opinions of different scientific circles as well as some individuals' views.

Advancement in molecular biology research has expanded the ability to diagnose and classify brain tumors. Using the latest molecular methods we can precisely determine the type or subtype of a particular tumor and choose the right therapy. Understanding mutations and signal pathways involved in brain tumor development helps differentiate clinically different subgroups and adapt therapies. Further research and discoveries of specific mechanisms and pathways will help develop even better therapies and guidelines for treating brain tumors in the future.

**Alen Juginović, Miro Vuković, Ivan Aranza: COGNITIVE EFFECTS OF ANTIEPILEPTIC DRUGS IN THE PEDIATRIC POPULATION: A LITERATURE REVIEW**

University of Split School of Medicine, Šoltanska 2, 21 000 Split, Croatia

**Introduction:** Epilepsy is one of the most common neurological disorders in the pediatric population. In Europe in 2005, epilepsy affected 0.9 million children and adolescents (age 0 - 19). Some of the known causes include brain injury, stroke, brain tumors, infections, etc. To treat epilepsy optimally, physicians have to carefully balance between types of antiepileptic drugs (AEDs) and their doses to achieve the desired and avoid adverse effects which can significantly impact learning capabilities and cause cognitive impairment in adults. Our objective was to examine the effect of these drugs in the pediatric population which can have more pronounced side effects due to active neurocognitive development.

**Materials and methods:** This review included PubMed (MEDLINE) available case reports, original articles, and data gathered from registered clinical trials that reported adverse effects of AEDs related to cognitive impairment that were associated with medication usage in the pediatric population up to 21 years of age. Search terms used were: antiepileptic drugs, adverse effects, cognitive impairment, children, epilepsy.

**Results:** Many commonly prescribed AEDs have at least some effect on cognitive function, especially in the pediatric population. The use of first-generation anticonvulsant (FGA) phenobarbital significantly impacted memory and attention. Phenytoin, a commonly prescribed FGA, may affect mental speed, but predominantly in higher dosing. Carbamazepine impaired attention and caused sleep and other behavioral disturbances, although there are conflicting reports. Similarly, conflicting data is found for the use of valproate which has less effect on cognitive impairment than carbamazepine. Second generation anticonvulsant (SGA) drugs have improved tolerability and safety, although this is very dose-related and patient-dependent. One study showed FGA valproate and ethosuximide to be more effective therapy options for pediatric absence seizures than the SGA lamotrigine. Then again, lamotrigine was shown to improve learning and alertness. Oxcarbazepine and pregabalin do not seem to influence cognitive function significantly. There is clear evidence that topiramate has a negative effect on learning, language function and attention in both children and adults. There is little or no evidence for cognitive impairment induced by gabapentin and levetiracetam, but few studies included the pediatric population. The data for third generation anticonvulsants is scarce, especially for children. Lacosamide therapy in the pediatric population can cause sleep disturbances and hyperactivity. Rufinamide, on the other hand, is generally well tolerated in children.

**Conclusion:** Reviewed studies reported that the use of certain AEDs, such as phenobarbital and topiramate in the pediatric population has negative effects on memory, attention, mental speed, learning, language function, and attention. On the other hand, some AEDs such as lamotrigine improved patient's learning abilities and alertness. Due to inconclusiveness for the correlation of some AEDs with behavioral disturbances, cognitive impairment, and other effects, further research is needed to better understand these effects which are crucial for better prevention in patients at risk.

**WORKSHOPS.**

**WORKSHOP HOW TO READ AND WRITE A SCIENTIFIC PAPER?**

**Anton Glasnović: NORMAL DISTRIBUTION AND RELATED TOPICS**

Zagreb University School of Medicine, Croatian Medical Journal, Zagreb, Croatia

When first encountering a set of data, scientists are faced with a simple question – is his/her dataset of normal distribution. Without answering that question, all other steps that follow can lead to false results, and subsequent false conclusions. Therefore, when reporting statistics in a scientific journal, it is crucial to see how study group decided to use various tests, that is, to see which normality testing did they use and why. After that, it is important to choose adequate testing, as they are different if the distribution is normal and if it is not normal. In this short lecture all these steps will be discussed with hope to give participants, that usually do not deal with data analysis, a glimpse into statistical methods usage in everyday practice when analyzing their results.

**Anton Glasnović: STUDY TYPES**

Zagreb University School of Medicine, Croatian Medical Journal, Zagreb, Croatia

Determining a study type is one of the first steps in designing a study. There can be different approaches to that depending on which questions our study aims to answer. Also, in this lecture, one of the keystones will be emphasizing the importance of hypothesis driven research which subsequently leads us to designing a study. That is why knowing which study types there are gives us very important tool before we even start the research. One of the main reasons why this is important is case very often seen in scientific publishing practice in which researchers did not design the study right, or they even did not do a hypothesis driven research which finally leads to many disappointments in both researchers when their manuscript is rejected for publication, but also in editors which see time and money invested into research that goes to waste.



**Srećko Gajović: NEW WAYS TO CONCEPTUALISE THE BIOMEDICAL KNOWLEDGE**

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

**Introduction/Objectives:** To understand the representation of the biomedical knowledge in the context of person-centered care and digital society.

**Participants, Materials/Methods:** Theoretical interdisciplinary study in the fields of biomedicine, sociology and philosophy.

**Results:** The knowledge was understood as a result of the vast amount of the biomedical research, but as well as a social construct, being tentative and approximative. The individual quest for knowledge represents a base for person-centered care.

**Conclusions:** Evidence-based medicine being combined with narrative-based medicine creates a new digitally based popular culture aimed to understand health and disease.

**WORKSHOP - CHILD AND ADOLESCENT PSYCHIATRY****Aldo Špelić: PSYCHOANALYTIC APPROACH IN PSYCHOTHERAPY OF AUTISM**

University J. Dobrila – Pula, Faculty of educational sciences, Pula, Croatia

Psychoanalytic psychotherapy of autism as a topic has very little presence in modern theoretical and practical discussions. This position is evident in the fact that contemporary scientific and professional debates about psychoanalytic psychotherapy of autism are mainly reduced to the question of its historical role in the development of treatment of autism. This position may be explained by new scientific trends in which dominate neuroscience and genetics. At the end of the 20th century these trends in science brought many changes in the field of understanding the genesis of many psychopathological phenomena. These changes were conditioned by the technological advances in the organization of researches which, especially within the period of the 'Decade of the Brain', gave special emphasis to the investigation of the role of organic factors in psychopathology. These new approaches led to a multitude of organic theories that put psychological theory in the background. These new trends in science further highlighted the "fault line" (Fonagy) that existed within the 20th century in the field of research of the human mind between, on one side psychoanalysis and psychotherapy and, on the other, the discipline of 'science of mind'. These contemporary scientific trends have manifested itself in the field of understanding genesis of autism. Many scientific researches have resulted in a multitude of different and mutually inconsistent theories about organic etiology of autism, which has led some authors to define autism as a "pervasive developmental disorder of different etiologies but in the same way of occurrence." Today this multitude of different and mutually inconsistent theories is largely used as an unmasked proof of organic etiology of autism, by which the importance of psychological factors is placed in the background of understanding autism. Therefore, contemporary scientific and professional discussions on psychoanalytic psychotherapy of autism are reduced to the question of its historical role in the development of autism therapy and at same time neglect its current contribution to understanding the genesis of autism and its therapy. The aim of this presentation is to indicate the sources of the existing "splitting" that exists between the biological and psychological concepts in understanding the genesis of autism and also to indicate the possible way of its overcoming. In support of the overcoming of the present situation, the knowledge of 25 years of experience in the application of psychoanalytic approaches in the psychotherapy with eleven autistic children is presented. Fundamentals of acquired knowledge presented in this lecture include the contributions of individual authors of the theory of object relations (Tustin, Mahler, Meltzer, Alvarez,) and the intersubjectivity (Trevarthen, Stern, Hobson) as well as the knowledge of neuroscientists which confirms this possibilities.

**Aleksandra Mindoljević Drakulić: SOCIAL NEUROSCIENCE OF ATTACHMENT-BASED TEACHING IN THE CLASSROOM**

Zagreb University, Faculty of Humanities and Social Sciences, Teacher Education Center, Zagreb, Croatia

Today, a good enough teacher stimulates student's minds and brains to learn. Why good enough teacher is successful and how he stimulates neuroplasticity and learning in the classroom? Teacher who is able to mobilize social instincts of it's students, is doing it through attachment-based teaching and attachment relationships. It is a well-known fact that relationships shape human brain throughout life. Across all human cultures, infants and young children display a specific reaction following separation from their stronger, older and wiser caregivers. After this early attachment, a good enough teacher becomes their secure base in the school. In this paper we will explore classroom teaching from the perspective of evolutionary model of attachment theory as well as capacity to learn which is deeply connected on the quality of our relationships with teachers and classmates.

## POSTERS PSYCHIATRY

### 1. “THAT LAWYER IS A SHARK BECAUSE HE HAS TEETH”: DISENTANGLING METAPHOR INTERPRETATION IN PATIENTS AFFECTED BY SCHIZOPHRENIA.

Giulia Agostoni

San Raffaele Hospital, Department of Clinical Neuroscience, Milan., Italy

**Introduction/Objectives:** The deficit of pragmatic abilities is a significant feature of schizophrenia (SCZ), affecting around 70% of patients, and it is a main determinant of functional disability, undermining patients' social well-being and quality of life. Patients with SCZ very often misunderstand the speaker's meaning, generally showing a concrete misinterpretation of figurative language, especially metaphors, relying also on Theory of Mind (ToM). In developmental age, it has been suggested a differential ToM contribution depending on metaphor characteristics, i.e. physical or mental features, however to date this aspect has not been considered yet in SCZ. In this study, we analyzed the interplay between metaphor comprehension and ToM in SCZ, with a focus on metaphors' misinterpretation and on the different comprehension of two types of metaphors (physical vs. mental).

**Participants, Materials/Methods:** 60 patients with SCZ were assessed for metaphor interpretation (Physical and Mental Metaphors tasks, PMM) and ToM (Picture Sequencing Tasks, PST). We run two Linear Mixed Effects Models, investigating the role of both ToM and the type of stimulus (i.e., physical vs. mental), respectively on accuracy and type of metaphor interpretation.

**Results:** Results showed a significant effect of type of stimulus on accuracy score, with mental metaphors being more difficult to correctly interpret than physical ones. A significant effect of ToM also emerged. Moreover, on the type of interpretation, we found significant effects of both type of stimulus and ToM, as well as a significant interaction between them. Post-hoc analysis showed that the effect of ToM was greater for interpretation mental of metaphors.

**Conclusions:** The study suggests that the two types of metaphors present differences in the profile of impairment, as well as in the contribution of ToM. Results show that physical and mental metaphors are not equal, and the latter seems to be more difficult to understand for patients with SCZ, since they require an inference about mental aspects of the metaphor's topic. These data also suggest that ToM influences the ability to both correctly comprehend

metaphors, as well as to interpret mental metaphors in a mental way. Our findings are in line with theories claiming that pragmatics and ToM are different domains, but with some degree of overlapping. Moreover, our data suggest that an integrated sequential rehabilitative approach, including both ToM and pragmatics interventions, can lead to greater benefits, with consequent effects on social well-being, employment, and quality of life.

### 2. CLINICAL ASPECTS OF SCHIZOPHRENIA COMORBID TO TYPE 2 DIABETES.

Marina Artemieva, Tatiana Varnakova, Roman Suleymanov, Anastasia Lazukova

RUDN University, Department of psychiatry and medical psychology department, Moscow, Russian Federation

**Introduction/Objectives:** The treatment of schizophrenia associated with brain damage is one of the most common issue in psychiatry. According to previous studies, about 8,8-14,5% cases of schizophrenia is comorbid to type 2 diabetes. The focus of the study was the evaluation and dynamics of positive (delirium, hallucinations, pseudohallucinations, asthenodepressive, hypochondriacal, obsessive, mood, conversion, dissociative and organic personality disorders) and negative (apathy, motivation deficit, cognitive dysfunction) symptoms in schizophrenia with type 2 diabetes.

**Participants, Materials/Methods:** 100 patients were divided in two groups: The first group (48 patients) was assigned to receive a monotherapy treatment with antipsychotic; The second group (52 patients) received the combination of antipsychotics, nootropics and antioxidants. The mean age of the patients was 53,7 years. The duration of treatment for both groups lasted 8 weeks. Questionnaires: Short-form 36 questionnaire (SF-36), which is an instrument for assessing quality of life, The Hamilton Anxiety Rating Scale (HAM-A) and Depression Rating Scale (HDRS), Scale for evaluation positive and negative symptoms (PANSS) were administered to evaluate the effective treatment approach for patients with the combined pathology measured in the beginning and the end of therapy.

**Results:** The patients of the second group showed visible clinical progress: exhibited more motor activity, less social avoidance and emotional withdrawal as well as greater cognitive functions. According to Quality of Life questionnaire combination of antipsychotic, nootropic, antioxidant was significantly more effective than monotherapy with antipsychotic. The physical component of health after treatment was 41,38% in the first group and 56,34% in the second group ( $p \leq 0,05$ ). The mental component of health was 39,79% in the first group and

50,8% in the second group ( $p \leq 0,05$ ). A comparison of scores of Hamilton Anxiety Rating Scale (HAM-A) and Depression Rating Scale (HDRS), Scale for evaluation positive and negative symptoms (PANSS) also displayed higher rates of improvement in the patients of the second group ( $p \leq 0,05$ ).

**Conclusions:** Patients with schizophrenia and comorbid type II diabetes were treated more effectually with both antipsychotic and metabolic drugs compared with monotherapy.

### 3. MAIN PSYCHOGENIC CAUSES OF NON-PSYCHOTIC NEUROPSYCHIATRIC DISORDERS IN RESIDENTS OF MOSCOW.

Marina Artemieva, Roman Suleymanov Ivan Danilin, Anastasia Lazukova

RUDN University, Department of psychiatry and medical psychology department, Moscow, Russian Federation

**Introduction/Objectives:** The purpose of the study was to identify the most significant psychogenic causes of non-psychotic neuropsychiatric disorders, in residents of Moscow.

**Participants, Materials/Methods:** 350 Muscovites hospitalized for the treatment of neurotic mental disorders were examined after the exclusion of somatic diseases, endogenous or personality disorders and addictions studying the levels of anxiety, depression and anhedonia in 2015-2018.

**Results:** The most frequent complaints were chronic sleep deprivation and insomnia, constant fatigue and irritability, apathy and depression, psychosomatic disturbances combined with increased patient fatigue, rapid exhaustion, vasomotor disorders, irritable weakness syndrome or nervous exhaustion, which is a neurasthenic "core syndrome" or "core". They were accompanied by a significant decrease in mental performance (lowering of "mental tone" - intentions, impaired active attention, etc.), developing on the background of altered well-being, emotional disturbances (depression, non-objective malaise, combined with displeasure, irritability, anxiety), psychosomatic dysfunctions - headache, hypertension, etc. In a broad sense, situations that contributed to the development of the disease were defined as a combination of subjective interpretation (something implicit, unique, based on common cultural traditions) and objective conditions as part of the environment or external stress as permanent negative circumstances requiring additional forces for adaptation. The internal stressors were the same characteristics (the ability to control the situation, the

subjective assessment of the impact force, variability, ambiguity, repeatability and personal experience of encountering a stressful situation).

The common causes and/or stress factors were: a conflict situation with another person (24%); frequent fears, especially of fatal diseases (cancer) (21%); long absence of holidays and good rest (19%); routine life or small amount of positive emotions, changes (18%); long-lasting chronic diseases or death of relatives (17%); loneliness (11%); sexual problems (4%); abrupt change of environment (10%); excessive physical activity, or adverse environmental conditions (6%); combined impact of multiple adverse factors was observed in 30% of cases.

**Conclusions:** Among all the above, common to all situations predisposing factor was housing shortage (64%), expressed in inability to improve living conditions, splitting out with a former family member. The second most stressful factor (27%) was low income, which did not allow care for chronically ill relatives living together, inability to hire a nurse for sick relatives, while at the same time keeping a job.

### 4. PSYCHOSOMATIC ASPECTS OF GASTRIC ULCER DISEASE AND HYPOTHYROIDISM.

Marina Artemieva, Vladimir Kuznetsov, Ivan Manyakin, Elena Basova, Sergey Safaryan

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**Introduction/Objectives:** The relevance of the study was determined by the high incidence of mental disorders and decrease of the quality of life (QL) in patients with gastrointestinal tract (GIT) diseases and hypothyroidism (the frequency of this combination of diseases-about 30%). Diseases of the digestive system and endocrine system will be at the leading place in the 21st century according to predictions of WHO experts.

**Participants, Materials/Methods:** The combination of gastric and thyroid gland disorders impairs the course of the disease, favors multiple organ failure, increases the cost of diagnostic and treatment of diseases. Evaluation of quality of life (based on questionnaire SF 36 and Hamilton's scale of Depression and anxiety) is widely spread and can also help to choose the effective treatment for patients with combined pathology. We analyzed questionnaires SF36 of patients with gastric ulcer and/or duodenal ulcer (two or more ulcers) in combination with thyroid pathology (hypothyroidism).

**Results:** Patients are divided in two groups: the first group – patients with ulcer disease (20 persons); the second group –

patients with ulcer disease and hypothyroidism (20 persons). The quality of life of patients from the second group is low. The physical component of health is 51,36% in the first group and 40,8 in the second group ( $p \leq 0,05$ ). Such indications are associated with the symptoms of hypothyroidism: metabolic disorders of protein, lipids, decelerate of carbohydrates utilization, weight gain, tendency to bradycardia, pain caused by biliary dyskinesia. The mental component in the first group is 41.22%, in the second – 30.75% ( $p \leq 0.05$ ). The score on the Hamilton Anxiety Rating Scale (HAM-A) is also high for both groups. High score indicates the course of the pathological process affects the personality of the patient and his emotional experiences. The mental component of QOL is various for somatic patients.

**Conclusions:** Ulcer disease manifests irritability, insomnia, emotional instability, hypochondria, carcinophobia, exhaustion of mental functions. The psychoorganic syndrome (decrease of memory, intelligence, attention) quickly appears in patients with hypothyroidism in addition to exhaustion of mental functions. Curmudgeonly, ipohondricescie, stereotyping behavior, decrease of intelligence are specific for these patients. Patients with combined pathology of peptic ulcer and thyroid dysfunction should be examined not only by general practitioner, gastroenterologist, endocrinologist, cardiologist, but also by psychotherapist because of pronounced somatogenic mental disorders.

##### 5. THE QUALITY OF LIFE OF PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE.

Marina Artemieva, Vladimir Kuznetsov, Ivan Manyakin, Elena Basova, Sergey Safaryan

RUDN University, Department of psychiatry and medical psychology department, Moscow, Russian Federation

**Introduction/Objectives:** The pattern of diseases changes: the pathology of the upper gastrointestinal tract (gastroesophageal reflux disease, gastritis, duodenitis) is the most prevalent. Gastroesophageal reflux disease (GERD) is one of the most common, recurrent and comorbid gastroenterological diseases, with a prevalence of 30% in Western Europe and 10% in East Asia in the adult population. Comorbidity of patients with GERD and thyroid diseases degrades the course of the disease, increases the cost of diagnosis and treatment, because the pathology of thyroid gland affects various organs and systems, also mental function.

**Participants, Materials/Methods:** Evaluation of quality of life (based on questionnaire SF 36 and Hamilton's scale of Depression and anxiety) is widely spread and can also help

to choose the effective treatment for patients with combined pathology. We analyzed questionnaires SF36 of patients with GERD only and GERD with hypothyroidism.

**Results:** Patients are divided in two groups: the first group – patients with GERD (15 persons); the second group – patients with GERD and hypothyroidism (15 persons). The quality of life of patients from the second group is low for such indications as “physical and mental components of health”, “social functioning”.

The intensity of pain in two groups significantly limits daily activities of patients. The physical component of health in patients with GERD is 48.82%, and in patients with comorbidity – 39.21% ( $p \leq 0.05$ ). A significant difference in the mental health component is observed: in the first group – 39.7%, and in the second group – 30.18% ( $p \leq 0.05$ ).

**Conclusions:** Patients with GERD suffer not only symptoms associated with erosive-ulcerative, catarrhal and/or functional disorders of the distal esophagus, but also neurotic disorders. Depression, memory impairment, attention disorders are more common. Thyroid dysfunction manifests with psychoendocrine syndrome (depressive and anxiety-phobic disorders), therefore the mental health component of the quality of life of patients with GERD and hypothyroidism decreases. Patients with combined pathology of GERD and thyroid dysfunction should be examined not only by general practitioner, gastroenterologist, endocrinologist, cardiologist, but also by psychotherapist because of pronounced somatogenic mental disorders.

##### 6. AN ANALYSIS OF HIGH RANGE IQ EXAMINATIONS.

Sriram Balasubramanian

Kalahasti Ashram Knowledge Ventures, Chennai, India.

**Introduction/Objectives:** Intelligence quotient measures a certain projective, logical and synthetic faculty of the mind in order to predict a quotient of functional capacity such as problem solving. and logical aptitude. While IQ ranges above 120 are considered superior numerous efforts have been undertaken to quantify high performance of in these tests upto accurately 145 and projected as high as 180. In this study the various sorts of questions in a high range IQ exam are examined addressing the question of what is being precisely tested in the high IQ exam ie. the precise manner In which the G factor is set up and how it correlates to subjective logical thought that is found in academic disciplines with a high correlation to IQ such as Mathematics and physics.

**Participants, Materials/Methods:** A total of 60 high range IQ exams with more than 1000 graded culture fair questions



were independently analysed for the mental functions measured with norms for each test set after 100 voluntary submissions from interested candidates worldwide with a wide cultural diversity in a strict online test room simulation. As a sample the LABCUB test with 26 items had 548 test takers with mean score 15.59 (IQ = 132) std mean error at 0.18 and raw variance at 13.745 (IQ=120) with 0.95 as std error. The lowest score was 2 (IQ=77) while highest was 26(IQ=182). Each of the test was analysed similarly.

**Results:** Various standard IQ schemes are first studied noting similarities in the essential mental functions being tested such as symmetry identification, projective ability of rotation and deletion, abstract figure manipulations with geometric shapes, geometric numerical correlations etc. Only culture fair spatial patterns are included in this study.

**Conclusions:** it is observed that problems above 145 fall into two categories that make them eligible for that categorization 1. Addition and compounding of simpler basic functions that make them tough but in principle workable from basic functions of mind and 2. Conceptually novel functions such as non linear thinking and correlation in pattern. While those in the category of 120-145 pose straight forward toughness of mental functions with sufficiently workable base and those below 120 just test the basic ability or existence of such faculties.

## 7. ONTOLOGICAL VALIDITY OF DEPRESSIVE REALISM EVIDENCED FROM PHILOSOPHY AND NATURE OF DEPRESSION DIAGNOSIS.

Sriram Balasubramanian

Kalahasti Ashram Knowledge Ventures, Chennai, India.

**Introduction/Objectives:** Depressive realism is a controversial conjecture that states that depressed states of minds do indeed perceive reality more accurately. This has spawned debates as to whether the perception of the depressed mind do correlate with objective reality perceived superiorly or whether they are figments of imagination and thus need treatment. In this gedanken consideration, depressive realism is analysed from the perspective of perceiving philosophical truths as found in the stoic philosophy which emphasises on the modus operandi of life that accentuates clinical depressive symptoms such as withdrawal and neglect of comforts. A case is made that depressive realism can be objectively true that brings into question the very nature of clinical depression diagnosis

**Participants, Materials/Methods:** The nature of the superiorly perceived reality in depressive realism is argued to be a philosophical penchant with the perception of

platonic thought forms and conclusions about issues of value, morals and justice. This conclusion is reached by the analysis of writings of stoic philosophers such as Marcus Aurelius whose philosophies imply lifestyle that explicitly overlap with modern clinical depression symptoms. The concept of Limbo in theology and the psychology of aolian mode is explored to be an inherently depressive ambience yet the theologically documented residing place for all the great ancient philosophers who were traditionally considered wise.

**Results:** This makes a circumstantial case that such a natural expression of depressive realism statistically do present in clinical cases as objectively as the phenomenon of giftedness but are not recognised due to the nature of depression evaluation questionnaires and standard diagnostic methods that do not take into account the nature of such a philosophical reality as true. This raises the possibility for objective psychiatric misdiagnosis of depression due to the lack of acknowledgement of objective truth in depressive realism perception.

**Conclusions:** An extension of this consideration leads to the position that depression is an inherently a spectrum condition with certain forms of the condition as a transformative evolution that disputes uniform cartesian clinical pharmacological intervention and methods of diagnosis. This form of depressive realism is not yet documented in the DSM nor acknowledged in current psychiatric practice.

## 8. “HYSTERICAL CHARACTER STRUCTURE” IN PATIENT WITH BIPOLAR AFFECTIVE DISORDER – A CASE REPORT.

Sarah Bjedov, Ivana Picek, Darko Marčinko

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

**Introduction/Objectives:** The aim of this paper is to present a case report of a female patient suffering from bipolar affective disorder, accompanied with anxiety and multiple somatizations, and to analyse how patient's personality organization affected her treatment.

**Case report:** We present a case of a 43-year-old female patient diagnosed with bipolar affective disorder sixteen years ago. She was hospitalized multiple times with similar presenting symptoms. She was complaining on frequent mood fluctuations in terms of experiencing periods of depressive mood, alternating with phases of elevated mood, often oscillating from hypomanic to depressive during the same day. She was describing having a lot of energy throughout the morning, being able to do few household chores simultaneously, but then feeling depressed in the

afternoon. She also reported intense diffuse anxiety accompanied with numerous somatizations, such as dizziness, headache and chest pain. She was treated with various medications, but mostly achieving only partial remission, with mood swings still being present in reduced form. Psychotherapy was included in her treatment, and during last hospitalization, she was also treated with transcranial magnetic stimulation, after which she reported better mood stabilization and significant reduction of anxiety, but she was still experiencing somatizations.

**Conclusions:** Considering complexity of symptoms in presented case, the question arises whether the patient's condition is an example of refractory bipolar affective disorder or is the therapy resistance in fact a result of interaction between bipolar symptoms and personality traits. Despite being treated with numerous treatment options (various combinations of psychopharmacs, individual and group psychotherapy, transcranial magnetic stimulation), patient continued to experience residual symptoms, which could suggest that personality traits may play a big role in patient's response to given treatments. It is possible that patient's "hysterical character structure" interferes with treatment, which implicates that further long-term psychotherapy is indicated.

### 9. AGGRESSION INCIDENCE, TYPE AND SEVERITY AMONG INVOLUNTARILY HOSPITALIZED PSYCHIATRIC PATIENTS.

Andreja Celofiga, Jure Koprivsek

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**Introduction/Objectives:** Aggressive incidents in acute psychiatric setting have significant impact and implications on clinical practice as well on the health, safety and wellbeing of patients and medical staff. When developing the programs to reduce the aggressive behavior and consequences as it is use of coercive measures like restraining, differentiating between types of aggressive behaviour and its severity is one of the first steps in developing of them.

The aim of this study was to investigate the incidence, severity and type of aggressive incidents among involuntarily hospitalized psychiatric patients.

**Participants, Materials/Methods:** The study was conducted in the first part of the National project of Slovenian Psychiatric Association aimed to reduce aggression in intensive psychiatric units and was carried out over 5 months period. The data were obtained from two intensive psychiatric units. Aggressive incidents occurred in the ward during the study period were assessed routinely

using the Staff Observation Aggression scale (SOAS-R). Aggressive incidence rate were calculated per 1000 hospitalization days. Differences in types and severity of aggressive incidents were evaluated with Chi square and owing to non-normal distribution with Mann-Whitney U test, with p values <0.05 used to determine statistical significance. SPSS software was used for data analyses.

**Results:** Of 813 psychiatric patients admitted to the units during the study period, 138 were responsible for 278 aggressive events. Aggressive incidents were reported in 41.5% involuntarily and in 10.5% of voluntarily hospitalized patients, resulting in significantly higher aggressive incidents rate among involuntarily compared to voluntarily admitted patients (19.4 versus 8.9 incidents per 1000 hospitalization days) ( $\chi^2(1) = 85.538$ ,  $df=1$ ,  $p=0.000$ ). SOAS-R scores were significantly higher among involuntarily hospitalized patients with 92% of aggressive incidents being severe (SOAS score  $\geq 8$ ) ( $U=6414.500$ ,  $p=0.000$ ). Verbal aggression only, was observed less frequent in the group of involuntarily hospitalized patients ( $\chi^2(1) = 8.062$ ,  $df=1$ ,  $p=0.005$ ). 59.3% of incidents in involuntarily hospitalized patients involved physical aggression, compared to 43% in voluntarily hospitalized patients ( $\chi^2(1) = 7.095$ ,  $df=1$ ,  $p=0.008$ ).

**Conclusion:** The study indicates significantly higher rate and severity of aggression among involuntarily hospitalized psychiatric patients, which implies for the need of special attention on this group of patients, when developing the programs to reduce the aggressive behavior and its consequences.

### 10. COMPARISON OF INCIDENCE AND DURATION OF COERCIVE MEASURES AMONG VOLUNTARILY AND INVOLUNTARILY HOSPITALIZED PSYCHIATRIC PATIENTS.

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University Psychiatric Clinic Ljubljana, Ljubljana, Slovenia

**Introduction/Objectives:** Use of coercive measures within acute psychiatric facilities in European countries varies widely with regard to its frequency, type, and legal regulations. Physical restraint is defined as a coercive measure that must be employed as the last resort under any circumstance to ensure the safety of the patients. In Slovenia use of coercive measures is governed by the Mental Health Law defining use of physical restraints and seclusion. In clinical practice the restraints are mostly used. The aim of this study was to investigate the differences in incidence and duration of coercive measures among voluntarily and involuntarily hospitalized psychiatric patients.



**Participants, Materials/Methods:** The study was a part of the first phase of the National project of Slovenian Psychiatric Association aimed to reduce aggression in intensive psychiatric units and was carried out in acute psychiatric units of two largest Slovenian psychiatric hospitals. Data about type of admission (voluntary/involuntary) were collected for five months for all admitted patients. The data about coercive measures were obtained from standardized paper forms, according to the terms of Mental Health Law. SPSS software was used for data analyses.

**Results:** Among the 1587 psychiatric patients admission during the five-month study period, 332 (21%) were involuntarily hospitalized. Use of coercive measures were more than four times higher by involuntarily hospitalized patients (37% versus 8.9%;  $\chi^2(1) = 85.440$ ,  $p=0.000$ ). Repeated coercive measures were introduced in a significant proportion of patients, which was contributed to the total number of 404 coercive measures. The median duration of coercive measures was 9.13 hours (mean 14.77 s.d.=19.36) in the group of involuntarily and 8.00 hours (mean 11.67 s.d.=19.51) in the group of voluntarily hospitalized patients. The difference in the duration was not statistically significant ( $U= 18130,00$ ,  $p=0.063$ ). The main reason for the use of coercive measures in both group was different types of aggressive behaviour.

**Conclusion:** The frequency of coercive measures in involuntarily admitted patients in our study was 37%, which is the same as in the large European study, where Slovenia was not included. Use of coercive measures in our sample were more than four times higher among involuntarily hospitalized patients. There was no differences in the duration of coercive measures and the reasons for its use between voluntarily and involuntarily hospitalized patients. Treatment programs for reducing aggression and use of restraints may be difficult and should be adjusted to focus on the specific groups, such as involuntarily admitted patients

### 11. EYES OPEN – THE ORGANICITY OF DIAGNOSIS IN A CASE OF VISUAL HALLUCINATIONS: A CASE REPORT.

Zenn Chua, Ambrose Cheng

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**Introduction/Objectives:** Visual hallucinations are often associated with underlying organic disorder. The diagnostic process itself is organic.

We present a patient for whom our understanding of his aetiology of visual hallucinations evolved as time unfolded. There were three working diagnoses altogether.

**Case report:** A 68-year-old man with near-total blindness secondary to glaucoma was admitted for gout flare in October 2017. He developed emotional lability and visual hallucinations, which improved when prednisolone was discontinued. Blood tests and CT brain were unremarkable. Diagnosis was steroid-induced psychosis. He was admitted in December 2018 for worsening visual hallucinations over the past month. He now saw faces and bodies, with partial insight. Family reported slight forgetfulness but not fluctuating cognition. He was not on steroids. MMSE was 25/26. Diagnosis was Charles Bonnet syndrome (CBS). Quetiapine was prescribed. He was re-admitted the same month for worsening visual hallucinations, paranoia and aggression. He reported tactile and elementary auditory hallucinations. Nurses noted episodes of disorientation. Retaking corroborative history, there was fluctuating cognition in previous months. Function was at baseline. There was mild cogwheel rigidity. Diagnosis was probable mild neurocognitive disorder with Lewy bodies. Rivastigmine was started.

**Conclusions:** CBS was diagnosed when only visual hallucinations were apparent, and revised subsequently in view of decreased insight, significant paranoia, multimodal hallucinations, fluctuating cognition, and rigidity. Although he performed well on MMSE, visuospatial/constructional function (usually affected earlier in Lewy body dementia (LBD)) could not be assessed due to vision. His blindness also decreased sensitivity in elicitation of functional decline. He likely had early LBD.

On PubMed search, 26% of CBS patients in a chart review subsequently developed dementia, commonly LBD. A systematic review suggested possible association between CBS and dementia. A paper stated hallucinations can be the unique early sign of LBD. A paper published a CBS case with functional imaging suggestive of LBD, before LBD was diagnosed years later. A study shared that CBS may be a marker for early cognitive difficulties. The literature documents early/prodromal symptoms of LBD to seek on history-taking, use of Froment's manoeuvre to elicit mild rigidity, and neuropsychological domains typically affected first.

This case highlights the importance of being attentive to evolution of the clinical picture. Notably, LBD can be misdiagnosed as CBS early in presentation. Ensuring longitudinal monitoring and knowing the subtleties to keep one's eyes open for might aid in earlier correct diagnosis and appropriate management.

**12. NEUROPSYCHOANALYSIS - BRAIN/BODY AND MIND.**

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**Introduction/Objectives:** Neuropsychoanalysis connects psychological experiences, thinking processes, personality and behavior with neurobiology, in order to compile a theory of mind applicable in general psychology and psychotherapy. The main objective is to postulate a version of a brain/mind functional model with additional emphasis on understanding human behavior. The presented work demonstrates building blocks of which the brain/mind is comprised, as well as how its functional complexity may be conceptualized. Etiological factors of psychological disorders are described along with psychoanalytical tools and goals through which psychotherapy induces changes. Various perspectives of affective, cognitive, and social neurosciences were used, including subdisciplinary ones from neurosciences of consciousness and self.

**Participants, Materials/Methods:** Clinical experience and scientific literature describing four fundamental neurobiological-psychological theories of emotion were used. The latter includes interoceptive (Damasio), construction of emotions (Barrett), functional (Adolphs), and seven primary emotions (Panksepp) theories. Their relation to cognition (thoughts, concepts, and categorization) and prediction theory with prediction error is showed. Damasio's hypothesis, on how consciousness emerges from the mind and which neurobiological components constitute it, is also included. Ultimately, multiple sources were used for the convergence and synthesis which schematically presents how the mind emerges from the brain and the body, which perpetually interact with the environment.

**Results:** All bodily systems highly intertwine with cognition, which is further comprised of concepts, categorizations, and one's social-cultural environment. Emotions are functional states that may be elicited by -homeostatic feelings (interoception), environmental factors (exteroception), behavior, and mental simulation of events or actions. Respective emotional states may produce various outputs, e.g. concepts, emotional expressions, behavior, and cognitive alterations. Self is a system associated with cognition/memory (autobiographical self), as well as with affective system and consciousness (core self). Functioning of affective-cognitive mind is akin to inference machine learning model. It enables better understanding of psychotherapy as an interpersonal communication game with the ultimate goal of achieving affective and cognitive balance.

**Conclusions:** Homeostatic feelings, emotions, and cognition are the building blocks of the human mind. Their interaction should be considered as being focal. Continuous dynamic relationships of the brain, body, and environment are reflected in one's mental health status. This work highlights how neuropsychoanalysis, as a discipline which combines psychological, psychopathological, and neuroscientific, may contribute to the understanding of the human mind.

**13. NEUROSENANCE AND PSYCHODINAMICS IN CONTEMPORARY PHENOMENOLOGY.**

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**Introduction/Objectives:** Neuropsychoanalysis combines neuroscientific insight into how brain creates the mind (feelings and emotions, cognition, memory, self) and psychoanalytical understanding of human behavior, mental disorders and their treatment. Contemporary neuroscience is unconscious in the field of gray structures surrounding the fourth chamber while the center of consciousness is in the prefrontal cortex. The assessment of the recognition of the experience is carried out by amygdala and orbital-frontal cortex. Amygdala is the first to enter and from the thalamus and from the cortex. As information comes in the amygdala from the thalamus before the cortex, thalamic injections have the ability to directly affect the amygdal response to cortical intake. That is why Freud was right when he assumed that behavior was influenced by unconscious motives, as well as in the assumption that they knowingly and unconsciously differ in the mode of funculation. Kendel (2001) points out that structural links between nerve cells can be changed through learning, and that the activity of the gene can be affected even by the environment.

**Participants, Materials/Methods:** Authors look at the present titles subject though scientific view of the eternal problem of psyche – soma diversity. They consult literature, have subjective experiences in several psychiatric practices and though objective observations.

**Results:** Modern neuroscience has given more insight into brain plasticity and its realization in the form of learning and memory processes. The human brain represents the body of adaptation to the social and physical world stimulated by growth and learning through positive and negative interactions with the environment. Psychotherapy from the perspective of neuroscience represents a special form of enriched environment designed to enable neuronal growth and integration of neuronal bonds. With a better understanding of the relationship of a psyche, the way of psychotherapy and neuroscience dialogue is overwhelming. The brain decade is marked by progressive progress in

understanding biology of mental function, the psychological basis of our inner world.

**Conclusions:** The brain is plastic and retains the ability to learn and develop throughout your life. The main criticism of many neuroscientists to psychoanalytic theories is to be poorly evidence-based, while psychoanalysts have long ignored a scientific confrontation, denying the need for an empirical back up outside the therapeutic setting. Psychoanalytical treatment does not quite affect the conscious conflict. It can change the deeper structure and functioning of the brain. Deep therapy can be profound for the brain as well.

#### 14. FORENSIC PSYCHIATRIC ASPECTS OF PERSONALITY DISORDER.

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**Introduction/Objectives:** Background. The greatest difficulty is the determination of the contingency of the clinical and dynamic characteristics of the disorder and the psychological criteria for sanity and procedural ability formulas. Objectives. Development of clinical, psychological and forensic psychiatric assessments of personality disorders.

**Participants, Materials/Methods:** 70 men with the diagnosis “Personality disorder” accused of committing various crimes were examined. Literature analysis, clinical, psychopathological, psychological, statistical methods applied.

**Results:** Personality disorder is a fairly stable pattern of behavior. The main manifestations are a violation of emotional regulation, volitional control over impulses, self-knowledge, other people. Violations, biological and social factors lead to criminalization of patients. Disorders are noted in the case of dynamic changes (affective, dissociative disorders, adaptation disorders), which contribute to the commission of criminal delicts. Expert problems - assessment of the impact of disorder on criticality, goal setting, ability to predict and self-regulate behavior in a legally significant situation acquires particular relevance. The study found that when there are regulatory violations, defendants with personality disorders have changes in the motivational and semantic sphere, difficulties in organizing activities and controlling behavior in, long-term adoption decisions. Thus, the criteria for the inability to realize the actual nature and public danger of their actions or to lead them are a violation of the ability to analyze holistic

analysis, awareness and assessment of the situation, form the goal of the activity and choose the means to achieve it, a significant distortion of the motivational sphere, a painful disorder critical ability and prediction. The criteria for limiting the ability to be aware of the actual nature and social danger of one’s actions or to lead them are insufficient focus and awareness of criminal actions, violation of the arbitrariness of choice. However, the list of expert questions may include the following tasks: determining the ability of the accused to independently protect his rights and legal interests, understand the meaning of criminal proceedings and his procedural position, ability to act, aimed at the implementation of his procedural rights. Procedural incapacity in defendants with personality disorders may be due to the occurrence of a transient psychotic disorder or a depressive moderate or severe episode. In these cases, psychogenic-induced disorganization of mental activity with anxiety, hopelessness, confusion, violation of rationality of judgments, the presence of delusions are stated. **Conclusions:** The main task of forensic psychiatric experts is to assess the substantive characteristics of personality disorder, its dynamics in a criminal situation.

#### 15. HOW TO TREAT TREATMENT-RESISTANT DEPRESSION – A CASE REPORT.

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**Introduction/Objectives:** The prevalence of affective disorders is on the rise in all age groups. Treatment-resistant depression (TRD) is a particular challenge for psychiatrist.

**Participants, Materials/Methods:** We present the course of treatment for a patient suffering from TRD. **Results:** A 54-year-old male, married, the father of one child, engineer, was admitted to psychiatric treatment for a major depressive disorder. He was hospitalized 4 times in the previous 6 months. He was treated with pharmacotherapy and supportive psychotherapy and biological methods: electroconvulsive treatment (ECT), repetitive transcranial magnetic stimulation (rTMS) and the light therapy. Despite all aforementioned treatments, no significant therapeutic benefits were achieved.

**Conclusions:** Covert challenges encountered by clinicians in treating such conditions range from undiagnosed bipolar disorder to comorbid dependence disorders or various psycho-social issues. Marital neglecting and psychological abuse in interpersonal area and a comorbid personality disorders are also common, as well as subtle brain changes in the middle-aged population. Careful clinical assessment

of each patient with TRD is required. Clinical experiences show that the reduction of symptoms is a realistic goal with the additional approach to each of these challenges.

Adjuvant psychotropic treatment with mood stabilizers such as lithium or antiepileptic's, and alpha 2 delta ligands can be considered. Substantive intrapsychical conflicts as well as comorbid personality disorders and psychosocial difficulties can be accessed through psychosocial methods as well as psychotherapy. In middle-aged people with TRD, it is also necessary to assess the possibility of abuse and neglect by family members who should care for them. Removing such adverse environmental factors can significantly improve affective status in those patients. Careful assessment of comorbidity and psychosocial issues might help in targeting those difficult-to-treat patients.

#### **16. ANHEDONIA AND THE SEVERITY OF DEPRESSION IN TWO PSYCHIATRIC DISORDERS.**

Dejana Jezernik, Lucija Šimunić, Marina Šagud, Lucija Tudor, Zoran Madžarac, Ivana Stefanović, Ivona Šimunović Filipčić, Bjanka Vuksan-Ćusa, Biljana Kosanović Rajačić, Alma Mihaljević Peleš, Suzan Kudlek Mikulić, Nela Pivac

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**Introduction/Objectives:** Anhedonia is a core feature of major depressive disorder (MDD). However, symptoms of depression are common in schizophrenia. Given that anhedonia is also a negative symptom of schizophrenia, we sought to investigate the relationship between anhedonia and symptoms of depression in patients with MDD and schizophrenia.

**Participants, Materials/Methods:** Patients treated for MDD or schizophrenia in the Department of Psychiatry, University Hospital Centre Zagreb were enrolled in this cross-sectional study. All participants filled in the revised Physical Anhedonia Scale (RPAS) to measure physical anhedonia (PA) and the revised Social Anhedonia Scale (RSAS) to assess social anhedonia (SA). The severity of depression was measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) in MDD patients, and using the Calgary Depression Scale for Schizophrenia (CDSS) in schizophrenia patients. The severity of psychopathology in schizophrenia was estimated by the Positive and Negative Syndrome Scale (PANSS).

**Results:** In respondents with MDD (n=178) the severity of depression was moderate (median MADRS score=20), while in those with schizophrenia, the depression severity was mild (median CDSS=4). Within the MDD group, in multiple linear regression, MADRS total score significantly predicted PA score (p=1.6E-5) and SA score (p=3.3E-7). In

schizophrenia patients, the significant correlation was found between both types of anhedonia and the CDSS total score (p=0.001 for PA and p=3.6E-6 for SA). The CDSS score has also significantly and positively correlated with all PANSS subscales, with the strongest correlation between CDSS and PANSS negative sub-score (p=3.7E-6). Of note, neither total antipsychotic dose in schizophrenia, presented as chlorpromazine equivalents, nor total antidepressant dose, shown as fluoxetine equivalents, correlated with any rating scale scores.

**Conclusions:** Anhedonia was associated with symptoms of depression in both MDD and schizophrenia. The lack of association between the severity of depression and severity/presence of anhedonia with antipsychotic dose, speak against the development of antipsychotic-induced dysphoria. This finding might be contributed to treatment with second- and third- generation of antipsychotics, which have low propensity to induce depression or emotional distress.

#### **17. FEATURES OF PARENT-CHILD RELATIONSHIPS IN FAMILIES OF MOTHERS WITH SCHIZOPHRENIA.**

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**Introduction/Objectives:** Mother's mental illness is associated with impaired family functioning and a negative style of parent-child relationships. The aim of the study was to investigate the features of family functioning and parent-child relationships in families of mothers suffering from schizophrenia.

**Participants, Materials/Methods:** A cross-sectional, comparative, case-control study was carried out. The study involved mothers suffering from schizophrenia (n = 58) and mentally healthy mothers (n = 43), having children aged 3 to 14 years and living with them. The evaluation and comparison of the socio-economic characteristics of the research participants were conducted. The assessment of the style features of the relationships between the mother and the child was conducted using the questionnaire for parents "Analysis of family relationships." The non-parametric Mann-Whitney criterion was used to assess intergroup differences, exploratory factor analysis was used to analyze the stylistic features of the child-parent relationship.

**Results:** Mothers with schizophrenia more often than healthy had a secondary and incomplete higher education, were more often unemployed and had a low professional status. In the families of mothers with schizophrenia, the unsatisfactory financial situation was more often, sick



mothers more often than healthy ones were dependent on their parents. The birth of children out of wedlock was more common in the group of mothers suffering from schizophrenia. The "Analysis of family relationships" profile of mothers with schizophrenia reflects higher levels of hyperprotection, indulgence, demands-responsibilities, instability of parenting strategies, minimal sanctions for violating a child's requirements, and higher levels of both excessive prohibitions and insufficient prohibitions. Among the possible causes of dysfunctional parent-child relationships, the psychological problems of the parent were revealed in the form of an expansion of parental feelings, a phobia for the loss of a child, lack of parenting confidence, confrontation with a partner in the area of parent-child relationships, underdevelopment of parental feelings, preferences of female qualities. An analysis of the internal structure of parent-child relationships in the studied groups showed that in families of mothers suffering from schizophrenia, the style of parent-child relationships has features that are typical for dominant hyperprotection, lack of parenting confidence and hypoprotection.

**Conclusions:** The most important socio-economic characteristics affecting family functioning are significantly lower in mothers with schizophrenia than in the group of mentally healthy mothers. The results of the study show that the styles of parent-child relationships in families of mothers suffering from schizophrenia are dysfunctional and are often caused by the psychological problems of the mother, solved by the child.

#### 18. DIFFERENTIAL DIAGNOSIS OF STUPOR IN THE ACUTE PSYCHIATRY - A CASE REPORT.

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**Introduction/Objectives:** Herein we present a case that is exemplary of the diagnostic complexity and treatment challenges often confronted in the acute psychiatry setting.

**Case report:** A 69-year-old female with a long-established diagnosis of schizophrenia was transferred to our inpatient unit after being treated for lobar pneumonia. Upon admission, her stuporous level of consciousness rang alarms, diagnostic doors were flung open, and an extensive work-up was initiated. She was on the following medications: risperidone 2mg tbl. bid; lorazepam 1mg tbl. bid; olanzapine pamoate 405 mg i.m. q 4 wks. Pertinent findings revealed by a laboratory and diagnostic work-up included: body temp. 37,5 C; BP 117/72 mmHg; pulse rate 100/min; serum glucose 5,4 mmol/L; sinus rhythm on ECG; CK 1460 U/L; D-dimers 3.20 mg/L; hs-cTnT 93 ng/L; total leukocyte 6.7

x109/L; CRP 73.2 mg/L; K 4.2 mmol/L; Na 130 mmol/L; MSCT brain scan revealed vascular lesions bilaterally in subcortical white matter, widened ventricles due to moderate atrophy, and a suspected aneurysm in the anterior circulation; serum olanzapine conc. 423 nmol/L; serum benzodiazepine conc. 0.4 umol/L. Neurological exam revealed a GCS of 8 and hypotonia.

The differential diagnosis of stupor in our patient aroused suspicion of the following aetiologies: iatrogenic or drug-induced; (atypical) neuroleptic malignant syndrome; hypoactive delirium due to GMC or multiple causes; catatonia associated with another mental disorder; and catatonia due to another medical condition. While awaiting test results, aggressive supportive measures were initiated, and psychotropic medications were withheld to potentially reverse over sedation due to antipsychotic medication, NMS, or delirium.

**Conclusions:** As our patient's mental status gradually improved during the following week, antipsychotic medications were inferred to be causative, *ex juvantibus*. Diagnostic ambiguity remained however, as additional mental status examinations, neurologic examinations, diagnostic and laboratory results lent support to all entities considered in the differential. Diagnostic complexity abounds in psychiatric practice – in this case, the complexity was concentrated into a single symptom, stupor.

#### 19. PERSON-CENTERED CARE AND ACCESS TO DRUGS IN THE DIGITAL ENVIRONMENT: TO CURE OR TO SELL.

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**Introduction/Objectives:** We live in an era where technology undoubtedly plays an important role in our daily lives, making us better and more efficient individuals. Moreover, it is fair to say that we have become increasingly technology dependent. The technology, and in particular digital technology is all around us, and it would be challenging to envision life without it. This is especially true when considering how much technology has improved medicine. Robotic surgeries and artificial organs are no longer science-fiction movie plots, but are implemented in medicine regularly. However, with the wealth of advantages technology has brought, many drawbacks have been overlooked or pushed aside. Thus, it is critical to examine both the beneficial and the negative effects of technology in medicine, and to understand the "invisible" bond between technology and modern medicine. Patients are exposed to

the resources that are suitable for their condition, which are curated by the professionals, but in the same way filtered according to the purpose. This is where it can become tricky. Although online resources can be very useful, problems may arise from the fact that, oftentimes, those resources present selective, simplified and biased information. Further, patients increasingly take that information at face value, and in turn, make potentially harmful health-related decisions based on that. Needless to say, these ill-informed decisions can lead to dangerous and chaotic outcomes.

**Conclusions:** As technology continues to thrive, its effects on modern-day medicine have shown to be both beneficial and potentially harmful. The development of available medications, how they are being accessed, as well as how they are marketed clearly shows the negative and morally questionable impact the digital environment can have on person-centered care. Without a proper channel that provides consumers with accurate information, the existence of misinformation regarding medications can have detrimental effects. As a result we would all be witnesses to a better health system that has minimized risks and maximized benefits.

## 20. THE CONNECTION OF THE NITROSATIVE AND OXIDATIVE STRESS WITH THE DEPRESSIVE DISORDER.

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**Introduction/Objectives:** Depression is one of the leading causes of disability and lessening of the functioning, that is, of the morbidity and mortal rate around the planet. In the recent years the effort has been made by some scientists to find the central cause of this and to find the right pathophysiological area of this disorder. The aim of this study is to research the potential role of nitrosative and oxidative stress in people who got ill from this disorder as well as the connection of the tested markers with the anxiety and suicidal intentions at depressive patients.

**Participants, Materials/Methods:** There were 70 participants included in the research (39 depressive patients and 31 healthy control subjects.). The participants were accustomed according to their gender, age, and place of living. By the analysis of the sample of the serum the amount of the malondialdehyd were specified (MDA), the amounts of nitrates and nitrites ( $\text{NO}_2 + \text{NO}_3$ ) as well as the activity of superoxidismutasis (SOD). With the aim to get the necessary data the following were applied: the general

semi-structural interview, PHO-9 scale, BAI scale, Scale For Suicide Ideation Of Beck, Holmes and Rahe Stress Scale. The statistical analysis was done by standard statistical methods.

**Results:** The values (amounts) of MDA were significantly higher and SOD significantly lower in the group of the depressive patients in comparison to the control group of subjects ( $p < 0.05$ ). SOD showed the negative correlation with the result for depression of PHQ-9 questionnaire as well as for the anxiety of BAI questionnaire. What was not noticed was the correlation between the intensities of stress as well as with the suicidal intentions with the tested biomarkers.

**Conclusions:** The results that were noted by this test confirm lowering of the oxidative capacity at within the depressive patients. The intensity of the anxiety included in a depressive disorder can be connected with the change in redox status.

## 21. CONCENTRATION OF THE BRAIN-DERIVED NEUROTROPHIC FACTOR IN DRUG FREE SCHIZOPHRENIC PATIENTS FOLLOWING ACUTE ANTIPSYCHOTIC TREATMENT WITH OLANZAPINE.

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**Introduction/Objectives:** Alterations in Brain-derived neurotrophic factor (BDNF) concentration could be responsible for disturbance in neuroplasticity and synaptic connectivity in the brain that could be connected to neuronal dysfunction in mental disorders, such as schizophrenia. The role of BDNF as possible biomarker for schizophrenia has been highly targeted with inconclusive results. Studies on the early effect of antipsychotic treatment correlated with changes in both serum and plasma BDNF in the same sample remain rare. Animal studies show increase of BDNF concentrations in brains of animals treated with olanzapine after exposure to chronic stress. Longitudinal studies in schizophrenic patients showed variable results on effect of olanzapine on changes in peripheral BDNF concentration. Aim of this study was to determine possible early effect of antipsychotic treatment on both serum and plasma changes in BDNF concentration in acute schizophrenic drug-free patients.

**Participants, Materials/Methods:** For the schizophrenic patients (N=28) who were in hospital treatment because of acute psychotic episode, BDNF was evaluated in three time points: baseline (without treatment), after 2 and 6 weeks of

the treatment with atypical antipsychotic olanzapine. Positive and negative syndrome scale (PANSS) and Clinical global impression scale (CGI) were used for clinical psychiatric assessment. Mean age of participants was 30 years. Participants were drug free from antipsychotic treatment at least 6 months before the inclusion in the study. Duration of psychosis was no longer than 5 years, with 0-1 prior psychotic episode.

**Results:** Results did not show significant changes in both plasma ( $\chi^2=.673$ ,  $df=2$ ,  $p=.714$ ) and serum ( $\chi^2=1.748$ ,  $df=2$ ,  $p=.280$ ) concentration of BDNF from baseline to after 2 and 6 weeks of treatment with olanzapine. Improvement in clinical status was followed with significant changes in both PANSS and CGI score. There were no significant correlation between plasma and serum BDNF concentration and changes in clinical status in PANSS and CGI. Correlation between the baseline values of plasma and serum BDNF concentrations was significant ( $r=.349$ ).

**Conclusions:** The role of BDNF in etiopathogenesis of schizophrenia is yet to be elucidated. Possible monitoring of the early brain function response to antipsychotic treatment related to BDNF could be valuable as marker of clinical and treatment outcome. Further studies should include larger samples, different periods of duration of psychosis and longitudinal follow up of BDNF changes on antipsychotic treatment.

## 22. EMOTIONS AND MOTIVATIONS IN CHILDREN AFTER SPINAL TRAUMA AT EARLY REHABILITATION.

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**Introduction/Objectives:** Psychological and psychiatric disorders of varying severity are revealed after a spinal trauma (ST). Emotions after SCI are studied in adults; data on the study of emotional disorders in children, and their medical treatment is not. Aims: to evaluate emotions and motivations in children after severe ST in early rehabilitation

**Participants, Materials/Methods:** Materials and methods: 35 children with severe ST (8-18 years old) admitted to treatment and rehabilitation. Psychological and psychopathological methods were used. Diagnostic scales and questionnaires used to detect depression, to assess the severity of individual symptoms.

**Results:** Results: three groups of children were identified, depending on emotional disorders and their severity: 1 -

with depression 6 (2 boys, 4 girls from 14-17 years old), 17.2%; 2 - with high anxiety, decreased motivation, with subdepressive prerequisites 11 (4 girls, 7 boys from 12-16 years old), 31.4%; 3 - no depression or depressive tendencies 18 (15 boys, 3 girls, 8-17 years old), 51.4%. Children with a lowering of emotions, with an average or low level of anxiety, but a safe motivation, needed only the accompaniment of a psychologist. Children with a decrease in emotions, medium or high levels of anxiety and low motivation needed the treatment of a psychiatrist and a psychologist. Children with depression, high anxiety and low motivation required the supervision and medical treatment of a psychiatrist.

**Conclusions:** Conclusions: 48.6% of children after severe spinal injury there are emotional and motivational disorders. These children should be treated by a psychiatrist and a psychologist at the early stage rehabilitation. Differentiated assistance will allow carrying out rehabilitation tasks with high efficiency.

## 23. THE NEED FOR A MULTIDISCIPLINARY APPROACH AND INDIVIDUAL SCOPE IN FOCUS.

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**Introduction/Objectives:** As there were several methods in practice commonly used in treatment of patients with alcohol dependencies (known as patients with high comorbidity and several mental disorders), there are common expectations about multidisciplinary approach as the best way to treat these patient. This article is also dealing with the second, very important need-the need for detailed insight in patient's specific somatic(biological), psychological, and social status, system of beliefs, working habits, motivation, expectation, responsibly built within the family, referral group and common society. Individual approach includes use of specific knowledge about patient, impression taken at the screening, but also during regular treatment what improve possibility for best individual approach and implementation of adaptive training, new learning what brings functionality and practice, and implementation strategies with idea to support individual to learn skills that may help patient to adapt to specific requests after being treated at Department for treatment of alcoholism and /or within Daily hospital Experiences taken in daily work with patients are described and summarized and serve as a starting point for short overview and efforts for implementation of specific programs that meets the needs of patients and daily practice. Treatment should be beneficial

for patient, make him/her much more stronger but also functional and able to cope with daily requirements.

**Participants, Materials/Methods:** Descriptive method; summary of activities performed with 20 patients within the treatment for patients treated at the Department for alcohol and other dependencies in Hospital Popovača/ Daily Hospital for alcohol dependencies working at two locations- is to be provided; include different methods that activate need for learning, adoption of new sights, adaptation, education process, learning about group and in the group, individual experience, training in self-presentation and self esteem, emotions expression, sharing and taking emotions, building trust and criticism, group spirit, interest for others, mirror experience, copying, taking responsibilities, playing roles, talking about planned steps when leaving safe "treatment area" and treatment period. etc

**Results:** Results (qualitative data) are summarized for several patients and families and considered as positive feedback and support for methods used and future improvement; results motivate team to continue to use multidisciplinary approach and individually centered methods with focus and awareness on patients specific characteristics and needs.

**Conclusions:** Results support use of psycho-bio-social model and underline importance of sharing all important data within multidisciplinary team with continued efforts for further investigation how to improve individual plan and treatment in accordance with patient's specific needs. These efforts are with a purpose patient to achieve best adaptation in accordance to family, work and social requests from one side, and from other side feel good, self confident, relaxed and motivated and accepted. From social and health-insurer-s level it is also very important to keep stable remission and make individual strong within local community and included in different support groups (also groups with support for treated alcoholics) trying to avoid return to the hospital within short timeframe. These efforts may be productive if relevant instances may be active support while planning and organizing these activities and active politics may do much more here.

#### **24. CHILDREN WITH MENTAL HEALTH DISORDERS IN EDUCATION SYSTEM.**

Filip Mustač, Vera Musil

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**Introduction/Objectives:** Mental health problems could affect children's functioning at home, in school and among peers. Mental health disorders belong to special needs, such

as developmental difficulties, disability and other severe medical conditions. The aim of this paper was to analyze education of children with mental health disorders.

**Participants, Materials/Methods:** For the purpose of this paper we analyzed data in Report on Disabled Persons in the Republic of Croatia 2017. Children with mental health disorders are educated according to Regulation on Primary and Secondary Education of Students with Difficulties. Children with special needs require suitable education program and receive suitable professional support. Depends on individual's capacities and capabilities, suitable education program could be: regular program with individualization, adjusted program, special program and program of autonomous life training. Suitable education program could be applied in regular class in regular school (complete inclusion), partly in regular and partly in special class in regular school (incomplete inclusion), in special classes in regular school or in special schools. If necessary, students could receive extended professional treatment or rehabilitation, be supported by personal assistant / professional communication mediator, or to attend temporary form of education at home or in healthcare facility.

**Results:** According to The Report on Disabled Persons in the Republic of Croatia 2017, there are 511910 people with disability and developmental difficulties. Out of them, 32101 (6.2%) are children (62% boys). Mental health disorders, intellectual disability (16.3%), mental and/or behavioural disorders (10%) and pervasive developmental disorder/autism (3.9%), are present in more than one third of children as a reason of disability. Five children were reported as tried to commit a suicide and 36 are registered as exposed to or suffer from some kind of violence. Suitable education program was applied for total of 21555 children (64% boys) in Croatian schools. In The Report, here is no data about number of children with mental health disorders included in suitable education program, being educated at home or in healthcare facility and stopped with education.

**Conclusions:** The results of the analysis showed the significance of care, treatment, follow up and multidisciplinary support of children with mental health disorders during education. Beside medical treatment and support it is necessary to ensure development and maintenance of student's cognitive, social, emotional and physical needs. The results imply necessity of improvement and empowerment of inter-sectoral cooperation - medical, educational and social, in care and support of children with mental health disorders.



## 25. DEPRESSION, LOWER URINARY TRACT SYMPTOMS AND SEXUAL DYSFUNCTION IN CROATIAN OBESE PATIENTS.

Filip Mustač, Katarina Ivana Tudor, Martina Matovinović, Nenad Jakšić, Andrej Kovačević, Zrinka Vuksan-Ćusa, Ervina Bilić, Bjanka Vuksan-Ćusa, Marina Šagud

University Hospital Center Zagreb, School of Medicine, University of Zagreb, Zagreb, Croatia; The Croatian Institute of Emergency Medicine, Zagreb County, Croatia; Department of Neurology, University Hospital Center Zagreb, School of Medicine, University of Zagreb, Zagreb, Croatia; Department of Internal Medicine, Division of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia; School of Medicine, University of Zagreb, Department of Psychiatry, University Hospital Center Zagreb, Zagreb, Croatia; Department of Neurology, General Hospital Virovitica, Virovitica

**Introduction/Objectives:** Depression is highly prevalent among individuals suffering from obesity, and so are various other somatic complaints and disorders. The aim of this research is to assess the association between symptoms of depression, lower urinary tract symptoms (LUTS) and sexual dysfunction in Croatian obese patients.

**Participants, Materials/Methods:** This cross-sectional study was carried out in a tertiary healthcare centre in an outpatient clinic for treatment of obesity. Overall, 111 participants (73% women), mean age  $49.03 \pm 12.21$  years, BMI > 30, were included. ICIQ-OABqol questionnaire was used to assess the quality of life in patients with LUTS. Sexual dysfunction was evaluated through Arizona Sexual Experience Scale (ASEX). Depression was documented with the general information questionnaire where patients marked all the illnesses they were being treated for. Statistical analysis included bivariate Pearson's correlations.

**Results:** Significant correlation was found between the presence of depression and the impact of urinary symptoms ( $r=0.21$ ,  $p=0.03$ ). Furthermore, significant correlations were observed between the impact of urinary symptoms and following complaints: pain/uneasiness ( $r=0.29$ ,  $p=0.001$ ), anxiety/melancholy ( $r=0.3$ ,  $p=0.001$ ) and sleep disorders ( $r=0.25$ ,  $p=0.01$ ). According to our study, sexual dysfunction was (significantly related to depression ( $r=0.22$ ,  $p=0.03$ ). Moreover, sexual dysfunction also significantly correlates with pain/uneasiness ( $r=0.22$ ,  $p=0.03$ ) and anxiety/melancholy ( $r=0.2$ ,  $p=0.04$ ).

In addition, a significant association was observed between obtaining an overall score above 3.8 (standard cut-off score) on the sexual dysfunction questionnaire (ASEX) and the presence of depression ( $r=0.27$ ,  $p=0.01$ ). Finally, an overall score above 3.8 on ASEX was significantly associated with

pain/uneasiness ( $r=0.23$ ,  $p=0.02$ ) and anxiety/melancholy ( $r=0.21$ ,  $p=0.04$ ).

**Conclusion:** While the presence of depression was associated with sexual dysfunction and the impact of urinary symptoms in obese individuals, cross-sectional data precludes causality assessment. It remains to be determined whether treating symptoms of depression might alleviate those somatic difficulties.

## 26. MENTAL HEALTH PROBLEMS IN MEDICAL STUDENTS.

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**Introduction/Objectives:** Mental health is essential part of well-being at each phase of life, from childhood to adulthood. It includes psychological, emotional and social comfort and influences way of feeling, thinking and acting. Mental health status regulates how person make choices, relate to others, and handle stress. Demanding medical education could influence mental health of students. The aim of this study was to examine and compare mental health problems of male and female first year medical students of two generations.

**Participants, Materials/Methods:** The study was conducted at first year of medical study University of Zagreb. Generation in academic year 2006/2007 comprised 186 participants (64.5% female) and in 2016/2017, 287 (60.3% female). Data was collecting using anonymous questionnaire. For the purpose of this study answers about mental health problems were analysed using descriptive statistics.

**Results:** Sense of apathy (F 20% vs. f 17%; M 16.7% vs. m 16%), feeling irritable (F 22% vs. f 20%; M 15.2% vs. m 11%) and being nervous (F 30% vs. f 27%; M 29.2% vs. m 18%) more than once a week were present more often among female compared to male students, in generation 2006/07 then in generation 2016/17. Sleeping difficulties more than once a week were reported more often among female students of generation 2016/17, while among male students were more present in generation 2006/07 (F 12.6% vs. f 14%; M 15.2% vs. m 7%). Sleeping pills were used more often among female compared to male students in both generation and among female students in generation 2006/07 (F 4% vs. f 2%; M 3.2% vs. m 3%). Anti-anxiety medications were used more often among female and male students of generation 2006/07 (F 10% vs. f 2%; M 4.8% vs. m 1%).

**Conclusions:** The results of this study showed that mental health problems were more present among first year students in generation 2006/07 compared to generation ten years later and more among female students. The results imply better mental health status, motivation and preparation for medical study among students of generation 2016/17 that could be possibly explained by increased quota for medical study in recent years and solid perspective of employment and carrier for medical doctors. Presence of mental health problems implies necessity of counselling and mental health services as a part of specific care within current organisation of health care for students.

## 27. OMNIPOTENCE AND HELPLESSNESS OF NARCISSISTIC CULTURE.

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**Introduction/Objectives:** Narcissism is on the rise, both in individual cases, as well as on the collective-cultural level. Perfectionism, which is present all around us, pushes the modern man to become a part of the consumer world where only power and wealth are appreciated. Technology is also having a remarkable progress and man's emotional life cannot keep track of it, which is the reason why people feel more alienated and empty. The aim of this review is to conceptualise narcissism in contemporary culture and to analyse how aspiration to perfectionism and grandiosity makes people seek for revenge and other destructive actions.

**Participants, Materials/Methods:** Various scientific papers and specialized psychotherapeutic and sociological literature are elaborated and discussed in this review, focusing on summarizing the problems of narcissistic culture.

**Results:** Today's culture is marked with abundance – there are more, better things and possibilities, technology progresses rapidly, people live longer with better living conditions etc., which indicates that we should be happier, but is it so? Unfortunately no, we are obsessed with omnipotence, success and perfectionism, in order to prevent facing the endless emptiness and boredom inside us. Money and consumerism became the focus of society, leading us to envy those who have more, which is constantly followed by feeling of our own inadequacy and less value. According to Lasch, superficiality is protecting us from our fears that enslave us. We live in an instant culture, everything needs to be done without or with minimal effort, but results must be grandiose, perfect, soaked in fame and wealth. In that instant culture we are unable to bear with even minor, everyday frustrations. When somebody doesn't do something, what

we only imagined in our grandiose entitlement that we deserve (narcissistic position), we impulsively want to destroy that object. That results with revenge fantasies, which in instant culture cannot be delayed and transformed into structured critic, but must be acted out as revenge acts. That is how we make narcissistic atmosphere prone to revenge and unable to love.

**Conclusions:** Narcissism presents a complex problem of society nowadays, with many examples of narcissistic features increasing in modern culture, which implicates that methods and approaches that offer a solution for reparation and forgiveness should be thoroughly explored. Future researches are needed for further examination of this widely spread sociological phenomenon.

## 28. PROBIOTIC SUPPLEMENTATION IN REDUCING SYMPTOMS OF PTSD – FUTURE POSSIBILITIES.

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**Introduction/Objectives:** Posttraumatic stress disorder (PTSD) is disturbing disorder with a delayed response triggered by the stressful events. That experience is so painful that those people cannot integrate it, nor they can move on. The most significant symptoms are recurrent, involuntary distressing memories, dreams and dissociative reactions (flashbacks), arousal alterations and similar experience. Croatian Homeland War Veterans are due to experiences in The Homeland War often burdened with symptoms of PTSD. 16% of them have PTSD, and even 25% of them have some signs of PTSD. Dysbiosis of the gastrointestinal tract is associated with many systemic diseases and neuropsychiatric disorders, including mood disorders and stress-related disorders (PTSD). This thesis aims to examine how does microbiota affect the course of the disease and does the use of the probiotics ameliorate the severity of discomfort.

**Participants, Materials/Methods:** Investigating existing studies about probiotics interventions on individuals with PTSD. We used relevant scientific papers from psychiatry and internal medicine as well as clinical nutrition findings.

**Results:** Gut microbiota consists predominantly of Bacteroidetes, Firmicutes and Proteobacteria phyla but various factors (environment, genetics, diet, antibiotics) can influence its content causing dysbiosis. Gut bacteria influence on the central nervous system via the gut-brain axis. There are several mechanisms including production of

short-chain fatty acids (butyrate, acetate) that can activate the sympathetic nervous system and alter the activity of cells located in the blood-brain barrier. Gut microbiota secretes neurotransmitters (serotonin, dopamine) which can affect emotion regulation. Furthermore, chronic stress affects microbiota composition and activates gut-brain axis. It can elevate pro-inflammatory cytokines that increase the permeability of the blood-brain barrier and regulate CNS function and behavior. Several studies showed that supplementation with specific probiotics could have positive effects on the brain and behavior implicating the role of the microbiome in the treatment of PTSD. Preexisting studies are showing promising effects with probiotics supplementation in combat-related PTSD. Studies showed the reduction of anxiety, derealization, panic, widespread infection and headache that represent the major issues in patients with PTSD. Also, supplementation with probiotics has a positive effect on the overall well being through different mechanisms of which the most pronounced are regulation of bacterial homeostasis on the gut level and improved bioavailability of food supplements and medication used to reduce the symptoms of PTSD.

**Conclusions:** Promising effects have been observed while also using probiotics in the amelioration of disease symptoms of PTSD. However, additional studies in this challenging therapeutic are needed.

## 29. THE UNBEARABLE SYMBIOSIS IN NARCISSISTIC/BORDERLINE INTERACTION.

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**Introduction/Objectives:** Personality disorders are characterized by maladaptive patterns of behaviour, which suggests that relationships of people suffering from these disorders can often be dysfunctional. The connection between a narcissist and a borderline can be particularly twisted, because they complement each other in their own pathology. The aim of this paper is to provide an overview of narcissistic/borderline interaction, to define problems they are facing with and to offer some solutions of resolving them.

**Participants, Materials/Methods:** A literature search was conducted, including both scientific papers and expert textbooks, in order to identify relevant publications and present current psychodynamic explanations of interpersonal relations on the example of two selected personality disorders.

**Results:** The relationship between a narcissist and a borderline is highly complex and fulfilled with opposite feelings that show regressive behaviour – love/hate, optimism/pessimism, power/hopelessness, intimacy/envy, shame/guilt and many others. These rapid changes from omnipotence to “disappearing” are the exact reason why, in any interaction, they are always on some kind of the edge and prone to a twisted, tangled conflict. The narcissistic omnipotence and entitlement can be easily injured by a provocation of a borderline, resulting in withdrawal of the narcissist. The borderline then struggles with the intense fear of abandonment and starts endlessly apologizing. At first, the narcissist is too angry to talk about continuing the relationship, but agrees to it later due to tremendous need of an object in which he/she can project all negative feelings and which will boost his/her own grandiosity, while simultaneously feeling more guilt than shame in comparison to borderline. Borderline is thrilled because he/she won't disappear and the vicious circle of this unbearable symbiosis continues.

**Conclusions:** Despite the fact that narcissist and borderline encounter many problems in their interaction and that psychotherapy for these couples can be challenging and demanding, there are various well developed techniques and procedures used in couple therapy, aimed at reaching conflict resolution, which can lead to improvement and advancement of their relationships.

## 30. DEPRESSIVE DISORDERS IN PATIENTS WITH PRIMARY HYPOTHYROIDISM.

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**Introduction/Objectives:** Early detection of mental disorders in somatic patients and the organization of their adequate therapy by physicians are extremely important, as stigmatization is still a strong counteracting factor - the negative attitude of patients to a psychiatrist due to the widespread misrepresentation of psychiatry in the population.

**Participants, Materials/Methods:** We examined 132 patients with primary hypothyroidism at age of from 25 to 55 years. Structural interview was the main method of assessment.

**Results:** In 108 patients (81.12%) there were various forms of nonpsychotic mental disorders, among which 12.04% patients had anxiety-depressive syndrome and 32.41% developed asthenia-depressive syndrome. Depressive disorders did not reach the level of severe with severe

depressive affect and were accompanied by apathy manifestations. There were pessimistic views on life, a sense of pointlessness, the lack of prospects of existence, the loss of the content of being, the decline of initiative and anhedonia; increased fatigue, distractability, inability to concentrate supplemented the clinical picture of asthenia-depressive syndrome. Along with violation of appetite, they showed a decrease in interests, energy and efficiency, indifference, lack of motivation to work, a tendency to underestimate self-esteem and a sense of confidence in themselves and their forces. Frequent and more profound among these patients were sleep disorders (violation of night sleep, presomnic, intrasomnic and postsomnic disorders, affectively saturated, anxious and frightening dreams). The balance between individual episodes of mild depression and periods relative to the normal state was very variable. Patients themselves indicated on weeks or days that they regarded as normal, but most of the time, they experienced a bad mood, decreased energy, disability, fatigue: from the words of patients, "everything became very difficult", "nothing pleases", "the outside world tired, " there is no prospect for the future", " existence is pointless, "something that previously had value, lost its value". These patients were prone to stubborn thoughts and intrapsychic processing of their own feelings.

**Conclusions:** Thus, biopsychosocial approach is of great importance in order to achieve high quality of medical help. It includes the application of elements of rational psychotherapy, in particular explaining to patients the mechanisms of their illness, explaining the need for an analysis of their emotional experiences and the situation surrounding them, in order to create a sense of control over their own state and the ability to absorb the negative effects that contribute to stabilization and compensation their general condition and quality of life.

### 31. A TUNNEL BETWEEN DEPRESSION AND DEMENTIA – FOLIC ACID , VITAMIN B12 AND HOMOCYSTEINE – A CASE REPORT.

Iva Radoš, Marina Šagud, Biljana Kosanović - Rajačić

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**Introduction/Objectives:** Depression is a common mental disorder, characterized by persistent sadness and a loss of interest in activities that you normally enjoy, accompanied by an inability to carry out daily activities, for at least two weeks. Dementia is a syndrome – usually of a chronic or progressive nature – in which there is deterioration in cognitive function (i.e. the ability to process thought) beyond what might be expected from normal ageing. It

affects memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgement. Consciousness is not affected. The impairment in cognitive function is commonly accompanied and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation.

**Participants, Materials/Methods:** A depressed patient ( female, 64 age ). Hamilton Depression Scales, Montgomery-Åsberg scale for depression and Mini mental state examination. Laboratory values of vitamin B 12 and folic acid values.

**Results:** The patient comes to the first hospitalization under the image of depressive disorder. The first symptoms occur one year back. The patient then feels bad, has low moods, worried, anxious, having difficulty sleeping and loss of appetite. The patient also provides information that she loses things, that she can not remember what to do and can not remember people and events. Determination of vitamin B 12 and folic acid which showed lower values, and Hamilton Depression Scales (26 points ) and Montgomery-Åsberg scale for depression (35 points ). We also have done Mini mental state examination ( 17 points ).

**Conclusions:** Previous research has shown that reduced values of vitamin b 12 and folic acid are present in some patients with depression and dementia. In our case report we want to point out that vitamin B12 and folic acid are probably the link between these two diseases and in the future one of the markers of these two diseases.

### 32. SLEEP AND RELATED HABITS IN PTSD PATIENTS.

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**Introduction/Objectives:** The symptoms of PTSD are categorized into three groups: re-experience, avoidance and hyperarousal. One of the main symptoms of hyperarousal is insomnia. Insomnia is defined by the presence of any of the following symptoms: persistent symptoms of trouble falling asleep, staying asleep or waking up too early in the morning – accompanied by at least one symptom of impaired daytime function. The aim of our study was to analyse sleep hygiene and related habits in PTSD patients and the difference between PTSD and Complex PTSD.

**Participants, Materials/Methods:** Participants of our study were 90 male war veterans diagnosed with PTSD who are currently in psychiatric treatment in Regional center for psychotrauma, Clinical hospital center, Split. For that purpose we used ITQ (International Trauma Questionnaire)



which represents newly developed instrument for distinction between PTSD and Complex PTSD. Three additional symptoms characterize complex PTSD: Affective dysregulation, Negative self-concept and Interpersonal difficulties. As an insomnia measure we used Sleep and related habits questionnaire providing us with information about sleep problems and physical activity.

**Results:** Results have shown that all participants have persistent sleep problems but the majority (73,33%) of them had trouble staying asleep. 56,66% of participants stated having trouble falling asleep while only 6,67% stated they sleep during the day. On the average our participants sleep only 5 hours during weekdays and on the weekend. 62,2% participants are currently using medications or alcoholic beverages to help them fall asleep. 50 (56,82) our participants engaged in activities leading to sweating or increased HR at least once a week. Average amount of time spent in vigorous activity was 3,5 hours per day, 2,5 hours of moderate activity per day and 2 hours of light activity per day while average sitting activity was 3,5 hours per day. We found no statistically significant difference in all measured parameters between PTSD and Complex PTSD patients.

**Conclusions:** This study showed that PTSD patients have major sleep problems. Even though a lot of participants are physically active and regularly use sleep medications they still sleep only 5 hours on average which additionally describes the severity of this problem. This is an important finding in the understanding of the sleep disorders in PTSD patient population. In future studies, more factors and therapeutic techniques should be considered when dealing with insomnia.

### 33. QUANTIFICATION OF PSYCHOSTIMULANT SELF-ADMINISTRATION IN DROSOPHILA MELANOGASTER.

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**Introduction/Objectives:** Self-administration is one of the behavioral endophenotypes associated to addiction and serves as a measure for the rewarding effect of the drugs. Voluntary consumption of addictive drugs can be studied in model organism, such as *Drosophila melanogaster*, fruit fly.

**Participants, Materials/Methods:** We have previously showed that *Drosophila* preferentially consumes cocaine (COC) and methamphetamine (METH) containing food over the regular food using the two-choice Capillary Feeder (CAFE) assay. To measure in more detail psychostimulant (COC and METH) induced increase in locomotion after

self-administration and preference to location of capillary containing drug on individual level we have developed a high-throughput assay using the concept of CAFE assay in combination with *Drosophila* Activity Monitoring system (DAMs). In this new assay, we can measure: the amount of psychostimulant that flies self-administer, locomotor activity during the exposure to drugs and percentage of time spent by the food capillaries.

**Results:** Our results show that the total amount of consumed food did not differ among control, COC or METH fed flies and there was no side preference in the control group with choice of sugar food only. When presented with the choice of sugar-based food with or without added COC flies did not show the preference for COC over sugar, likely due to the fact that COC is a bitter tasting alkaloid. However, COC containing food did not lead to aversion, suggesting that in spite of bitter taste COC-containing food was as palatable as sugar-based food. Flies voluntarily administered and showed distinct preference for METH over sugar-based food, suggesting that METH activates motivational and reward circuits in *Drosophila*'s brain.

**Conclusions:** These findings indicate that complex drug-related behaviors such as voluntary drug consumption can be successfully quantified in invertebrates. In the future this method can be used in a genetic screen to identify genes that influence regulation of preferential drug consumption or in selective breeding experiments to select for high versus low METH preferring flies.

### 34. AN AUDIT OF SODIUM VALPROATE PRESCRIBING TO FEMALES OF CHILD BEARING AGE WHO ATTEND AN INTELLECTUAL DISABILITY SERVICE.

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**Introduction/Objectives:** The European Medicines Agency introduced stricter regulations in 2018 to minimize the teratogenic risk associated with valproate use during pregnancy. These state that valproate is contraindicated unless the pregnancy prevention program conditions, which include the use of highly effective contraception, are fulfilled. The regulations also apply to women who are not sexually active unless there are 'compelling reasons' to indicate that there is a low risk of pregnancy. For those without the capacity to make an informed decision the same

information advice should be provided to their parents/caregiver or responsible person. Objectives: To audit females of child bearing years prescribed valproate across Daughters of Charity, Dublin, services and assess: • The prescribing of highly effective contraception. • The capacity to understand the pregnancy protection plan requirements

**Participants, Materials/Methods:** Data was collected for all females aged 24 to 60 years prescribed valproate. A minority of the cohort was screened directly and the remainder through collateral from a familiar carer or nurse. Participants were given the valproate patient information booklet in advance and interviewed with a standard questionnaire regarding their understanding the teratogenic risks associated with valproate use. Parameters gathered included; indication for valproate, degree of intellectual disability (ID), capacity, psychiatric diagnosis, prescription of contraception and highly effective contraception.

**Results:** In total 51 females were identified, aged between 24 to 60 years inclusive. The vast majority lived in residential services (92.1 %, n= 47) the remainder being day attendees (7.8%, n= 4). Level of ID; mild (9.8%, n=5), moderate (49%, n=25), severe (39%, n=20), profound (1.2%, n=1). Indication for valproate; epilepsy (84.3%, n=43), mental health (15.8%, n=8). Capacity present = (5.9% n=3). Contraception was prescribed for (11.8 %, n=6) but only (5.9 %, n=3) were prescribed highly effective contraception

**Conclusions:** The majority of this cohort lacked capacity and highly effective contraception was rarely prescribed and then for reasons other than pregnancy prevention. Further guidance is needed around the ethics and risk/benefit of prescribing highly effective contraception to women on valproate with intellectual disability who lack capacity.

### 35. DE NOVO ARTERIAL HYPERTENSION IN PATIENTS WITH POST TRAUMATIC STRESS DISORDER.

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**Introduction/Objectives:** Post-traumatic stress disorder (PTSD), according to the DSM V is a direct experience either of observation or knowledge of an event or traumatic events to which the person responded with fear, impotence and horror, which produced symptoms consistent with this pathology. such as persistent experimentation of the traumatic event, the avoidance of stimuli associated with trauma, a decrease in the ability to react and symptoms that activate the sympathetic nervous system in a repetitive manner, which leads to sleep disorders, mood disorders and

even organic diseases. which is the central axis of this research.

**Participants, Materials/Methods:** participants: authors materials: medicine databases: Ovid, Pubmed, Embase, among others Method: state of the art **Results:** It has been found in different scientific literature that there is a relationship between PTSD and cardiovascular problems, mainly hypertension (HBP); The most prevalent cause of mortality in this population are cardiovascular diseases, with the incidence of HBP being 34% in the population over 50 years of age. In the pathophysiology of PTSD we can find an alteration in the endogenous opioid system which is responsible for the release of analgesic substances, in addition there is alteration in the serotonergic system since it modulates brain activation or the aero-al and noradrenergic system, due to the PTSD, serotonergic levels decrease, which makes it difficult to control the level of brain activation, producing symptoms consistent with inappropriate behavior in humans characterized by aggressiveness, hypersensitivity and hyperirritability. The pathophysiology of hypertension is characterized by endothelial dysfunction due to the alteration of vasodilator and vasoconstrictor factors, and an increase in intravascular volume is also involved in this process. Hypertensive patients have stiffer arteries, which is a prediction of acute cardiovascular problems.

**Conclusions:** Regarding the pathophysiology of both diseases, there are several shared pathophysiological mechanisms between these two pathologies. Among the various mechanisms that have been studied and probably produce PTSD, we find a hyperreaction of the sympathetic nervous system which is in tune with fear which causes the amygdala and the ceruleal locus to deregulate and their dopaminergic bodies to produce an increase in dopamine; In addition, it increases the production of catecholamines, which, if they occur chronically due to stressful hyper stimulation, will produce arteriosclerosis as a consequence, which ultimately produces cardiac ischemia. In conclusion, patients who suffer TEPT are more likely to develop arterial hypertension.

### 36. THE EMOTIONAL DISTURBANCES IN PATIENTS WITH THYROTROPINOMA.

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**Introduction / Objectives:** Thyrotropinoma (TSH-secreting pituitary adenomas, TSH-AG) is a rare tumor of the pituitary gland (0.5-2% of all pituitary adenomas). Localization of the tumor with the appropriate neuroendocrine disorders has been featured in the clinical presentation. This is due to the direct damage to the nucleus and the structures of the pituitary gland with hypersecretion of TSH, which leads to overstimulation of the thyroid gland and the emergence of a clinical picture of "central" hyperthyroidism. Differentiated diagnosis of these disorders will help physicians to set the correct diagnosis of thyrotropinoma with an interdisciplinary approach. The aim of the study was to analyze emotional disturbances in the structure of the clinical picture of thyrotropinoma.

**Participants, Materials / Methods:** 26 patients with pituitary adenomas, normal or elevated TSH levels in combination with elevated levels of St.T4, St.T3, administered to the Institute for treatment (2002-2017). 14 women (54%) and 12 men (46%), 15-67 years old (median 38.5 years). All tumors belonged to macroadenomas (by MRI), the diameter was 14-64 mm (median 26 mm). All patients underwent a study of the levels of TSH, St. T4, St. T3, prolactin, cortisol, LH, FSH, estradiol / testosterone, in 18 cases - the study of the levels of ICF-1. The reference values were: TSH (0.4-4.0) mU / l, St. T4 (11.5-22.7) mmol / L, St. T3 (3.5-6.5) mmol / l, antibodies to the TSH receptor (<1.0 mU / l). The criteria for inclusion in the study were high levels of free fractions of thyroid hormones and elevated levels of TSH.

**Results:** The clinical presentation was shown with symptoms of hyperthyroidism in 21 (80.7%) patients, anamnesis from 1 to 13 years (median 3 years). Emotional pathology was detected in 57.6% (n = 15): anxiety-phobic disorders in 50%, panic attacks-46.1%, depression-11.5%. Patients complained of: increased fatigue and weakness - 8 patients, heartbeat - 13, "anxiety" - 9, mood lability - 14, sleep disorders - 5, sweating - 5, hand tremor - 3, subfebrile temperature - 2, weight loss - 2. And these symptoms combined with each other. The severity of psychopathological symptoms was often moderately severe (65%). 8 patients received psychotropic therapy before diagnosis, 5 of them were seen by a psychiatrist for a long time.

**Conclusions:** The clinical picture of TSH-AH consists of the symptoms of hyperthyroidism and the mass-effect of the tumor. Emotional disturbances occur in 57.6%. The interdisciplinary approach will allow: 1) to carry out an early diagnosis of these tumors with the specification of the differential diagnosis of conditions with hyperthyroidism; 2) to conduct adequate medical treatment, including specialized neuropsychopharmacotherapy.

### 37. THE NEUROPSYCHIATRIST IN THE MULTIDISCIPLINARY TEAM IN REHABILITATION AFTER BRAIN INJURY IN CHILDREN.

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**Introduction/Objectives:** Based on the experience of treatment and rehabilitation of children after severe traumatic brain injury (sTBI) in CRIEPT in early recovery of mental activity a multidisciplinary team includes a psychiatrist, to be more precise - a neuropsychiatrist.

**Participants, Materials/Methods:** The rehabilitation tasks of the neuropsychiatrist include clinical diagnosis of the disorders and their drug correction. According to the structure of the Institute, it is accepted that these tasks are performed in the departments of intensive therapy, neurosurgery and rehabilitation. The neuropsychiatrist determines: 1) the level of consciousness, 2) disorders in emotional, personal, motivational, cognitive and motor function, 3) psychotic symptoms.

**Results:** The neuropsychiatrist identifies the main specialized syndrome and compares it with the general clinical picture of the course of the disease, determining the significance of the syndrome of recovery in the dynamics of the general condition, the degree of its influence on the severity of the course of the disease, and the effectiveness of rehabilitation measures. Accounted for: 1) of the developing child's organism and mental development; 2) pathogenesis processes. The neuropsychiatrist recommends drug therapy for correction: 1) of mental recovery, 2) of psychotic disorders. At present after sTBI most drugs are prescribed on the "off-label" principle. The drugs are recommended taking into account the pharmacological effect depending on the disorders of the neurotransmitters: affecting the metabolism of glutamate, GABA, dopamine, choline (acetylcholine), serotonin. Neuromodulating effects have: 1) anti-parkinson medication; 2) muscle relaxants; 3) anti-dementia medication; 4) antidepressants; 5) antipsychotics; 6) hypnotics; 7) anticonvulsants; 8) other neurotropic drugs.

**Conclusions:** A differentiated approach to diagnosis and medical treatment in children after sTBI with regard to the level of lesion, pathogenesis mechanisms resulting from the trauma itself and reactive processes in response to trauma, taking into account the mental development and recovery increases the chances of more effective rehabilitation, recovery mental functions with minimal defects.

**38. THE INTERACTION BETWEEN AGE AT ONSET AND CATECHOL-O-METHYLTRANSFERASE POLYMORPHISM (COMT) ON COGNITIVE FUNCTIONING IN SCHIZOPHRENIA: A 10 YEARS STUDY.**

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**Introduction/Objectives:** Cognitive deficits are core features in schizophrenia. Although longitudinal studies suggested that the impairment of cognitive functioning (CF) is stable over time, the development of CF throughout time has not been investigated yet. Two important features that have been associated with the degree of CF impairment are age at onset and Catechol-O-Methyltransferase (COMT) polymorphism. In details, young-onset patients have more impaired CF than late-onset patients, similarly subjects with the Val/Val genotype were most likely to exhibit cognitive deficits compared to Met carriers. In this regard, the present study aims at evaluating: 1) longitudinal stability of CF over 10 years of illness; 2) longitudinal differences in CF in patients with onset before and after 24 years-old, based on the sample's median value; 3) the role of the interaction between age at onset and COMT polymorphism on CF over time.

**Participants, Materials/Methods:** Sixty-two patients with schizophrenia were assessed for neurocognitive measures at baseline and at 10 years follow-up with Brief Assessment of Cognition in Schizophrenia (BACS) and genotyped for COMT Val158Met polymorphism from peripheral blood sample. Descriptive statistics, paired-samples t-test, repeated-measures ANOVA and general linear model were performed.

**Results:** Our findings supports CF stability over 10 years of illness in the whole sample. However, we found a significant difference in CF between patients with different onset. Moreover, Val/Val homozygous have a different development according to age at onset: an onset before 24 years predicts a significant CF worsening. While, Val/Val patients with an onset after 24 years and Met Carriers present a CF stable over time.

**Conclusions:** The present study highlights the effects of the interaction between age at onset and COMT polymorphism on CF over time. Our results support the protective role of Met genotype on CF, regardless age at onset; instead, Val/Val genotype acts as a vulnerability factor interacting with age at onset, which impact on prognosis of illness in patients with schizophrenia.

**39. ANHEDONIA AND SUICIDE ATTEMPTS IN DEPRESSION AND SCHIZOPHRENIA: IS THERE A LINK?**

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**Introduction/Objectives:** Anhedonia, the diminished capacity to experience pleasure from pleasurable experiences, is cardinal symptom of depression and negative symptom of schizophrenia. While numerous studies reported correlations between anhedonia and suicidality in patients with major depression (MDD), less is known whether those features correlate in patients with schizophrenia. The aim of the present study was to explore the associations between anhedonia and past suicidal attempts in patients with MDD and schizophrenia.

**Participants, Materials/Methods:** Patients diagnosed with schizophrenia or MDD were recruited at the Department of Psychiatry, University Hospital Center Zagreb. All respondents fulfilled the revised Physical Anhedonia Scale (RPAS) to estimate physical anhedonia (PA) and revised Social Anhedonia scale (RSAS) to measure social anhedonia (SA). In addition, patients with schizophrenia were rated by Positive and Negative Syndrome Scale (PANSS), and those with MDD by the Montgomery-Åsberg Depression Rating Scale (MADRS).

**Results:** Overall, 207 participants with schizophrenia (60.9% males, median age 44 years, 21.3% with previous suicide attempts) and 178 subjects with MDD (28.1% males, median age 54 years, 28.1% with suicide attempt history) were included in this cross-sectional study. Within MDD group, in multiple linear regression, MADRS total score significantly predicted PA score ( $p=1.6E-5$ ) and SA score ( $p=3.3E-7$ ). Individuals with prior suicide attempts had higher both PA and SA scores than those without such attempts, although no differences were observed in MADRS total scores (Mann-Whitney test). On the contrary, in respondents with schizophrenia, in multiple linear regression model, neither PA nor SA total scores were associated with the history of suicide attempts. Similarly, the presence of PA or SA was not associated with previous suicide attempts (Mann-Whitney test).

**Conclusions:** Anhedonia was associated with the presence of life-time suicide attempts only in MDD patients, despite similar prevalences of suicide attempt history in both clinical samples. Depressed patients with anhedonia require



particular clinical attention, since anhedonia, rather than depression severity, might relate to suicidal behavior. Suicidality in schizophrenia might be related to symptoms other than anhedonia, such as impulsivity and imperative hallucinations.

#### **40. ARIPIPRAZOLE INDUCED PATHOLOGICAL GAMBLING IN PATIENT WITH ALCOHOL INDUCED PSYCHOSIS.**

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**Introduction/Objectives:** Aripiprazole is a D2 receptor partial agonist. Dopamine agonist drugs (including aripiprazole) can induce pathological gambling, as it was reported before.

**Case report:** We will present the case of a 42 year old male patient with alcoholism complicated with psychosis. At first, the patient used risperidone and sulpiride for psychosis, but this combination of drugs induces sexual dysfunction. The risperidone and sulpiride combination was switched to aripiprazole. The patient used to gamble before, but only for fun and without significant financial loss. After starting to use aripiprazole, he lost control after a few months and started to lose a significant amount of money gambling on the internet, and he had an urge to gamble all the time. In the beginning if we exclude aripiprazole use it seems that one addiction switches to another (alcoholism to gambling), but that was not the case. After switching back to risperidone monotherapy after two weeks the patient stopped feeling the urge for gambling, and no other intervention was necessary. Still, sexual dysfunction emerges again after a month of therapy with risperidone. After that, the patient was switched from risperidone to ziprasidone monotherapy which resulted in restauration of sexual function.

**Conclusions:** Aripiprazole is a potent antipsychotic with agonist D2 properties which is very convenient when we want to avoid sexual dysfunction, but we have to be aware of its potential pharmacodynamics side effects connected with aripiprazole agonistic properties.

#### **41. SEVERE HEADACHE IN A PATIENT WITH BORDERLINE PERSONALITY DISORDER.**

Ozren Veselić, Javor Vouk Kamenski, Maja Vincek, Duje Krstulović-Jelić

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**Introduction/Objectives:** Borderline personality disorder (BPD), also known as emotionally unstable personality disorder (EUPD), is a long-term pattern of abnormal behavior characterized by unstable relationships with other people, unstable sense of self and unstable emotions. There is often dangerous behavior and self-harm, people may also struggle with a feeling of emptiness and a fear of abandonment, symptoms may be brought on by seemingly normal events. The behavior typically begins by early adulthood and occurs across a variety of situations. Substance abuse, depression, self-harm behavior and eating disorders are commonly associated with BPD. Up to 10% of people affected die by suicide.

**Participants, Materials/Methods:** Our poster shows a female patient with BPD whom we treated psychiatric stationary due to her suicidal thoughts, self-harm tendencies and anxiety symptoms due to severe headache and vision difficulties that she was experiencing so we consulted neurologist, radiologist, otolaryngologist and neurosurgeon and we did a neuroradiological imaging of the brain (CT, MRI) which showed 4x2 cm neoplastic process at the skull base clivus area with expansion to the left internal cerebral artery.

**Results:** A biopsy was made and she was diagnosed with chondroma, a benign tumors arising from the long bones, pelvis, or scapulae. Intracranial chondromas, however, are extremely rare. These lesions usually arise at the base of the skull from embryonic chondrocytic cell remnants, but may also originate in the falx, and convexity dura. The tumor is expanding at a very low pace and because of the delicate positioning of the tumor, there is no indication for surgical treatment.

**Conclusions:** After finding out that tumor is not malignant and with the help of escitalopram, diazepam, Quetiapine in sedative doses and Ibuprofen, the patient felt relieved and her mental condition has been stabilized. She is now without suicidal thoughts and with a lot less anxiety but still in constant fear for her future making the treatment of this type of patient with BPD challenging. She has regular psychiatric, neurological and neurosurgical check ups with new MRI scans and is taking her medication regularly.

**42. COMPLEX VISUAL HALLUCINATIONS EMBEDDED IN DELUSIONAL CONTEXT FOLLOWING OCCIPITAL LOBE INFARCTION: A CASE REPORT.**

Javor Vouk-Kamenski, Ozren Veselić, Duje Krstulović-Jelić, Draženka Topolnjak-Pavišić, Maja Vinček

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**Introduction/Objectives:** Infarction of the occipital lobe is known to cause homonymous hemianopsia, frequently accompanied by visual hallucinations which are often localized in the affected part of visual field. These hallucinations vary in content and complexity, while their etiology remains poorly understood.

In this case report we present a 63-year-old female patient, who began experiencing intense delusions related to complex visual hallucinations which appeared within one month after an ischemic stroke in the left occipital lobe. In addition, she developed right homonymous hemianopsia.

**Case report:** The patient was admitted to our inpatient psychiatric ward in a disorganized state, following a short history of emotional lability, agitated depression and visual hallucinations embedded in delusional context. In addition to newly developed right homonymous hemianopsia, signs of moderate cognitive impairment, marked by short-term memory loss and severe temporal disorientation were also present, as shown in neuropsychological assessment. Her past medical history records revealed a visit to emergency ward one month prior to admission. She complained of intense vertigo and malaise, while medical examination found severe hypertension - 220/110 mmHg. MSCT scan revealed massive left occipital lobe infarction and cerebellar atrophy. While immediately complaining of severe loss of vision, visual hallucinations were not present until 2 weeks later. She started perceiving progressively more complex visual hallucinations, culminating with severe delusions and agitation, leading to her hospitalization. Prior to admission she reported seeing unfamiliar men with hostile intentions damaging her house and threatening to murder her family. Delusions and agitation subsided completely within two weeks, possibly related to the start of psychopharmacological treatment consisting of risperidone and oxazepam. She was discharged with a low maintenance dose of risperidone and hasn't shown any signs of agitation, delusions or hallucinations during follow-up.

**Conclusions:** The emerging neurobiological insights led to renewed interest in the etiology of visual perceptual disorders, resulting in vastly improved hodologic/topologic framework based on earlier associationist models. Based on radiological imaging findings, we hypothesize that both the lesion in occipital cortex and the subcortical lesion, followed

by plastic changes involved in neural excitability and connectivity of visual pathways could provide the pathophysiological basis of visual hallucinations experienced by our patient, supporting both topological and hodological perspective in this case. Cognitive impairment possibly contributed to delusional interpretation of hallucinations and consequent disorganized agitated state.

**43. DEMOGRAPHIC CHARACTERISTICS OF CROATIAN WAR VETERANS WITH PTSD AND COMPLEX-PTSD.**

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Regional Center for Psychotrauma, Department of psychiatry, Clinical Hospital Center Split, Split, Croatia

**Introduction/Objectives:** Post-traumatic stress disorder (PTSD) is a psychiatric disorder that can occur after people experienced or witnessed a traumatic event such as a natural disaster, a serious accident, a terrorist act, war/combat, rape or other violent personal assault. It has been observed that one group of war veterans, along with PTSD symptoms, appear symptoms of affective dysregulation, negative self-concept and difficulties in interpersonal relationships that are contained within the diagnosis of Complex PTSD. That seems to be a new and still unexplored diagnostic category. Therefore, we were interested in the sociodemographic characteristics among Croatian war veterans with PTSD and those with Complex PTSD.

**Participants, Materials/Methods:** The participants of our study were 90 war veterans diagnosed with PTSD who were part of Daily hospital programs in 2018 in Regional Centre for Psychotrauma, Split. The diagnosis of PTSD was confirmed using CAPS V in accordance with DSM V and the diagnosis of Complex PTSD using International Trauma Questionnaire. This questionnaire was developed for distinction between PTSD and Complex PTSD. In order to gather data about age, marital status, offspring, level of education, economical and work status we used sociodemographic questionnaire.

**Results:** The average age of our participants was 54,015 years, 77 (85,56%) of them are currently married, 80 (88,89%) have children. Regarding education, 17,78 % had graduated from elementary school education, 71,11% graduated from high school while 11,11% of them have higher level of education than high school. Most of our participants stated self-perceived economical status as below average or average. Considering their work status, majority (41,11%) of our participants are retired due to disability, 27,78% are currently unemployed, 7,78% were on a long-term sickness leave while only 23,33% participants are

currently employed. On average, majority of our participants sought psychiatric help for the first time 12-14 years after the traumatic war experience occurred. When comparing groups with more severe symptoms (Complex PTSD) and less severe symptoms (PTSD) there was no statistically significant difference in any mentioned parameter.

**Conclusions:** Results of our study show no difference in sociodemographic data between war veterans suffering from PTSD and those suffering from Complex PTSD leading us to conclusion that sociodemographic data is not correlated with diagnosis of Complex PTSD. Our sample size and inability to reason out the level of family or workplace functioning using sociodemographic questionnaire could be a reason for such results.

#### **44. PSYCHOPHARMACOLOGICAL TREATMENT OF BEHAVIOUR AND PSYCHOLOGICAL SYMPTOMS IN ALZHEIMER'S DISEASE - A CASE REPORT.**

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**Introduction/Objectives:** Dementia with early onset is often accompanied by significant degradation of higher cortical functions with impaired speech and behavior. The onset of affective symptoms is more frequent at the beginning of the illness, while the psychotic symptoms and delirium occur with the progression of the disease. Follow up the treatment with anti-dementia drugs requires an assessment of the functioning, counseling of the caregiver and the family.

**Case report:** A 56 years old man, railway tracker, in the divorce process, father of 4 children, sent by employer to psychiatric examination because of workplace disfunction. Present hipobulia, forgetfulness, anxiety, gastric disturbances. CT brain: atrophic changes. Psychological test: reduction of mental efficiency, deficit in specific cognitive functioning psychoorganical etiology, and anxiety-depressive symptoms. Ordered antidepressant, monitoring, neurocognitive assessment. Next two years he lived with his mother and girlfriend, worked simple jobs. In psychological monitoring there is a deficit in mental functioning, memory, executive and motor skills. In the age 59 hospitalized due to dementia with apraxia, alexia, paranoid thoughts, disorganization. MR brain: supratentorially subcortical frontally and peritrigonally right hyperintensive changes in the sense of nonspecific gliosis with cortical brain atrophy changes. MMSE 21/30. Treated with quetiapine, diazepam, memantine. Daughter take care

of him at home awhile, but because of the delusional conditions being hospitalized again, then placed in nursing home, threatened with haloperidol, diazepam, memantin. Extended hospitalization occurred because of paranoid, aggressive symptoms, treated with breksipiprazol during the study, then zuklopentixol along with memantine. Next two years he lived at home with his daughter and mother, was self-sufficient about daily routine, attend unwanted leg movements and speech difficulties. Half a year before death at 62, dementia progress, MMSE 5/30.

**Conclusions:** Fast-developing dementia patient with early onset, previously monitored neurocognitive function over two years. Anti-dementia drug started at age 59, also significantly expressed Behaviour and psychiatric symptoms of dementia (BPSD). A combination of anti-dementia drug, anxiolytics and antipsychotics is needed in the treatment of agitation and psychotic symptoms et AD.

## POSTERS NEUROLOGY

**45. ARTERY OF PERCHERON INFARCTION – A CASE REPORT.**

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**Introduction:** The artery of Percheron is an anatomical variant of the paramedial thalamic vasculature that supplies blood to the medial part of the thalamus and the rostral midbrain. The main symptoms are vertical gaze palsy, memory impairment and consciousness disorder. Other symptoms include oculomotor disturbances, hemiplegia, cerebellar ataxia and movement disorders. We present a rare stroke syndrome of bilateral paramedial thalamic and mesencephalic infarction – artery of Percheron infarction in a male patient.

**Case report:** In November 2018 a 63-year-old male with non-obstructive coronary disease, atrial fibrillation, arterial hypertension and cardiomyopathy was admitted to the Department of Neurology due to sudden consciousness disturbance to the level of coma, pinpoint pupils, decerebration type of arm movements, without lateralization of the extremities, bilaterally positive Babinski sign, GCS=5 and NIHSS=16. Because of the suspicion for stroke an urgent brain CT scan was performed, but there were no pathological findings. CT angiography showed a possible thrombus in the start of left posterior cerebral artery with a gracile posterior cerebral circulation. On the second day he was intubated because of the decreased level of consciousness and respiratory insufficiency. Brain CT scan showed ischemia in the posteromedial, dominantly left thalamus and to the less extent right thalamus and in the paramedial part of the left midbrain which corresponds to artery of Percheron infarction. During the following days the patient became febrile, he developed left eye ptosis and mild abduction of the right eye bulb while the left eye couldn't perform adduction. Vertical gaze palsy was present, left pupil became wider than the right one and there was a central type palsy on the right side, motoric dysphasia, mild weakness of the right arm and bilaterally positive Babinski's sign. The patient was treated first with low-molecular-weight heparin and then with novel oral anticoagulants. On the 17<sup>th</sup> day brain digital subtraction angiography didn't show artery of Percheron, nor aneurisms or AV malformations. The patient was discharged from hospital with vertical gaze palsy, mydriasis on the left, partial left eye ptosis, cognitive impairment, milder right side weakness and speech impediments and is currently undergoing a daily hospital treatment.

**Conclusion:** Artery of Percheron infarction is a rare infarction and it presents a diagnostic challenge. Because of the wide range of symptoms and often normal initial radiological assessment it is generally overlooked. After the discharge from hospital due to multiple neurological

impairments patients need extensive multidisciplinary rehabilitation approach.

**46. LIGHT POLLUTION AND COMMUNITY NOISE AS PREDICTORS OF SLEEP QUALITY AMONG UNIVERSITY STUDENTS.**

Terezija Berlančić, Dorian Laslo, Maja Miškulin, Ivan Miškulin

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**Introduction/Objectives:** Sleep disturbances from noise and light can lead to shorter sleep duration, increased daytime fatigue, and poorer daytime cognitive performance. Noise and light levels are higher in the city where most universities and dormitories are located. The aim of this study was to determine the frequency of sleep disturbances in the student population and their correlation with the level of light pollution and the level of community noise.

**Participants, Materials/Methods:** This on-line, anonymous, cross-sectional questionnaire study was done during January and February 2019 among university students at the University of Osijek, Eastern Croatia. The specially designed questionnaire that contained questions regarding students' demographic characteristics, their sleeping habits and questions about light and noise pollution was used as a research tool.

**Results:** There was a total of 202 participants, aged 21.8 years (range 18 to 31 years); 79.2% females and 20.8% males. The poor quality of sleep (QS) was determined in 23.3% of students. There was a statistically significant correlation between QS and light pollution related health issues ( $p=0.002$ ) where higher levels of light pollution caused poorer QS. There was also statistically significant correlation between QS and noise related health issues ( $p=0.016$ ) where higher levels of community noise caused poorer QS. There was a statistically significant correlation between QS and intensity of community noise ( $p=0.002$ ). Considering the extent of disturbance in everyday life caused by road traffic noise there were 26.2% of students who were not disturbed by this source of noise at all; 27.7% of students who were slightly disturbed by this type of noise; 22.8% of students who were moderately disturbed by this type of noise; 13.4% of students who were significantly disturbed by road traffic noise and 9.9% of students who were extremely disturbed by road traffic noise in their everyday life. The study further revealed statistically significant correlation between difficulties to fall asleep and light pollution related health issues ( $p<0.001$ ) however there



## Posters Neurology

was no statistically significant correlation between difficulties to fall asleep and intensity of community noise ( $p=0.322$ ).

**Conclusion:** This study demonstrates the effect of noise and light pollution on university students sleeping habits. It was confirmed that light pollution and community noise have significant negative influence on university students' quality of sleep. Further studies are needed to evaluate details of established interconnections.

#### 47. ETIOLOGY OF STROKES IN YOUNGER PATIENTS.

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**Introduction/Objectives:** Stroke, a leading cause of disability has a significantly fewer occurrence amongst adults < 45 years of age, with its incidence accounting for 10-15% of all strokes. Even though there has been considered able improvement in primary prevention, diagnostic evaluation, and management, stroke is still in second place on a mortality list, and when it comes to the younger population it has larger economic impact compared with stroke in older because it's leaving victims disabled during their most productive years. Our aim was to find the most common causes of stroke in younger people in Hospital Center Rijeka.

**Participants, Materials/Methods:** A retrospective audit was performed amongst patients under 45 years of age that were admitted to the Clinical Hospital Center Rijeka from January 2010 to December 2016. Using TOAST criteria to derive the etiology of cases.

**Results:** Cerebral infarction is most common although a greater proportion of strokes are due to subarachnoid hemorrhage and intracranial hemorrhage (40-50%) compared to the general stroke population (15-20%). Stroke of undetermined etiology is the most common etiology among young stroke patients and as such younger patients require more extensive investigations to determine a cause of stroke.

**Conclusions:** Moreover, the etiology of stroke is more complex and heterogeneous than that of older patients resulting in uncertainties about diagnostic evaluation and treatment. The etiology of strokes in younger people is certainly more heterogeneous than in older populations. More studies should be done to collect more precise epidemiology data.

#### 48. REFRACTORY STATUS EPILEPTICUS COMPLICATED BY SEPSIS – A CASE REPORT.

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**Introduction/Objectives:** Status epilepticus is neurologic emergency which can manifest as many different syndromes. Whatever is the cause, status epilepticus requires rapid evaluation and treatment due to major morbidity and mortality. Refractory status epilepticus occurs in about 20% of patients with status epilepticus.

**Participants, Materials/Methods:** We report 60-year-old male patient who was admitted to emergency department because of frequent partial and tonic clonic seizures. 8 years ago he was hospitalized because of atypical intracerebral hemorrhage due to rupture of aneurysm of anterior communicating artery which was resolved by clipping. 3 years ago he was hospitalized in our Clinic because of status epilepticus. Since then he took antiepileptic drugs because of symptomatic epilepsy. In emergency department he was treated with diazepam intravenously but despite the use of standard therapy he progressed to status epilepticus and was admitted to Intensive care unit. Extensive diagnostic work up was performed: blood findings, CT scan, lumbar puncture were all within normal range.

**Results:** He was intubated, mechanically ventilated, sedated with midazolam but despite the high dose of midazolam he continued having frequent convulsive seizures. He was monitored with continuous EEG so thiopental drip was started and titrated to burst suppression. He was treated with thiopental and midazolam infusion for 3 days and after tapering there was no epileptiform discharges in the EEG and he had no new seizures. Treatment was complicated due to sepsis which was successfully treated according to antibiogram. After 15 days he was discharged in home alert, without focal neurologic deficits, with levetiracetam and lamotrigine in therapy.

**Conclusions:** Adult survivors of status epilepticus are at higher risk for recurrent seizures and status epilepticus.

#### 49. STUDY OF THE MENTAL ACTIVITY OF CHILDREN AFTER SEVERE NEUROTRAUMA (EARLY STAGE OF REHABILITATION).

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University ; Department of Rehabilitation; Department of Neurosurgery; Moscow, Russian Federation

**Introduction/Objectives:** Restoration of mental activity in children after severe traumatic brain damage has its own characteristics. The study of the degree of manifestation of the disorders will allow the use of a differentiated approach to the restorative treatment of children after TBI. This will increase the effectiveness of rehabilitation activities and classes, reduce the percentage of detectable post-traumatic mental and pedagogical consequences in the long-term period after a brain injury. The interdisciplinary participation of doctors and specialists of pedagogical defectologists in the rehabilitation of children after severe traumatic brain damage is necessary for a favorable recovery of mental activity. And should be applied in the medical and educational fields. Objective: to study the options for mental activity in children after STI.

**Participants, Materials/Methods:** 210 children 2.5 -18 years old (median 10) with organic brain damage (HBT, hypoxia, hydrocephalus) who were admitted for treatment and rehabilitation at the Research Institute NDHiT (2016-2018). Pedagogical and clinical psychopathological methods were used; assessment of the level of consciousness and recovery of mental activity on the scales (CRS; RLAS; MSMA (2015))

**Results:** 3 groups of children identified with variants of mental activity depending on the degree of manifestation: 1 - children with high values of mental activity(37, 18%): physical activity, understanding and implementation of simple instructions, emotional responses. Minimum consciousness "+". 2 - children with medium values of mental activity (67, 32%): sensorimotor actions not related to instructions, low and rare emotional reactions. Minimum consciousness "-". 3 - children with low values of mental activity (106, 50%): physical, cognitive and sensory actions are limited. Vegetative state/vegetative output.

**Conclusions:** Evaluation of mental activity with an interdisciplinary approach will allow to differentiate determine the tasks of rehabilitation in children after severe brain damage. Understanding the variability of manifestations of mental activity will increase the effectiveness of rehabilitation treatment at an early stage of hospitalization, reduce the risk of post-traumatic mental and pedagogical consequences in the remote period after trauma.

## 50. COULD RADIOLOGICAL IMAGING TECHNIQUES GIVE US THE RIGHT ANSWER?

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**Introduction/Objectives:** Magnetic resonance imaging (MRI) is a radiologic imaging technique used frequently in neurology. MRI is superior to other techniques, especially in neurology, because it provides more detailed information about the inner organs (soft tissues), it gives better resolution and has a wide range of different types of techniques that could explain the etiology of the lesion.

**Case report:** We report a 52-year-old man with transitory paresthesia of the left side of the face, instability, nausea (without vomiting) and left-sided hearing loss. He was examined by the neurologist-on-call. The patient did not report any other symptoms (headache, double vision, blurred vision, tinnitus or vertigo); neurologic exam has not showed any deficits and the blood pressure levels were normal (130/80 mmHg). MSCT of the brain was made and the patient was admitted on neurology department. Through the hospitalisation neurosonologic (US CD of carotid and vertebral arteries, TCD of vertebral and basilar arteries) and neuroelectrogenic (EEG) diagnostic procedures were made. The patient was examined by ENT doctor, due to the loss of hearing. Additionally, audiologic diagnostics and MR of the brain with emphasises on the temporal regions were made. Radiologist described expansive lesion in the left pontocerebellar angle that would probably correspond to acoustic Schwannoma. After being examined by an anesthesiologist, the patient was transferred to the department of neurosurgery. Instead of finding the expected lesion, the neurosurgeon found only some blood in the area.

**Conclusion:** Eventhough the technology and knowledge have never been on higher levels, sometimes the correct diagnose is a great challenge for medical practitioners. A thorough history and neurological examination are essential for differential diagnosis. However, MRI is another tool that is most often confirmatory, but may cause uncertainty at times too.

## 51. QUALITY OF LIFE IN DIABETIC PATIENTS WITH PAINLESS DIABETIC POLYNEUROPATHY - THE RESULTS OF 8 – YEARS FOLLOW-UP STUDY.

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**Introduction/Objectives:** In our previous study, we have presented the quality of life parameters in an initial cohort of 240 subjects, divided into three groups – diabetics with painless neuropathy (D), diabetics with painful neuropathy (P) and controls (C). In this report, we present the results of the first follow-up study on the quality of life-parameters in the cohort of 38 subjects from the D group, at Clinical Hospital Merkur - University Clinic Vuk Vrhovac.

**Participants, Materials/Methods:** Mean follow-up time was 8,05 years (SD = 0,39 years). In this period subjects significantly increased their BMI, with average difference of 1,2 kg/m<sup>2</sup> (SD=2,53, p=0,007), and mean HbA1c values decreased from 7,34 to 7,28 mmol/L (p=0,772), total cholesterol decreased from 4,64 to 4,08 mmol/L (p=0,021), HDL decreased from 1,49 to 1,45 mmol/L (p=0,560), LDL decreased from 2,50 to 2,17 mmol/L (p=0,044) and triglycerides showed the tendency with decrease from 1,41 to 1,28 mmol/L (p=0,260).

**Results:** The most important goal of this follow-up was to assess differences in eight Short Form Questionnaire (SF-36) dimensions after the 8-year period. As expected, all dimensions have shown decrease; physical functioning changed from average 64,9 (SD=25,18) to average of 57,4 (28,63) points (p=0,114), role limitations due to physical health from 69,7 (39,06) to 55,9 (47,01) (p=0,126), role limitations due to emotional problems from 78,9 (36,69) to 73,1 (39,11) (p=0,203), vitality from 61,9 (16,74) to 57,2 (20,55), (p=0,094), mental health from 71,7 (18,88) to 65,5 (20,38) (p=0,085), social functioning from 82,2 (19,20) to 78,6 (20,93) (p=0,361), bodily pain from 58,7 (18,60) to 53,5 (21,88) (p=0,160) and general health from 49,7 (16,68) to 47,9 (17,12) (p=0,441). We have also noticed an significant (p=0,004) increase in Beck's depression inventory (BDI) values, from the mean 9,2 (7,70) at the initial visit to 12,8 (9,33) at the follow-up assessment.

**Conclusions:** In conclusion, after the 8-year follow-up period in 38 diabetic subjects, we found an expected increase in BMI, combined with unexpected, but positive decrease in laboratory parameters. This may be a consequence of the education the subjects at our institution, reflecting in better control of blood glucose and additional attention to quality (but not quantity) of their diet.

Furthermore, all dimensions of the SF-36 scale decreased, as expected. Lack of the statistical significance here could be explained with higher variability (SD) of results at the follow up visit. Decrease in BDI scale values is also clearly detectable, as expected with increase of subjects' age.

## 52. CEREBELLAR STROKE AND WALENBERG'S SYNDROME – A CASE REPORT.

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**Introduction/Objectives:** Cerebellar stroke (CS) is frequently caused by a combination of inferior posterior cerebellar artery (PICA) and superior cerebellar artery (SCA) infarction. We present a case of CS in a young person with simultaneous infarction in the territory of PICA and SCA and partial lateral medullary syndrome-Wallenberg's syndrome (WS) with ipsilateral hemiparesis.

**Case report:** In December 2018, a 32-year-old male, with diabetes and hyperlipidemia, was admitted to the Department of Neurology for occipital headache on the right, dizziness, nausea, vomiting, hiccups, diplopia, ptosis on the right, nystagmus, semipronated right forearm with dysmetria, ataxia to the right, inability to stand or walk and preserved sensation. National Institutes of Health Stroke Scale (NIHSS) score was 2 and Modified Rankin Scale (mRS) score was 4. The clinical picture indicated CS and partial WS. Computerized tomography of the brain showed the acute ischemic lesion on the right side of cerebellum in territory of SCA. The Computed Tomography Angiography demonstrated a hypoplastic right vertebral artery (RVA). Color Doppler Flow Imaging displayed narrower RVA with lower flow. Digital subtraction angiography showed absence of blood flow in RVA from the beginning to the height of the atlas, RVA was hypoplastic, blood flow in PICA was absent as well. Magnetic resonance imaging confirmed ischemic lesion on the right side of cerebellum. Magnetic resonance angiography verified the filiform RVA before the entrance to the basilar artery, while the distal parts weren't shown. Due to the suspicion of RVA dissection patient was treated with low-molecular-weight heparin and acetylsalicylic acid, atorvastatin due to hyperlipidemia, thiethylperazine and pantoprazole due to nausea and vomiting. He was discharged with Horner syndrome and gait ataxia to the right; NIHSS score of 0, mRS score of 3. He was readmitted in January and February of 2019 due to previously existing symptoms and newly developed left arm numbness, mild weakness of the right arm, moderate

weakness of the right leg, and sensory decrease on the left side with preserved pain and temperature sensation; NIHSS score of 3, mRS score of 3. The magnetic resonance imaging showed sequelae of earlier ischemia on both hemispheres of cerebellum, more pronounced on the right, in the territory of SCA and PICA. Magnetic resonance angiography showed hypoplastic RVA. Patient was treated with acetylsalicylic acid, atorvastatin; Fluvoxamine due to depression, Metformin due to diabetes. He was discharged home with improved strength in the right arm and coordination.

**Conclusion:** According to clinical picture this case report showed probable RVA dissection with occlusion of the PICA and SCA which led to partial WS and combined CS of PICA and SCA territory. Ipsilateral hemiparesis as part of WS is rare and is known as Opalski's syndrome. It is attributed to the involvement of corticospinal fibers to the pyramidal decussation. Hypoplastic vertebral artery is a predisposing factor for vertebral artery dissection and frequent monitoring is required because of the higher possibility for stroke in the brain's posterior circulation.

### 53. ATYPICAL CLINICAL PRESENTATION OF MULTIPLE SCLEROSIS: A CASE REPORT.

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**Introduction/Objectives:** Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. Typical signs and symptoms that point to MS onset include vision problems, numbness or tingling of face and extremities, and involuntary muscle spasms. Diagnostic tools, such as magnetic resonance imaging, analysis of evoked potentials and/or cerebrospinal fluid, are used to search for demyelination in both central and peripheral nervous system. However, many cases of MS start with atypical symptoms, and here we present such a case.

**Case report:** Since 2013, an otherwise healthy 62-year-old male, has been suffering from trigeminal neuralgia, a chronic pain disorder that affects the trigeminal nerve. In his case, he has been presenting as short (about 10 seconds long), painful attacks, located in the right temporal area. The patient had positive clinical reaction to carbamazepine. His neurological status didn't indicate any other possible disorders. In 2014, the MRI showed suspected demyelination (frontoparietal, left parietal, and peritrigonal lobes), but there were still no other symptoms that would point to anything else but trigeminal neuralgia. In 2014 and

2015 the EEG testing was performed, which showed dysrhythmic changes. Thyroid hormones were within normal limit values, and the ultrasound of cervical blood vessels was normal as well. However, in 2017, a fresh brain MRI (using the demyelinating protocol) was performed, which conclusively proved the existence of primary demyelinating lesions. After extensive hospital treatment, vascular etiology of the lesions had been ruled out, and cerebrospinal fluid was sampled as well - despite several viruses and bacteria present in the serum (Epstein-Barr Virus, Herpes Simplex Virus, Cytomegalovirus, Borrelia burgdorferi), there were none found in the cerebrospinal fluid. However, IgG bands (type 2) were positive. The patient is still not presenting with any of the typical signs and symptoms that would indicate multiple sclerosis.

**Conclusions:** The patient presented with an atypical clinical presentation of the primary demyelinating disease of central nervous system, in this case multiple sclerosis. It is an important case to discuss, since this particular symptom (trigeminal neuralgia) is extremely rare, especially when it occurs at that age (at 60-years-old) and as a sole, isolated, symptom (only about 15% of patients exhibit it). Furthermore, the diagnosis of multiple sclerosis itself, that late in life is a rare case as well.

### 54. POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME AS A COMPLICATION OF MULTIPLE SCLEROSIS: A CASE REPORT.

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**Introduction/Objectives:** Multiple sclerosis (MS) is characterized by worsening of neurological symptoms as the disease progresses, among others, urinary disorders, respectively, urinary retention that can potentially lead to renal decompensation and hypertension, which can cause an uncommon neurological entity – posterior reversible encephalopathy syndrome (PRES).

**Participants, Materials/Methods:** We describe an 18-year-old woman diagnosed with relapsing-remitting MS in 2017, previously treated with interferon beta-1a, but due to highly active disease, also with the first cycle of ocrelizumab, who presented in our Clinic with altered mental status, cognitive deficits, speech and visual disturbances, difficulties in walking and urinating. Examination confirmed encephalopathic disorder with urinary retention, high blood pressure (BP 220/135 mmHg) and tachycardia (HR 140/min).

**Results:** Laboratory tests revealed renal dysfunction so ultrasound of kidneys was performed and showed bilateral



hydronephrosis; secondary causes of hypertension were excluded. Analysis of cerebrospinal fluid was without pathological findings, as the results of testing for JC and other neurotropic viruses. New pathological findings on MRI of the brain were T2/FLAIR hyperintense lesions and mild thickening of the pons. The patient was treated with a multidisciplinary approach which included neurologist, nephrologist, urologist and psychiatrist; urinary catheter setup and antihypertensive and psychiatric therapy lead to the recovery of renal function and neurological status with normalization of blood pressure, while control MRI of the brain showed regression of previously described changes. Therefore, it was concluded that our patient developed PRES of atypical localization due to high blood pressure caused by acute postrenal obstructive nephropathy as a consequence of urinary retention which is one of the well-known symptom of MS.

**Conclusions:** PRES is a dramatic neurological condition which should be considered in the differential diagnosis of MS patients with urinary disorders who develop encephalopathic symptoms; also the urinary disorders should be carefully monitored in patients with MS to prevent the development of this type of complication.

#### 55. PSYCHOTIC PRESENTATION OF SPORADIC HEMIPLEGIC MIGRAINE- A CASE REPORT.

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**Introduction/Objectives:** Sporadic hemiplegic migraine is a rare disorder and psychiatric presentations are described in a few case studies. We present a unique and intriguing case of migraine with a newly formed motor weakness and psychotic symptoms.

**Participants, Materials/Methods:** A middle-aged man has been suffering from migraine with aura over the last 20 years. The migraine was refractory to triptans, it would last for a few days and resolve without medication therapy spontaneously. In June 2017, after one of the migraine attacks, he started his medical diagnostic in the daily hospital of the Department of Neurology in the University Hospital Centre Zagreb. During the work-up, his medical condition rapidly deteriorated. He started to present with severe headache, aura, temporary visual impairment, vomiting and left-sided motor weakness. MRI showed cortical oedema and meningeal enhancement contralateral to hemiparesis and a methylprednisolone therapy was induced for five days in a dose of 1000 mg per day. After two days

he became agitated, aggressive, confused and dysphoric, started to mention suicidal ideas, and he was transferred to the psychiatric department. There he was treated with haloperidol (20 mg per day), promazine (300 mg per day), diazepam (20 mg per day), clozapine (25 mg per day) and clonazepam (1,5 mg per day). However, his state persisted; he was still unable to communicate adequately, agitated and confused. He was then transferred back to the neurologic department and another MRI showed an extensive area of left cerebral hemisphere oedema. Immunoglobulin therapy was indicated in dose 0,4mg per kg per day and the symptoms decreased rapidly. Motor weakness and psychotic symptoms were completely resolved. Thorough medical examinations excluded all but a sporadic hemiplegic migraine.

**Results:** Diagnostic criteria for sporadic hemiplegic migraine include aura with reversible motor weakness and neurological impairment accompanied by headache. According to our knowledge, only a few cases have reported concomitant psychiatric symptoms; mostly psychotic and depressive. MRI in psychotic symptoms is usually indicated for excluding lesions, demyelinating disorders or stroke, and the changes in psychosis are very unspecific. The presence of cerebral oedema usually manifests as headache, vomiting and nausea, seizures and altered mental status. Our patient presented with headache, vomiting and altered mental status, however, those are clinical manifestations of a broad disease spectrum. Therefore, the first psychotic episode in adults should always be thoroughly investigated for underlying neurological aetiology.

**Conclusions:** This case represents a diagnostic challenge within an overlapping neurological and psychiatric field.

#### 56. NEW MATERIAL IN MEDICINE AS A PROTECTOR OR POSSIBLE CAUSE OF STROKE – A CASE REPORT.

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**Introduction/Objectives:** World Health Organisation defines stroke as a „brain attack“ that is caused by the interruption of the blood supply to the brain, usually because of a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue. Within minutes, brain cells begin to die. With this case report we want to indicate that even if a prospective clinical trial has proved that >60% patients don't have bleeding or risk for stroke, we have to think

about other 40% of patients because every patient is an individual person.

**Case report:** In this case, we present a 34 years old woman who comes to the Clinic with symptoms of speech difficulty and left side body weakness. She was presented as a Transient ischemic attack (TIA). A brain MRI showed signs of cytotoxic edema caused by micro embolism which was evidence of a stroke. The new discovery was also the left ophthalmic artery occlusion. From the history of the disease, we find out that she had surgery of stenosis of the aortic valve and ascending aortic aneurysm and also aortic valve replacement with a mechanical prosthesis. After surgery, the doctor determined the international normalized ratio (INR) values between 1.5 and 2.0 because this mechanical prosthesis is a new model of On-X Aortic Valve. The On-X Aortic Valve is a newer generation heart valve made of a unique material - pure pyrolytic carbon and design characteristics compared with earlier generations of mechanical heart valves. This material has antiaggregation properties which prevent platelet adhesion. The On-X Aortic Valve is the only mechanical valve with FDA and CE approval as being clinically proven safe with significantly less blood thinner (warfarin) and lower values of INR. On-X Aortic Valve patients with a reduced blood thinner dose had > 60% fewer bleeding events without an increase in the risk of stroke.

**Conclusions:** In this case, the INR values and new modern unique material were not enough to prevent the occurrence of the thrombus and stroke. During the treatment of the patient, an INR was determined between 2.0 and 3.0. That was optimal INR for preventing stroke or potential brain bleeding in this case.

#### **57. A DURAL ARTERIOVENOUS FISTULA OF CEREBELLOPONTINE ANGLE AS A CAUSE OF TRIGEMINAL NEURALGIA IN A PATIENT WITH HYPERINTENSIVE LESIONS OF CNS OF UNDETERMINATED ETIOLOGY - A CASE REPORT.**

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**Introduction/Objectives:** Secondary trigeminal neuralgia is a rare neurological condition that can be caused by tumors or vascular abnormalities of cerebral blood vessels.

**Case report:** We reported a 50-year-old woman who came to our Clinic for the second opinion dominantly because of neuropathic pain in the area of innervation of the left trigeminal nerve, but also intermittent vision disorder, tingling of the right extremities and weakness in both legs. In a neurological examination, paresthesia of the right

cheeks and right extremities as the mild paresis of the right arm were established. Previously she was treated by a dentist who fixed the teeth in painful region and neurologist who prescribed carbamazepine which reduced a patient's level of pain but was soon abolished because of side-effects. MRI of the brain was performed and revealed a suspected dural arteriovenous fistula (DAVF) in the area of the left trigeminal nerve (in the left pontocerebellar cistern); T2/FLAIR hyperintensive lesion unknown etiology localized bilaterally periventricular and subcortical were also described.

We performed extensive diagnostic work up: blood findings (including results of hematological tests) were all within normal range except positive IgM for *Borrelia burgdorferi* confirmed with Western blot; analysis of cerebrospinal fluid showed positive IgM for EBV, preserved function of the blood-brain barrier with negative oligoclonal bands and all other infectious agents. Due to potential borreliosis and EBV infection, we consulted infectologist who concluded that positive EBV IgM is a sign of benign reactivation, neuroborreliosis was excluded, but doxycycline was prescribed for positive serum test for *Borrelia burgdorferi*. Because of suspected DAVF digital subtraction angiography was performed and confirmed the dural fistula which supply is driven from the left AICA, the branches of the left vertebral and carotid artery and the middle meningeal arteries, and it drains through a medium peduncular vein. DAVF was excluded from cerebral circulation with an endovascular procedure which was performed in two occasions (first procedure of embolization was only partially successful), after the second treatment patient reported regression of symptoms of neuropathic pain.

**Conclusions:** To conclude, it's important to consider the potential secondary causes of trigeminal neuralgia so we could successfully treat neuropathic pain; regarding hyperintensive lesions of CNS, our patient needs further monitoring.

#### **58. TAU PROTEIN SPREADING AFTER INJECTION OF TAU OLIGOMERS INTO THE RAT ENTORHINAL CORTEX.**

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**Introduction/Objectives:** Alzheimer's disease (AD) is the most common secondary tauopathy characterized by progressive loss of cognitive functions and behavioral impairment. The hyperphosphorylation and aggregation of

tau proteins progress in a stereotypical manner with the first changes seen in the entorhinal cortex and locus coeruleus from where they spread to the hippocampus and other cortical regions, respectively. Here, we aimed to explore if intracerebral injection of tau oligomers and tau fibrils will induce trans-synaptic transfer of pathological tau proteins, and will those changes be associated with cognitive decline.

**Participants, Materials/Methods:** Three to four month old male Wistar rats (n = 96) were stereotaxically injected into the lateral entorhinal cortex with tau oligomers, tau fibrils, and phosphate-buffered saline. Animals were analyzed after post-injection interval of 4 months. Cognitive performance was tested using open field, T-maze task, novel object recognition (NORT), and object-location test (OLT). To detect tau protein changes and perform staging of tau pathology, we used anti-tau antibodies AT8, T22, HT7, and PHF1. Possible amyloid changes were assessed using anti-amyloid antibody 4G8. Proteins isolated from the entorhinal cortex and hippocampus were analyzed by immunoblotting.

**Results:** In comparison to the control and the tau oligomer group, rewarded learning in the T-maze showed slower learning curve with more incorrect choices in rats injected with tau fibrils (-25%,  $p < 0.05$ ). Immunohistochemistry revealed HT7-positive signal in the brainstem and transentorhinal region only in the group injected with tau fibrils. Here, oligomeric tau was found both ipsilaterally and contralaterally to the injection site. In comparison to sections from control animals where no immunoreactivity was observed, the Ser202/Thr205 phosphorylated tau epitope visualized by AT8 antibody showed weak immunoreactivity in both tau fibril and tau oligomer group.

**Conclusions:** The results obtained suggest that stereotaxic injection of tau oligomers or tau fibrils into the lateral entorhinal cortex induces phosphorylation of AT8 epitope of tau in the rat brain at 4-month post-injection. Using antibody HT7, which recognizes human (and not murine) tau, we found a signal present in the brainstem after injection of tau fibrils into the lateral entorhinal cortex. Therefore, we concluded that understanding of the role of tau oligomers and tau fibrils in this rat model of neurodegeneration has a great potential for revealing mechanisms underlying development and progression of AD and other tauopathies in humans. This work is funded by the Croatian Science Foundation HRZZ (IP-2014-09-9730) and by Scientific Centre of Excellence for Basic, Clinical and Translational Neuroscience (project "Experimental and clinical research of hypoxic-ischemic damage in perinatal and adult brain"; GA KK.01.1.1.01.0007 funded by the European Union through the European Regional Development Fund), University of Zagreb

### 59. BASAL GANGLIA MATTERS IN THE PRIMARY BURNING MOUTH SYNDROME-TRANSCRANIAL SONOGRAPHY STUDY.

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**Introduction/Objectives:** Primary burning mouth syndrome (BMS) is chronic intraoral burning sensation without medical or dental cause. Potential causes are neuropathic dysfunction and central mechanisms with involvement of the nigrostriatal dopaminergic system (NDS). BMS could also be premotor symptom of Parkinson's disease (PD). The aim of this study was to determine the frequency of NDS dysfunction in BMS using TCS.

**Participants, Materials/Methods:** 120 patients with BMS, 120 with PD and 74 healthy individuals are included. Using standardized transcranial sonography (TCS) protocol, basal ganglia echogenicity as well as ventricular system diameter and brainstem raphe echogenicity were measured. Degree of intraoral burning sensation and affective status were also determined.

**Results:** Frequency of substantia nigra (SN) echogenicity was the highest in PD, also significantly higher in BMS in comparison to controls (90% vs. 62% vs. 10%;  $p < 0.01$  respectively), while there were no differences in other basal ganglia echogenicities. The third ventricle diameter was significantly higher in PD and BMS compared to controls ( $8.4 \pm 2.2$  vs.  $8.2 \pm 2.1$  vs.  $5.3 \pm 1.9$ ;  $p < 0.01$ ). Frequency of brainstem raphe hypoechogenicity was significantly higher in both patients groups compared to controls (75% vs. 74% vs. 10%;  $p < 0.01$  for PD and BMS vs. controls). Significant correlation was found between raphe and substantia nigra echogenicity and the degree of depression ( $r = 0.351$ ;  $p = 0.012$ ).

**Conclusions:** TCS is noninvasive method to identify BMS patients with NDS damage that in some could be early premotor PD symptom. This finding could have important therapeutic implications.

### 60. LAMINAR SHIFTS OF SOX2 EXPRESSION PATTERN IN THE HUMAN FRONTAL CORTEX DURING MIDGESTATION.

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**Introduction/Objectives:** Complex organization of cerebral cortex is established by orchestrated histogenetic and neurogenetic processes i.e. cell proliferation, migration, differentiation, and synaptogenesis, which are regulated by differential gene expression. During fetal brain development, neurons are born in proliferative zones, ventricular (VZ) and subventricular (SVZ) zone, by division of stem cells and other progenitors, and migrate to their final destination in the cortex forming a transient fetal cortical lamination. Gene SOX2 encodes the transcription factor that maintains the identity of neural stem cells and such is critically involved in cortical development. However, SOX2 protein expression pattern during the human neocortical development remains elusive. Our aim was to analyze shifts in the SOX2 expression pattern through transient fetal zones in human frontal cortex during fetal development.

**Participants, Materials/Methods:** SOX2 expression pattern was studied by immunohistochemistry and immunofluorescence on fixed-paraffin-embedded sections of postmortem human brains, as a part of the Zagreb Neuroembryological Collection that has an approval of the Internal Review Board of the Ethical Committee at the School of Medicine, University of Zagreb.

**Results:** At early fetal development (10-12 post-conception weeks (PCW)) SOX2 is mainly expressed in cells of the VZ, while during the early mid-fetal period (13-15PCW) there is a shift in SOX2 expression pattern to the neural stem cells of the SVZ, which gradually diminishes at the late mid-fetal period (17-20PCW). Besides diminished SOX2-immunoreactivity in proliferative zones, SOX2-immunoreactive cells were found scattered throughout the subplate (SP), and less frequently in the cortical plate (CP) during the late mid-fetal period.

**Conclusions:** Our study shows shifts in the distribution of SOX2-immunoreactive cells throughout transient fetal zones during fetal cortical development. Interestingly, SOX2-immunoreactive cells were sparsely distributed throughout the SP, and CP during the late mid-fetal period, whose developmental role remains elusive. Therefore, SOX2 expression shifts to the SP and CP during late mid-fetal cortex is raising functional questions that will open new avenues for stem cell research. This work was supported by

Adris Foundation (ZK) and Croatian Science Foundation CSF-IP-09 2014-4517 (IK).

### 61. LOWER URINARY TRACT SYMPTOMS IN PATIENTS WITH OBESITY.

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**Introduction/Objectives:** Patients with obesity may have lower urinary tract symptoms (LUTS) (1). Little is known about these symptoms in patients with obesity in Croatia.

The aim of the study was to assess LUTS in patients with obesity in Croatia.

**Participants, Materials/Methods:** This was a prospective study carried out in tertiary healthcare centre. 111 participants (81 women (72.97%), 30 men (27.03%), mean age  $49.03 \pm 12.21$  years) were included. Following questionnaires, were used to assess LUTS: ICIQ-OAB (currently under validation for Croatian language) and recently validated for Croatian language ICIQ-UI (1).

**Results:** On ICIQ OAB patients reported following symptoms: 34.23% (N=38) increased frequency of urination (38.27% (N=31) women, 23.33% (N=7) men), 42.34% (N=47) nocturia (48.15% (N=39) women, 26.67% (N=8) men), 25.23% (N=28) urgency (28.4% (N=23) women, 16.67% (N=5) men) and 46.85% (N=52) urgency urinary incontinence (51.85% (N=42) women, 33.33% (N=10) men).

On ICIQ-UI patients reported following symptoms: 43.06% (N=31, 51.92% (N=27) women, 20% (N=4) men) urgency urinary incontinence, 44.44% (N=32, 61.54% (N=32) women, 0 men) urinary incontinence when coughing and sneezing, 2.78% (N=2, 3.85% (N=2) women, 0 men) urinary incontinence when sleeping, 22.22% (N=16, 28.85% (N=15) women, 5% (N=1) men) urinary incontinence during exercise/physical activity, 18.06% (N=13, 17.31% (N=9) women, 20% (N=4) men) urinary leakage after having urinated and getting dressed, 6.94% (N=5, 7.69% (N=4) women, 5% (N=1) men) urinary leakage for no obvious reasons.

Women were found to be more significantly affected by



increased incidence of urinary frequency and mixed urinary incontinence than men ( $p < 0.05$ ).

Significant correlations ( $p = 0.001$ ) in the overall results on the ICIQ OAB were found with the following variables: mobility  $r = 0.29$ , self-care  $r = 0.28$ , pain/uneasiness  $r = 0.27$ , sleep disturbances  $r = 0.34$ , spinal injuries  $r = 0.25$ . Significant correlations were found among other between nocturia and the following variables: age  $r = 0.28$  ( $p = 0.001$ ), tea  $r = 0.21$  ( $p = 0.03$ ), mobility  $r = 0.22$  ( $p = 0.02$ ), self-care  $r = 0.23$  ( $p = 0.01$ ), pain/uneasiness  $r = 0.3$  ( $p = 0.001$ ), anxiety/melancholy  $r = 0.19$  ( $p = 0.05$ ), sleep disturbances  $r = 0.34$  ( $p = 0.001$ ).

**Conclusions:** According to our preliminary results in patients with obesity, women were found to be more significantly affected by increased incidence of urinary frequency and mixed urinary incontinence than men. In the future our study will be oriented on causal connection in greater patient number.

## 62. SEXUAL DYSFUNCTION IN PATIENTS WITH OBESITY.

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The Croatian Institute of Emergency Medicine, Zagreb County, Croatia; Department of Neurology, University Hospital Center Zagreb, School of Medicine, University of Zagreb, Zagreb, Croatia; Internal Clinic, Department of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia; Department of Neurology, General Hospital Virovitica, Virovitica

**Introduction/Objectives:** Patients with obesity may have symptoms of sexual dysfunction (SD). Little is known about these symptoms in patients with obesity in Croatia. The aim of the study was to assess SD in patients with obesity in Croatia.

**Participants, Materials/Methods:** This was a prospective study carried out in tertiary healthcare centre. 103 patients (72 female, 31 male, mean age  $48,7 \pm 11.87$  years) were included. SD symptoms were assessed using questionnaire - Arizona Sexual Experience Scale (ASEX) that is currently under validation for Croatian language, where higher score represents more pronounced symptoms of SD (2).

**Results:** 20.42% ( $N = 20$ , 6.45% ( $N = 2$ ) male and 25% ( $N = 18$ ) female) patients had higher score than average (3.8) on ASEX. 27.18% ( $N = 28$ , 12.9% ( $N = 4$ ) male and 33.33% ( $N = 24$ ) female) patients answered at least one question with a score 5 or greater than 5. Significant correlation was found between having answered at least one question with a score

5 or greater than 5 and the depression  $r = 0.31$  ( $p < 0.001$ ). Women obtained statistically significant much higher mean results than men (3.46 vs. 2.81):  $t(91.098) = 3.53$ ,  $p < 0.001$ . The percentage of women who obtained a score higher than average (3.8) is statistically significantly much higher than the percentage of men (25% vs. 6.45%):  $\chi^2(1) = 4.76$ ,  $p = 0.03$ . The percentage of women who chose the answer 5 or greater than 5 is statistically significantly higher than the percentage of men (33.33% vs. 12.9%):  $\chi^2(1) = 4.57$ ,  $p = 0.03$ . Women had more pronounced symptoms of SD, which was found both in the group of patients that had, as well as in those that did not have sexual intercourse in the previous week ( $p < 0.05$ ). Significant correlations in the overall results on the ASEX are found with the following variables: depression  $r = 0.22$  ( $p = 0.03$ ) and anxiety/melancholy  $r = 0.2$  ( $p = 0.04$ ).

**Conclusions:** This study brings valuable observations on the presence of SD symptoms in obese patients in Croatia, found to be more present in women, and regarding patient-oriented management brings indispensable information.

## 63. SLEEP DISORDERS AND LOWER URINARY TRACT SYMPTOMS IN OBESE PATIENTS.

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**Introduction/Objectives:** Sleep disorders (according to ICSD-3, International Classification of Sleep Disorders, 3<sup>rd</sup> ed.; in DSM-5, Diagnostic and Statistical Manual of Mental Disorders – 5<sup>th</sup> ed. Sleep-Wake Disorders) are common nowadays problem. They are caused by many reasons (psychiatric, neurologic, environmental, endocrine etc.). Also, there is various spectrum of symptoms and signs what we understand under the term sleep disorders and classifications vary. Most common entities are: insomnia, hypersomnolence, sleep apnea, narcolepsy etc. Lower urinary tract symptoms (LUTS) are disturbing and can be connected to sleep disorders. We wanted to assess connection between sleep disorders and lower urinary tract symptoms in obese patients in Croatia.

**Participants, Materials/Methods:** This was a prospective study carried out in tertiary healthcare centre. 111 participants (81 women (72.97%), 30 men (27.03%)), mean age  $49.03 \pm 12.21$  years, BMI >30 were included. Following questionnaires, were used to assess LUTS: ICIQ-OAB and ICIQ-OABqol (both currently under validation for Croatian language). Sleep disorders were evaluated through general information questionnaire where patients needed to mark all illnesses (out of 14) they have problem with. Pearson's correlation coefficient was used.

**Results:** Our study found significant correlation in the overall result on the overreactive bladder questionnaire (ICIQ-OAB) and sleep disorders:  $r=0.34$  ( $p=0.001$ ). Also, increased urinary frequency and sleep disorders are significantly connected:  $r=0.21$  ( $p=0.03$ ). Nocturia and sleep disorders significantly correlate as  $r=0.34$  ( $p=0.001$ ). Sleep disorders are significantly related to urinary urgency  $r=0.3$  ( $p=0.001$ ). Moreover, significant correlation is found between urinary incontinence and sleep disorders:  $r=0.23$  ( $p=0.02$ ). Significant correlation is found between the overall results of the impact of urinary symptoms on the quality of life questionnaire (ICIQ-OABqol) with sleep disorders:  $r=0.25$  ( $p=0.01$ ). On the last question on the impact of urinary symptoms on the quality of life questionnaire – ICIQ-OABqol (where patients need to assess overall impact of urinary symptoms on everyday life choosing a number between 0 (not at all) and 10 (a great deal)) is significantly correlated to sleep disorders:  $r=0.24$  ( $p=0.01$ ).

**Conclusion:** This study has shown significant preliminary results in addition to indicating a correlation between sleep disorders and LUTS in Croatian obese patients. In the future, our study will consider a possible causal connection using the Pittsburgh Sleep Quality Index, Insomnia Severity Index and Epworth Sleepiness Scale.

#### 64. THE IMPORTANCE OF AN INTERDISCIPLINARY APPROACH TO RETT SYNDROME THERAPY - A CASE REPORT.

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**Introduction/Objectives:** Rett syndrome (RTT) is a progressive neurodevelopmental disorder mostly affecting females, presenting with a wide array of neurological, psychological and other symptoms which in turn cause profound mental impairment in girls and lack of social integration. There is no known cure for Rett syndrome, but through an interdisciplinary approach, there are treatment options that could help alleviate some of the symptoms, thus

helping maintain a better quality of life. We report a case of a 22-year old Rett syndrome patient, along with the clinical presentation and the challenges that arise with her treatment.

**Case report:** A 22-year old patient comes for a regular neurological check-up accompanied by her parents. She demonstrates typical neurological symptoms of Rett syndrome including signs of slowed undeveloped speech and communication patterns, abnormal movements followed by spasticity, tremor and ataxia as well as psychological symptoms like anxiety, irritability, unprovoked crying and smiling with abnormal gaze symptoms like intermittent staring and eye contact avoidance. So far, she's been treated by various child psychiatrists symptomatically with anti-psychotics, anxiolytics and neurologists with anti-epileptics for seizures typically accompanying Rett syndrome, as well as physical therapy. On more than one occasion, her parents reported a worsening of everyday functioning and behavior due to treatment and discontinued it. At her last check-up, she is functioning well, does not demonstrate aggressiveness and her sleep cycles are balanced, with regular therapy including valproate for seizure prevention, propranolol which proved beneficial for her tremor, vitamin D due to deficiency and physical therapy for motor symptoms. We recommended further treatment by an interdisciplinary team including a speech therapist, work therapist and physical therapist as well as regular regular neurologic and psychiatric controls for the optimal treatment result.

**Conclusions:** Rett syndrome has no known cure, but an integrated symptomatic therapy demonstrated the optimal results for better social integration and everyday quality of life. Our case demonstrates the necessity for an interdisciplinary approach because of the span of symptoms that the disease encompasses, since in some instances it actually worsened the basic symptoms due to a lack of an interdisciplinary approach. A balanced collaboration between neurologists, psychiatrists, physical therapists, speech therapists and others could tackle and milden the symptoms if working effectively together, not only in Rett syndrome but in others as well.

#### 65. SEXUAL DYSFUNCTION AND DEPRESSION IN MULTIPLE SCLEROSIS.

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**Introduction/Objectives:** : Both depression and sexual dysfunction (SD) may be present in people with multiple sclerosis (pwMS) (1-5). The aim of this study was to evaluate a possible association between SD and depression in pwMS.

**Participants, Materials/Methods:** This was a prospective cross-sectional study carried out in tertiary healthcare centre over 10 months, which included 101 consecutive pwMS (mean age 42.09 (range 19-77) years, 75 female, 25 male, 1 missing, EDSS score 3.1 (range 0.0-7.0)). SD was assessed with Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ), while information on treatment for depression was obtained during the medical interview. Data were analysed and interpreted using parametric statistics (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

**Results:** 89 patients completed MSISQ. 25 patients were in treatment for depression, while 75 did not have depressive symptoms. There were no significant differences between female and male patients regarding treatment for depression ( $\chi^2=0.018$ ,  $df=1$ ,  $p>0.05$ ). Results in all subcategories on t-test found that depressive patients had higher impact on SD when compared to non-depressive: overall ( $t=-2.691$ ,  $df=87$ ,  $p<0.01$ ) and in regards to primary ( $t=-2.086$ ,  $df=87$ ,  $p<0.05$ ), secondary ( $t=-2.608$ ,  $df=87$ ,  $p<0.05$ ) and tertiary ( $t=-2.460$ ,  $df=86$ ,  $p<0.05$ ) SD.

Depressive patients on 7 questions showed significantly ( $p<0.05$ ) higher SD symptoms: Muscle tightness or spasms in my arms, legs, or body; Tremors or shaking in hands or body; Pain, burning, or discomfort in their body; Feeling less attractive; Fear of being rejected sexually because of MS; Lack of sexual interest or desire; Less intense or pleasurable orgasms or climaxes.

**Conclusions:** This study found that both depression and SD are present in pwMS and that depressive patients have more pronounced SD symptoms.

#### 66. VALUE OF HEAD CT SCAN IN THE EMERGENCY DEPARTMENT IN PATIENTS WITH VERTIGO WITHOUT FOCAL NEUROLOGICAL ABNORMALITIES.

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**Introduction/Objectives:** Vertigo is a common symptom and reason for admission to emergency department (ED). The aim of this research was to determine the incidence of clinically significant findings on computed tomography (CT) in patients with vertigo without focal neurological abnormalities in ED.

**Participants, Materials/Methods:** The results of the native CT scans in ED were retrospectively analyzed. Exclusion criteria included: focal neurological abnormalities, underlying malignancy, brain metastasis, previous brain operation, headache, fever, nausea, vomiting, head trauma, coagulopathy. As a clinically significant finding we took into account tumour, hemorrhage and acute ischemic lesion. 72 patients fulfilled the set criteria, present vertigo, without focal neurological abnormalities. Out of 72 patients with median age of 62 (23-87) years old, 54% of the patients were female and 46% were male.

**Results:** Normal CT findings were found in 44 patients (61.1%). 28 patients (38.9%) had pathological findings, out of that number 23 (31.9%) findings were clinically irrelevant and 5 (6.9%) were clinically significant. Out of the 5 clinically significant findings, tumor process was found in 3 (4.2%) patients, hemorrhage was found in 1 (1.4%) patient and ischemic lesion was found in 1 (1.4%) patient. Additional evaluation of five clinically significant findings showed change of initial diagnosis in one case, but significance of the finding remained the same.

**Conclusions:** Our study demonstrates a low diagnostic yield of head CT examination with 6.9% of clinically significant findings in patients with vertigo without focal neurological abnormalities.

#### 67. RAMSAY HUNT SYNDROME - A CASE REPORT.

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**Introduction/Objectives:** Ramsay Hunt syndrome (RHS) is a rare neurological disorder caused by reactivation of latent Varicella-zoster virus (VZV) in the geniculate ganglion. A triad of ipsilateral facial paralysis, ear pain and herpes zoster oticus is the typical presentation. Cochleovestibular impairment such as hypoacusis, tinnitus and vertigo may occur. The involvement of other cranial nerves, such as V, IX, X, and XII is rare. Objectives : Review of clinical manifestations and treatment of patient with Ramsay Hunt syndrome caused by VZV reactivation.

**Case report:** A 24-year-old female patient was admitted to the hospital on the third day of illness, presenting with fever, symptoms of upper respiratory tract infection (sore throat, lymphadenitis on left side on neck), loss of salt taste on the front 2/3 of the left side of the tongue, left ear pain without hearing loss, and ipsilaterally a herpetiform vesicular eruption the auricle and external acoustic meatus. On the fifth day of the disease, the patient developed an inability to close left eye and a facial asymmetry with the lower left corner of the lips. A complete clinical examination revealed herpes zoster oticus and peripheral facial nerve paralysis a House-Brackmann grade III on the left side. Diagnosis was performed based on laboratory, physical and neurological examinations.

Hematological-biochemical tests were within reference range (erythrocyte sedimentation rate, CRP, blood cell count, liver and kidney enzyme analysis, urine analysis), MRI brain scan was normal, the patient had a bilateral type A tympanogram and stapedial reflex was absent in the left ear. The serological test (EIA) confirmed reactivation of VZV ( IgM antibodies 11-positive, IgG antibodies 38-positive , IgA antibodies-borderline). Patient was treated with acyclovir 800 mg PO q4h (5 times daily) for 10 days and oral prednisolone (1 mg /kg q24 h) for 5 days, then the dose was tapered for 10 days. On follow-up four weeks later, complete recovery of neurological deficit was noted.

**Conclusions:** Early diagnosis and prompt treatment of RHS with combination of steroids and acyclovir within 72 hours of rash appearance achieved the higher rate of recovery and prevention of complications such as permanent hearing loss and facial weakness, eye damage and postherpetic neuralgia. Treatment of our patient was started on the third day of the rash, recovering completely within four weeks.

#### 68. CLEVELAND CLINIC ABU DHABI STROKE REGISTRY (CCADSR) METHODOLOGY.

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**Introduction/Objectives:** United Arab Emirates (UAE) is a federation of seven emirates. Its population grew from 1971 from 235,499 to 9,157,000 in 2015 according to United Nations. The forecast suggest further growth to 13,163,548 by the year 2050. The UAE population is mainly composed of expatriates and only 11% are UAE Nationals. In UAE has a high cardiovascular risk population as 60% is overweight, 20% has diabetes and 18% more is at risk of developing this condition.

**Participants, Materials/Methods:** The epidemiological stroke data for UAE is limited to a few small studies. In addition to this UAE population is mixed with majority of it being expatriates which makes any epidemiological extrapolation futile. Collection of stroke epidemiological data is critical for further development of proper larger scale primary and secondary stroke preventative strategies. CCADSR was approved by CCAD Ethical Committee (A-2018-020). CCADSR collects hospital level data. All patients' entries are anonymised with consecutive and unique serial numbers. All patients with acute stroke as main diagnosis admitted to CCAD are included (ischemic stroke, hemorrhagic stroke, subarachnoidal haemorrhage). The following data domains are collected: demographics, premorbid functional status, vital parameters, cardiovascular risk factors, time of onset of symptoms, stroke type/subtype, diagnostic results, initial clinical presentation, etiological stroke subtyping, treatment received, vital status at discharge.

**Results:** Until May 2018 we included 1013 stroke patients (mean age 55.9 y; min 17, max 98y; 68.4% men; 36.7% UAE Nationals). There were 590 ischemic strokes (58.73y; 17-98y; 68.5% men; 40% UAEN), 176 ICH (52.8y; 20-97y; 71.6% men; 46.8% UAEN) and 117 SAH (46.74y; 18-77y; 61.53% men; 21.36% UAEN).

**Conclusions:** Further prospective studies are needed to further explore stroke epidemiology in UAE and to understand the differences in stroke epidemiology between UAE Nationals and Expats.

#### 69. EFFECTIVE CORTICOSTEROID THERAPY IN MELAS – A CASE REPORT.

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**Introduction/Objectives:** MELAS (Mitochondrial myopathy, Encephalopathy, Lactic Acidosis and Stroke-like episodes) is a rare syndrome characterized by the presence of seizures, headaches, loss of appetite, vomiting, muscle weakness blindness, myoclonus, altered consciousness and loss of intellectual function. The therapy is symptomatic as a cure or specific therapy has been found for MELAS, while only a small number of cases reported the use of corticosteroids in MELAS with contradictory results. We report a case of a 25-year old female with a clinical picture and biochemical and genetical findings of MELAS, who responded well to corticosteroid therapy.

**Case report:** A 25-year-old female was admitted to the hospital after two grand mal seizures after a history of



seizures that were controlled with sodium valproate. Brain MRI revealed cortical area of ischaemia in the non-vascular territory of the left occipital lobe. The cerebrospinal fluid (CSF) analysis revealed a mild proteinorachy and lactate elevation. Infectious causes, autoimmune encephalitis and malignant diseases were ruled out. The symptoms progressed and at fourth week of treatment the patient had increased tiredness, loss of vision on both eyes, stronger headache and was unable to walk, eat or dress properly. A follow-up brain MRI visualized a new cortical ischemic lesion in the right temporal and occipital lobes, along with a lactate increase in the CSF. The diagnosis of MELAS was suspected and genetical analysis confirmed the presence of a point mutation A3243. Methylprednisolone was administered intravenously after exacerbation, with a regression of symptoms. Impairments at discharge were slight disorientation in time and space, slower motions and a speech impairment. No further progression of cognitive decline was noted in a control visit twelve months later. **Conclusions:** Corticosteroid therapy brought a recovery to our patient and we propose that corticosteroid therapy should come into consideration whenever a case of MELAS is suspected in patients with progressive worsening.

**70. ADVANCED 3D MODELING FOR PREDICTION AND QUANTIFICATION OF THE PERIHEMATOMAL BRAIN EDEMA FORMATION AFTER INTRACEREBRAL HEMORRHAGE: IMPLICATIONS OF BIOCHEMICAL, RADIOLOGICAL AND CLINICAL VARIABLES.**

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Department: University Clinic of Neurosurgery

**Introduction/Objectives:** The worst neurological deterioration after intracerebral hemorrhage (ICH) occurs due to the formation of perihematoma brain edema, a significant risk factor for poor prognosis and increased in-hospital mortality. The formation of the edema significantly contributes to the secondary brain injury after ICH as a result of its mass effect, thus stimulating increased intracranial pressure. Therefore, the identification of the main risk factors which directly or indirectly drive the brain edema formation is particularly challenging, allowing prediction of the brain edema formation on the basis of initial biochemical, radiological and clinical variables.

**Participants, Materials/Methods:** 70 conservatively-treated ICH patients were included in the study. Advanced

mathematical modeling for prediction and 3D visualization of the brain edema formation, as well as quantification of its volume was performed by using several statistical approaches in JMP® 14 (SAS Institute Inc).

**Results:** All models have stressed the importance of the initial TNF- $\alpha$  and glutamate levels at admission and the initial volume of ICH as the main drivers for formation of the edema volume, five days after ICH. The constructed 3D models were characterized by high overall characteristics and fit and high overall predictive capacity, allowing precise quantification of the volume of the edema on the basis of initial characteristics. Since all characteristics pointed out to reliability and validity of the developed models, interactive 3D surface plots were also constructed which can serve for instant estimation of the edema volume.

**Conclusions:** We believe that the constructed models and the developed interactive plots could be beneficial for clinical decision making between conservative treatment and surgical intervention, especially in the group of threatened ICH patients where high volumes of the edema are expected to occur during the patient's hospitalization trajectory.

**71. ANTI-GQ1B ANTIBODY SYNDROME: A CASE REPORT.**

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**Introduction/Objectives:** Studies have shown that serum samples from patients with Miller Fisher syndrome (MFS), Guillain-Barré syndrome (GBS), Bickerstaff's brainstem encephalitis (BBE) and acute ophthalmoparesis often have positive anti-GQ1b antibodies. The aim of this case report was to present challenges in diagnosis and treatment of a young patient with overlapping GBS and MFS syndrome.

**Participants, Materials/Methods:** A 31-year-old man presented in our emergency room due to the sudden onset of binocular diplopia. One week prior to the symptom onset he had diarrhea. Other past medical history didn't reveal any significant diseases. The physical examination was unremarkable, while the neurological examination revealed diplopia with right abducens nerve palsy and right ptosis with preserved pupil function. During first days after the hospitalization, the clinical state continued to worsen with the progression of neurological deficit affecting multiple cranial nerves, the absence of myotatic reflexes, paresthesias in the hands and feet and tetraparesis. Initial negative CT scan was followed by magnetic resonance (MR) of the brain and the magnetic resonance angiography (MRA) of the brain vessels. Neither showed any significant pathological

findings. The lumbar puncture revealed increased protein level (0,61 g/L) with normal cell counts (2 cells) and normal CSF glucose levels. Electroneurography performed on day 7 of the illness revealed moderate loss of motoneurons in all examined muscle groups. Neurographic analysis showed low amplitude sensory nerve action potentials (SNAP) in all sensory nerves. Serum tests for antiganglioside antibodies were sent for analysis and came positive for anti-GD1b and anti-GQ1b.

Considering the clinical presentation of overlapping Miller Fisher and Guillain-Barré syndrome, treatment with plasma exchange was initiated. Despite the treatment, the clinical state continued to worsen to the state of the respiratory arrest due to which the patient was urgently intubated and mechanically ventilated. In total, five plasma exchanges were given which gradually resulted in the separation of the patient from the mechanical ventilation. However, there was no other clinical improvement and since the slight progress of the motoric deficit in the arms was observed, therapy with intravenous immunoglobulin was indicated in dose 2g/kg over 5 days. Three months after the admission, the patient was discharged from the hospital and referred to rehabilitation. The first follow-up after the discharge from the hospital was two months later. The neurological exam revealed significant improvement with residual gait ataxia, dysarthria and slight weakness of the proximal musculature of both arms. On the second follow-up, four months after the discharge, the patient was independently mobile, without speech disturbances and with the residual mild motoric deficit of the left arm (motor strength 3/5).

**Conclusions:** The optimal management for most severe cases of GBS remains uncertain. The current clinical practice requires further investigations to identify clinical predictors of early deterioration and to define the treatment modalities in patients with anti-GQ1b overlapping syndromes.

## 72. CRYOGLOBULINEMIA AND SENSORIMOTOR POLYNEUROPATHY: A CASE REPORT.

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**Introduction/Objectives:** Cryoglobulins are immunoglobulins that produce precipitate or gel in reduced temperatures. These precipitate dissolve when the temperature returns to normal values. Cryoglobulinemia can be essential - without a detectable underlying disease, or it can be secondary to other conditions, such as an infection (most commonly hepatitis C), lymphoproliferative or an

autoimmune disease. It can lead to a variety of systemic complications, including peripheral neuropathy.

**Case report:** A 69-year-old woman was admitted to the Department of Neurology due to progressive gait difficulties with distal motor weakness of extremities, tingling sensation in the hands and feet and skin changes. The symptoms began two years prior with gradual numbness of both hands and feet. Past medical history revealed arterial hypertension and operation of the kidney in the childhood that required a blood transfusion. Neurological examination at admission revealed distal motor weakness with hypotrophy, reduced sensation in the hands and feet, and absent Achilles reflexes, while the physical examination revealed skin ulcerations of the lower extremities.

Laboratory testing showed elevated sedimentation rate (ESR) and C-reactive protein (CRP) levels, while immunological testing revealed normal ANA; p-ANCA, c-ANCA, anti-CCP anti dsDNA levels, increased RF and CIC, C4 hypocomplementemia and positive cryoglobulin type III. Neuroradiological imaging (MR of the cervical and lumbar spine) did not reveal any significant findings, and the lumbar puncture revealed slightly increased protein level (0,51 g/L) with normal cell counts (5 cells) and normal CSF glucose levels. Serologic studies for viral hepatitis were performed and came positive for HCV virus. Also, the skin biopsy was performed and revealed leukocytoclastic vasculitis with necrosis. The patient was diagnosed with cryoglobulinemia and treated with high doses of glucocorticosteroids while in the hospital. She was discharged home with prescribed immunosuppressive therapy (prednisone) and antiviral therapy (ombitasvir, paritaprevir and ritonavir) for hepatitis C. On follow-up exams there were a gradual and substantial recovery of skin lesions, eradication of chronic HCV infection with residual distal motor leg weakness.

**Conclusions:** Hepatitis C infection is associated with a broad spectrum of manifestations and cryoglobulinemia is believed to be one of the most common extrahepatic expressions. The patients with cryoglobulinemia can develop various complications affecting multiple organ systems, and the most common neurological complication is distal sensorimotor polyneuropathy. In the clinical setting, it is important to think about the association between these conditions. Screening of the patients with hepatitis C infection by electrophysiological testing is necessary to detect patients with neurological complications in the early stages to begin treatment since they can be sometimes quite difficult and challenging to treat later on.

**73. EPILEPTIC SEIZURES IN PATIENTS WITH LARGE AND GIANT PROLACTINOMAS.**

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**Introduction/Objectives:** The aim of the study was to analyze epileptic seizures in patients with large and giant prolactinomas.

**Participants, Materials/Methods:** the study group included 45 patients with large prolactinoma (more 36 mm in diameter) and 23 patients with giant prolactinoma (more than 60 mm in diameter). 55 men and 13 women aged 16-67 years (mean 39). Patients were followed by hormone measurements, magnetic resonance imaging (MRI), electroencephalogram (EEG) and endocrinological, psychopathological, neurologic examinations. Mean serum prolactin level ranged between 12990 and 1038000 mU/l (mean 198000 mU/l).

**Results:** Epileptic syndrome was revealed in 14 patients (21%): partial seizures with secondary generalization (64%), complex (28%) and simple (14%) seizures or their combinations. Seizures differ red in structure depending on growth of the tumor. Partial seizures with secondary generalization were mostly revealed in patients with growth of adenoma to temporal region on left (50%) and right (14%). Complex partial seizures were revealed in patients with growth of the adenoma to temporal region on left (21%) and into the III ventricle (7%). Simple partial (psychosensory) seizures were in patients with growth of adenoma into diencephalic region (14%). Diagnosis of epileptic seizures was based on clinical presentation and ry EEG.

**Conclusions:** 21% patients with large and giant prolactinomas have epileptic syndrome. Structure of epileptic seizures depends on extension of the adenoma and intrusion in different regions of the brain.

**74. PATIENT WITH NEWLY DIAGNOSED MESENCEPHALIC GLIOMA AND TREMOR – A CASE REPORT.**

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**Introduction/Objectives:** Parkinsonism is a syndrome characterized with hypokinesia and bradykinesia, rigor, resting tremor and postural instability. Etiologically, it mostly occurs within idiopathic Parkinson's disease; secondary causes are iatrogenic, vascular, metabolic, endocrine, infections, traumas and tumours.

Gliomas are the most common tumours of CNS; their symptoms and clinical presentation are consequence of brain parenchyma destruction, elevated intracranial pressure and convulsive seizures.

**Case report:** During 2015, 58-years-old patient started treatment at the Department of Psychiatry, due to depression and disturbances in cognitive functioning. Despite the introduction of antidepressants, there wasn't any therapeutic response. Patient's forgetfulness became worse and interfered with his functioning and, because of that, he was referred to neurologist. In 2016, patient developed incontinence and unilateral tremor of his right hand at rest, during posture and action. Performed MRI of the brain was described as normal. Since no other associated symptoms (bradykinesia and rigor) were present in clinical status, patient was instructed to perform SPECT scintigraphy of the brain with ioflupan, which showed scintigraphic deficit of striatal DAT gr. I-II on the left. Pramipexole has been introduced in therapy without any therapeutic response; during next visits, amantadine, rasagiline and levodopa were introduced in therapy as well, but also without any therapeutic response. Over time, patient noticed tremor of the right leg, reduction of strength of the left leg, frequent falls, daily sleepiness and lack of sleep at night, disturbances of attention, dizziness, frequent headaches and limited left-hand mobility. Neurological status did not present any clinical signs in favour to atypical parkinsonism syndromes. Due to symptoms worsening, control MRI of the brain has been recommended. Patient became acute sexually disinhibited; therefore urgent hospitalization at Psychiatry was performed. Control cognitive testing indicated deterioration in cognitive status with initial dementia followed by disinhibited behaviour, depression and social dysfunction. Performed MRI of the brain has shown low grade glioma located in mesencephalon with irregular cystic areas in tectum and without obstruction of CSF drainage. **Conclusion:** Secondary parkinsonism, with clinical presentation of pharmacoresistant depression and pharmacoresistant tremor, along with appearance of early postural instability and tendency of falling, in our case, was caused by tumour process in mesencephalon. DATScan, as method for diferentiation between Parkinson disease and secondary parkinsonism, was not useful in this case.

Therefore, we emphasize the importance of reviewing the diagnosis and need for additional diagnostic treatment in atypical Parkinson's disease cases.

### 75. STROKE AND ULCERATIVE COLITIS – A CASE REPORT.

Ivana Šimić, Darko Kotromanović, Jasna Hanižjar-Berlančić

Institute of Public Health Osijek Baranja County, Osijek, Croatia; Faculty of Medicine Osijek, Josip Juraj Strossmayer University in Osijek, Osijek, Croatia; University Hospital Center Osijek, Department of Neurology, Osijek, Croatia

**Introduction/Objectives:** Ulcerative colitis (UC) is idiopathic, chronic inflammatory bowel disease characterized by remissions and exacerbations. Venous thromboembolic events are well known complications of inflammatory bowel disease but arterial thrombosis is rare, especially stroke. Inflammation plays a role in the development of atrial fibrillation (AF), therefore UC can be associated with AF. We present a case of a stroke patient and newly discovered UC with existing AF.

**Case report:** In May 2018, an 82-year-old male, with cardiomyopathy, hypertension and implanted permanent pacemaker for left bundle branch block with AF on warfarin therapy, was admitted to the Department of Gastroenterology and Hepatology for stomach pain, constipation and bloody mucus in stool. Electrocardiography showed pacemaker rhythm of 72/min, and one ventricular extrasystole. Blood test showed normochromic normocytic anemia, elevated alanine transaminase, gamma-glutamyltransferase, blood glucose levels, urea, and C-reactive protein. His prothrombin time-normalized international ratio was 5,03. Clinical picture indicated active UC which was confirmed by colonoscopy, colon and rectum biopsy and computed tomography scan of the abdomen. He was treated with mesalazine, gastroprotective and antibiotic therapy, while warfarin was substituted with low-molecular-weight heparin because prothrombin time-normalized international ratio was above optimum values. Applied UC therapy was effective, which was confirmed by control colonoscopy. Two days after control colonoscopy, patient developed right facial palsy of central type, motor dysphasia and severe weakness of right arm and leg. National Institutes of Health Stroke Scale (NIHSS) score was 18. Computed tomography scan of the brain confirmed left frontal acute ischemic lesion. He was moved to the Department of Intensive Neurological Care with Stroke Unit. Electrocardiography showed AF. Color Doppler flow

imaging revealed initial morphological stenosis of the right common carotid artery and the possible occlusion of the right vertebral artery. Mesalazine, gastroprotective, antihypertensive, antiarrhythmic and diuretic therapy continued. Pneumonia and urinary infection have been treated with targeted antibiotic therapy. Low-molecular-weight heparin was gradually substituted with warfarin. Due to urinary incontinence, urinary catheter was set up. Physical and speech therapy were continuously performed during his hospitalization. On the 48th day of hospitalization the patient was discharged with stabilized UC, right facial palsy of central type, motor aphasia, severe weakness on the right side, incontinence of urine and stool. NIHSS score was 17. Further rehabilitation at home was advised.

**Conclusion:** Active UC is associated with increased risk of AF and stroke. The risk of stroke after colonoscopy in patients with AF with optimal anticoagulant therapy is low. The risk is higher in older people with severe comorbidity and additional risk factors for stroke. Patients with AF and active UC have increased risk of stroke during and immediately after the colonoscopy despite well regulated anticoagulant therapy.

### 76. HOW TO LABEL SOMEONE TREATED FOR EPILEPSY?

Ana Sruk, Latica Friedrich, Ivan Bielen

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

**Introduction/Objectives:** The debate on how a person with diagnosed epilepsy should be referred to still continues, but views of those living with epilepsy are rarely researched. The aim of this study is to identify which label patients treated for epilepsy and persons close to them prefer.

**Participants, Materials/Methods:** For one month, starting from 28th May 2017, an anonymous online questionnaire was offered to all visitors of the Croatian Association for Epilepsy's website. The first question was "What do you think is the most appropriate label when talking about someone treated for epilepsy?", with 5 possible answers: 1. Epileptic, 2. Person with epilepsy (or depending on the context child/older person/woman with epilepsy), 3. A person having epilepsy (or depending on the context child/older person/woman having epilepsy), 4. Patient with epilepsy/diseased with epilepsy, and 5. I think all the suggested labels are equally appropriate. The second question was a yes/no question: "Would you mind if someone called you (or your child/family member/friend/acquaintance) an 'epileptic'?" The remainder of the questionnaire collected demographic data (age, gender, country of residence, level of education) and the



relationship with a person with epilepsy, which was then checked for associations with label preference.

**Results:** In total, 328 responses were analysed. Mean age was  $35 \pm 9.6$  years, 85% were female. Fifty-three percent of subjects had epilepsy; 31% were parents of someone with epilepsy, and the remainder stated other kind of relationship with someone with epilepsy. The majority of subjects preferred the label “person having epilepsy” (28%) followed closely by “person with epilepsy” (27%). Parents were more likely to mind the term “epileptic” (71.6 %), while the opposite was true for patients (43.4%).

**Conclusions:** We believe our study has brought an additional insight from those living with epilepsy into the language debate. These results can help with shaping future recommendations for terminology in epilepsy.

#### **77. DISTRIBUTION OF DEMYELINATING LESIONS WITHIN THE CEREBRAL WHITE MATTER SEGMENTS AND THEIR CORRELATION WITH NEUROLOGICAL DISABILITY IN PATIENTS WITH MULTIPLE SCLEROSIS.**

Sarah Stančić-Rokotov, Milan Radoš, Anton Vladić

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

**Introduction/Objectives:** The development of human cerebral white matter (WM) represents a complex set of developmental processes characterized by precisely regulated timetable of axonal growth and their spacial arrangement within cerebral wall. When reading radiological report, WM is roughly divided into periventricular, deep and subcortical WM. Since this division does not involve developmental and functional complexity of WM, no significant correlation can be made between radiological and clinical findings. Clinical symptoms identified in patients with MS and their neurological outcome oftenly do not correlate with the extent of demyelination of MS lesions on MRI. In same severe demyelinated lesions induce only discrete neurological symptoms while in other patients discrete lesions can cause severe clinical impairments. This study was based on the hypothesis that correlation between the neuroradiological and clinical findings could be improved if distribution of demyelinated lesions would be analysed more precisely using segmentation according to Von Monakow (IV) which appreciate developmental and functional complexity of WM. Each segment of WM (I-V), as classically described by von Monakow, can be visualized by using magnetic resonance imaging.

**Participants, Materials/Methods:** This study will have a prospective character of MR brain examination involving

100 patients with MS. The inclusion factors are based on McDonald Criteria for MS from 2017. The age of the patient will be greater than 18 and less than 60 years. Patients with MR scans done according to the 3D demyelinating disease protocol, including FLAIR intercepts, will be analyzed from which the volume distribution of MS lesions can be calculated within the white matter segments. Lesions will be distributed according to its spatial distribution into one of the five segments of white matter. For manual segmentation and volumetric lesion analysis, the ITK-SNAP 3.2 program will be used (University of Pennsylvania, USA, open code program) (2). A particularly well-trained and experienced neurologist will examine each patient prior to the MR examination of the brain to a clinical neurostatus according to Expanded Disability Status Scale and Multiple Sclerosis Functional Composite scale.

**Results:** Four patients were thoroughly processed for this analysis. First, they were examined by an experienced neurologist, who determined their neurological status, MSFC and EDSS scale. The same day an MRI scan was done with 3D FLAIR sequence and volumetric analysis of demyelinating lesions by segments. Mean volume of lesions in all patient is  $3950,9 \text{ mm}^3 \pm 520,5$ , thereof in 1st segment lesion volume is  $5417 \text{ mm}^3 \pm 1074$ , in 2nd segment  $3247,1 \text{ mm}^3 \pm 1106,6$ , in 3rd segment is  $5172,1 \text{ mm}^3 \pm 1319,5$ , in 4th segment is  $1887,9 \text{ mm}^3 \pm 326,3$ . and in the 5th segment is  $79,65 \pm 0,5$ . The 5th segment which represents intracortical white matter lesion is not possible to quantify in a reliable manner. In this small sample of patient's statistical analysis of lesion volumes and neurological status is inadequate. The study is still in progress and the results are still not complete. The study should be continued and date subjected to more detailed statistical analysis to have definitive conclusion.

**Conclusions:** Gathering the patients for the study was slower than expected due to the excluding factor, absence of cervical demyelinated lesions, with the intent of better correlation of neurological disability and presence of demyelinating lesions in segments of white matter. Our research will contribute to a better correlation of neuroradiological and clinical findings in patients with multiple sclerosis. We hope that the analysis of the distribution of demyelinating lesions in the white matter segments to Von Monakow will show which segments of white matter have the greatest significance for the development of disability.

**78. THE PREVALENCE OF MCI IN RURAL CHILE.**

Pablo Toro, Claudia Bambs, Caterina Ferreccio, Johannes Schröder

Heidelberg University, Section Geriatric Psychiatry, Heidelberg, Germany

**Introduction/Objectives:** Little is known on the prevalence of mild cognitive impairment (MCI) in rural South American regions although an increasing life expectancy underlines the importance of dementing disorders and calls for appropriate preventive measures. In this respect potential effects of education and gender have to be considered since this population had limited access to advanced education in the past; an effect that particularly applied for females. We therefore sought to establish the prevalence of MCI in Molina i.e. an agriculture centre in rural Chile by using data from the (MAUCO).

**Participants, Materials/Methods:** Eligible subjects were literate participants aged 50 (range: 50 – 76a) and above from the MAUCO, a population-based cohort study of chronic disease in the city of Molina, Maule, Chile. Subjective cognitive complaints were examined on a questionnaire, neuropsychological performance on the Addenbrooke's Cognitive Examination. Data from subjects with a history of cancer (n=221) and cerebrovascular disorder (n=126) were excluded, as these conditions may cause symptomatic cognitive decline.

**Results:** 3610 persons (age  $58.9 \pm 6.5$  a; years of formal school education  $9.1 \pm 6.1$  a) were eligible for this analysis. Women were slightly younger ( $58.7 \pm 6.5$ ) than men ( $59.3 \pm 6.5$ ;  $p < 0.01$ ) and had less educational years ( $8.9 \pm 3.6$ ) than men ( $9.4 \pm 3.6$ ;  $p < 0.0001$ ). 16.1% of women but 10.9% of men met criteria for MCI ( $p < 0.0001$ ); female gender (OR=1.49, CI= 1.22- 1.82,  $p < 0.0001$ ) and education (0.91, CI=0.89- 0.94,  $p < 0.001$ ) but not chronological age ( $p = 0.93$ ) were confirmed as risk and protector factors respectively. For detailed analysis, neuropsychological performance was compared between female and male subjects with MCI vs. female and male control subjects with education as a covariate. The MANOVA revealed highly significant effects of diagnosis and gender on all neuropsychological domains (abstract thinking, memory, attention, verbal fluency, visuo-spatial thinking and mental flexibility) examined. However, solely the effects of diagnosis but not those of gender were confirmed when education was entered as a covariate. In contrast gender effects were only significant for verbal fluency, with women showing a better performance than men.

**Conclusions:** Our findings demonstrate that MCI is a frequent condition in an older rural population. Risk factors for MCI involved both, gender and education. According to a detailed analysis of neuropsychological performance,

however, these effects can be solely referred to school education. As social progress continues, future studies involving later born cohorts who enjoyed a better and more equal access to education in their youth will demonstrate lower prevalence rates of MCI than observed in this study.

**79. PRELIMINARY EVALUATION OF CROATIAN VERSION OF THE NON-MOTOR SYMPTOMS SCALE IN PARKINSON'S DISEASE.**

Zvonimir Uzarevic, Anamarija Soldo Koruga Ivana Kampic, Zeljka Popijac, Silva Butkovic Soldo

Faculty of Education, University of Osijek, Osijek, Croatia,; Clinic for Neurology, Clinical Hospital Centre Osijek, Osijek, Croatia; Faculty of Medicine, University of Osijek, Osijek, Croatia

**Introduction/Objectives:** Non-motor symptoms (NMS) of Parkinson's disease (PD) are common and have a great impact on PD patients. They are often under-recognized and remain untreated. The non-motor symptoms scale (NMSS) is an instrument specifically designed for the comprehensive assessment of NMS in PD patients. The objective of this study was to preliminary evaluate the psychometric properties of Croatian version of the NMSS as an instrument for measuring NMS in Croatian-speaking PD patients.

**Participants, Materials/Methods:** In this research was analysed data on 23 PD patients, which included 8 women and 15 man which underwent neurological care at Clinical Hospital Centre Osijek in Croatia. Our research problem was examined using the NMSS which includes nine domains: cardiovascular including falls, sleep/fatigue, mood/cognition, perceptual problems/hallucinations, attention/memory, gastrointestinal tract, urinary, sexual function and miscellaneous. The data was descriptively analysed and Chronbach's  $\alpha$  coefficient assessed internal consistency. Pearson r correlations were performed on the nine domains of the NMSS. The level of significance was set to  $p < 0.05$ .

**Results:** The mean age was  $70.8 \pm 10.4$  years, and mean disease duration was  $6.5 \pm 4.2$  years. The mean NMSS score was  $112.70 \pm 60.89$ , where the more common non-motor symptoms in PD patients were related to the following domains: mood/cognition (21.64%), sleep/fatigue (18.86%), sexual function (14.93%) and urinary (12.51%). Cronbach's  $\alpha$  coefficient for the NMSS total score using the entire sample was 0.93, indicating high internal consistency. For domains, the Cronbach's  $\alpha$  coefficient ranged from 0.43 to 0.97. The total NMSS score was highly correlated with each of the nine domains, the Pearson r correlation coefficient ranged from 0.43 to 0.78).

**Conclusions:** This preliminary results suggests that Croatian version of NMSS can be considered a comprehensive and reliable measure for NMS in Croatian-speaking PD patients.

#### **80. CLINICAL CHARACTERISTICS, DIAGNOSTIC PROCEDURES AND THERAPY OF CEREBRAL VENOUS AND SINUS THROMBOSIS – A CASE REPORT.**

Ivana Vuković, Borislav Vuković, Dobrinka Petković

Clinical Hospital Center Rijeka, Department of Pediatrics, Rijeka, Croatia

**Introduction/Objectives:** Cerebral venous and sinus thrombosis (CVST) is a rare type of cerebrovascular disease which accounts for <1% of all the strokes and is characterized by widespread thrombus within the central venous sinus system. CVST can occur at any age and is more frequent in young adultst. The incidence in the adult population is 3-4 cases per 2 million per year, and in children is 0.67 cases per 100 000 children below 18 years. The predisposing factors include the use of oral contraceptives, pregnancy, childbirth, congenital and acquired coagulation disorders, neoplastic processes, cardiac defects, systemic diseases of the connective tissue etc. Risk factors cannot be identified in about 15% of cases. CVST are associated with accelerated coagulation and increased blood density, and occurs following endothelial damage and slowed blood flow. Diagnosis was based on neuroimaging – computed tomography, magnetic resonance imaging, computed tomography angiography, magnetic resonance angiography, digital subtraction angiography, magnetic resonance venography. Objectives: Review of clinical characteristics, diagnostic procedures and therapy patient of cerebral venous and sinus thrombosis.

**Case report:** 73-year-old female hospitalized after the onset of severe headache, dizziness, nausea, vomiting and the right-sided hemiparesis 4/5 degree. Hyperdense signal and empty delta sign on computed tomography image and the combination of absence of a flow void with alternation of signal intensity in the dural sinus on MRI were the suggestive signs of CVST. Except the elevated D-dimer values, other laboratory findings were within the reference range. Genetic and acquired coagulation disorders were excluded, and the laboratory and radiology processing for detection of malignancy were negative. The patient was treated with body weight-adjusted subcutaneous low-molecular-weight heparin with a good clinical response—dissappearance of signs and symptoms and the absence of

complications. After the acute phase of the disease she took oral anticoagulant therapy for 1 year.

**Conclusions:** We reported a case of multiple segmental sinovenous thrombosis with good prognosis. Early diagnosis and application of anticoagulant therapy affect the outcome of CVST. The aims of antithrombotic therapy in CVST are to recanalise the occluded sinus or vein, to prevent the propagation of the thrombus and to prevent the recurrence of CVST.

#### **81. RESTORATION OF THE MENTAL HEALTH OF CHILDREN WITH STBI: PEDAGOGICAL MEANS IN REHABILITATION.**

Alla Zakrepina, Yuliya Sidneva

Clinical and Research Institute of Emergency Pediatric Surgery and Trauma; Institute of Correctional Pedagogy of the Russian Academy of Education; Burdenko Neurosurgery; Department of Rehabilitation; Department of Nerosurgery, Moscow, Russian Federation

**Introduction/Objectives:** Severe traumatic brain injury (sTBI) causes a high level of disability in children population. Reducing the risk of insufficient psychological adaptation after sTBI represents a considerable social challenge. Its solution depends not only on the high quality rehabilitation in hospitals but also on the timely contribution and pedagogic assistance to the patient and its family. Objective: To provide the background and the content for the pedagogic assistance to children with severe traumatic brain injury.

**Participants, Materials/Methods:** The experiment was performed for 98 children aged 1.5 to 15 including 19 children of the early age, 36 preschool children and 43 scholars. Were used: observation, ascertaining and training experiments, analysis of medical histories of hospitalized patients (case histories), surveys of parents or adult caregivers, talks with attending doctors and relatives.

**Results:** The first group (expansive character) - 25%. Children have a more pronounced interest: a more active physical and emotional state. These children were characterized by low motivation for targeted actions; however, they understood the instructions and, in joint activities with adults, showed interest in studying their surroundings. The second group (border type) - 30%. Their sensorimotor reactions were active, simple manipulations with objects were observed. The third group (stagnant type) - 45%. The reactions of the children were weak, but after training there were changes: increased mental tone, signs of adaptation to the environment, selectivity to contacts of adults and regime procedures. Pedagogic activity with



children after sTBI constitutes an element of complex rehabilitation. In the present study the researchers have identified pedagogic background for the correctional education of children with sTBI, revealed and described the traits of mental activity of children with sTBI. Finally, the stages of correctional education of children with sTBI were defined to assist the recovery of children mental activity. Findings of the primary pedagogic examination of the studied children have allowed differentiating methods and procedures for diagnostic trainings as an initial stage in the correction-pedagogic activity. During the training experiment three diagnostic programs were developed.

**Conclusions:** In the course of correctional education a positive recovery dynamics was seen: in the majority of cases one could detect a shift to upper level of a child activity, signs of orientation behavior, child's engagement into joint activity with adults. In the most difficult cases a positive dynamic was identified in qualitative changes in the mental activity at the initial level: selective reactions to adult's activity, widening variety of reflex response.

## 82. THE STUDY ON MANIFESTATION OF MENTAL ACTIVITY IN PRESCHOOL CHILDREN WITH SEVERE CRANIOCEREBRAL TRAUMA.

Alla Zakrepina, Yuliya Sidneva, Elena Strebeleva

Clinical and Research Institute of Emergency Pediatric Surgery and Trauma; Institute of Correctional Pedagogy of the Russian Academy of Education; Burdenko Neurosurgery; Department of Rehabilitation; Department of Neurosurgery, Moscow, Russian Federation

**Introduction/Objectives:** This study investigates the leading factors in the manifestation of mental activity in children with severe craniocerebral trauma. The groups of factors demonstrate not only "sensitive" zones in the manifestations of mental activity during severe brain trauma injuries in children at early stages of recovery, but also serve as reference points for the selection of socially significant methods of rehabilitation. Objective: The aim of this research was to identify leading factors in the structure of mental activity in children with severe traumatic brain injury (STBI).

**Participants, Materials/Methods:** The experiment involved 80 preschool children as participants (35 of them girls and 45 boys). The following research methods were used: observation of a child; educational and clinical psychopathological methods were used with the assessment of the consciousness level and mental activity recovery according to CRS (Coma Recovery Scale, Giacino J.T., Kalmar K., 2004); RLAS (Runcho Los Amigos Scale,

Hagen C., Malkmus D., 1989); MSMA (Method of studying mental activity, Zakrepina A.V. 2015) scales. Scientific examination of children was carried out during one year in the period of early stages of rehabilitation in the hospital.

**Results:** The results showed a disharmonious distribution of the factors load in the structure of mental activity, depending on the severity of its manifestations in the early stages of rehabilitation. The first factor encompasses characteristics that reflect the emotional-sensory level of mental activity; the second factor combines elementary arbitrary movements and actions, combined with involuntary manifestations, which may indicate difficulties in understanding the meaning of the speech addressed to the child; the third factor is saturated with the characteristics of arbitrary actions associated with the perception and purposefulness of movements and actions.

**Conclusions:** Despite similar diagnosis of STBI in terms of clinical parameters, three groups of factors were distinguished, among which the third - as the least sound, reflected spontaneous forms of behavior, nevertheless, determining the most important social parameters of mental activity with respect to recovery dynamics.

## USEFUL INFORMATIONS

### CONGRESS VENUE

Hotel Park Plaza Histria, Verudela 17, Pula Croatia

### POSTER PRESENTATIONS

Neurology and Psychiatry: Friday, May 31st 2019, 18:00-20:00 (PP Histria – Ulika Hall)

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

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

Posters can be mounted from 16:00 Friday 30th May 2019 and can stay exhibited until Sunday.

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Type of registration	Early Bird Until March 31 <sup>st</sup>	Regular From April 1 <sup>st</sup>	Late On- Site From May 20 <sup>th</sup>
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Prices in Kuna (HRK) will be charged at the middle rate of the Croatian National Bank on the day of payment

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Thursday 14:00-19:30 / Friday 08:00-19:00 / Saturday 08:00-19:00 / Sunday 08:00-12:00

### **SOCIAL PROGRAM**

Thursday, May 30th, 2019 – 20:00 - Welcome reception / cocktail  
Friday, May 31st, 2019 & Saturday, June 1st, 2019 - 13:15-14:30 – Lunch  
Friday, May 31st, 2019 & Saturday, June 1st, 2019 - 10:00-17:00 Coffee break  
Saturday, June 1st, 2018 – 20:30 - Farewell cocktail / Joint Dinner – Park Plaza Histria

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