# **ABSTRACT BOOK**



## 55<sup>th</sup> International Neuropsychiatric Congress

Pula, Croatia May 27-30, 2015

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55<sup>th</sup> International Neuropsychiatric Congress

May 27-30, 2015 Pula, Croatia



This meeting is endorsed by the World Federation of Neurology and European Academy of Neurology.



### The 55<sup>th</sup> International Neuropsychiatric Congress

under the High Patronage of the President of Republic of Croatia Her Excellency Mrs. Kolinda Grabar-Kitarović

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### **PROGRAM** 55<sup>th</sup> International Neuropsychiatric Congress

#### Wednesday, May 27th

16:00 – 16:30 <b>Belica</b>	<b>STRESS MANAGEMENT</b> Alexey Danilov (Moscow, Russia)	
16:30 – 18:30 Belica	8 <sup>th</sup> INTERNATIONAL EPILEPSY SYMPOSIUM IN PULA "EPILEPSY AND COGNITION" <i>Chairperson:</i> Hrvoje Hećimović (Zagreb, Croatia)	
	AURA IN EPILEPSY Hrvoje Hećimović (Zagreb, Croatia)	
	FUNCTIONAL STUDIES USING PET/CT IMAGING - WHAT DO THEY TELL US? Sunčana Divošević (Zagreb, Croatia)	
18:30 – 19:30 Ulika	ACADEMIC LECTURE - <b>WFN THE WAY AHEAD</b> Raad Shakir, President of the World Federation of Neurology	

19:30 – 20:30 Welcoming drink and traditional Istrian folk dances performed by Artistic group "Mendula" from Medulin

#### Thursday, May 28th

09:00 - 10:00 Opening ceremony

Ulika MAIN THEME – HIGHLIGHTS IN NEUROLOGY AND PSYCHIATRY What have we learned in the last 55 years in:

10:00 – 11:30 *Chairpersons:* Vida Demarin (Zagreb, Croatia), Kurt Niederkorn (Graz, Austria)

STROKE

Kurt Niederkorn (Graz, Austria) POSTSTROKE DEPRESSION

Wai Kwong Tang (Hong Kong, China)

HEADACHE AND PAIN Vida Demarin (Zagreb, Croatia)

- 11:30 12:00 Break
- 12:00 13:30 Chairpersons: Vesna Šerić (Zagreb, Croatia), Franz Fazekas (Graz, Austria)

MULTIPLE SCLEROSIS Franz Fazekas (Graz, Austria) EPILEPSY Francesco Paladin (Venice, Italy) NEW VISTAS IN NEUROREHABILITATION Vesna Šerić (Zagreb, Croatia)

13:30 - 14:30 Break

#### 14:30 - 16:00 CONTROVERSIES AND NEWS IN PSYCHIATRY

Chairpersons: Francesco Benedetti (Milano, Italy), Martin Brüne (Bochum, Germany)

CLASSIFICATION OF FIRST-EPISODE PSYCHOSIS Paolo Brambilla (Udine, Italy)

NEW FINDINGS ON THE MILD ENCEPHALITIS HYPOTHESIS OF SEVERE MENTAL ILLNESS Karl Bechter (Günzburg, Germany)

THE PROFILE OF SERUM IMMUNE AND GROWTH FACTORS IN RELATION TO NEUROIMAGING Francesco Benedetti (Milano, Italy)

#### 16:00 - 16:30 Break

#### 16:30 – 18:00 EVOLUTIONARY PERSPECTIVES IN PSYCHOPATHOLOGY

Chairpersons: Karl Bechter (Günzburg, Germany), Norbert Müller (Münich, Germany)

BORDERLINE PERSONALITY DISORDER: INSIGHTS FROM LIFE HISTORY THEORY Martin Brüne (Bochum, Germany)

PSYCHIATRIC CONDITIONS IN CROSS-CULTURAL PERSPECTIVE Wulf Schiefenhövel (Andechs, Germany)

THERAPEUTIC IMPLICATIONS FROM EVOLUTIONARY PSYCHIATRIC INSIGHTS Alfonso Troisi (Roma, Italy)

#### Friday, May 29th

#### 09:00 - 10:30 4th SYMPOSIUM ON INTERFACE PROVIDERS IN NEUROREHABILITATION

Ulika Chairpersons: Raphael Béné (Zagreb, Croatia), Natko Beck (Zagreb, Croatia)

TRACKING AND REWIRING THE RIGHT NEURAL NETWORKS IN NEUROREHABILITATION Raphael Béné (Zagreb, Croatia)

AFFECTIVE REACTIONS: WHAT CAN BE RECORDED? Siniša Popović (Zagreb, Croatia)

WHAT TECHNOLOGY CAN OFFER TO NEUROREHABILITATION-NEW VISTAS Natko Beck (Zagreb, Croatia)

AUTISM: INSIGHTS INTO NEW COMMUNICATION NETWORKS Goran Đingalašević (Zagreb, Croatia)

#### 10:30 – 11:00 SPECIAL LECTURE Ulika WILSON'S DISEASE

Anna Czlonkowska (Warsaw, Poland)

- 11:00 12:00 Satellite Symposium sponsored by Medis
- Ulika Tecfidera new option in the treatment of Multiple Sclerosis

#### 12:00 – 13:00 **POSTER SESSION - Psychiatry**

Bianca Istriana Chairpersons: Karl Bechter (Günzburg, Germany), Francesco Benedetti (Milano, Italy), Johannes Schröder (Heidelberg, Germany)

13:00 – 14:00 **Break** 

 14:00 - 15:00
 Joint meeting with Central and Eastern European Stroke Society and WFN Applied Research Group

 Ulika
 on the Organisation and Delivery of Care

 CURRENT STATUS OF STROKE MANAGEMENT IN THE REGION

Chairpersons: Vida Demarin (Zagreb, Croatia), Hrvoje Budinčević (Zagreb, Croatia)

STROKE NEUROLOGY IN MEDITERRANEAN COUNTRIES Vida Demarin (Zagreb, Croatia)

MANAGEMENT OF STROKE IN CENTRAL AND EASTERN EUROPEAN COUNTRIES Hrvoje Budinčević (Zagreb, Croatia)

**Discussion: Similarities and Differences** 

#### 15:00 - 16:30 ACUTE STROKE TREATMENT

Ulika Chairperson: Kurt Niederkorn (Graz, Austria)

INTRAVENOUS THROMBOLYSIS Thomas Gattringer (Graz, Austria)

MECHANICAL THROMBECTOMY Hannes Deutschmann (Graz, Austria)

CERVICOCRANIAL DISSECTION Günther Erich Klein (Graz, Austria)

#### 16:30 - 18:00 SYMPOSIUM OF THE ASSOCIATION OF PEOPLE'S HEALTH "ANDRIJA ŠTAMPAR"

Ulika HEALTHY LOVE AS A PREREQUISITE OF HEALTH

Ivan Vukoja (Požega, Croatia) THE 6 YEARS OF ASSOCIATION'S PUBLIC HEALTH ACTIVITIES

Jakov lvković (Zagreb, Croatia)

BE COOL, DON'T BE A BULLY – PRESENTATION OF A PROJECT Maksimilijan Mrak (Zagreb, Croatia), Romano Antunović (Zagreb, Croatia)

HEALTH FOR ALL - PRESENTATION OF A PROJECT Ana Asančaić (Požega, Croatia)

### 16:30 – 18:00 POSTER SESSION - Neurology Chairpersons: Kurt Niederkorn (Graz, Austria), Vesna Šerić (Zagreb, Croatia), Zlatko Trkanjec (Zagreb, Croatia)

18:00 – 19:00 Kuratorium meeting

20:00 Farewell cocktail - Istrian eno-gastronomy evening

#### Saturday, May 30th

08:30 - 09:30 BEST POSTERS AWARDS PRESENTATIONS

09:30 – 13:00 Joint Meeting with Alps-Adria Neuroscience Section, WFN Applied Research Group on the Organisation and Delivery of Care and Central and Eastern European Stroke Society

Chairpersons: Leontino Battistin (Padova, Italy), Vida Demarin (Zagreb, Croatia)

DISEASE COURSE MODIFICATION IN PARKINSON'S DISEASE Amos Korczyn (Tel Aviv, Israel)

BIOMARKERS IN CEREBROSPINAL FLUID (TAU, PHOSPHO-TAU (181) AND NEUROFILAMENT LIGHT) IN CLINICALLY ISOLATED SYNDROME CONVERTED TO MULTIPLE SCLEROSIS Euphrosyni Koutsouraki (Thessaloniki, Greece)

ENHANCEMENT OF MOTOR ABILITIES IN PARKINSON'S DISEASE PATIENTS Vladimira Vuletić (Zagreb, Croatia)

CHRONIC PELVIC PAIN - EVIDENCE BASED PHARMACOTHERAPY Oleg Davidov (Moscow, Russia)

PATIENTS WITH MIGRAINE: A SUBJECTIVE APPROACH WITH QUALITATIVE STUDIES Marjan Zaletel (Ljubljana, Slovenia)

THE CLINICAL OUTCOME IMPROVEMENT RATE WITH ENDOVASCULAR THERAPY IN PATIENTS WITH ACUTE STROKE – OUR EXPERIENCES Bojana Žvan (Ljubljana, Slovenia)

SMALL ARTERY DISEASE AND COGNITIVE IMPAIRMENT Nadežda Čovičković-Šternić (Belgrade, Serbia)

NON-MOTOR STROKE SIGNS AND SYMPTOMS Osman Sinanović (Tuzla, Bosnia and Herzegovina)

### **AURA IN EPILEPSY**

Hećimović H.

Aura is the only ictal phenomenon that strickly points to the epileptogenic region. It is of high importance to define aura in epilepsy as closely as possible that will help in further EEG and neuroimagiung correlation. Clinical semiology can depend on involvement of sensory and motor system, autonomic network, speech area, but also cognition and the emotional brain.

Some human brain networks are involved in cognitive functions, emotions, and other feelings that may explain neuropsychiatric correlates.

Auras are generated in the seizure-onset zones and have highest localizing value for epileptic focus. Abdominal aura is mainly characteristic in patients with temporal lobe epilepsy, but it is also described in smaller number of patients with extratemporal epilepsy. When temporal epileptic regions are studied, the abdominal aura is more characteristic for patients with the mesial temporal lobe epilepsy. In retrospective study of 67 patients who had temporal lobectomy by French et al in 1993, major risk factors for mTLE were history of seizures during early childhood, especially febrile seizures, then head trauma and birth trauma. In this study more patients with hippocampal sclerosis had history of febrile seizures and epigastric aura than patients with extratemporal epilepsy. More subjects had early oral automatism, but less early motor involvement of upper extremities. Patients would more readily recognise their aura if they suffer less from secondarily generalized seizures and had more lateralized ictal EEG.

Clinical semiology of the frontal lobe seizures consist of complex motor automatisms and hypermotor activity. Ictal vocalization, abrupt onset, occurrence during sleep and brief duration are main characteristics. Pre-ictal and ictal features for non-epileptic seizures is that patients usually have their eyes closed, their motor activity is discontinuous, have more lateral movements and duration of seizures can be longer. Postictally there is no confusion, but people complain of general fatigue.

### FUNCTIONAL STUDIES USING PET/CT IMAGING – WHAT DO THEY TELL US?

#### Divošević S.

Although the primary imaging modality in the management of epilepsy is magnetic resonance imaging MRI, functional neuroimaging with positron emission tomography (PET) provides important complementary information or sometimes even unique information that cannot be obtained with MRI. PET is important in lateralization and localization of epileptogenic cortical areas, improving the success of surgical treatment.

PET with 18F FDG shows regional brain glucose hypometabolism ipsilaterally to the seizure focus, and hypometabolic region is usually larger than the structural pathologic abnormality on MRI, because of the dysfunctional neural network.

With PET radiopharmaceuticals that bind to different types of brain receptors, we can evaluate the neurochemistry basis of the illness.

Binding of 5-HT1A receptor antagonists is decreased ipsilaterally to the epiletogenic zone, showing also decreased density of receptors or higher concentrations of endogenic serotonin, as well as stronger contralateral binding. Binding capacity of the hippoccampus can also be evaluatued, finding lower values in hippoccampal sclerosis and atrophy, suggesting loss of neurons, but normal values in patients with normal hippoccampal volume. Similar to FDG, decreased binding is not found just in the region of the epileptogenic zone, but also in the regions of the seizure spread, sugesting loss neurons involved in the temporo-limbic epileptogenic network, with stronger binding in the regions beyond the epileptogenic zone, maybe as a compensatory mechanism for high electric activity and neuron hyperexcitability. The 5-HT1A receptor is closely involved in the pathogenesis of anxiety and depression, which is common comorbidity in patients with temporal epilepsy.

Binding of radiopharmaceuticals to GABA receptors is also lower on the side of the epileptogenic focus, correlating negatively with the frequency of epileptic seizures, as well as binding of dopamine D2/D3 receptor antagonists.

The number of opioid receptors is more prominent in the epileptogenic temporal lobe.

In comparison to FDG, several studies show higher sensitivity for identification of the seizure onset zone and better delineation of the size of the epileptogenic area, predicting good surgical outcome.

With further development of new tracers highly sensitive and specific for epileptogenic brain regions, the presurgical evaluation of refractory epilepsy will be significantly improved.

### **POSTSTROKE DEPRESSION**

Tang W.K.

Stroke represents a major public health problem in the China and worldwide, but relatively little work has been directed toward identifying and treating the common neuropsychiatric disorders occurring after stroke. I will review the epidemiology, clinical and pathological correlates and treatment of depression after stroke. These disorders have been shown to inhibit physical recovery from stroke and reduced the quality of life. There are very few controlled trials examining the effectiveness of treatments for these disorders after stroke. Both pharmacological and psychological treatments, however, can alleviate symptoms of this disorder.

### HEADACHE AND PAIN

Demarin V.

The first systematized classification of headaches was reported in the literature in 1962. (Friedman et al). Today there are a number of different classification systems for headaches, The International Classification of Headache Disorders, published by the International Headache Society, classify more than 150 types of primary and secondary headache disorders. Headache is the most common form of pain. In the last decades chronic pain, including headaches, evolved in a widespread healthcare problem with a negative impact on mental health, professional and family life of the patients.

In many patients, headaches can be well controlled with a combination of medicines and complementary therapies. Treatment is most successful when it is tailored to the patient needs. The causes and treatment of headaches continue to be an active area of scientific research. A number of current researches seek to understand the underlying causes of headaches, brain mechanisms of headaches, social, racial and psychiatric factors that may relate to headaches, and genetic predispositions for headaches. There are also many ongoing clinical studies seeking to relieve and manage headache pain.

Headaches are causing significant burden for both the individual and the society. Therefore the diagnosis and treatment of headaches and pain should continuously improve. The known pain therapies have significant adverse events limiting patient's normal functioning. Therefore the new findings on neuroplasticity are providing an important role in pathophysiology of chronic pain; the neuroplastic changes are recognized during pharmacological treatment of pain and in the last years new approaches in headache and pain treatment using principles of neuroplasticity are emerging.

### **MULTIPLE SCLEROSIS**

Fazekas F.

The past decades have seen enormous progress in the pathophysiologic understanding, diagnosis and treatment of multiple sclerosis (MS). The advent of magnetic resonance imaging (MRI) certainly was a driving force in this development as it enabled for the first time to visualize the hallmark finding of the disease, i.e. MS lesions in vivo. After some initial concerns about the specificity of such findings it rapidly became clear that MRI was also more sensitive to follow the evolution of the disease by depicting new lesions than by the more rare clinical correlate of relapses. The introduction of contrast enhanced MRI using Gadolinium chelates added the potential to identify acutely inflamed, i.e. active lesions and thus paved the way for MRI to be able to demonstrate MS lesion dissemination both in space and time. MS thus became the first neurologic disorder the diagnosis of which is nowadays largely based on MRI findings according to formally agreed criteria.

The morphologic insights made possible by MRI also opened new questions which revived neuropathologists' interest in the disease and fuelled their efforts to look beyond MRI visible changes. This led to the notion that MS does not just affect the white but also the grey matter and entails much more complex and diffuse abnormalities than expected. The direct occurrence of axonal damage in addition to demyelination, a high frequency of cortical lesions and evidence for "neurodegeneration" as a possible second element of the disease are just some of the new insights that were generated.

Finally the past decades saw MS become a treatable disease. After hundreds of years and innumerable methods and drugs claimed to beneficially impact on the disease clear evidence for a significant treatment effect was generated for the first time with the results of the pivotal ß-interferon 1b trial now more than 20 years ago. Again MRI played an important role as it gave credential to the clinical findings by showing the ability of ß-interferon to reduce lesion accumulation in a rather objective, i.e. patient and physician independent manner. From there on MRI rapidly developed into a tool to screen new drugs for their efficacy in early drug development and MRI measures have continued to be a valuable secondary outcome in phase 3 trials for the disease. This has contributed to a nowadays already rather rich armemantarium of drugs for fighting MS which reaches from injectable to oral and from immunomodulatory to immunosuppressive drugs.

### **CLASSIFICATION OF FIRST EPISODE PSYCHOSIS**

Brambilla P., Squarcina L., Peruzzo D., Castellani U., Perlini C., Marinelli V., Bellani M., Rambaldelli G., Lasalvia A., Ruggeri M.

Currently, most of the classification studies of psychosis focused on chronic patients and employed single machine learning approaches. To overcome these limitations, we here compare, to our best knowledge for the first time, different classification methods of First Episode Psychosis (FEP) using multimodal imaging data exploited on several cortical and subcortical structures, white matter fiber bundles and vascular organization. FEP patients and age-, gender-, and race-matched healthy controls underwent multimodal MRI imaging. The distribution of values of structural MRI (sMRI), diffusion tensor imaging (DTI) and dynamic susceptibility contrast (DSC) MRI indexes were used as features in innovative support vector machine classifiers.

Regions with an accuracy greater than 70% on sMRI and DTI were middle and superior frontal gyrus, parahippocampal

gyrus, uncinate fascicles and cingulum. Linear SVM reached an accuracy of 83% in the classification of patients and normal controls using DSC-MRI, with the highest accuracy associated with right frontal lobe and left parietal lobe.

In conclusion, we found evidence that multivariate machine learning approaches integrating multimodal and multisource imaging data can classify FEP patients with high accuracy. Interestingly, specific grey matter structures and white matter bundles reach high classification reliability when using different imaging modalities and indices, potentially outlining a prefronto-limbic network impaired in FEP with particular regard to the right hemisphere. Also, brain perfusion, particularly cerebral blood volume, is shown to be useful as a potential marker to classify patients with psychosis.

### NEW FINDINGS ON THE MILD ENCEPHALITIS HYPOTHESIS OF SEVERE MENTAL ILLNESS

#### Bechter K.

The mild encephalitis (ME) hypothesis proposed an actual how level neuroinflammatory process as the core pathomechanism in a considerable subgroup of affective and schizophrenic disorders.

Review of own results and of results of others.

Infections and autoimmune disorders additively increase the risk of severe mental illness in time relationship to respective insults. The pathogenicity of infections varies by age, variation fits with preferred age of onset of psychosis. Key to clinical diagnosis of neuroinflammation is cerebrospinal fluid (CSF) investigation. CSF spaces play an autochthonous role for CNS functioning and protection. In therapy resistant affective and schizophrenic disorders we found in about 40 % some CSF abnormalities with conventional methods, in addition in 30 % increased CSF neopterin, and in 100 % some CSF cytokine pattern abnormalities.

These findings support ME hypothesis for a large patients subgroup. New therapy approaches are discussed on this background. Literature: Maxeiner H. G., et al. Cerebrospinal fluid and serum cytokine profiling to detect immune control of infectious and inflammatory neurological and psychiatric diseases. Cytokine 2014;69:62-67 Bechter K. Updating the mild encephalitis hypothesis of schizophrenia. Progress NPBP 2013; 42: 71-91 Bechter K., B. Schmitz. Cerebrospinal fluid outflow along lumbar nerves and possible relevance for pain research: case report and review. Croat Med J. 2014;55:399-404

### **BORDERLINE PERSONALITY DISORDER: INSIGHTS FROM LIFE HISTORY THEORY**

#### Brüne M.

Borderline personality disorder (BPD) is characterised by unstable interpersonal relationships, impulsivity and unprecedented risk-taking including risky sexual behaviour. These behaviours are commonly explained at the level of altered neurotransmission, e.g., dysfunction of the serotonin system, or as being caused by early life stressors. How these factors interact in BPD is, however, poorly understood. Here, we seek to conceptualise BPD as a syndrome comprising patterns of behaviour, emotions, and cognitions, which can be understood from the viewpoint of life history theory. This theory proposes that humans can flexibly adopt behavioural strategies in terms of mating and reproduction depending on the predictability of environmental resources, that is, accelerating or decelerating life history patterns.

One hundred patients diagnosed with BPD were examined using questionnaires tapping into the domains of early childhood experiences, attachment, mating, and biological development.

Preliminary evidence suggests that BPD represents the (pathological) extreme of variation of a "fast" life history strategy that could be adaptive under environmental strain. In line with predictions, patients with BPD were more likely to experience adverse early rearing conditions including parental marital discord, emotional neglect and sexual abuse, and had more unstable short-term intimate relationships compared to a control sample resembling the opposite type of interpersonal orientation. No difference was found regarding biological maturation. BPD can be conceptualised within an evolutionary framework as the extreme of variation of a "fast" life history strategy based on environmental contingencies.

### PSYCHIATRIC CONDITIONS IN CROSS-CULTURAL PERSPECTIVE

Schiefenhoevel W.

Somatic diseases in patients treated in New Guinea (appr. 90% infectious diseases) have a very different morbidity profile than in European patients; most striking is the almost complete lack of allergies, hypertension, cardiovascular and chronic diseases. The major psychiatric diseases do occur in Melanesian populations, yet with partly very different prevalences, depending on the different environments (traditional village versus acculturated town life). In 50 years of research on topics of ethnomedicine and evolutionary medicine, cry babies, ADHD, Alzheimer's dementia, schizophrenia, post traumatic stress disorder, burn-out and paranoia were rarely seen. Prolonged depression occurred in some old persons and especially in younger

women, of whom some committed suicide because they were distraught about a sexual and partnership conflict, often involving breaking the customary incest taboo relating to members of the same clan. Pain tolerance is very high, already in small children; anxiety disorders do not seem to occur.

I attribute the last two points to the fact that everyone is, from early age on, subject to real pain and real danger and that this creates, in an evolutionarily paved process of adaptation and much in contrast to commonly held viewpoints of modern pain therapy and psychiatry, a protection against pain and anxiety becoming medical and psychiatric problems.

### THERAPEUTIC IMPLICATIONS FROM EVOLUTIONARY PSYCHIATRIC INSIGHTS

#### Troisi A.

As a branch of medicine, psychiatry has as its main objectives the diagnosis, treatment, and prevention of mental disorders. Yet these clinical aspects have not been a major focus of research and discussion in evolutionary psychiatry. Almost certainly, this is the most important reason that can explain why the evolutionary approach has had so little impact on clinical psychiatry. When evolutionary psychiatrists suggest ultimate explanations of vulnerability to psychopathology based on phenomena such as evolutionary trade-offs (different traits are adaptive in different environments), genome lag (evolved traits may be out of step with modern environments), and historical constraints (how a trait has evolved may result in particular susceptibility to disease), certainly they are offering a deeper understanding of the origin of psychiatric disorders. However, this is not enough for clinical psychiatrists. When people experiencing mental distress arrive at the hospital or psychiatrist's office, what they need is a proper diagnosis and an effective treatment. And evolutionary hypotheses and explanations, as currently presented by most articles and books on Darwinian psychiatry, do not

seem to be of great help to address patients' needs. In this presentation, contrary to the belief of skeptics, I will try to convince the audience that Darwinian psychiatry has a great potential in terms of clinical utility. My ambition is not to demonstrate that the evolutionary approach can match the practical applications of those disciplines that are revolutionizing contemporary psychiatry, such as, for example, brain imaging or psychopharmacology. This is not only untrue for the present but also highly improbable for the future. More modestly, I would show that the inclusion of evolutionary theories and methods within the clinician's know-how can improve to some extent the diagnosis, treatment, and prevention of mental disorders. There are many clinical applications of the evolutionary approach that testify its practical utility. This presentation deal with those activities that clinicians exert in their everyday practice and that people suffering from mental disorders expect to progress at a fast pace: diagnosis, therapy, and prevention. Each of these clinical tasks can already benefit from the contributions of evolutionary theory.

### TRACKING AND REWIRING THE RIGHT NEURAL NETWORKS IN NEUROREHABILITATION

#### Béné R.

Over the past two decades it has been increasingly recognized that sensory, motor and cognitive cortical maps are not static and permanent entities, but instead undergo continuous dynamic remodelling in response to behaviorally important experiences throughout the entire life span.

The symptoms occurring after the brain damage are not just direct manifestations of loss and/or malfunction of affected brain region; they are also manifestations of the ongoing plastic changes in the remaining brain parts, especially perilesional brain regions. It has been recently suggested that, in contrast to widespread cortical activation, the focal brain activation of perilesional regions is more correlated with better rehabilitation outcomes. Thus, the aim of the person-oriented neurorehabilitation is to enhance specific inputs from intact brain regions to perilesional brain regions. Therefore, the key question is how to target and specifically stimulate these brain regions.

### **AFFECTIVE REACTIONS: WHAT CAN BE RECORDED?**

Popović S.

Elicitation of startle reflex and affective reactions by visual, auditory and tactile stimuli, as well as synchronized measurement of the corresponding physiological, speech and facial responses has been conducted in healthy participants, using a developed laboratory system.

Ten female first-year university students passed through five elicitation paradigms: (1) acoustic startle probes lasting 40 ms, with intensity 108 dB (A) SPL; (2) airblasts to the occiput lasting 250 ms, using air pressure of 140 p.s.i.; (3) loud aversive sounds lasting 1 s; (4) aversive images lasting 2 s; and (5) simultaneous deliveries of aversive images, sounds and airblasts having the same properties as in the prior respective paradigms. Each paradigm lasted two minutes and included three pseudorandomly ordered presentations of stimuli and three occasions when stimuli were omitted. In order to capture the impact of stimuli on speech responses, the participants were given onscreen visual reminder to start sustained phonation of vowel 'a' shortly before the stimulus could potentially occur. All participants went through the same paradigms in the same order, 1 through 5, with approximately three-minute breaks between successive paradigms. Recorded physiological, speech and facial features have been analyzed for response differences between stimulus and no-stimulus conditions within each paradigm, as well as to reveal potential differences in responding to various paradigms.

Among recorded physiological features, skin conductance response showed the largest differences between stimulus and nostimulus conditions. The most prominent stimulus/no-stimulus differences among speech features were observed in the energy (intensity) of the voice signal and fundamental frequency (F0), while the major stimulus/no-stimulus differences among facial features occurred in eye blinks, eye gaze direction and head distance from camera. Physiological, speech and facial responses to image stimuli (paradigm 4) had the lowest intensity; this paradigm was the only one that did not elicit startle response at all. The largest median responses in physiological and speech modality were obtained during paradigm 5 (combination of stimuli), and in facial modality during paradigms 2 and 5. Overall, paradigm 5 can be regarded as the paradigm that elicited the most intense responses across all modalities.

The tested paradigms generated significant physiological, speech and facial responses to the presented aversive stimuli in the selected sample of participants. The obtained results are encouraging for further work on the laboratory system and elicitation paradigms for multimodal affective responding, in the context of the authors' research spanning stress resilience and affective computing topics.

### WHAT TECHNOLOGY CAN OFFER TO NEUROREHABILITATION-NEW VISTAS

#### Beck N.

Although new technologies have only recently made their appearance in the field of neurorehabilitation, they are now widely accepted by a majority of clinicians and therapists as supporting tools in clinical routine. The general consensus is that these technologies should be used on the basis of individual patient requirements and training goals in order to ensure a safe, tailormade and successful rehabilitation.

In recent years advances in interface and mobile system technology made it possible to develop light, low cost interface devices that can, inspired by scientific breakthroughs especially in neuroscience (Connectome, Human Brain Project, BRAIN Initiative), lead to new alternative communication systems, cognitive rehabilitation devices/programs and cognitive enhancement devices/programs. New mobile body monitoring systems allow feedback implementation in everyday rehabilitation, also making it mobile and patient friendly.

# AUTISM: INSIGHTS INTO NEW COMMUNICATION NETWORKS

#### Đingalašević G.

We all use communication strategies when we make facial expressions or gestures, point to pictures, or write. People with severe speech or language challenges may use alternative communication strategies to supplement existing speech or replace speech that is not functional. Special augmentative aids, such as picture and symbol communication boards and electronic devices, are available to help people express themselves. Autism represent a challenge

For individuals with autism, an augmentative communication system should:

- increase participation in the classroom, work, community and home
- address IEP, work and personal goals
- support timely and interactive communication
- provide meaningful language to the recipient
- support language and literacy learning
- encourage successful day to day, face to face, real time interaction
- be age and level appropriate
- provide positive behavioral supports

### WILSON' S DISEASE

Czlonkowska A.

Wilsons disease, was described by Kinnier Wilson over one hundred years ago. He focused on neurological aspects of the disease, however he also made critical observation that the liver was affected. He postulated that a toxic agent was responsible for both neurological and liver injury. We just know the toxin is copper and that it accumulates in toxic levels in tissues due to a defect in a specific geneATP7B, that is critical to copper transport and metabolism in liver. Injury to other organs mainly brain is secondary to copper overload in liver and increased copper level in blood. Both hepatic and neurological symptoms of the disease are very variable, from mild developing over years to rapidly progressing leading to severe disability and death. Diagnosis is crucial for WD patients. It is based on combination of clinical features, studies of copper metabolism, genetics analysis, and neuroimaging. Anticopper therapy is based either on copper chelation (d-penicillamine, trientine) or inhibition of copper absorption from gut (zinc salts). Both types of therapy seem equally effective, and choice depends on center experience, patient's preference and drug availability. Liver transplantation is performed only in cases with fulminant liver injury and progression of liver failure despite of therapy. Anticopper therapy must be lifelong. In majority of cases which are not diagnosed in the terminal stage pharmacotherapy leads to clinical improvement. It is important to screen asymptomatic siblings and children of affected patients. Early therapy prevents symptoms development. Critical for therapeutical success is patients' compliance.

### STROKE NEUROLOGY IN MEDITERRANEAN COUNTRIES

Demarin V.

According to WHO data, the global burden of diseases is shifting from infectious diseases to non communicable diseases (NCDs), with chronic conditions such as heart disease and stroke now being the leading causes of death worldwide. Stroke is the second largest leading cause of disability, after dementia.

About 15 millions of people experience stroke each year, 6 millions of them die and majority are left more or less disabled. Apart from extreme financial burden, stroke is devastating disease for patients, their families and the whole society.

According to data gathered by questionnaire from majority of participants at the Siena meeting, there are differences in incidence of stroke between Mediterranean countries, with even more pronounced difference in mortality and overall outcome, as well as related to specific therapy for ischaemic stroke, (thrombolysis), stroke units and rehabilitation. Special emphasis should be pointed out to management of environmental risk factors such as smoking, lifestyle, regular excersise and control of so called metabolic risk factors – arterial hypertension, heart diseases, diabetes mellitus, dislipidemia etc., all being preventable and controlable.

Mediterranean diet is proved, by results of many recent clinical trials, to be one of a major factor in stroke prevention.

More organized common research is needed in the field of stroke, which will contribute greatly to emphasize the World Stroke Organization (WSO) premise that Stroke is a treatable and preventable catastrophe.

Thus, knowledge from our part of the world would be more then welcome in the global fight against stroke.

### MANAGEMENT OF STROKE IN CENTRAL AND EASTERN EUROPEAN COUNTRIES

Budinčević H., Tiu C., Bereczki D., Kõrv J., Tsiskaridze A., Niederkorn K., Czlonkowska A., Demarin V.

Stroke is one of the leading causes of disability in Europe. Central and Eastern European countries have the highest incidence and mortality rates through Europe. The improvements in stroke prevention and treatment in Central and Eastern European countries did not completely reach the quality parameters present in Western European countries. The current management of stroke in Central and Eastern European countries will be discussed.

### MECHANICAL THROMBECTOMY

Deutschmann H.

Immediate recanalization of the occluded vessel is the key factor for predicting functional clinical outcome in patients with acute ischemic stroke. Early clinical trials utilizing either only guidewires or first generation thrombectomy devices, such as the MercyÒ device failed to demonstrate a significant clinical benefit of mechanical thrombectomy compared to standard i.v.lysis (IMS III, MR Rescue, Synthesis). However, with the introduction of dedicated medical devices, the so called "stent retrievers", a powerfull tool for quick removal of clots had been developed. Wide acceptance among the interventionalists has led to many successfull procedures and in many cases to a good clinical outcome. But unfortunately, the scientific evidence for the widespread use of the new technique compared to the gold standard, i.v.lysis was lacking. Within the last few months, several prospective randomised trials comparing iv.lysis to iv.lysis plus mechanical thrombectomy have been published (MrClean, Revascat, Swift Prime) finally demonstrating a clinical benefit of mechanical thrombectomy compared to i.v.lysis as the sole treatment in patients with acute stroke due to occlusion of the distal internal carotid artery, the middle cerebral artery, or the anterior cerebral artery. Proximal vessel occlusion caused by large thromby with a length of more than 8mm is well suited for mechanical thrombectomy. Patients treated with this technique within 6 hours of stroke onset will benefit more from

mechanical clot removal compared to i.v.lysis. The published randomized trials generated new evidence for acute stroke treatment. This was also recongnized by the scientific societies such as the European Stroke Organizytion (ESO) publishing new guidelines, including mechanical thrombectomy as inherent part of stroke treatment. In parallel, another technique emerged, the aspiration of clots (ADAPTÓ technique) by using specially designed distal access catheters and large lumen aspiration catheters. However, the only randomized trial comparing this technique to i.v.lysis failed to demonstrate a significant clinical benefit for the treated patients (Therapy trial). One limiting factor of this trial is, that only in 27% of the patients, the latest version of the aspiration catheter (ACEÒ) was used. Thus, the efficacy of the most recent version of the device could not be assessed by the trial.

Regardless of the applied technique for mechanical thrombectomy, the clot removal is only one part of acute stroke treatment. Immediate transfer of the patients into a dedicated stroke center and sufficient stroke imaging is at least as important as successfull clot removal. In line with the "time is brain concept", every discipline concerned with acute stroke patients has to work together closely based on standardized operating procedures and according to guidelines to achieve the best clinical outcome of the patients.

### SYMPOSIUM OF ASSOCIATION OF PEOPLE'S HEALTH "ANDRIJA ŠTAMPAR"

Vukoja I., Ivković J., Relić D., Plazibat O., Mašić M., Njavro L., Antunović R., Asančaić A., Jureša V., Demarin V., Božikov J.

Association of people's health "Andrija Štampar" (hereinafter Association) was founded in the year 2009 at the School of Medicine, University of Zagreb. Main goals of the Association are promotion of awareness about public and people's health and humanity, promotion of healthy lifestyles and prevention of diseases. Association works strongly on promotion of personal and people centered medicine, on promotion of nonviolent behavior and social equality. Association is bringing together medical students, physicians and other academic citizens through multidisciplinary approach. Members of the Association promote learning of Andrija Štampar who said that person is physical and mental and also spiritual and social being. During the 55<sup>th</sup> INPC you'll be able to hear about logotherapy approach to love with lecture "Healthy love as prerequisite of the health", about projects of the Association such as"Days of Andrija Štampar", "Be cool, don't be a bully", "Health to all".

### BIOMARKERS IN CEREBROSPINAL FLUID (TAU, PHOSPHO-TAU (181) AND NEUROFILAMENT LIGHT) IN CLINICALLY ISOLATED SYNDROME CONVERTED TO MULTIPLE SCLEROSIS

Koutsouraki E.

Several cerebrospinal fluid (CSF) proteins have been studied as potential predictors of clinically isolated syndrome (CIS) converted to multiple sclerosis (MS). Among the multitude of biomarkers which have been tested, neurofilaments and tau protein, markers of axonal and neuronal damage, seem to stand out for potential prognostic value.

The aim of the present study was to evaluate CSF biomarkers indicating axonopathy and neuronal loss in CIS patients converted to clinically definite MS in comparison with controls.

Total tau (tTau), phosphorylated Tau 181 (pTau) and neurofilament light (NF-L) were analyzed and determined using the Elisa technique in 31 CSF samples, of 18 CIS patients (36.5±11.4) and 13 controls (39.7±12). CIS patients were 15 females and 3 males, and controls were 4 females and 9 males. CIS patients converted to clinically definite MS in a 3-year period. According to our results biomarkers of axonopathy such as NF-L and tTau start to increase from the initial stage of MS; this finding is in accordance with the results published by other authors, demonstrating higher values in CIS patients compared with the healthy controls. Biomarkers of both axonal and neuronal loss like pTau, do not correlate with the initial stages of MS but probably with the progression of MS where brain atrophy appears, as demonstrated by the lack of statistical significant difference between CIS patients and controls. Lower levels of the protein in the CIS patients group were demonstrated in comparison with the other MS patients' group, with the highest values noted in the PPMS cases.

The combination of high values of tTAU, NF-L and low value of pTAU could be indicative of a possible predictive role of this signature in the CSF of CIS patients.

## ENHANCEMENT OF MOTOR ABILITIES IN PARKINSON'S DISEASE PATIENTS

#### Vuletić V.

The treatment of movement disorders, especially advanced ones, has been always a challenge. With this presentation we want to show how we can improve motor abilities in Parkinson's disease (PD). All antiparkinsonian oral and transdermal drugs have an important place in enhancement of motor abilities. In advanced fazes there are invasive methods like deep brain stimulation and levodopa-carbidopa intestinal gel that can successfully ameliorate them. Patients with Parkisnon's disease usually have a life style with decreased physical activity. Physical therapy and neurorehabilitation are very important in all phases. Neurorehabilitation principles include physiological concepts incorporated in physiotherapy, occupational therapy and speech therapy and also therapeutic schools such as Bobath, Maitland's manual therapy or Vojta treatment. That helps them with safe mobility while walking, improvement of balance, coordination and fall prevention. The aim of the neurorehabilitation process is to get maximal possible functional ability and independency. The aim of this presentation is to show how we improve motor abilities in our Center especially

after invasive procedures. A multidisciplinary team is involved in the process of motor ability's improvement in every level with continual, complex and multidisciplinary approach. The individual, planed and problem orientated neurorehabilitation treatment is necessary after careful evaluation of the various dysfunctions and psychophysical condition. Novel and engaging training regimes are also: augmented feedback, knowledge of results available, repetition and intensity facilitated, possibility for transfer practice and encouraging explicit and implicit learning. We followed 30 patients with Parkinson's disease before and after surgical intervention during one year using all recommended scales for the international survey of DBS. Great outcome results were found concerning motor and disability improvement and quality of life perception in all investigated patients. In conclusion our results have shown that DBS implantation has a great benefit for movement disorders' patients and is effective in maximizing patients' functional improvement. Likewise, the other methods with multidisciplinary approach are successful in increasing motor ability.

## CHRONIC PELVIC PAIN - EVIDENCE BASED PHARMACOTHERAPY

#### Davidov O.

Chronic pelvic (CPP) and urogenital pain is a common and debilitating problem that has a significant impact on the quality of life of patients. Many urological, gastrointestinal, and gynecological disorders appear to cause or are associated with chronic pelvic pain, which often produces a diagnostic dilemma. There is no generally accepted definition of chronic pelvic pain. IASP defines chronic pelvic pain without obvious pathology as chronic or recurrent pelvic pain that apparently has a gynecological origin but for which no definitive lesion or cause is found. This definition is problematic from a clinical perspective, since it implies absence of pathology, which might not necessarily be the case-for example, many patients with endometriosis suffer from pelvic pain. At the same time pelvic pain in men is also missing in this definition. The definition also excludes cases where pathology is present, although it may not necessarily be the cause of pain.

Chronic pelvic and urogenital pain is more common than previously expected. Epidemiological data show that 14.7% of women of reproductive age reported chronic pelvic pain and that the estimated number of female pelvic pain sufferers is 9.2 million in the United States alone. Analysis of a large primary care database from the United Kingdom demonstrated that the annual prevalence of chronic pelvic pain in women is 38/1000, which is comparable to the prevalence rate of asthma and low back pain. Prostate pain syndrome without demonstrated infectious or inflammatory etiology is the most common urological diagnosis among men under age 50, and the third most common in those over 50, with an estimated 6 million men affected in the United States. Community studies suggest that vulvar pain is common, and prevalence rates are as high as 18%. Careful clinical history and examination show that patients with pelvic and urogenital pain often suffer from "more than

one pain." Data from the Interstitial Cystitis Data Base Study show that 93.6% of patients enrolled with a diagnosis of IC reported having some pain in some part of their body. Of the patients having pain, 80.4%, 73.8%, 65.7%, and 51.5% reported having pain in their lower abdomen, urethra, lower back, and vaginal area, respectively.

Diagnosis of CPP remains difficult even for Pain specialist, especially taking into the account uncertainty with definition of the syndrome. In clinical practice much emphasis has been placed on finding a specific etiology and specific pathological markers for pelvic disease. Patients with CPP typically undergo many diagnostic tests and procedures. However, often the examination and workup remain unrevealing, and no specific cause of the pain can be identified. In an attempt to improve diagnostic approach, Shoskes et al were the first to propose a clinical phenotype–based classification system with six domains: urinary, psychosocial, organ specific, infection, neurologic/systemic, and tenderness (UPOINT). UPOINT aims to improve the understanding and management of CPP, especially prostate and bladder pain syndromes and its clinical applicability has been clearly demonstrated.

Treatment approach to CPP varies significantly, although in last decades several recommendations from different Societies and Working Groups on CPP management have been issued. The International Association for the Studying of Pain, The European and American Urology Associations, The American Congress of Obstetricians and Gynecologists made and attempt to elaborate rational strategies for CPP management. But still, the evidence base for the treatment of CPP by pharmacological therapies is poor. Thus far, no randomized controlled trials have been conducted that support the use of nonsteroidal antiinflammatory drugs (NSAIDs) for treating CPP. However, there are enough studies in populations with other chronic pain syndromes that indicate NSAIDs can be helpful potentially as a first-line treatment, and particularly for patients with dysmenorrheal and inflammatory-based conditions. Paracetamol should be considered as an alternative to or given with nonsteroidal anti-inflammatory drugs (NSAIDs) because it is well tolerated with few side-effects. Based on the potential pathologic mechanisms in the nervous system and the structures involved in CPP, tricyclic antidepressants and anticonvulsants may be valuable alternatives, especially for neuropathic pain or central sensitization. Some Guidelines recommend that vulvar pain can be managed with topical treatments such as lidocaine 5% ointment or eutectic mixture of local anesthesia (EMLA) cream. Opioids also have a role in managing CPP, as they are an established option in the analgesic armamentarium for controlling moderate-to-severe chronic nonmalignant pain. Opioids can have a clinically significant benefit, but current data on longtermuse of these analgesics are limited. Oral contraceptives can effectively reduce pain associated with endometriosis, although limited clinical trial data support their use. According to recent large randomized controlled trial the use of a-blockers for pain management is considered not effective.

The management of patients with CPP is nowadays challenging. Because of the multifactorial causes and multidimensional consequences of this type of pain, practitioners should be aware of well-described mechanisms outside the usual organ limits. The guidelines on chronic pelvic pain propose that treatment strategies are most successful if they are based on mechanism-based treatment approach and implemented by Interdisciplinary Team, including pain specialist.

## PATIENTS WITH MIGRAINE: A SUBJECTIVE APPROACH WITH QUALITATIVE STUDIES

#### Zaletel M.

The impact of migraine on quality of life has been traditionally evaluated by quantitative analysis, but diverse aspects remain insufficiently assessed, so a complementary qualitative approach may have advantages. In addition, Migraine is poorly managed despite a high level of morbidity. The majority of sufferers use non-prescription medications and are reluctant to seek help but the reasons for this are not understood. Furthermore, Prophylactic treatment is an important but under-utilised option for the management of migraine. Patients and physicians appear to have reservations about initiating this treatment option.

Qualitative methodologies aim to explore and understand situations, interpret phenomena and develop concepts in their natural context, with emphasis on meaning, significance and opinions of those taking part (1). These techniques focus more on subjective aspects and personal experiences of routine and problematic moments and meanings in individual lives, and are therefore based on a relatively small number of individuals, selected according to specific criteria. Among the qualitative techniques, focus groups and individual interviews seem more suitable in this setting. Usually groups are designed to obtain information on a predefined area of interest, in a non-directive, permissive atmosphere so that participants express their subjective experiences and opinions. Discussion is relaxed and comfortable, since a group of persons sharing a number of common characteristics. Furthermore, the views of patients' relatives and migraine-related health professionals are not usually considered in classical studies, but may be of great interest, as the opinion of those migraineurs that do not usually seek medical advice but self-medicate instead; qualitative analysis represents the ideal approach to gain knowledge in this respect (2).

Once all the focus groups had met, the summaries of the sessions, notes and transcriptions were read and the tapes were listened to by the researcher responsible for the data analysis in order to organize data into initial codes and then into higher codes that provided insight into identified themes. Grounded theory involves rigorously extracting and systemising the concepts, categories and themes from the evolving data (3). Validity, or trustworthiness, is checked by ensuring that the emergent theory be recognisable and relevant to those studied.

The main results of qualitative studies suggest that migraine has a negative affect on the quality of life, including physical, emotional and social aspects of daily life such as family, work and social relationships. Family environment and psychological well-being of patients were the aspectsmost affected according to patients and relatives. Health professionals emphasized work impairment and focused on pharmacological management and on the need for adequate information about migraine for nonmedicated patients and patients' relatives. In addition to the functional impact of migraine, the decision to start prophylaxis is based on a complex of considerations from the patient's perspective (e.g. perceived burden of migraine, expected benefits or disadvantages, interaction with relatives, colleagues and physician). Therefore, when advising migraine patients about prophylaxis, their opinions should be taken into account. Despite a significant impact on the quality of life of

migraine sufferers and their families, their needs remain largely unmet. Useful insights can be obtained when patients and professionals work together in true partnership but the time and effort involved should not be underestimated.

The Qualitative methodologies open up new areas for further research.

## THE CLINICAL OUTCOME IMPROVEMENT RATE WITH ENDOVASCULAR THERAPY IN PATIENTS WITH ACUTE STROKE – OUR EXPERIENCES

Žvan B., Jeromel M., Miloševič Z., Zaletel M., Švigelj V., Oblak P.

Although endovascular therapy is an evolving treatment for acute stroke patients, its ability to improve clinical outcomes has not yet been established. Our objective was to determine the clinical outcome improvement rate with endovascular therapy by analyzing the outcomes of patients from 2009 to 2012 at the University Medical Centre.

134 acute stroke patients with normal computerized tomography (CT) findings were treated with endovascular therapy at a single center from 2009 to 2012. Based on CT perfusion and CT angiography findings, they all had large vessel occlusions. Intravenous thrombolysis was used in eligible patients. The recanalization rate, time to recanalization, periprocedural complications and clinical outcome at discharge from the hospital (National Institutes of Health score, modified Rankin Scale) were analyzed. The recanalization rate during the study interval increased from 70% (2008/2009) to 93% (2011/2012) ( $p \le 0.01$ ). The procedure duration time was reduced from 124 minutes (2009) to 43 minutes (2012) ( $p \le 0.01$ ), while the periprocedural complication rate decreased from 21% (2009) to 2% (2012) ( $p \le 0.01$ ). A patient had a 2.21-times greater probability for a mRS post score  $\ge 2$  in 2009/2010 compared to 2011/2012 (95% CI: 1.0 - 5.0). If the procedure lasted 15 minutes longer, the prospect for a mRS post score  $\ge 2$  was 1.30-times greater (p=0.02). High recanalization rates, low procedural complications and improved clinical outcomes were achieved using endovascular therapy in selected acute stroke patients over four years. According to our experience, endovascular therapy is an evolving safe and effective treatment for intracranial large vessel occlusion.

### NON-MOTOR STROKE SIGNS AND SYMPTOMS

Sinanović O.

Behavioural neurology is discipline which was revived in the 1960s by Norman Geschwind with his description of the disconnection syndromes (Geschwind, 1965; Cummings and Mega 2003). This discipline is cornerstone of neuropsychiatry or clinical neuropsychology which includes both the psychiatric manifestations of neurological illness (primary brainbased disorders) and neurobiology of «idiopathic» psychiatric disorders (Geschwind, 1965; Rizzo and Eslinger, 2004; Cummings, 1995). Neurological primary brain disorders provoke broad spectrum of brain pathophysiology that cause deficit sin human behaviour, and the magnitude of neurobehavioral-related problems is a world wide health concern. Although there are recognized specialists in behavioural neurology/ neuropsychology, the filed is not a conventional discipline but rather a broad sphere of interest to which experts in different disciplines, medical and non medical, have made important contributions (Rizzo and Eslinger 2004).

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 more frequent non-motor disorders then it verified in routine exam, not only in the developed and large neurological departments (Sinanovic, 2011; Sinanović et al., 2012). 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 (Brkić et al., 2009; Pederson et al., 2004; Sinanovic et al., 2011). Unilateral neglect is a disorder that mostly effects 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 stoke (Sinanović i Vidović, 2005; Vidović et al., 2006: Sinanović, 2010).

There are different reports on frequency of delirium in acute stroke, from 24 to 48%, and it is more frequent in hemorrhagic then ischemic stroke. Post stroke depression (PSD) 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. Cognitive impairment are part of clinical picture of many stroke patients. 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 (Sinanović, Trkanjec i suradnici, 2015).

This presentation gives an overview of type and frequency nonmotor stroke signs and symptoms.

### CHALLENGING CHILD AND ADOLESCENT IN MODERN SOCIETY

#### **Bianchera hall**

#### Friday, May 29th

09:00 – 10:00 REFLECTION OF CHANGES IN FAMILY RELATIONSHIPS ON THE CHILD'S MENTAL STATUS AND THERAPY SUCCESS Dubravka Kocijan Hercigonja (Zagreb, Croatia)

RECENT CHANGES IN EARLY BEHAVIORAL FEEDING PROBLEMS AND FAMILY DINAMICS Mara Vukadin (Zagreb, Croatia)

INFLUENCE OF MODERN TECHNOLOGIES AND SOCIAL NETWORKS ON PEER RELATIONSHIPS IN ADOLESCENCE Mihaela Rister Zec (Zagreb, Croatia)

- 10:00 10:20 Discussion
- 10:20 10:40 Break
- 10:40 11:40 NONSPECIFIC CLINICAL PICTURE OF DEVELOPMENTAL DISORDERS IN CHILDREN DIAGNOSTIC PROBLEM Dina Koren (Zagreb, Croatia)

RECENT CHANGES AND CHALLENGES OF DIAGNOSTICS AND TREATMENT IN CHILD AND ADOLESCENT PSYCHIATRY POLICLINIC Tikana Karan (Zagrah, Creatic)

Tihana Koren (Zagreb, Croatia)

WHEN FEELING HURTS – INFLUENCE OF ABUSE AND NEGLECT ON DEVELOPING BRAIN Vanja Slijepčević Saftić (Zagreb, Croatia)

INTENTIONAL DRUG POISONING IN MINORS: RISK FACTORS Nenad Jakušić (Zagreb, Croatia)

EFFECTS OF CHILDHOOD TRAUMA ON DEVELOPMENTAL PROCESSES Mirjana Graovac (Rijeka, Croatia)

- 11:40 12:00 Discussion
- 12:00 13:30 Break
- 13:30 14:30 RESTLESS, IMPULSIVE AND IRRITABLE CHILD-DIFFERENTIAL DIAGNOSIS AND TREATMENT Nikolina Antonia Domokuš (Popovača, Croatia)

CHILDHOOD AND ADOLESCENT DEPRESSION – DISORDER WITH MANY DIFFERENT FACES Nela Ercegović (Zagreb, Croatia)

CHARACTERISTICS OF DELIBERATE POISONING IN MINORS Nenad Jakušić (Zagreb, Croatia)

- 14:30 15:00 Discussion
- 15:00 16:00 Break

#### 16:00 – 18:00 ROUND TABLE THE EFFICIENCY OF THE PRESENT AND THE NEED FOR NEW THERAPEUTIC APPROACHES IN CHILD AND ADOLESCENT PSYCHOTHERAPY

Debate questions:

Qualifications of experts for therapy Multidisciplinary and cooperation What therapeutic approaches should include? Terapeutic work coordinatet with Europea standards (education)

MODERATOR: Prof. dr. sc. Dubravka Kocijan Hercigonja

#### Participants:

Prof. dr. sc. Dubravka Kocijan Hercigonja Dr. Mirjana Graovac Dr. Nenad Jakušić Tihana Koren, prof.psihologije Dr. Nela Ercegović Dina Koren, prof.soc.ped.



## **REFLECTION OF CHANGES IN FAMILY RELATIONSHIPS ON THE CHILD'S MENTAL STATUS AND THERAPY SUCCESS**

Kocijan Hercigonja D., Koren T., Prvčić I., Rister Zec M., Koren D., Hercigonja Novković V.

In modern society changes in family relationship dynamics which are associated to social expectation and pressures leads to change of previous family values. A number of other factors leads to changes in parenting styles as well, especially related to a quality and length of time spent with children. Mentioned changes result in altered patterns of attachment which are very important for child's mental development. It could also lead to many developmental difficulties and subsequent psychopathology in adolescence.

Furthermore, there is a problem of a necessity with taking a responsibility for a participation in the treatment process and resolving issues.

In such situations, very often parents and schools come into a state of mutual accusations, which intensify children's problems and their state of confusion and insecurity. The authors present the most common changes in the family and reflection on the mental health as well as the problems associated to inadequate participation in the treatment process between family – school. As well as among family members, especially parents in mutual accusations who might intensify children's problems. This problems also might prevent separation processes, creation of child 's identity. The most common problem is placing the children in the role that is inadequate with their age and developmental stage causing the sense of guilt and too big responsibility for them, which is one of the essential factors in the development of numerous variations, both in adolescence and in adulthood.

## RECENT CHANGES IN EARLY BEHAVIORAL FEEDING PROBLEMS AND FAMILY DINAMICS

Vukadin M., Prvčić I., Rister M., Koren T., Barišić I., Bukovina I.

In recent years there is a significant increase in incidence of early behavioral feeding problems evidenced in Children's Hospital Zagreb. Analyses of cases suggest that such changes are linked to shifts in family dynamics and parental attitudes towards feeding in a modern society context. As feeding is among first interactive activities with others, it is prone to a great deal of interpersonal, emotional and context influences. Major underlying processes connected with development of pathology which are child oriented are identified and discussed. Parent related processes include parental cognitive distortions towards food, feeding and normal child behavior, perception of food abundance, growing health concerns and related feeling of insecurity and impatience in parents during feeding process, as well as role ambiguity in nuclear family. In addition to that objective factors such as availability of food in modern societies, diversity of different diet's, ubiquity and pressure of organic and healthy nutrition, great quantity of different information and suggestions via modern technologies increase parental confusion and significantly increase the risk of early behavioral feeding disorder development.

# INFLUENCE OF MODERN TECHNOLOGIES AND SOCIAL NETWORKS ON PEER RELATIONSHIPS IN ADOLESCENCE

Rister Zec M., Barišić I., Prvčić I., Vukadin M., Koren T..

Research data on peer relationships from 1990s show that adolescents spend twice as much time in interactions with friends compared to any other activity. Development of technology and social networks influenced a significant change in that aspect of adolescence. Today's adolescents most of their times spend on-line, even during the real interactions with peers they tend to communicate simultaneously through social networks. Previously empirically proven data on positive feeling in peer relations is now burdened with constant need in teenagers to prove themselves in on-line friendships. Such tendencies can be linked to the research findings of increased loneliness in today's adolescents as well as to reported less positive experiences in on-line friendships. The goal is to discuss nature of the changes in perception of peer support due to social networks experiences and to discuss what are the consequences of virtual friendships on face-to-face peer communication in light of clinical experiences and recent research data.

## NONSPECIFIC CLINICAL PICTURE OF DEVELOPMENTAL DISORDERS IN CHILDREN - DIAGNOSTIC PROBLEM

Koren D., Kocijan Hercigonja D., Hercigonja Novković V., Gajski M., Koren T.

According to experts about 10,000 children with autistic spectrum disorders live in Croatia. Early diagnosis and early intervention are crucial for these children, because a degree of independence and integration of children in their older age depends on its quality and availability.

Experts diagnose a disorder in children on the basis of the presence or absence of certain behaviors, characteristic symptoms or developmental delays.

What if the clinical picture is unclear and children's behavior can not be assessed in the existing classifications used as DSM-V?

A diagnosis is made by a psychiatristst and valuation and diagnostic is carried out by a multidisciplinary team. It is particularly important to get information from parents and educators. The clinical picture is very different, from the difficulties in language and speech, the complete absence of the mentioned, from the development damage to the stereotyped behavior, avoidance of sounds through covering the ears to the children who in this spectrum disorder work well.

The clinical picture described above lead to the dilemma of whether it is a developmental disorder with non-specific clinical picture or autistic spectrum disorder.

The authors give an overview of the analysis of children with the described characteristics and their experience in the diagnostic evaluation and treatment.

## RECENT CHANGES AND CHALLENGES OF DIAGNOSTICS AND TREATMENT IN CHILD AND ADOLESCENT PSYCHIATRY POLICLINIC

Koren T., Prvčić I., Rister Zec M., Vukadin M., Barišić I.

Recent changes in society affect conceptualization and understanding of the childhood itself, and consequently our understanding of psychopathology of childhood and adolescence. Accordingly, we can expect changes of conceptualization of psychopathology due to theoretical and empirical progress, as well as due to changes in social values and norms. Analysis of referral reasons for psychological examination and support in Children's Hospital Zagreb in last few years shows that the most common reason for parental concern and referral are early developmental problems. From parental perspective such disorders are highly maladaptive, but from clinical perspective they often don't meet existing diagnostic criteria for specific disorder. Given collected data and everyday clinical practice, difficulties of differentiation between existing diagnostic entities and developmental challenges are discussed. Special emphasis in this discussion is on two newly identified significant processes in interpersonal parent-child relationship. First is parental deficiency to adequately perceive normative developmental changes due to changes in family dynamics in modern society. Second, changes in family dynamics obstruct natural developmental transition from one stage to next, which in turn interfere with clinicians diagnostic process, especially when we consider developmental symptom substitution.

## WHEN FEELING HURTS - INFLUENCE OF ABUSE AND NEGLECT ON DEVELOPING BRAIN

#### Slijepčević Saftić V.

The aim of this review is to analyse how significant adversity, such as abuse and neglect, experienced in early childhood, alters to developing of the brain. Chronic stress can become toxic to developing brains and biological systems when a child suffers significant adversity. Toxic stress response can occur when a child experience strong, frequent, prolonged adversity, such as physical or emotional abuse, chronic neglect, caregiver substance abuse or mental illness, exposure to violence, without adequate adult support. Trauma ("fight or flight" mode) can leave a lasting signature on the genetic predispositions caused neurobehavioral changes in childhood and long-term mental health problems. The high levels of fear and intense stress which are the result of chronic and/or multiple exposure children to abuse, result in increased levels of cortisol being produced under the influence of the hypothalamic-pituitary-adrenal gland

(HPA) through epigenetic programming of glucocorticoid receptor expression. Toxic stress cascade cause disturbance process in the establishment of synaptic connections, which results in changes in the cytoarchitecture in hypocampal region, amygdala, corpus callosum and prefrontal cortex. In these regions the physiological process of migration and integration may be lacking, including the establishment of associative connections. Brain cells still being produced at normal rate, but large percentage of the new cells were dying off before fully maturing. In abused child volume of gray matter in numerous brain areas had significantly lower volume. The dysfunction of these systems and structures has a negative effect on the regulation of emotional reactions with lack of capacity for emotional self-regulation, learning problems and causes changes in a child's perception of himself and others, and in understanding and interpreting events.

## INTENTIONAL DRUG POISONING IN MINORS: RISK FACTORS

Jakušić N., Klobučar A., Rešić A.

Predictors or risk factors for suicidal behaviour encompass psycho-pathological factors, family and environmental factors, and biological indices.

In this paper we analysed the risk factors for suicidal behaviour in 51 cases of intentional drug poisoning in minors, admitted for treatment to Children's Hospital 'Zagreb', Klaiceva 16, during 2013 and 2014. The patients reside in the City of Zagreb or Zagreb County: the area with over 95.000 residents aged 11-18. Diagnostic and treatment in case of poisoning is conducted by paediatricians, child and adolescent psychiatrists and psychologists. A detailed medical record is maintained for each patient and some of the data from the record have been used in this paper.

Psycho-pathological Factors In 40 of 51 cases, some form of pre-existing psychiatric condition (one or more) was diagnosed. All our patients with pre-morbid diagnosis had contact with psychiatric services. Here are the names of the disorders and their frequency : Mixed disorders of conduct and emotions (N=11), Conduct disorders (N=6), Depressive episode (N=2), Recurrent depressive disorder (N=4), Mixed anxiety and depressive disorder (N=9), Obsessive-compulsive disorder (N=1), Transsexualism (N=1), Eating disorders (N=4), Abuse of cannabinoides (N=2), Multiple drug abuse (N=1), Acute and transient psychotic disorders (N=1). Physical abuse: fathers (N=2); Sexual abuse (genital contacts): two cases, mother's boyfriend and one case, adult outside the adolescent's family; Psychological abuse: mothers (N=3); Bullying: (N=3). Family Factors The family relationships were described as seriously disrupted in 31 of 51 cases. The patients mainly live with both parents (N=28), in single parent household (N=18), or do not live with their parents (N=5). In 11 cases, children grow up without father and in three cases without mother; in five cases the children are without parents; in 4 cases the mother is described as a disturbed person; in 7 cases the father is described as a disturbed person. Environmental Factors In 27 cases there are problems at school (poor grades, absenteeism from school, the feeling of not being accepted in the company of peers etc.). In all observed cases, the responsible person did not take adequate care of the unavailability of medicines. The average family income is between under average to average relative to the area of residence. In our sample the main risk factors in intentional drug poisoning in minors are: psychiatric disorder, dysfunctional family, low economic status, school related stress, female sex.

## EFFECTS OF CHILDHOOD TRAUMA ON DEVELOPMENTAL PROCESSES

Graovac M., Petrić D., Kaštelan A.,

Children and adolescents can experience traumatic situations in family, school and society, as well as participants in natural disasters, terrorism, war and civilian casualties. Clinical entities associated with the traumatic experience in children and adolescents are common in psychiatric practice. Frequent manifestations of these experiences are classical clinical picture of PTSD, as well as depression, anxiety, somatization, feeding and behavior disorder, dissociative reactions, etc.

The child's perception of the traumatic event, and subsequent developing psychiatric symptoms depended on age and sex, the individual ego strength, coping strategies, but also on the reactions of the surrounding were the aims of this report. We present difficulties in growing in childhood and adolescence that we recognize and treat in our clinical practice. Faced with the traumatic situation, patients usually use a selfprotective mechanisms suppressing negative emotions and memories to combat the negative effects of traumatic experience. Ways of coping are mostly associate with the low degree of reliance with mothers. During adolescence patients presente symptoms of anxiety and/or depresion, guilt to encourage a sense of protection.

Secure attachment is the first line of defense against psychopathology launched traumatic experience. In terms of traumatic events in the child unless objective factors related to the traumatic event affects a child's perception of danger / threat, and perceptions of care required and provided by others. In that space shape the emotional experience of the child, which includes a sense of helplessness, loss, anger and betrayal.

## RESTLESS, IMPULSIVE AND IRRITABLE CHILD -DIFFERENTIAL DIAGNOSIS AND TREATMENT

Domokuš N.A., Boričević Maršanić V.

Children's minds and emotions are constantly changing and developing, and they do not all develop at the same rate, so it is important to distinguish and acknowledge some entities in child's behaviour that can indicate a disorder. Restlessness can occur in children in preschool and school period, and is an expression of interest in discovering new things, objects and phenomena. Differential diagnosis of such behaviour include generalized anxiety disorder (GAD) and attention deficit /hyperactivity disorder (ADHD). ADHD is a neurodevelopmental disorder that occurs in children and adults. It is described as a "persistent" or repeating pattern of inattention and / or hyperactivity / impulsivity that interferes with the functioning or development. Sometimes GAD can be replaced with ADHD. Diffuse anxious children often have difficulty in maintaining attention and their anxiety can also lead to psychomotor restlessness (hyperactivity). The key difference is that children with ADHD are not prone to anxiety than children without ADHD, while children with GAD have many serious concerns. In order

to to differentiate irritable and impulsive behavior in a child ADHD, depresive disorder, posttraumatic stress disorder, intermittent explosive disorder, oppositional defiant disorder, disruptive mood dysregulation disorder and drug abuse have to be taken into consideration. It is important to emphasize that the expression of symptoms varies significantly depending on the developmental stage of the child. When it comes to depressive disorder prepubertal children express more physical complaints, anxiety, fears of separation whereas adolescents express hopelessness, negative expectations of the future, excessive sleeping, changes in body weight, suicidal thoughts and attempts. Psychotherapy, especially cognitive behavioral therapy is used in treatment together with pharmacotherapy. Play therapy using toys, puppets, and drawings may help young children recognize and express their fears and psychodynamic therapy may help older children understand some of the sources of their anxiety. The best results are achieved by combination of these methods.

## CHILDHOOD AND ADOLESCENT DEPRESSION – DISORDER WITH MANY DIFFERENT FACES

Ercegović N., Boričević Maršanić V., Juretić Z., Franić T., Dodig Ćurković K., Štimac D.

Depression is a serious health problem that can affect people of all ages, including children and adolescents. Depression is more than just feeling sad. It is a form of mental illness that affects the entire person. It changes the way the person feels, thinks, and acts and is not a personal weakness or a character flaw. Childhood and adolescent depression negatively impacts growth and development, school performance, and peer or family relationships and may lead to suicide.

More than 70 percent of children and adolescents with depression do not receive appropriate diagnosis and treatment. One possible reason may be atypical presentation. Diagnostic criteria for depression in children and adolescents are essentially the same as those for adults; however, juvenile depression may manifest in different forms and symptom expression may vary with developmental stage.

Younger children may not be able to describe their internal mood state and may express their distress through vague somatic symptoms or pain. Irritable mood may be the cause of angry, hostile behavior. Impaired attention, poor concentration, and anxiety may resemble attention-deficit/hyperactivity disorder.

Adolescent depression tend to be similar to adult depression, so adolescents may show symptoms of insomnia, guilt, brooding, apathy, inconsolable crying, weight and appetite changes, irritability, anhedonia, and deficits in memory and cognitive ability.

Children and adolescents may display different symptoms at different times and in different settings. Although some children may continue to function reasonably well in structured environments, most kids with significant depression will suffer a noticeable change in social activities, loss of interest in school and poor academic performance, or a change in appearance. Adolescents may also begin using drugs or alcohol as means of self-medication for depression.

Psychiatric comorbidities are frequent in juvenile depression; the most common of these are dysthymic disorder, anxiety disorders, attention-deficit/hyperactivity disorder, oppositional defiant disorder, and substance use disorder and can affect clinical presentation of depression in children and adolescents. It is essential that physicians recognize and treat associated psychiatric comorbidities in pediatric depression.

Given the serious impact of pediatric depression on individuals, families and the community, early preventive, detection and treatment interventions should also be an important component of management of this serious disorder.

### **CHARACTERISTICS OF DELIBERATE POISONING IN MINORS**

Jakušić N., Rešić A., Klobučar A.

Adolescence is a challenging period of life and when accompanied with unfavourable environment multiple risks tend to emerge. Adolescents are prone to act emotionally with little consideration to potential consequences of their behaviour. In this paper we analysed the characteristics and patterns of 51 cases of deliberate prescription drugs poisoning in minors, admitted for treatment to Children's Hospital 'Zagreb', Klaiceva 16, during 2013 and 2014. The patients reside in the City of Zagreb or in Zagreb County: the area with over 95.000 residents aged 11-18. As for the medical attention in case of poisoning almost half of those adolescents reside in the catchment area of Children's Hospital 'Zagreb'. Diagnostic and treatment in case of poisoning is conducted by paediatricians, child psychiatrists and psychologists.

Out of 51 cases in our sample, 6 were diagnosed as suicide attempts. Out of all cases of poisoning for the majority (N=40) the first, second (N=5) and third (n=2) incident. For the remaining 4 patients no data on previous poisoning were available. In 40 cases, some form of pre-existing psychiatric condition (F 32, F 92, F 93, F 91, etc.) was diagnosed. Prescription drugs used were easily accessible to minors. Mostly (N=23) of those were legally prescribed, mainly for psychiatric treatment. Benzodiazepines predominate among abused substances (N=39), either alone or in combination with others. Girls-boys ratio was 43 to 8. The average age was 15, 5; the youngest adolescent was 11. Admissions mainly occurred by the end of school terms, either winter or summer (N=27), while only one occurred during the school break. Thirty adolescents attended secondary school, 15 attended primary school and 6 dropped out from education. The average school performance was about 3, 5 (1-5 scale). The patients mainly live with both parents (N=28), in single parent household (N=18), or do not live with their parents (N=5). The family relationships were described as seriously disrupted in 31 cases. The average hospitalization duration was 2, 5 days. After discharge from Paediatric Department some form of psychiatric treatment was continued: in-patient (N=11), daily hospital (N=7) or outpatient clinic (N=33). Majority of deliberate poisoning in minors is an expression of immature behaviour patterns (temporary escape from problems, attention seeking, call for assistance, revenge etc.), while suicide attempts are relatively rare. Poisoning is associated with: female sex, pre-existing psychiatric conditions, dysfunctional family, school related stress, but also unjustifiably easy access to prescription drugs.



### 4<sup>th</sup> EUROPEAN PSYCHOPATHOLOGY SUMMER SCHOOL

Taverna hall Chairpersons: Karl Bechter, Francesco Benedetti, Martin Brüne

#### Friday, May 29th

#### 08:30 - 10:00 INTERACTIVE COURSE SESSIONS

*Chairpersons:* Martin Brüne (Bochum, Germany), Karl Bechter (Günzburg, Germany)

POSSIBLE ROLES OF OXYTOCIN ON EXAPTATION AND MIS-EXAPTATION OF THE INNER SPEECH VIA ITS ACTIONS ON D2R RECOGNITION/DECODING PROCESSES IN NEURONS AND ASTROCYTES Luigi Agnati (Modena, Italy)

ETHICAL IMPLICATIONS OF THE MILD ENCEPHALITIS HYPOTHESIS Sabine Müller (Berlin, Germany)

#### 10:00 - 14:00 Break

14:00 – 15:30 Chairpersons: Francesco Benedetti (Milano, Italy), Antonio Vita (Brescia, Italy)

META-ANALYSIS AND META-REGRESSION OF BRAIN IMAGING DATA IN SCHIZOPHRENIA Antonio Vita (Brescia, Italy)

INFLAMMATION IN ALZHEIMER'S DISEASE: A LECTURE ON THE OCCASION OF THE 100. OBIT OF ALOIS ALZHEIMER Norbert Müller (Münich, Germany)

2 short presentations selected from submissions by course participants

- 15:30 16:00 Break
- 16:00 17:30 *Chairpersons:* Francesco Benedetti (Milano, Italy), Paolo Brambilla (Udine, Italy)

YOUNG RESEARCHER SYMPOSIUM: 6 short presentations selected from submissions by course participants

#### Saturday, May 30th

#### 09:00 - 10:30 INTERACTIVE WORKSHOP WITH CASE VIDEOS AND NEUROPSYCHOLOGICAL TESTING

Chairperson: Johannes Schröder (Heidelberg, Germany)

Mild cognitive impairment (MCI) is generally considered to represent the preclinical phase of Alzheimer's disease (AD). The aim of the present workshop is discuss the diagnostic work up and treatment concepts with reference to typical clinical cases. This will also include differential diagnosis, neuropsychological testing and important biomarkers.

10:30 - 11:00 Break

#### 11:00 - 12:00 PILOT SESSION CASE SUPERVISION

*Chairpersons:* Karl Bechter (Günzburg, Germany), Johannes Schröder (Heidelberg, Germany)

Participants can present own cases (speaking, paper or video) and pose specific questions to be discussed with the group and the supervisors.



Under the patronage of EPA.

## POSSIBLE ROLES OF OXYTOCIN ON EXAPTATION AND MIS-EXAPTATION OF THE INNER SPEECH VIA ITS ACTIONS ON D2R RECOGNITION/DECODING PROCESSES IN NEURONS AND ASTROCYTES

Agnati LF., Marcoli M., Cervetto C., Genedani S., Borroto-Escuela D., Romero-Fernandez W., Guidolin D., Maura G., Fuxe K.

Human beings have unique mental abilities such as the "inner speech" that have been crucial for development of complex social organizations. Related to inner speech is imagination, which is a feature of human self-awareness and of crucial importance for critical analysis of virtual scenarios provided by simulation processes. Thus, inner speech plays a fundamental role in predictive psychic homeostasis, especially through its participation in the Internal Theatre shaping where consequences of future actions can be simulated.

Inner speech has also become a target for mental disorders, which result in a reduced fitness and conflicts between the individual and society. To account for this evolutionary maladaptation, we have advanced the concept of "mis-exaptation", derived from Gould and Vrba's concept of exaptation (1982). Mis-exaptation is a characteristic that, although conferring positive effects in one field of activity, may reach an inappropriate degree of specialization to have deleterious effects in that or in another field thereby leading to a decrease in fitness.

Although inner speech favours learning and reasoning, it may cause the emergence of mental disturbances, hence altered social behaviours and hallucinations, characteristic of schizophrenia. There are, nevertheless, two traits associated with the inner-speech mis-exapted state namely altruistic behaviour and heightened creativity, the latter being over-expressed in relatives of schizophrenic patients.

As far as the neurotransmitter-identified neurons are concerned, it has been shown that oxytocin and dopamine neurons of Complex Cellular Networks (CCNs) in limbic and cortical areas could play regulatory roles both in social behaviours and schizophrenia. As a side-effect antipsychotic drugs, acting on nucleus accumbens (Acb) D2R, bring down dopamine/oxytocin interactions and thus oxytocin function. This leads to a reduction of normal social behaviours. Furthermore, D2R and oxytocin receptor heteroreceptor complexes (D2R^OTR) have been demonstrated in Acb and striatum. Accordingly, in membrane preparations from Acb, oxytocin increases density and affinity of high-affinity agonist state of D2R, increasing D2R/Gi/o coupling. Morphological and functional data obtained by our group demonstrate OTR interactions with A2A and D2R in native astrocytes, possibly due to the presence of OTR^D2^A2A heteromers. Thus, astrocytes could play a critical role in integrating these Volume Transmission signals hence in modulating CCNs involved in inner speech and social behaviours.

## ETHICAL IMPLICATIONS OF THE MILD ENCEPHALITIS HYPOTHESIS

#### Müller S.

The mild encephalitis hypothesis characterizes schizophrenia as a neurological disorder with psychiatric symptoms that can be triggered by external factors, including viruses, particularly in humans with a hereditary vulnerability. If the mild encephalitis hypothesis would be largely adopted in the medical community, then schizophrenia would be shifted from psychiatry to neurology, and the social status of many patients would shift from chronically, refractory ill and mentally disabled to temporarily or chronically ill but treatable.

This talk will discuss two major ethical issues that would be raised if the mild encephalitis hypothesis would be largely adopted by the medical community and the public:

First, compulsive treatment: In many countries, legal regulations have been strengthened in order to protect patients with psychiatric disorders from being treated compulsively. This legal development is strongly connected with the UN Convention on the Rights of Persons with Disabilities. In Germany, the Federal Constitutional Court has established the "right to be sick", particularly with regard to patients diagnosed with schizophrenia who refuse antipsychotic medication. If (subtypes of) schizophrenia) would be recognized as a primarily neurological condition, that often comprises the reality perception and the capability to give informed consent, but that might respond to anti-inflammatory medication, then the attitude of legal theorists to compulsory treatments might change. If compulsory treatment would often be successful in restoring the patients' capabilities for autonomy, and if the treatments would not have the feared adverse effects of neuroleptics, then the attitude to compulsory treatment of patients with schizophrenia might be reconsidered.

Second, stigmatization: If the mild encephalitis hypothesis would be accepted by the public, it will influence the stigmatization of people suffering from schizophrenia. Stigmatization research has shown that for most disorders, stigmatization is increased by biological, particularly by genetic causal explanations. It is hypothesized that the mild encephalitis hypothesis of schizophrenia will cause less stigmatization than explanations that focus on genetics: Genetically caused psychiatric conditions are considered by laypeople as belonging to the core of the personality, and therefore as unchangeable, whereas acquired brain disorders are seen as possibly treatable, and not as part of the personal identity. Therefore, the mild encephalitis hypothesis could be helpful for better integrating patients with schizophrenia into the society.

# INFLAMMATION IN ALZHEIMER'S DISEASE: A LECTURE ON THE OCCASION OF THE 100. OBIT OF ALOIS ALZHEIMER

#### Müller N.

Alois Alzheimer died at 19. December 1915, two years after his change from Munich to Wroczlaw. In Munich, he had described in 1907, a peculiar severe illness-process of the cortex', which named the head of the department, Emil Kraepelin, Alzheimer's disease (AD). 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 chapter 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.

### INTERNATIONAL SPORTS PSYCHIATRY MEETING

#### **Belica hall**

Chairpersons: Karl Jürgen Bär, Valentin Markser

#### Friday, May 29th

- 07:30 Participants meet on the main entrance for the morning warm-up (sportswear required)
   10:30 – 12:30 SPORTS THERAPY IN DEPENDENCE DISORDERS Tobias Freyer (Freiburg, Germany)
   SPORTS AND MOTOR ACTIVITY IN DEMENTIA Karl Jürgen Bär (Jena, Germany)
   SPORTS PSYCHIATRY: ISSUE, METHODS AND WORK OUT Valentin Markser (Köln, Germany)
   INTERNATIONAL HIGH PERFORMANCE SPORTS, TRAUMA AND CULTURAL BACKGROUND Thomas Wenzel (Wien, Austria)
   14:00 – 15:30 SPORTS AND PHYSIOTHERAPY IN PSYCHIATRIC DISORDERS
  - Case presentation and discussion
- 15:30 16:00 **Break**
- 16:00 17:30 MENTAL HEALTH IN HIGH PERFORMANCE SPORTS

Case presentation and discussion

## SPORTS PSYCHIATRY: ISSUE, METHODS AND WORK OUT

#### Markser V.

Sport psychiatry encompasses two sides of one coin. On the one side, it deals with the therapeutic potential of sport for mental illnesses. On the other, it can be defined as a discipline to prevent, diagnose and treat the psychiatrically related medical issues confronting the athlete.

In psychiatric care, sport has been used as a rather unspecific additional method for standardized treatment. However, during the last decade more and more studies suggest that sport has a specific therapeutic potential for various disorders and requires therefore a more prominent role in the entire treatment regime. The best explored disorders are depression, anxiety and various dependencies. Professional athletes are subject to massive somatic, as well as social and emotional strains. Despite the great public interest in athletic achievements, the emotional strains are rather poorly investigated. This was caused by the assumption that only the emotionally very strong athletes are able to compete at the highest professional level and therefore mental disorders do not exist in professional sports. However, available research suggests that this selection hypothesis has to be revised. Mental disorders are as common in professional sports as in the general population. Nevertheless, there are sport-specific variations to certain types of mental disorders. This will be discussed using depression and overtraining syndrome. In addition, various preventive strategies for the athlete will be discussed.

## **POSTERS PSYCHIATRY**

#### 1. THERAPEUTIC EFFICACY OF LAMOTRIGINE IN A PATIENT WITH BORDERLINE PERSONALITY DISORDER AND DEPRESSION EPISODES: A CASE REPORT

Arsova S., Manusheva N., Bajraktarov S. University clinic of psychiatry Skopje Macedonia, Republic of Macedonia

The aim was to present therapeutic efficacy of lamotrigine in patients with borderline personality disorder and depressive symptoms.

This is a case-report of a 35-year-old patient, with completed secondary education, employed in the public administration, single, who lives with her family. The patient has been treated at the Psychiatric Clinic for more than ten years and she has been hospitalized four times. Her last three hospital visits were realized in the Day Hospital. All admissions were a result of severe psychological difficulties manifested with unstable and intense interpersonal relationships with her family, at work (with the authorities), partners and her friends. Following these conflict situations she exhibited rejection sensitivity, she felt neglected, receiving no gratitude from the others, for her deeds, having feelings of emptiness, anger, distress, lack of motivation and willingness, and reduced working capacity. Thus, all these led to self-harming thoughts and actions. On admission a marked distress has been observed, accompanied by outburst of weeping, severe problems with self-worth, rejection sensitivity and feeling disrespected by her family members (mother, daughter-inlaw, brother), as well as by occupational and social environment. Concerning her emotional condition on admission a depressed mood has been noticed and expressed anxiety with rage, anger, despair, but not with obvious sorrow. In conditions like these she displays cognitive difficulties, eating disorders, occasional insomnia, social withdrawal, occasional impulsive self-destructive behavior. During her two-week hospital stay her sensitivity was very much expressed, her adaptation to group environment, veering from extreme closeness with some members of the group to quick disappointment and dislike by these members, experiencing "abandonment fears" and insufficient understanding. These experiences and behavior have also been noticed by the team from the Day Hospital. Family medical history shows that her mother is being treated for chronic mental illness. Over the years of pharmacological treatment she was receiving SSRI anti-depressive drugs, low dose of anti-psychotic drugs and recently a psychostabilizer has been introduced, firstly carbamezapine and then lamotrigine at a dose of 25, 50 to 2x100 mg/day. At the moment she is in a stable condition regarding her everyday functioning, relatively stable emotional state, without significant interpersonal conflict situations and normal occupational functioning.

Lamotrigine has shown therapeutic efficacy in this patient with BD personality disorder and occasional depressive episodes in stabilizing her emotional condition, behavior and interpersonal and occupational functioning.

#### 2. THE PRESENCE OF CHRONIC PAIN IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER AND ITS INTERCORRELATION

#### Batinic B., Nesvanulica J., Stankovic I. Clinical Center of Serbia, Clinic of Psychiatry, Belgrade, Serbia

Chronic pain is a common experienced symptom among patients diagnosed with Major depressive disorder. The intensity of depression and chronic pain intercorrelated, having negative impact on the daily functioning of the patients. Our objective was to explore the presence of chronic pain in patients diagnosed with Major depressive disorder (single episode or recurrent), correlation between intensity of depression and chronic pain, its interference on daily functioning, as well as sex differences regarding to the explored variables

The study sample consisted of 51(62.2%) female and 31(37.8%) male patients diagnosed with Major depressive disorder (N=82), age between 18 and 65 years (mean age of 46.21). Assessment instruments included The Beck Depression Inventory-II (BDI-II), The Brief Pain Inventory-Short Form (BPI) (consisting of BPI-I factor of pain intensity, and BPI-II-factor of pain interference with daily functioning), and semistructured questionnaire for sociode-mographic characteristics. Chronic pain was defined as of duration of 3 months, at least a moderate level of intensity, which interferes with daily functioning.

The presence of chronic pain was found in the 51 (62,2%) of patients with Major depressive disorder. The mean score on the BDI-II for the whole sample was 22.5 (SD 12.8). There was a positive correlation between intensity of depression (BDI-II) and intensity of chronic pain (BPI-1), and its interference on the level of daily functioning (BPI-2) (p <0.01). Furthermore, there was a sex differences regarding to the explored variables: women diagnosed with Major de-

pression experienced chronic pain of higher intensity and with greater interference on daily functioning.

Our research data show a high frequency of chronic pain among patients diagnosed with Major depressive disorder and its positive intercorrelation which results in negative impact on daily functioning, so psychiatrist's regular evaluation of depressive symptoms should necessarily include evaluation for the presence of chronic pain, especially in women. Pharmacology and cognitive–behavioural approach to major depression in the presence of chronic pain should be modified from standard treatmant in order to target chronic pain (considering dual antidepressants- SNRI in pharmacotherapy, and focus on pain cognition and emotions in cognitive-behavioural therapy).

#### 3. WWOX MAY BE RELATED WITH SLEEPLESSNESS SYMPTOM OF BIPOLAR MANIA: A GENOME-WIDE ASSOCIATION STUDY

Chul-Hyun C., Heon-Jeong L., Leen K. Korea University College of Medicine, Seoul, South Korea

Even though bipolar disorder (BD) is highly heritable psychiatric disorder, the investigation of specific genetic variations has suggested limited findings. It has been suggested that dividing BD to subgroups according to clinical subphenotypes is a possible approach for further genetic studies in BD. We performed a genome-wide association study (GWAS) of sleeplessness symptom of bipolar mania (SBM) vs. non-sleeplessness symptom of bipolar mania (NSBM) in bipolar I disorder subjects.

A total of 2,200 cases, 1,436 controls, and 703,012 SNPs in the merged samples of the Translational Genomics Institute (TGEN) and the Genetic Association Information Network (GAIN) were investigated.

We identified 44 associated SNPs with P<10-4 in this caseonly analysis, the most significant of which was rs10492908 (OR=0.1832; P = 9.27 × 10-7; Permuted P = 1.00 × 10-6) which is located within a region of the gene encoding WW domain containing oxidoreductase (WWOX) on chromosome 16q23. We identified a total of eight of genomic regions of interest (ROIs) on chromosomes 3, 5, 8, 9, 12 and 17 defined as regions containing at least two SNPs with P<10-4 and adequate support for association (i.e., P<10-3) from surrounding SNPs within 100 kb. ROI5 and ROI7 showed matching genes ROR2 and ANKFN1, respectively. The functional enrichment analysis showed a significant enrichment of cell development-related, cell adhesion-related, signal transduction-related, cell recognition-related, synaptic transmission-related, and cell motility-related pathways. WWOX is known as a putative tumor suppressor gene. But, several studies show that WWOX is involved in regulation activity of GSK3beta which is important in circadian rhythm and lithium mechanism of action. ROR1 is known to be related to insomnia, and it modulates neurite growth and synapse formation in complex with ROR2. A GWAS of cannabis dependence reported ANKFN1 as significantly related gene.

We have explored about BD by using of a subphenotype, which is SBM, for more homogenous group of subjects with more similar clinical courses. Taken together, we speculate several candidate genes and pathways are related to sleeplessness bipolar mania. In the future, more replication study will confirm the results of present study.

#### 4. SEXUAL ORGANIZATION OF THE BRAIN: NEURODEVELOPMENT, GENDER DIFFERENCES AND RELATION TO GENDER IDENTITY DISORDER

Duišin D., Batinić B., Barišić J. Clinic of Psychiatry, Clinical Centre of Serbia, Belgrade, Serbia

Introduction The differences between men and women could be observed not only in their anatomy, but also in their behaviour. The importance of sex-related hormonal influence during specific hormone-sensitive periods in early development and the impact of sex differences on brain and behaviour has been proven using animal models. Objectives To highlight the complexity of neurodevelopment in relation to gender differences based on interaction between genetic, epigenetic and hormonal factors during early development. The emphasis will be on the development of neurofunctional brain physiognomy and its implications on sexual orientation and gender identity disorder (GID). Methods Review of available literature through electronic Kobson database, particularly experimental investigations of animal model, including advanced brain research in genetics and endocrinology.

Results Available data indicate that beside sex differentiation, gender-dependent differentiation of the brain is primarily controlled by differences in gonadal steroid hormone levels during prenatal development. Such differentiation has been detected at morphological, neurochemical and functional level of brain organization. The role of testosterone, particularly as inductor male gender role behavior and heterosexual orientation has been proven through clinical evidence, while estradiol involvement in the development of a human female brain is not yet clarified. Influences and impact of postnatal experiences as well as gonadal hormones and underlying neural mechanisms could involve the same neural circuitry. Gender specific patterns of sex hormones in specific prenatal and postnatal periods are reflected in human brain sex differences in gonadal hormone receptors. Local hormone dependent changes during development in some areas of the brain may follow a different course than the development of genitals during the process of sexual differentiation. This could result in partial or complete brainbody sex reversal phenomena, in other words, to brain development incongruent with body differentiation or vice versa. Such occurrence can happen to particular brain areas involved in the establishment of an individual's sexual orientation or gender identity, leading to sex reversed partner preference or gender identity. This provides new neurobiological evidence for supporting explanation of sex reversed brain status in persons with GID/GD e.g. transsexuals.

Conclusions Prenatal and around birth hormonal exposure can influence sexual differentiation of the brain, including development of gender identity. Extensive clinical and experimental research has provided new neurobiological evidence that can explain sex reversed brain status in persons with GID e.g. transsexuals. Contemporary standpoint regards transsexualism (gender identity disorder-GID/ Gender dysphoria-GD) as a neuro-developmental condition.

#### 5. THE EFFECT OF SUPPORT GROUP THERAPY ON PARENTALLY BEREAVED ADOLESCENTS: A RANDOMIZED CONTROLLED TRIAL

#### Elkeshishi H.E., Abuhegazy H.

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Bereavement is considered to be the most stressful life event, and it becomes particularly distressing when it concerns the death of a parent, such an event is very traumatic to children. The literature suggests various interventions for bereaved children including individual counseling, music therapy, and support groups. The present study aims to examine the effect of a support group therapy for parentally bereaved youth on self concept, and symptoms of depression and anxiety.

The sample of the study have been collected from 4 governmental schools at Cairo, and the interventions given between September 2012 and July 2013, participants were students in grades 7th, and 8th who had experienced the death of one parent for 1 year or more prior to the study, all eligible participants - who themselves and their parents gave consent to participate- were randomly assigned in 1:1 ratio to either supportive therapy intervention group or control group, the intervention group children were divided into groups each of 8-12 children which undergoes 12 weakly supportive group treatments led by the main investigators. The primary outcome was symptoms of anxiety, depression as well as self concept at 12 months; it was assessed at the baseline and 12 months after by three self-completed questionnaires: self concept scale, children's anxiety scale, and children's depression inventory. Analysis was by intention to treat.

60 (50%) of participants were assigned to supportive therapy intervention group, and the other 60(50%) to control group, at 12 months we recorded differences between control and supportive therapy groups in child depression inventory scores (19.2[SD 5.55] vs 13.2[SD 5.51]T= 4.25, P=< 0.001), children anxiety scale scores ( 27.66[5.29] vs 24.61[4.62]T= 7.69, P=<0.001) and self concept scale scores (49.29[11.07] vs 58.18[4.55], t=6.24, p=<0.001). we also noted significant differences between baseline and 12 months assessments in supportive therapy group, but not in control group on all outcome measures.

School based systematically delivered supportive therapy groups for bereaved youth found to be effective in reducing anxiety and depression symptoms, as well in enhancing their perceived self concept.

#### 6. PROBABILITY DISTRIBUTION OF R-R INTERVALS DURING SLEEP IN NORMAL AND OSA CHILDREN

Eui-Joong K.<sup>1</sup>, Young Min A.1, Jong Won K.<sup>2</sup> <sup>1</sup> EMC Eulji University School of Medicine, Seoul, Republic of Korea <sup>2</sup> Woolcock Institute for Medical Research, Seoul, Republic of Korea

Heart rate variability (HRV) has been investigated to evaluate autonomic nervous system (ANS) during Sleep. Increasing sympathetic activity was regarded as one of the important pathophysiology of obstructive sleep apnea syndrome (OSA) because of its cardiovascular complication. Is it still true for OSA children? We tried to figure out the characteristics of R-R intervals between OSA and normal children.

A single night PSG was performed to 12 OSA children (6.0  $\pm$  3.7 yrs.; 10 boys) and 14 normal children (5.8  $\pm$  2.1 yrs.; 7 boys). ECG recorded at 200 Hz in modified II position during sleep. Probability distributions of R-R intervals were obtained and compared to the Gaussian distribution function.

The mean value of R-R intervals in OSA was  $0.69 \pm 0.12$  sec. and in control was  $0.76 \pm 0.11$  sec. The group difference was not significant (p=0.11). The probability distribution of each patient usually fits to the bell-shaped Gaussian distribution curve. However, non-Gaussian, a double-bell shaped distribution was also found in both groups. Numbers of double-bell shaped were 2 out of 12 in OSA, and 1 out of 14 in control.

The double-bell shaped distribution may imply a sign of car-

diac abnormality, which could provide a new method to characterize R-R interval. Probability distribution might give a light on detection of abnormal cardiac function which couldn't found through usual HRV variables such as mean R-R intervals and standard deviation of NN intervals.

## 7. ALTERNATIVE MEDICINE TREATMENTS OF PAIN

#### Greš A., Radovančević Lj.

#### Croatian Association for Patients Rights, Zagreb, Croatia

The authors describe, discuss, comment, contextualize and operationalize the treatment of pain in the domain of alternative non-official medicine. So, the authors remain critical about alternative procedures. Nevertheless, today in rural, but also in urban settings semi educated people practice that unorthodox medicine. There are various methods and techniques of prevention ant therapy of pain, especially when standard medicine procedures did not bring any success. Herbal therapy (phitotherapy), decocts, teas, herbal extracts are used by alternative "doctors" with various results. Distraction of concentration on pain can be achieved by various remedies in the sphere of alternative medicine which attracts people with pain. The authors critically comment such approaches.

The authors collected their material from various books about alternative medicine describing methods used by quack doctors, but also by some medically educated individuals.

This is a review article. The paper deals with various nonscientific methods used in alternative medical practice of modern time. Some of them, as chiropractic and acupuncture are particularly recognized and known in the field of official medicine. However, Ayurveda, Christotherapy, color and light therapy, crystalotherapy, parts of hagiotherapy prayers, exorcism, etc., base their attempts on suggestion and auto-suggestion, placebo effect of belief in higher beings, gods, demons, fairies, holy spirits and other entities from the underworld. Implementation of such attempts brings only temporary success.

It is inevitable to escape to alternative medicine practices because the official medicine sometimes fails. Ill, sick, diseases people tend to apply anything they believe can help them.

#### 8. BODY AND SECONDARY GAIN

Greš A., Esapović Greš N. Croatian Association for Patients Rights, Psychiatry Clinic-KBC Zagreb, Croatia

Secondary gain, with it s tendency for gratification for reality, places a body as an important instrument and the aim of gratification. Besides, the body is a source of a psychic energy, which by a secondary gain patients, has not been evaluated to mature level of mentallization. The body is also an object of projection for unsolved conflicts through which becomes a symbolic form of communication

Four patients, with phobic disease, psychosomatic reactions, somatic projections and somatic violations, has been presented. All of them offered the body, as a serious damage of the personality, which is incompatible with a work capability. All patients where treated in individual psychoanalytically oriented psychotherapy.

The body of the secondary gain patient is a frequently used instrument. Emotional problems are expressed by body, the body is a symbolic speech of unsolved conflicts. The body also becomes the place of a psychosomatic disease and an acting out reaction.

Patients who have tendency towards gratification in reality very often use their body as one of their the most important real objects. Structure of patients with secondary gain, at which dominates incapability of solving conflicts on mental level is conditional that instead of psychic instrument, body is used in aim of obtaining gratification and avoiding frustration. Somatic diseases are crystal nucleus for conflicts projection on body of the patients whose aim is to keep symptoms. Regressive processes of patients with secondary gain have the deepness of the body level. Acting out is not only an obstruction in therapeutic process, but it is the frequent cause of somatic violations which become the instrument for obtaining the aim: gratification in reality.

#### 9. WHAT A CHILD AND ADOLESCENT MEET IN CONTEMPORARY SOCIETY

#### Greš A., Radovančević Lj. Croatian Association for Patients Rights, Zagreb, Croatia

Young people are nowadays exposed to several negative challenges which do not do any good to them. Bullying is one of horrible phenomena that can results in physical and mental victimization of involved children and teenagers. There is a number of events, for example, two girls fighting out of various reasons, and all other pupils stand by and stimulate one or another, enjoying themselves. Causes of such happenings lie in sentimental love affairs. Another challenge lies in computer games addiction. Writing in Facebook, is the possibility of getting acquainted to some hetero or homosexual predatory pedophiles of all ages. Offenders often seduce children and put photos on the internet to seen by everyone. Gambling addiction and habituation are also negative pathological evils awaiting the naïve, neglected adolescents and children. Exposition to psychostimulative means, starting with nicotine, marijuana and hashish is also one of negative challenges. Consumers go on to harder narcotic drugs as heroin, cocaine, LSD, crack and various other substances. This

is the trap for inducing severe pathology.

The authors have collected the information and materials about described topics from their everyday psychiatric practice, from articles in periodicals and newspapers and also from TV broadcasts on such unwanted events.

Society has to make efforts to eradicate such events in school settings. The American culture with competition and rivalry is a fruitful ground for such happenings.

We are the witnesses of various challenges and traps awaiting today our youth, society, culture and civilization. In this rapid development and progress, they brought a lot of various good things, but also the good ones. Among the bad thing in the first place is drug addiction, alcohol abuse, smoking, etc. Another unhappy phenomenon which affects children and teenagers is their addition to internet and computer games. Consequently, they neglect their school tasks and duties, become tired, somnolent, exhausted psychastenic, neurasthenic and weak. Pedophiles, perverse maniacs are waiting to chatter with eager girls and boys. They want to attract and to meet them in person, pretending to be of the same age. Many of kidnap cases, murders and exploitations through the years can occur. School setting can be places of bullying, brachial attacks of stronger pupils towards the weak and the smallest one, maltreatment and harassment.

#### **10. CORRELATION OF NOCTURNAL BRAIN ACTIVITY TO DAYTIME PVT PERFORMANCE IN OSA PATIENTS: A PILOT STUDY**

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Having a good sleep is essential to maintain physical and mental health, as well as to enhance daytime vigilance and performance. The quality of nocturnal sleep has been quantified via polysomnography (PSG) that monitors dynamic changes in various bio-signals, such as electroencephalogram (EEG), while psychomotor vigilance task (PVT) is widely used to measure the level of vigilance/performance. The purpose of this pilot study is to explore correlations of EEG measures to PVT outcomes, which may provide some insights in to the importance of good sleep in enhancement of daytime functioning, in an obstructive sleep apnea population.

Standard polysomnography (including six-channel EEG, ECG, EOG, etc) was performed for 8 obstructive apnea patients (All male; Age: 45.3 +- 8.5. yrs; BMI: 32.6 +- 5.3 kg/m^2; RDI: 49.8 +- 24.7 per hr.). 5 s epochs of artefactfree EEG epochs were analyzed using detrended fluctuation analysis (DFA), and averaged for each sleep stage. PVT was performed twice in the following day (8am and 10am), and the inverse of mean reaction time was used to quantify the level of vigilance/performance. For the correlation study, the ratio of mean DFA scaling exponents in sleep stage 1 to 2 was associated with the ratio of PVT at 10am to 8am. Person's correlation coefficient and its significance was obtained at p<0.05. The paired t-test was performed to examine the differences between DFA scaling exponents in sleep stage 1 and 2, as well as PVT at 8am and 10am.

The total sleep time and sleep efficiency of patients were 410.3 + 50.9 minutes and 84.6 + 9.1 %, respectively. The mean DFA scaling exponents in sleep stage 1 to 2 were 0.94 + 0.04 and 1.13 + 0.05, respectively (p<0.01). The PVT at 8am and 10 am were 2.79 + 0.48 and 2.69 + 0.65, respectively (p=0.57). The ratio of DFA scaling exponents showed a negative correlation to the ratio of PVTs (Pearson's correlation coefficient r = -0.708 and p = 0.049).

The strong correlation between nocturnal EEG activity and PVT performance suggest that our quantitative study could provide a good estimate for daytime vigilance/performance via nocturnal PSG.

#### 11. AN OVERVIEW OF THE REASONS FOR THE MEASURE OF HOSPITAL FORENSIC COMPULSORY TREATMENT FOR PATIENTS AT THE SLOVENIAN UNIT OF FORENSIC PSYCHIATRY (UFP) AND THE APPROACHES TO THEIR FURTHER CARE AFTER RELE

#### Koprivsek J., Celofiga A. University Medical Centre Maribor, Slovenia

The Unit of Forensic Psychiatry (UFP) of the Department for Psychiatry at the University Medical Center Maribor is the main and only forensic facility for Slovenian forensic patients and prisoners. It was opened in 2012, when all forensic patients were transfered from other psychiatric hospitals to the new location.

We reviewed reports of all 244 patient admittions to the UFP (during a 3-year period) about the reasons for treatment (diagnosis and type of offense as a reason for addmission) and types of further interventions after their discharge from UFP.

The majority of patients can be divided into three major groups : - previously often hospitalized patients with resistent symptoms or functional deterioration of severe chronic mental illness with different levels of offense, - "dual diagnosis patients" as offenders of a moderate to serious offense, - patients with personality disorders, mostly with substance use commorbidity, commited moderate to serious offense. After discharge patients were usually treated under the measure of outpatient compulsory treatment, or within community mental health services or were transfered in the supported housing institution.

We believe that in the field of forensic psychiatry in Slove-

nia some legislative changes are necessary that would allow a wider range of treatment options after the legal deadline of the measure of compulsory hospital treatment (maximum duration is 5 years). It is also necessary to consider additional institutional and functional ways of care for patients after their discharge from the UFP.

## 12. CASE REPORT OF THE DIAGNOSTIC ROLE OF ELECTROENCEPHALOGRAPHY IN DEMENTIA

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To acknowledge the role of the electroencephalography (EEG) during the diagnostic process in dementia. This is a case report of 63 year old female patient treated for dementia for the last seven years. Last four years she received Donepezil and Risperidone for behavioral changes and psychotic symptoms. Actual examination was performed because of the severity of the symptoms (with amnesic symptoms and difficulty in recognition of close relatives). In the mental status we observed psychomotor retardation, stereotype and poor thinking and speech, reduction in intensity and reactivity of affect, mood and drive, with no insight. Laboratory analysis was within normal limits. EEG was with theta dysrhythmic activity. Urgent CT of the brain was performed with present atrophy and no brain lesions but with sub-acute subdural hematoma with diameter of 2 cm. She was referred to a neurosurgeon.

Electroencephalography as a non invasive method should be used more often in dementia patients because it could point to possible complications or progression of the psycho-organic process.

#### 13. ARIPIPRAZOLE IN BIPOLAR DISORDER: A META-ANALYSIS OF EFFICACY AND SAFETY IN RANDOMIZED CONTROLLED TRIALS AND OBSERVATIONAL STUDIES

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Bipolar disorder (BD) refers to a group of affective disorders leading to significant personal distress or social dysfunction [1]. Even though psychological and psychosocial interventions may have an important part to play [2], the primary treatment in acute mania is pharmacological [3,4]. Aripiprazole is a recently FDA and EMA approved second-generation antipsychotic drug [5]. It seems to have a favourable efficacy and tolerability profile for the treatment of bipolar disorder [6], both in adult and pediatric population [7]. Bipolar disorder (BD) refers to a group of affective disorders leading to significant personal distress or social dysfunction . The primary treatment in acute mania is pharmacological. Aripiprazole is a recently FDA and EMA approved secondgeneration antipsychotic drug. It seems to have a favourable efficacy and tolerability profile for the treatment of bipolar disorder, both in adult and pediatric population. To assess the efficacy and safety of aripiprazole (ARP) alone or in combination with other antimanic drug treatments compared with placebo and other drug treatments (lithium or haloperidol). The acute (3 weeks) and the stabilization (4-to-12 weeks) phases of treatment were considered, both in adult and paediatric population.

Relevant studies were systematically located by searching electronic sources till 2014, August 19th, using EMBASE, MEDLINE, CINHAIL, PsychINFO, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus and ClinicalTrials.gov. The reference lists of other systematic reviews and meta-analyses were checked. The primary outcomes were ARP efficacy (mean change from baseline in Young Mania Rating Scale) and safety (specific adverse events). Twenty-two studies met our inclusion criteria. Sixteen were randomized clinical trials (RCTs) and 6 were observational studies. A total of 2505 patients were included in the analyses in the acute phase and of 2932 in the stabilization phase. Acute Phase - The efficacy of ARP was superior to placebo (SMD -0.31, 95%CI -0.46, -0.16) and comparable to traditional drugs (SMD 0.01, 95%CI -0.12, 0.13). The safety profile of ARP was overall comparable to other drugs, with a lower risk of hyperprolactinemia when compared to placebo but no studies were available for a comparison with other drugs. Stabilization Phase - ARP showed greater effect than placebo (SMD -0.48, 95%CI -0.78, -0.18), especially in paediatric patients (SMD -1.08, 95%CI -1.32, -0.85), and performed comparably to traditional drugs (SMD-0.14, 95%CI -0.29, 0.01). When excluding non-RCTs from analyses, results were overall comparable. The risk of adverse events with ARP was similar to other drugs, except for hyperprolactinemia, significantly lower.

To the best of our knowledge, this is the first meta-analysis evaluating ARP efficacy and tolerability that includes both randomized controlled trials and observational studies. ARP is an effective treatment in children and adults with Bipolar Disorder, similar to other drugs, both at 3 and 4 to 12 weeks. Its safety profile is similar to other drug treatments, but it is not associated with hyperprolactinemia. Further studies in the maintenance phase are needed.

## 14. THE NECESSITY FOR ANTIDEPRESSANTS IN THE ELDERLY

#### Milosavljevik P. Institute of Gerontology"13 November", Skopje, Republic of Macedonia

Depression is the most common mental health problem in the elderly that affects patiens, their families and communities.But it is still goes undertreated and untreated. In elderly, untreated depression can last for years. It can lead to or make worse other problems in physical and mental health and inrelationships with others. It also makes suicide more likely. However,it can be treated successfully. But it is challenging to identify and diagnose depression in a population owing to communication difficulties caused by hearing or cognitive impairment, other comorbidities and the stigma assosiated with mental illness.

Geriatric depression scale(long form) at the first day of hospitalization. We analysed 149 patients from 65 to 91 years of age at the first day of hospitalization in a period of 12 months(01.01.2014- 31.12.2014).

65 patients were with result from GDS(10-30) or 43.6 % were with mild and severe symptoms of depression, and only 26 or 17.45% of all were treated with antidepressants and all of them still with symptoms of depression.

Depression is a common but undertreated and untreated condition in the elderly.

#### **15. TIME PERSPECTIVE IN PSYCHODRAMA PSYCHOTHERAPY GROUP**

#### Mindoljević Drakulić A.

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The components of time in psychodrama include not only psychotherapeutic but the phenomenological and philosophical component as well. All three time dimensions of past, present and future coexist in the life of a protagonist in a psychodrama group and as such may be successfully integrated by psychodrama techniques through psychotherapy process. Time in psychodrama may speed up or slow down, suspend or freeze. In psychodrama all action takes place in the "here and now" and is carried out in a context that offers psychological safety through configuration and personalisation. The expression "here and now" refers to the overall process and the current actions that take place in group therapy between the group therapist, group members and the protagonist. However, there are also recollections of past events to be found in group therapy. This linking of the "there and then" with the "here and now" situation is crucial to the therapist and the group. This paper describes the past events in order to understand and change the present events in the psychodrama psychotherapy process. In this flexible

and creative distortion of time the protagonist, group members and the therapist can easily see a series of therapeutic benefits. This case uses the time-line method to engage a member of the psychodrama group in the action so as to combine his past and present events with the anticipation of future feelings and events, that is to say to combine the here-and-now observations and experience with the thereand-then observations and experience.

#### 16. EPIDEMIOLOGICAL FEATURES OF ACUTE ALCOHOLIC POISONING IN CHILDREN (2000-2010) POSTER PRESENTATION

#### Močenić I., Močenić D., Jašić M., Gazibara I., Mladinov O. General Hospital Pula, Croatia

Target is to determine basic epidemiological and clinical characteristics of tested patients.

Metod: A retrospective analysis of hospitalized patients in the period of ten years.

All of 80 children is hospitalized in acute alcohol intoxication state. Middle age of alcohol intoxication is 13.5. It is dominated by female and the most common place for drinking is out of house. Alcohol is purchased in the free markets and it is combinated by various alcoholic drinks, mostly on weekends and in summer months. Middle value of alcohol in blood is 2:02 ‰. The greatest value was 11.4 ‰ and the lowest value was 0.8 ‰ . In clinical picture dominates sleepines and ataxy. It is enough to keep body heat and infusion in the treatment.

The number of acutely intoxicated children in recent years is in a significant increase. From ESPAD study (European school survey project on alcohol and other drogs) Croatia was on the 13 position on the scale of 36 countries. The reason of drinking is a try to socializate, believing that after drinks they feel more relaxed and cheerful. Also an affirmation in society, a desire to be different from others and curiosity. Prevention measures imply properly oriented education, increasing the age limit of allowed public drinking, measures to prevent drinking in public places, reducing the availability of alcohol, limit permitted hours of sale, tax policy that will made high prices of alcohol less accessible, change societal attitudes about alcohol, positive role models (parents, celebrities), influence of the media on the negative public opinion about the consumation of alcohol (ban on advertising of beer (as well as "brandy" and wine)). We need to offer a better and more rational organization of leisure time and entertainment to children. Also appealing, attractive and useful content of socializing.

#### 17. PREVALENCE OF POSTPARTUM DEPRESSION IN INPATIENTS HOSPITALIZED OVER TWO YEAR PERIOD – IN CLINIC OF GYNECOLOGY AND OB-STETRICS IN PRISHTINA

#### Obertinca B., Ibishi N., Paqarada M. University Clinical Center of Kosovo, Prishtina, Kosovo

Mental diseases are one of the most common complications associated with pregnancies and childbirth. It was reported that postpartum depression (PPD) is one of the important public health problems affecting maternal and child health. Postpartum psychological disorders lead to maternal disability and disturbed mother-infant relationship. Postpartum depression is a serious disorder which has been estimated to affect 13-20% of women in industrialized nations. The objective of this study was to determine the prevalence of postpartum depression and socio demographic characteristics among women attending public health service in University Clinical Center of Kosova-Clinic of Gynecology and Obstetrics.

In this prospective cross-sectional study conducted at Clinic of Gynecology and Obstetrics in Prishtina, during January 2013-December 2014, participated 385 postpartum women. The participants were interviewed on days 2-3 after delivery and at 4 and 6-months after delivery. The women were screened for depression using the Edinburgh Postnatal Depression Scale (EPDS), and Adult Self Report/Adult Behavior Checklist( ASR/ABCL) for assessment of adaptive functioning scale, syndrome, DSM-IV oriented and substance use scale.

The mean age of woman included in the study was  $28.8 \pm 5.6$ , mostly living in rural area 53,95, and unemployed status in 82,6% of cases, 49% were multiparous, 41,7% had natural delivery, 15,1% unplanned pregnancy, 11,5% experienced stressful life events, being abused was rare reported in 0,8% of cases, and 15,9% of total sample reported for tobacco abuse during pregnancy. The prevalence rate of depression according (EPDS  $\geq 12$ ) criteria was 17,6% in the immediate postpartum week, and 5,45% at 4 months and 6 months after delivery. We didn't find significant difference between groups using t-test, regarding age and employment status, but our results find significant difference between groups regarding natural vs caesarean delivery. Natural delivery mothers reported to be more depressed.

Postpartum depression is common among Kosova women and can be detected early in the postpartum period, using simple screening methods. Health care workers at primary care should be educated about postpartum depression, and mental health interventions must be integrated into routine postpartum care to prevent adverse maternal and infant outcomes.

#### 18. TOBACCO USING AND IT'S ASSOCIATION WITH POST PARTUM DEPRESSION-IN INPA-TIENTS HOSPITALIZED OVER TWO YEAR PERIOD IN CLINIC OF GYNECOLOGY AND OBSTETRICS-PRISHTINA

#### Obertinca B., Ibishi N., Paqarada M. University Clinical Center of Kosovo, Prishtina, Kosovo

Postpartum depression (PPD) is a serious public health concern and this condition has become more common in routine obstetric care, while data are now more readily available to assist researchers in identifying patient characteristics that may be associated with increased risk of PPD. There is also a higher prevalence of cigarette consumption among depressive women than among those with no sign of depression. However, there are few studies available focused on investigating the prevalence of depressive symptoms among pregnant women and after delivery period. To evaluate the association between tobacco using and post postpartum depression in pregnant women and after delivery. The objective of this study was also to investigate the predictive role of tobacco using on postpartum depression.

Subjects of our study were women who gave birth between January 2013-December 2014, at Clinic of Gynecology and Obstetrics in Prishtina. 385 women, hospitalized inpatients prospectively fulfilled the selection criteria and completed self-reporting questionnaires on postnatal depression at 2-3 days, 4 month, and 6 months after childbirth, using the Edinburgh Postnatal Depression Scale (EPDS) and a Adult Self Report/Adult Behavior Checklist (ASR/ABCL).Inpatients characteristics included the method of delivery ( natural birth vs cesarean section), socio demographic data and smoking habits.

Showed that 385 subjects with mean age 28,8±5,6, years of education 11±2,8, mostly living in rural area 53,9%, and underwent caesarean section delivery in 58,3% of cases , 324 or 84,15% were non-smokers while 61 or 15,9% continued smoking during pregnancy and after delivery. Smoking habits were significantly associated with PPD, and analysis of t- test showed that tobacco using group of woman's compared to non users, showed significantly higher level of depressive symptoms in p<0,02 value. Women who smoked during pregnancy presented a 1.3 fold [R = .119, ( (1, 381) = 5.43, p = .02, OR = 0.14], higher probability of being depressed after delivery.

Our findings suggest a positive relationship between tobacco using and depressive symptoms after delivery women, and present predictive factor for PPD. This national public health concern and harmful behavior needs immediately prevention programs regarding the management and the providing evidence-based recommendations to health-care professionals and other related service providers, in our country.

## 19. COMT MODULATES WORKING MEMORY AND IMPULSIVITY CONTROL IN BIPOLAR DISORDER

## *Piccin S., Bonivento C., Fabbro D., Marinelli V., Bell University of Udine, Italy*

Cognitive deficits are commonly reported in bipolar disorders (BD), mainly involving the domains of attention, working memory and executive functions. However, the genetic basis of such impairments is still not fully elucidated. In this line, catechol-o-omethyltransferase (COMT) has been suggested to be involved. It contains the functional polymorphism Val108/158Met (rs4680) that results in two common variants of the enzyme (Val and Met). This polymorphism is responsible for modulating dopaminergic levels in the pre frontal cortex (Val being associated with higher activity). In the present study we investigated the role of COMT on cognition and control functions in BD with tasks assessing working memory and emotional inhibition.

The Brief Assessment of Cognition in Affective disorders (BAC-A) was administered to 42 BD patients (27 females, mean age = 44,26 years) and 99 healthy controls (HC) (66 females; mean age= 32,31 years). The single nucleotide polymorphisms COMT SNPs rs4680 were expressed and all the subjects were typified for the COMT variant as AA (Met/Met), GG (Val/Val) or AG (Val/Met). The statistical analyses were performed using the SPSS software. The raw scores obtained by the subjects at each subtest of the BAC-A were entered as dependent variables in Multivariate analysis of variance (MANOVA) with 'Group' (BD and HC) and 'COMT\_variant' (GG, AA, AG) as between subjects' fixed factors. The MANOVA does not need p value adjustment.

The analyses showed a significant main effect of 'Group' for almost all the tasks administered, with patients reporting the lower scores (all p<0.0001) In the Number Sequencing task, beside the main effect of 'Group' (p< 0.0001), a significant main effect of the COMT variant emerged (p=0.038), together with a significant interaction Group x COMT\_variant (p=0.048). As a whole, the BD group obtained lower scores than HC. However, post-hoc Bonferroni corrected ttests revealed that BD in the AA COMT\_variant subgroup performed at the same level as all the HC subgroups (p>0.05) while the BD in GG and AG subgroups did worse than both all HC and BD in AA group (all p <0.005). There were no differences between COMT\_variant subgroups within HC. Also, a main effect of 'Group' (all p< 0.0001) and a significant interaction between 'Group' and 'COMT\_variant' emerged in Emotional Inhibition with both neutral (p=0.038) and affective words (p=0.042). All the three BD subgroups (i.e. AA, GG and AG) performed worse than controls. Moreover the post-hoc t-tests (Bonferroni corrected) showed that BD patients in GG subgroup had significantly poorer performance than BD in the AA subgroup at the Emotional Inhibition task with both neutral (p=0.025) and affective (p=0.023) words. As for Number Sequencing there were no differences between HC COMT\_variant subgroups.

Compatibly with few previous investigations, the present study shows that only BD carriers of allele G from COMT SNPs rs4680 present deficits in working memory and impulsivity control, being potentially the targets for future innovative pharmacological medications. It would also be interesting to explore how personality traits or stress impact on such genetic modulation in BD.

#### 20. A RISK ASSESSMENT SCORE TO QUANTIFY AUTONOMIC CHANGES IN PATIENTS SUFFERING FROM SCHIZOPHRENIA

#### Refisch A., Bär K.J., Schulz S. Jena University Hospital, Germany

Cardiovascular mortality is significantly higher in patients suffering from schizophrenia. Several mechanisms leading to the increased risk are currently under discussion, including pro-arrhythmic effects of antipsychotic medication and lifestyle factors like obesity, smoking and poor access to health care services. Additionally an altered autonomic function, which is not present in healthy individuals, must be taken into consideration. The current study aims to establish a scoring system based on HRV measures from patients compared to age- and gender matched healthy controls to quantify autonomic changes with an assumed cardiac risk profile.

A high-resolution, short-term electrocardiogram (1000 Hz sampling) was recorded from 119 unmedicated patients with schizophrenia and 120 controls. The data records were analyzed for HRV indices from time- and frequency domain as well as from non-linear dynamics (symbolic dynamics, compression entropy, multiscale entropy, detrended fluctuation analysis, Poincaré-plot analysis). We developed a risk set by calculating the mean value (mean) and the corresponding standard deviation (mean±(x\*std)) with x<1, 2 and 3 for 13 highly significant HRV-indices from the healthy control group. Every schizophrenic patient was categorized in a risk subgroup according to its individual indices compared to the previously calculated values. In addition to the HRV indices clinical psychiatric scoring systems like SAPS, SANS and PANSS were determined as well as risk markers like BMI, smoking habits, education level, sport activity and coffee consumption.

Considering the composition of the risk groups, 85 % of schizophrenic patients show dramatic differences in their autonomic function compared to healthy individuals. According to this, only 15% of schizophrenic patients (no risk group) are comparable to healthy subjects regarding their autonomic function. Furthermore we were able to show that nearly 41% at medium and high risk are below the second standard deviation of control subjects. Comparing the three risk groups of schizophrenic patients to healthy subjects, highly significant differences became obvious in the medium and high risk group and only marginal significant in the low risk group. Comparing the risk subgroups with themselves revealed strong differences between the no risk group and any other. Only marginal differences were found by comparing the medium risk group with the high risk group. At least 41 % at medium and high risk group show profound autonomic abnormalities with an increased cardiac risk profile. They revealed strong pathological findings regarding HRV changes. This suggests that both groups are mainly responsible for the dramatic HRV changes in the entire schizophrenic group compared to healthy subjects. Concerning the clinical rating scales, a subdivision of schizophrenic patients in risk group regarding SANS, SAPS and PANSS did not show significant findings to HRV changes. As psychiatric symptoms are less correlated with HRV indices, this might be a further confirmation of an evident genetic background for the impaired heart rate regulation in schizophrenic patients.

#### 21. ALTERATIONS IN NEURAL REWARD PROCESSING IN EUTHYMIC PATIENTS WITH BIPOLAR DISORDER

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Bipolar disorder (BD) may be characterized by abnormalities in reward-processing neurocircuitry. Due to the emotional lability and dysregulation that characterizes the illness, studies suggested a reward hypersensitivity model that was supported by findings of increased activity in striatal and orbifrontal cortical regions (OFC). On the other hand recent findings that investigated antipsychotic and mood-stabilizer-naive Patients with BD II or BD not otherwise specified showed decreased striatal activity during reward anticipation. In the present study we examined reward activity in the ventral and dorsal striatum in participants with BD I and II disorders and healthy subjects. In addition we performed connectivity analyses to further explore associations among reward related brain regions.

20 euthymic patients with bipolar disorder and 20 matched healthy controls completed a monetary event-related fMRI paradigm as previously described to examine reward-related brain function to anticipation and receipt of monetary reward and loss. Data were collected using a 3T Siemens Trio Scanner.

Region-of-interest analyses revealed that BD participants

displayed decreased left ventral striatal (VS), but not dorsal striatal (DS), activity during anticipation, but not outcome, of monetary reward relative to healthy controls. Connectivity analyses showed increased negative functional interaction between VS and prefrontal cortical regions in BD patients compared to healthy controls.

This is the first study showing decreased ventral striatal activity in medicated BD patients and utilizing connectivity analyses approaching reward-processing circuitry in patients with BD. Our findings contrast with research reporting increased activation supporting a reward hypersensitivity model of BD, and add to the body of literature suggesting that blunted experiences of reward may be a vulnerability factor for mood disorders. Furthermore our findings suggest an inhibitory control of prefrontal cortical regions over the ventral striatum in patients with BD.

## 22. NEW FINDINGS ON ALCOHOL RELATED BRAIN DAMAGE

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Alcohol related brain damage (ARBD) is newer term for psychoneurological and cognitive disorders associated with alcohol abuse and addiction, that takes into consideration co-existing comorbid states. Formerly known disorders (Wernicke encephalopathy, Korsakoff psychosis, Hepatic encephalopathy, Delirium tremens etc.) have been undertreated and underdiagnosed due to overlapping symptoms and signs, research limitations, diagnosing inconsistencies and treatment recommendations. Most of our knowledge on the mentioned disorders derives from published case reports, clinical observations and post mortem pathohistological analyses. In the past twenty years, following the development of new imaging techniques, a better understanding, diagnosing of and research on ARBD is evident. Moreover, more specific operational criteria have been recommended for the diagnosis of Wernickes encephalopathy (Caine et al. 1997.). Studies on animal models have given us important insights into the specific patopshisiology of ARBDs.

We have conducted a mini review on PubMed, using the key term ARBD, then limited the search to the past five years (2010.-2015.) and finally sorted papers and reviews by relevance.

The key term ARBD retrieved a total of 676 articles. 21 of them were clinical trials, 418 related to studies on humans, 133 published within the past five years and 144 review articles. Further search limited to the past five years and review articles retrieved 29 articles.

Although ARBDs have been undertreated and underdiagnosed up until now, it is evident that they embody a very important clinical entity. A new set of criteria, MR imaging and prompt treatment, give patients with ARBD better prognoses and quality of life. Such an approach would significantly improve healthcare and social care cost-effectiveness. There are clear, important implications for further research, a need for an integrated approach to such groups of patients, public awareness and prevention campaigns.

#### 23. DEPRESSION IN PATIENTS ON DIALYSIS

#### Uglešić B., Lasić D., Vujnović Z., University Hospital Centre Split, Croatia

Depression is a common psychiatric problem in patients undergoing dialysis. Several studies have been performed to validate depression in haemodialysis patients. The objective of this study was to compare the incidence of depression in the patients on dialysis (on hemodialysis /HD/ and on continuous ambulatory peritoneal dialysis /CAPD/). Some inflamation parameters such as the levels of C-reactive protein (CRP) and interleukin-6 (IL-6) were assessed, due to numerous reports which connect depression with inflammatory status.

52 patients on HD and 36 on CAPD were enrolled in this study. Depressive symptoms were measured with the Beck Depression Inventory (BDI). The BDI is a 21-item self-report instrument, and the elevated symptoms of depression were defined as a BDI score ≥16. HD patients were treated with high-flux polysulphone biocompatible dialyzers and CAPD patients were treated with usual dwell time (4-6 hours during the day and 8-10 hours at night). Depression (BDI  $\ge$  16) was present in 28.4% of dialysis patients, 35% of patients on hemodialysis (HD) and 18.1% of patients on continous ambulatory peritoneal dialysis (CAPD). The BDI score was significantly lower in CAPD patients comparing to HD patients, as well as the levels of albumin, C-reactive protein (CRP) and interleukin-6 (IL-6). IL-6 serum levels were similar in patients with depression and patients without depression in the whole group, as in HD patients. In CAPD patients without depression IL-6 levels were significantly lower.

The prevalence of depression was higher in HD comparing to CAPD patients. Although IL-6 level was higher in HD compared to CAPD patients, the relationship between depression and presence of inflammation parametars were observed in CAPD, but not in HD patients.

## 24. AN EXTREME TARDIVE DYSTONIA DUE TO THE NEUROLEPTIC THERAPY

#### Vitorovič S., Velikonja I., Vučko Miklavčič I., Kores Plesničar B. University Psychiatric Clinic, Ljubljana, Slovenia

33-year old female patient was admitted to University Psychiatric Hospital due to the side effects of antipsychotic therapy where she was treated for three months. She had severe symptoms of tardive dystonia which presented a life-threating condition for the patient due to a severe tongue protrusion and inability to eat.

Diagnosed with a mild mental retardation in her childhood, the female patient was occasionally treated by a child psychiatrist. At the age of 22 she was hospitalised for the first time at the regional psychiatric hospital due to a psychotic decompensation. She was hospitalised three more times until the age of 32 when she was eventually admitted to the institutional unit because it was no longer possible for her to live with the family. The patient has been treated with antipsychotics for more than 10 years; upon her last admission to the psychiatric hospital she received depot therapy. She was hospitalised due to the side effects of the antipsychotic therapy which demonstrated as neurological symptoms including tremor, prolonged muscle contractions, choreatic movements and a severe tardive dystonia with extreme tongue protrusion. Initially the antipsychotic treatment side effects only had an impact on the patient's social life but eventually their intensity resulted in a life-threating condition for the patient: she wasn't able to eat and she had difficulties breathing. She was presented to a neurologist who suggested the therapy with tetrabenazine and botulinum toxin injections in tongue muscles.

As can be seen from the pictures enclosed, our patient had a very rare case of extreme tongue protrusion due to the neuroleptic therapy. The side effects intensified to the point when thy posed a life-threating condition for the patient. Extreme tongue protrusion can be a life- threating condition demanding an interdisciplinary approach.

### **POSTERS NEUROLOGY**

#### 25. THE COMT VAL158MET POLYMORPHISM MODULATES THE ASSOCIATION BETWEEN COGNITIVE PERFORMANCES AND WHITE MATTER MICROSTRUCTURE IN A SAMPLE OF SCHIZOPHRENIC PATIENTS

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Cognitive impairment is a core features of schizophrenia, and it is associated with functional outcome, occupational, interpersonal and problem-solving skills. Catechol-Omethyltransferase (COMT) Val158Met polymorphism could moderate cognitive performance in schizophrenic patients, with Val subjects showing poorer performances. Both COMT polymorphism and cognitive functions associated to white matter (WM) integrity. Here we investigated if COMT polymorphism could modulate the association between WM microstructure and cognitive functions.

We recruited 69 patients diagnosed with chronic schizophrenia. Diffusion Tensor Images (DTI) were acquired using a 3.0 Tesla MR scanner. Voxelwise DTI analyses were performed using Tract-Based Spatial Statistics using TFCE correction (p=0.05). Cognitive Functions have been assessed through the Brief Assessment of Cognition in Schizophrenia. Cognitive functions were correlated with DTI measures separately in Val/Val and Met carriers.

The distribution of genotype was in Hardy-Weinberg equilibrium (Val/Val = 21/69, Val/Met = 35/69, Met/Met = 13/69) (X2=0.055, p=0.81). Cognitive functions resulted associated with DTI measures in Val homozygotes, but not in Met-carriers. Cognitive performance showed positive relationships with Axial Diffusivity (AD), Mean Diffusivity (MD), and Radial Diffusivity (RD) and a negative association with Fractional Anisotropy (FA).WM tracts include corpus callosum, thalamic radiations, corona radiata, forceps major and minor, superior and inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, corticospinal tract and cingulum.

Performances in working memory, executive functions, and attention and speed of information processing were associated with WM microstructure in fiber tracts crucial to the functional integrity of the brain and affected by schizophrenia. Better cognitive functions seem to be associated with increased structural integrity and directionality of axons, including their intracellular microtubular structure (higher AD), and changes of myelination, possibly including remodeling of myelin sheaths and remyelination (increased RD and lower FA). Association of reduced FA with better cognitive performances is in agreement with the reported association of higher FA with schizophrenic psychopathology. Higher FA could be due to a number of pathological factors that may cause higher directionality such as increases in myelination, or microscopic deficits of axonal structures, or decreases in axonal diameter, packing density, and fiber branching. Brain catecholamines affect the biological process of myelination. Considering that the basal transcriptional activity of Met homozygotes is one-third less than Val ones, differences in cathecolaminergic signaling to oligodendrocytes could result in different behavior of these cells. These results show the importance of combined DTI and genetic analysis to better understand the neurobiological underpinnings of schizophrenic pathology.

#### 26. NEUROPATHIC AND CHRONIC PAIN OUTCOMES FOLLOWING CAESAREAN SECTION: A COMPARATIVE STUDY

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Research examining long-term outcomes five and more year in women after childbirth performed with different techniques of Caesarean section has been limited and don't provide information on long-term morbidity such a chronic and neuropathic pain

The study compare two group of patients operated with the "Traditional Method" where is used Pfannenstiel incision and patients operated with "Misgav-Ladach" method five and more year after the operation. They was randomized and allocated in two groups each of 50 patients. Widely utilized and validated questionnaires was used to screen for neuropathic pain conditions such as the Leeds assessment of neuropathic symptoms and signs (LANSS) and was paired with results from the clinical exam.

When chronic and neuropathic pain is detected the nerve cause of the chronic and neurophatic pain was the iliohypogastric in all the patients, only in one patients the nerve damaged was the ilioinguinal and iliohypogastric. In 16% of patients in the "Traditional Method" group suffer of neuropathic pain compare to patients in "Misgav-Ladach" group that suffer in 2 % of neuropathic pain. When we compare the results of chronic pain which comprises pain that persist more than 2 month we find also differences in the two groups of patients. In "Traditional Method" group 44% refer some element of chronic disturb that persist more than 2 month after CS, in "Misgav Ladach" group 12%. The VAS score also have also better results in "Misgav Ladach" group. There were more satisfied patients with the cosmetic apparence of the scar in "Misgav Ladach" group compare to "Traditional Method" group with statistically significant difference (p 0,009).

In our study we find better long term postoperative results five and more year after the Caesarean section in patients that was operated with "Misgav Ladach" compare to the "Traditional Method". The results was statistically better on intensity of pain, presence of neurophatic and chronic pain and level of satisfaction about the scar.

#### 27. CLOCK GENES ASSOCIATE WITH WHITE MATTER INTEGRITY IN DEPRESSED BIPOLAR PATIENTS: A TRACT-BASED SPATIAL STATISTICS STUDY

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Bipolar disorder (BD) is a progressive and disabling psychiatric condition associated with neurostructural changes and disruption of circadian rhythms. CLOCK and Period3 (PER3) genes are involved in the control system of circadian rhythms. A single nucleotide polymorphism in the 3' flanking region of CLOCK (3111 T/C; rs1801260) is known to influence occurrence of insomnia, response to treatment of sleep complaints, and lifetime recurrence rate of illness episodes in BD. A variable-number tandem-repeat polymorphism of PER3 (PER34/5) was found to influence age at onset in bipolar patients, and to influence cognitive performances in response to sleep loss in healthy subjects. A growing body of literature suggests that bipolar symptomatology is associated with dysfunctions in white matter (WM) integrity. Thus, we hypothesized that these two polymorphisms of the biological clock could be associated with WM microstructure in bipolar patients.

We studied 98 depressed bipolar patients. First we compared the DTI measures of C carriers and of T homozygotes for rs1801260. Then we analyzed differences in WM microstructure between the two homozygote groups for PER34 and PER35 alleles. We used whole brain tract-based spatial statistics with TFCE on the DTI measures: axial (AD), radial (RD), and mean diffusivity (MD), and fractional anisotropy (FA).

In regard to rs1801260, we found that, compared to T homozygotes, C carriers showed an increase of MD in several WM tracts, including superior and inferior longitudinal fasciculus, corpus callosum, uncinate fasciculus, medullary lamina of thalamus, and corona radiata. Additionally, PER34/4 showed reduced FA and increased RD compared to PER35/5 in thalamic radiations, inferior longitudinal and

fasciculus, and internal capsule. fronto-occipital MD measures the magnitude of water molecules diffusion and reflects the presence of boundaries to the free diffusion of water in each voxel, and correlate with membrane density and myelin integrity. Increased MD indicates myelin degeneration. RD represents the water diffusivity perpendicular to the axonal fibers, reflecting the integrity of myelin sheaths, while FA indicates the magnitude fraction of the diffusion tensor that is anisotropic, thus reflecting the structure of axonal cell membranes, myelin sheaths, and bundle coherence within the WM tracts. Our results highlight greater damages to myelin in rs1801260 C carriers, and in PER34/4. These findings suggest that CLOCK and PER3 genes could enhance the negative influence of BD on WM microstructure, with specific detriments resulting from effects on specific WM tracts contributing to the functional integrity of the brain and involving critical networks for bipolar symptomatology.

## 28. INTRACEREBRAL HEMORRHAGE AND ATRIAL FIBRILLATION

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Intracerebral hemorrhage causes 10-15 % of first ever strokes and is one of the major causes of stroke-related death and disability. Atrial fibrillation is a well-established risk factor for ischemic stroke. Antithrombotic therapy is effective for primary and secondary cardioembolic – ischemic stroke prevention. However, antithrombotic therapy represents also a risk factor for intracerebral hemorrhage. The aim of this study was to determine the outcome, the localization of intracerebral hemorrhage, and the prescribed therapy in patients with atrial fibrillation.

This retrospective study enrolled consecutive patients with non-valvular atrial fibrillation (AF) who were hospitalized for non-traumatic intracerebral hemorrhage (ICH) during the period from 1.1.2004 until 31.12.2013 at the Stroke and Intensive Care Unit, Department of Neurology, University Hospital "Sveti Duh" in Zagreb. Analysis of medical records included demographic data (age, gender), previous CHADS2 score, previously diagnosed atrial fibrillation, and previous ischemic stroke. In patients with prior anticoagulant therapy, data on the values of INR (within 24 hours of admission) were collected. The localization of the intracerebral hemorrhage (lobar versus non-lobar bleeding) was evaluated in accordance to the relevant neuroradiology findings (CT or MRI). Stroke severity was assessed on admission, according to the National Institutes of Health Stroke Scale. Stroke outcome was assessed with the modified Rankin scale at discharge from the hospital.

A total of 85 eligible patients were enrolled. The group receiving antithrombotic therapy (AT+) consisted of 49 patients: 14 patients had platelet antiaggregation therapy (acetylsalicid acid) and 35 patients were anticoagulated (warfarin). The group without antithrombotic therapy (AT-) included 36 patients. The AT- group had lower proportion of previously diagnosed atrial fibrillation (90% vs. 47%, p<0.001). The mortality rates in both groups were high (43% in AT+ group, 47% in AT- group), but there were no significant differences regarding mortality, outcome, and initial clinical presentation. There were no significant differences between groups regarding localization of intracerebral hemorrhage. Patients received antithrombotic therapy for ischemic stroke prevention more often in AT+ group (AT+ 60% vs. AT- 26%, p<0,005). Patients' mean INR in AT+ group was 2.61±1.51, but there were no significant differences between patients AT+ group regarding mortality, localization, outcome, and initial clinical presentation. Intracerebral hemorrhage and atrial fibrillation is relatively uncommon in routine clinical practice, but it might be challenging because of higher mortality rates and issues regarding the usage of antithrombotic treatment in ischemic stroke prevention.

#### 29. EFFECTIVE CONNECTIVITY ON NEURAL RESPONSE TO EMOTIONAL PROCESSING IN BIPOLAR DISORDERS IS INFLUENCED BY THE INTERACTION BETWEEN LITHIUM AND GSK—3ß

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Lithium is the mainstay for the treatment of bipolar disorder (BD) and inhibits glycogen synthase kinase3-b (GSK-3ß). GSK3-b polymorphism and lithium influence brain gray and white structure in psychiatric conditions and variants of GSK-3ß have been suggested as potential endophenotypes of BD. Consistent findings suggest the involvement of the frontolimbic network and emotional processing in BD, in particular the hyppocampus (HYP), in its anterior portion, which is related to emotions and affective processing and supported by anatomical bilateral connection with the amygdala(AMY). To our knowledge, no previous findings explored how lithium and GSK-3ß interact in affecting the connectivity between these limbic areas. Functional magnetic resonance images (fMRI) were acquired on a 3.0 Tesla scanner (Gyroscan Intera, Philips, Netherlands) using a 6 channels SENSE head coil. We used fMRI, Dynamic Causal Modeling (DCM), to study the effect of lithium and GSK-3ß on the response to emotional faces and effective connectivity in 28 BD patients. Four DCM models on the right hemisphere, exploring model

space between AMY-HYP were constructed. Bayesian Model Averaging provided DCM parameters, subsequently entered into statistical analyses as dependent variables with lithium and GSK-3ß as predictors, and age and BDI as nuisance covariates. Moreover, we compared BD with 34 healthy controls (HC), to investigate differences on DCM parameters.

Both DCM parameters were associated with clinical history of illness. A significant interaction between GSK-3ß and lithium was observed on both the endogenous connection HYP-AMY(F=4.94, p=0.034) and the modulatory effect (ME) on HYP-AMY (F=5.91, p=0.021). Whereas C-carriers taking lithium showed higher endogenous connection and lower ME compared to those not taking lithium, T/T subjects showed the opposite pattern. Moreover, the two groups differed only among subjects treated with lithium, in both endogenous connection (p=0.031) and ME (p=0.033) HYP-AMY. Furthermore, compared to BD, HC showed significantly higher endogenous connection on HYP-AMY(F=4.50, p=0.36) and a trend of a lower ME on HYP-AMY.

Our study reveals an interaction between lithium and GSK-3ß polymorphism on the effective connectivity on neural response to emotional processing in BD patients. In particular, the administration of lithium was associated with an increased endogenous connectivity HYP-AMY, and decreased ME on HYP-AMY in C carriers. This pattern is similar in HC, suggesting the positive effect of this drug treatment especially on C carriers. These results are consistent with previous findings, and with the hypothesized role of lithium on hyppocampal neurogenesis.

# **30. THE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) ON PAIN IN SPINAL CORD INJURED PATIENTS.**

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Spinal Cord Injury (SCI) causes several health related problems affecting not only the patient's physical state, but also all aspects of his live such as mood and health-related quality of life. Pain following SCI is notably difficult to manage and often refractory to treatment. Novel treatments targeting mechanisms associated with pain maladaptive plasticity, such as neural stimulation, may be desirable[1],[2],[3]. To date few small clinical trials have assessed the effects of invasive and non-invasive nervous system stimulation on pain after SCI [4],[5]. In our study we used transcranial direct current stimulation (tDCS) of the motor area (M1) on the scalp to evaluate its effects on the perception of pain in spinal cord injury patients and to determine the possible duration of pain reduction.

Double blind, randomised, single centre clinical trial. Analysis of data collected on 18 patients enrolled between August 2012 and May 2014 at the National Spinal Injury Centre, Stoke Mandeville Hospital, Aylesbury, UK, and randomly allocated to the active group or the sham group by mean of a standard randomization procedure. Table 2 summarizes the demographic and clinical characteristic at the baseline. The anodal electrode was placed over the M1 area of the dominant hemisphere, the reference electrode over the contralateral frontal area. Validated measures for pain and depression were administered during the baseline, intervention period and follow up until 1 month post stimulation. Statistical analysis was undertaken in SPSS; t-test for baseline measurements between groups and ANOVA for repeated measures and appropriate adjustments to F ratios using Huyn-Feldt corrections were used.

While there were no statistically significant differences between Sham and Active groups in self-reported VAS pain, a significant effect over time was seen, but non-significant time x treatment. There was a reduction in other pain and depression figures, particularly during the treatment phase, but comparisons between groups indicated that this could be a partial placebo type effect.

The real efficacy of tDCS for treatment of chronic pain has not yet been proved, and from the analysis of our data, we are yet not ready to prescribe it as a treatment for chronic pain in spinal cord injured patients.

#### **31. FATIGUE IN MULTIPLE SCLEROSIS PATIENTS**

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The aim of the study was to assess the relationship of fatigue in patients suffering from multiple sclerosis (MS) with respect to gender, age, duration of disease, level of incapacity and disease course.

The respondents were 60 patients older than 18 years of age with a confirmed multiple sclerosis diagnosis who in the period from 1 September to 31 December 2014 underwent inpatient rehabilitation in the Lipik Special Hospital for Medical Rehabilitation. The exclusion criteria were serious cognitive damage, a recent infectious illness, other acute complications in the previous 3 months or any chronic illness characterised by fatigue. The assessment of fatigue was done using the Modified Fatigue Impact Scale (MFIS) questionnaire. The MFIS is a structured, 21-item self-report questionnaire that provides an assessment of the impact of fatigue in terms of physical, cognitive, and psychosocial functioning. The total MFIS score is the sum of the scores for the 21 items, and can range from 0 - 84. Higher scores indicate a greater impact of fatigue on a patient's daily activities. The level of incapacity was determined for each patient based on a score obtained from the Expanded Disability Status Scale (EDSS), whereas an assessment of the cognitive status was performed using the Mini Mental Status.

The number of subjects totalled 60, of which 37 were women (61.7%) and 23 were men (38.3%). The average age was 49.5 years (29-71). The average time that had elapsed since patients were diagnosed with MS was 12.2 years (0.5-32 years). The average EDSS score was 4.9 (1.5-9). Of the total number of patients, 30 (50%) patients had experienced a relapsing-remitting course of the disease (RRMS), and 30 (50%) a secondary progressive course (SPMS). The average MFIS score for women was 49.5 (SD 12.85), and 47.9 (SD 16.04) for men. A positive correlation between the higher MFIS score and the time that had elapsed since MS being diagnosed (P=0.107) was found. There was no significant correlation in the MFIS score with respect to gender (P=0.682), age (P=0.083), level of incapacity (P=0.250) and disease course (P=0.716).

There is a positive correlation between the impact of the fatigue on daily activities and MS duration. None of the other analysed variables were predictive for the grater impact of the fatigue.

# 32. NEUROPATHIC PAIN IN PATIENTS WITH LUMBOISCHIALGIA

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The aim of this study was to determine the prevalence of neuropathic type of pain in patients with chronic lumboischialgia and determine their relation with respect to age, sex, duration and intensity of pain and depressive syndrome.

The respondents were patients from the neurological polyclinic at the Lipik Special Hospital, in the period from 20/12/2014 - 20/2/2015, with a duration of pain exceeding 3 months. The Pain DETECT questionnaire was used as the screening test for identifying the type of pain, and the Patient Health Questionnaire-2 was used as a test to screen for a depressive syndrome. The intensity of pain during the past month was measured using the visual analogue scale (VAS). Exclusion criteria were the presence of a neuropathic pain caused by other factors and more serious cognitive damage.

In all, there were 62 respondents. Neuropathic pain was experienced by 19 (30.6%), nociceptive by 22 (35.5%), and a undetermined type of pain by 21 (33.9%) of the respon-

dents. The results were compared with the group of patients with neuropathic and the group with nociceptive pain. The neuropathic group comprised 7 (36.8%) women and 12 (63.2%) men, with an average age of 53.37 years (38-78), an average duration of pain 13.6 years (SD 10. 587), and an average pain intensity on VAS of 7.11 (SD 1.487). The screening for depression resulted in 11 (57.9%) of respondents being positive. The nociceptive group comprised 12 (54.5%) women and 10 (45.5%) men, with an average age of 52.05 years (35-67), an average duration of pain 11.3 years (SD 10.759), and an average intensity of pain on the VAS of 4.64 (SD 2.013). The screening for depression resulted in 5 (22.7%) respondents being positive. The group of patients with neuropathic pain had significantly higher intensity of pain (t = 4.41, p < 0.001) and had a significantly more frequent positive screening test for depression (2 =5.299, p < 0.05) compared to the group with nociceptive pain. Between the groups there was no difference in age (t = 0.44, p > 0.05), duration of pain (t = 0.668, p > 0.05), and gender distribution (t = 1.134, p > 0.05).

Among the respondents, 30.6% had a predominantly neuropathic type of pain. In comparison to subjects with a predominantly nociceptive pain, they had a significantly higher intensity of pain and more frequent symptoms of depression.

## 33. THE QUALITY OF LIFE IN PATIENTS WITH DIABETIC POLYNEUROPATHY

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The quality of life (QOL) is a good indicator of international development and successful healthcare. Diabetes mellitus has high prevalence and ascending trends in the number of patients, especially in younger patients. Diabetic patients with longer duration of the illness have an elevated comorbidity, which significantly affects QOL. The aim of this study was to determine QOL in diabetic patients with painful diabetic polyneuropathy (DPN) compared to group of diabetic patients with DPN but without painful manifestation

160 diabetic patients in Clinical Hospital Merkur University Clinic Vuk Vrhovac Zagreb, were included in the study and were divided in two cohorts, depending on the presence or absence of neuropathic pain. DPN was diagnosed accorsding to European Federation of Neurology Societies (EFNS). Pain was assessed by Visual analogue scale (VAS) and Leeds Assessment of Neuropathic Sympoms and Signs (LANSS). QOL was assessed by SF-36 (Short Form Health Survey) questionnaire. Patients underwent detailed medical history, laboratory, somatic and neurological status, colordoppler flow imaging (CDFI) of leg arteries and electromyoneurography (EMNG) of upper and lower extremities. Diabetic patients with painful DPN had significally lower values in all 8 dimensions and both summary values of th SF-36 scale than diabetic patients without pain. Diabetic patients without neuropathic pain had higher average values of QOL compared to general population of Croatia in 4 of 8 dimensions- vitality (VT), social functioning (SF), roleemotional (RE) and mental health (MH), which was unexpected result.

Painful DPN is a major factor that influences various aspects of QOL in diabetic patients, which indicates the need for faster and better diagnostics and treatment of neuropathic pain.

#### 34. THE PARIETAL LOBE IN BIPOLAR DISORDER: A CROSS-SECTIONAL AND LONGITUDINAL STUDY USING STRUCTURAL MRI

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The parietal lobe (PL) is crucial in supporting specific cognitive-emotional domains (attention, emotion regulation, planning and motor control) that are impaired in bipolar disorder (BD). However, few studies have investigated the PL in the BD, finding some volumetric abnormalities [1]. The present study aimed: 1) to assess volume differences in PL white matter (WM) and grey matter (GM) in patients with BD and healthy subjects (cross-sectional study); 2) to investigate volume changes over time (longitudinal study); 3) to explore the possible relationship between the PL and the global functioning, as measured by the Global Assessment of Functioning (GAF).

Thirty-eight right-handed patients with BD and 42 righthanded healthy volunteers, comparable for race, gender, age, and years of study underwent a magnetic resonance imaging (MRI) at 1.5T. In addition, 17 patients and 16 controls underwent a second MRI (inter-scan interval= $2.74 \pm 1.31$ years). The PL was manually traced in the sagittal plane with the software Brains2 and PL WM and GM volumes were calculated.

The cross sectional comparison at baseline showed a significant group effect on the bilateral PL WM and GM (all p <0.05), with patients showing reduced PL compared to controls. Moreover, only in controls, but not in patients, the asymmetry index of PL WM was significant different, with the left region larger than the right (p <0.05). In the longitudinal study, we have observed a significant effects of group

and time on the WM (all p <0.05), but not the interaction timeXgroup (p> 0.05). Finally, we have found a positive correlation between the GAF scores and the WM volumes in patients with BD (p <0.001).

The results of this study suggest a potential involvement of the PL in the pathophysiology of the BD, with particular interest in the WM. In particular, it is highlighted a significant reduction in the parietal WM and GM in patients with BD, in line with recent studies showing an overall reduction [2]. Moreover, the asymmetry of the PL WM suggests the possibility that changes in the parietal connectivity between the two hemispheres might interfere with the process of lateralization of hemispheric dominance in the BD [3]. Finally, a reduced volume of the parietal WM may be associated with a lower global functioning in bipolar disease, in agreement with other studies in the literature [4]. 1] Frazier et al. (2005). Bipolar Disorder, 7, 555-569. 2] De Peri et al. (2012). Current Pharmaceutical Design, 18(4):486-94. 3] Crow et al. (1997). International Review of Psychiatry, 19(4):449-57. 4] Forcada et al. (2011). Journal of Affective Disorder, 130(3):413-20.

#### 35. LATE-ONSET CASE OF RASMUSSEN ENCEPHALITIS – A CASE REPORT

#### Friedrich L., Sicaja G., Sruk A., Budincevic H., Bielen I. Sveti Duh University Hospital, Zagreb, Croatia

Rasmussen's encephalitis is a rare inflammatory disease which usually occurs in children. We report a case of a probable late-onset Rasmussen's encephalitis.

A 57-year-old male with a 4 day history of confusion and walking instability was hospitalized at our department. His medical history included only weight loss and inappetence with episodes of forgetfulness in the former 5 months. His neurological examination revealed a horizontal gaze evoked nystagmus, slight confusion, and inability to perform tandem gait. EEG showed focal changes with epileptiform potentials in the left parieto-occipital area, where a small hyperintensity was found on FLAIR MRI. He soon developed focal motor seizures of his right side of face and body which occasionally progressed to status epilepticus, so valproate therapy was introduced. Extensive workup (metabolic, endocrinologic, infectious...) could not find a plausible cause of the symptoms. Three weeks later he developed a right hemiplegia with partial motor status epilepticus. MRI showed progression of the FLAIR hyperintensities in the left hemisphere. He had continuous cognitive deterioration in the following 4-5 months up to a point where he could no longer hold a simple conversation. His condition then remained relatively stable, and he skipped his neurologist appointments. MRI performed 40 months after the initial

presentation showed a severe atrophy of the whole left cerebral hemisphere.

Although a brain biopsy was not performed due to technical reasons, we believe this to be a case of late-onset Rasmussen's encephalitis. This diagnosis should be considered in patients of any age.

#### **36. PNES IN PATIENTS WITH EPILEPTIC SEIZURES**

#### Gashoska M., Atanasovski P., Miftari V. PHO University clinic of neurology, Skopje, Macedonia

This is a short presentation dedicated to the topic of: Psychogenic non-epileptic seizures (PNES) vs epileptic attacks Essentially we would start with is the glaring frequency of PNES. Epidemiologically: Between 20-30% of incorrectly treated epileptic attacks are actually PNES. PNES are almost as frequent as MS and trigeminal neurology. In order to make the topic even more intriguing, we discuss dilemmas: \* Can among patients with confirmed epilepsy also occurs PNES as comorbidity situation? \* What is the reason for the occurrence of psychogenic attacks of epileptic patients? \* Finally, how to cure PNES of epileptic patients?

In order to put more insight, we analysed 100 patients hospitalized during a six-month period (01 May - 21 November 2014) at the Department of Epilepsy-University Clinic of Neurology-Skopje. The analysis comprised: detailed history, EEG (standard, sleep-deprived and prolonged video EEG monitoring) and neuropsychological tests, in order to make reliable distinction between PNES and actual attacks. Out of all 100 hospitalized patients: 75 patients diagnosed with epilepsy, 8 patients only had psychogenic seizures, 3 patients with syncope, 7 patients had epileptic seizures and psychogenic seizures, 1 patient with other convulsive disorder, 6 patients with other neurological diseases. As stated in the text above, 7 out of 100 hospitalized patients, after certain period of having epilepsy were also diagnosed with PNES. Our small research also showed that: six out of the seven patients with epilepsy and PNES are women, and only one such patient is man. The age of these patients with epilepsy and PNES is between 21 and 55 years. Also for all 7 patients their primary disease epilepsy was pharmacoresistent and afterwards PNES occurred. For all 7 patients the epilepsy was diagnosed more than 15 years ago. Two of the 7 patients have GTKN, whereas five patients have complex partial epileptic seizures with occasional generalization. During neuropsychological testing of all 7 patients it was noticed chronic depressive sympthomatology with inclination towards psychogenic upgrading of already existing symptoms. All 7 patients with diagnosed epilepsy and PNES developed afterwards are in depraved socio-economic situation - unemployed. The most frequent cause for the occurrence

of psychogenic seizures among our patients with epilepsy is: specific traumatic event (often within the close family), unfavorable socio-economic situation (unemployment mainly). Other causes are: depression as a result of epilepsy and denial of the state, discrimination of these patients from the surrounding.

PNES also occurs among patients with epilepsy (as comorbid situation), it is difficult to detect and therefore they are not always treated. Most often, doctors first treat the more serious disease (therefore many psychogenic seizures are misdiagnosed and mistreated as epileptic). \* Most often the cause for the occurrence of psychogenic seizures among epileptic patients is specific traumatic event (physical, sexual abuse, divorce, death of close relative, huge changes in life, socio-economic status). \* PNES seizures may resemble epileptic seizures (of course they are not triggered by abnormal brain electric activity). Most often, the biggest differentially diagnostic problem being GTK attacks, absence seizures and complex partial attacks. \* It is noticed that the chronic pain can also be a cause for psychogenic non-epileptic seizures. \* Treatment. With respect to the treatment of PNES, a psychiatrist must be involved in order to treat the coexisting depression and anxiety. In the case of PNES as coexisting disease among epileptic patients, the multidisciplinary approach in the treatment is definitely useful (psychiatrist and neurologist). The treatment is with medication or psychotherapy, both are with success. We treat our patients, depending on the medical file, weight, comorbidity and their financial power, SSRI inhibitors, antipsychotics and tranquilizers.

#### 37. MANAGEMENT OF PATIENT WITH RIGHT COMMON CAROTID ARTERY OCCLUSION AND LEFT INTERNAL CAROTID ARTERY STENOSIS: CASE REPORT

#### Govori V., Hundozi Z., Shala A. University Clinical Center of Kosovo, Prishtina, Kosovo

Common carotid artery (CCA) occlusion is a rare cause of cerebrovascular events. The prevalence is approximately 0.24–5% in stroke patients. CCA occlusion is generally associated with occlusion of the distal vessels (internal carotid artery (ICAs) and external carotid artery (ECA)). Carotid artery stenos is increasingly prevalent from the fifth decade of life onward We report the clinical case of a patient with vascular disease and multiple risk factors (HTA, hyperlipidemia, smoking), family history of atherosclerosis and coronary artery disease.

This case involved a 57- year old male patient, hypertensive, with history of ischemic stroke 3 years ago with left upper limb paresis and amaurosis fug ax. He was admitted in Neurology Department. Brain CT, Brain MRI showed ischemic stroke in parietal temporal region, hypo density focal lesion in right cerebellar hemisphere. Duplex scan showed ICA occlusion in his origin, and stenos is 36% of left Internal Carotid Artery . Infra nuclear left facial palsy (two years ago), Neo larynx (operated eleven years ago), extirpation a glandular formation at left neck region (ten years ago), treated with radiotherapy. In the two last years, this patient showed headache and loss of vision with left eye. The patient was submitted to a new duplex scan of the carotid arteries, which showed stenos is greater than 55% in left ICA. Neurological examination: amaurosis with left eye, infra nuclear left facial palsy, and partial bulbar palsy; muscles atrophy on left neck region; but the upper and lower extremities, gait and consciousness are in good condition, physically active. Physical examination and routine blood test were unremarkable. In addition, cardiac and abdominal sonology revealing no specific pathology. Eye examination, loss of vision with left eye.Brain MRI and angio showed vascular chronic lesion, Echo-Color Doppler ultrasonography showed Right Common Carotid Artery occlusion and left internal Carotid artery stenos is greater than 55% This case shows the possibility of connectivity for Common Carotid Artery occlusion after operating Neo larynx and radiotherapy, and support the idea that Internal Carotid Artery stenos is and/or occlusion not due a significant neurological motor deficiency. Echo-color Doppler ultrasonography is the screening method of choice, noninvasive and low-cost. Carotid angiography still represents the gold standard, however, less invasive techniques as MR angiography and Angio CT are becoming increasingly common.

#### 38. CAROTID PLAQUE ECHOGENICITY IN PRE-DICTING SYMPTOMS: A SYSTEMATIC REVIEW AND META-ANALYSIS

#### Jashari F., Ibrahimi P., Henein M.

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Carotid artery atherosclerosis is an important cause of ischemic stroke. Several studies have already shown that hypoechoic carotid plaques on ultrasound (US) are more frequently associated with cerebrovascular symptoms than hyperechoic ones. In this meta-analysis we aimed to determine the role of carotid plaque echogenicity in predicting cerebrovascular symptoms.

Studies with US-based characterization of carotid artery plaque echogenicity and its association with ipsilateral symptoms (Stroke, TIA, amaurosis fugax) were eligible. We systematically searched electronic databases (PubMed, ME-DLINE, EMBASE and Cochrane Center Register) up to January 2015, for studies evaluating the effect of statins on carotid plaque echogenicity. The search terms used were: "carotid atherosclerosis", "carotid plaque", "ultrasound" "symptoms", "Stroke", "TIA" and "amaurosis fugax", in various combinations. In the meta-analysis we have included all studies reporting a risk ratio (RR) or hazard (HR) or presenting data amenable to RR and HR calculation. Heterogeneity was measured using I2 statistics. Publication bias was examined with the Begg–Mazumdar test.

13 out of 385 identified studies met the inclusion criteria to be included in the meta-analysis. A consistent increase risk of symptoms in patients with echolucent carotid plaque was found. Pooled weighted RR for symptoms associated with plaque echolucency was 2.04 (95% CI, 1.67 to 2.49), p<0.001, I square=82.1%. Pooled weighted HR for symptoms associated with plaque echolucency was 4.75 (95% CI, 1.54-14.62), p<0.001, I=68%.

Texture analysis of carotid plaques by ultrasound can identify patients at higher risk of cerebrovascular events in symptomatic and asymptomatic events. This association was confirmed even after adjusting for the degree of stenosis.

#### **39. CEREBRAL MATTER ATTACKED BY EPILEPTIC ATTACKS SECONDARY TO CEREBRAL VASCULAR ACCIDENTS CASES**

#### Jashari R., Jashari F., Koliqi-Lila R. Medical Schol in Prishtina, Kosovo

Attack of cerebral parenchyma presents a particular problem among patients with Cerebral Vascular Accidents and this might cause secondary epilepsy. To pinpoint location of attacked cerebral parenchyma, as well as nature of Cerebral Vasculat Accidents in cases with epilepsy.

The source of data was patients hospitalized in the Clinic for Neurology during the five year period, from January 2006 until December 2010. The conducted study was retrospective.

Results: Total number of Cerebral Vascular Accidents cases accompanied with epilepsy was 187. In 87 cases the cerebral cortex was involved, in 56 cases the lenticular capsule was involved, in 35 cases was thalamus involved, and in 9 cases the silent areas were involved. These data correspond with data from literature.

Among the large number of patients with CVA, responsible area for epileptic attacks is cortex, also white subcortical matter is involved, or often both regions might be involved in attacks. Capsular of strio-capsular region present deep lesions and rarely yield epileptic crises. These zones may have direct or indirect impact on insular cortex. The age of onset of illness is typically among the aged individuals. Diagnose is ascertained based on clinical and neuroimaging (EEG, CT, MRI) investigations.

#### 40. CORTICAL AND SUBCORTICAL LESIONS ARE MOST FREQUENTLY ASSOCIATED WITH EPILEPSY AFTER STROKE

#### Jashari R., Jashari F., Koliqi-Lila R.

Medical Schol in Prishtina, Clinic for Neurology in Prishtina, Kosovo

Background and Aim: Ischemic stroke is the most common cause of seizures among elderly. However, only few patients with seizures early after stroke will have epilepsy in the future. The aim of this study is to determine the association between ischemic brain lesions and their location with the incidence of epileptic seizures after stroke.

Material and methods: In this study we have retrospectively analyzed hospitalized patients in the Clinic for Neurology during the five-year period, from January 2006 until December 2010. The conducted study was retrospective. Diagnose is ascertained based on clinical and neuroimaging (EEG, CT, MRI) investigations.

Results: Epileptic seizures were more frequent among elder (>65 years old) patients. Total number of stroke accompanied with epilepsy was 187. In 87 cases In 87 cases the cerebral cortex was affected, in 56 cases the lenticular capsule, in 35 cases thalamus, and in 9 cases the silent areas were affected by ischemic or hemorrhagic lesions. These data correspond with those reported previously on the literature. Conclusion: Among the large number of patients with stroke, responsible area for epileptic attacks is cortex, also white subcortical matter is involved, or often both regions might be involved in patients with epileptic seizures. Lesions located in the deep regions of the brain including strio-capsular regions are rarely associated with epilepsy. These zones may have direct or indirect impact on insular cortex.

#### 41. TYPES OF EPILEPTIC ATTACKS TRIGGERED BY CEREBRAL VASCULAR ACCIDENTS

### Jashari R., Rakacolli M., Lila G.

Medical Schol in Prishtina, Kosovo

In the clinical practice, vascular epilepsies among VCA in most of cases have partial pattern. Also, depending on the attacked area and cerebral matter, cerebrovascular accidents have generalized pattern and may be followed up also by epileptic status. Cerebral Vascular Accidens is seldom associated by epileptic status, also generalized crises are lesser presented in comparison to partial crisis. Purpose: of this paper is to analyze cases of partial and generalized attacks, epileptic status in Cerebral Vascular Accidens as well as pathology of Cerebral Vascular Accidens followed by epilepsy. Source of information were patients hospitalized in the Clinic for Neurology during the five year period, from January 2006 to December 2010. The conducted study is retrospective. Results: From the total number of 187 patients diagnosed with ischemic Cerebral Vascular Accidens, 110 cases were with partial attacks, 71 cases with generalized attacks, and 6 cases with epileptic status.

If epileptogenic source is in the cortex of large brain, localization of epileptogenic focus will determine type of epileptic attack. If discharge is localized in the brain cortex, consciousness will be preserved same as in the case of focal attacks triggered by VCA. If attack involves subcortex, subsequent generalized attacks shall follow up with loss of consciousness, same as in the case of extensive VCA which can trigger epileptic status. Epilepsy secondary to CVA poses a particular problem for society, because along with care that require a large number of patients due to lifelong handicapping, among significant number of patients special attentions shall be paid to patients with epilepsies that are secondary to cerebrovascular insults. The age of onset of illness is typically among the aged individuals.

#### 42. MELKERSSON -ROSENTHAL SYNDROME

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This syndrome is characterized by chronic swelling of the lips and face, peripheral facial paresis which can be bilateral and recurrent, and same case with lingual plicata. Beginning is usually in childhood or young age with a heart of peripheral facial paralysis. The cause of MRS is unknown, and many believe that there is a genetic predisposition. It can be symptomatic for Chroh'n disease or sarcoidosis(1,2,3). Treatment is symptomatic and, with nonsteroidal anti-inflammatory drugs, corticosteroids for reduce swelling, antibiotics and immunosuppressants. Surgery may be recommended to relieve pressure on the facial nerves and to reduce swollen tissue. (4, 5).

B.A. 13-year old girl presented with complaints of right facial paralysis, lips edema and difficulty of speech. A month ago she was treated for the peripheral facial paralysis of the left side. On November 2012 peripheral facial paralysis of the right side and she was treated with symptomatic therapy and she had complete rehabilitation. On January of 2013, again she had peripheral facial paralysis of the right side. Physical examination: Swollen lip, soft, elastic, lip mycosis slightly red rough tongue (fig.1, 2). Placated tongue (Figure1,2). Neurological examination: peripheral facial paralysis of the left side. The biochemistry was in normal value. Nose and throat swab; no pathology found.CRP-18mg/l No IgG and IgM antibodies against Bordetella Pertussis, Rubella, HSV2, Toxoplasma gondi, Borrelia Burgdorferi were found. In the examined sample there are present specific antibodies of IgG class against Cytomegalovirus.Brain MRI: No pathology found. Abdominal ultrasound: no pathology found.

The axonal lesion of the left facial nerve in electrophysiological finding was found. Patient was treated with oral prednison tablets 1mg/kg of the body weight, H2 receptor blockers, antibiotics and vitamins and physical therapy. Melkersson -Rosenthal s' syndrome is characterized with three major symptoms; lip edema ,facial paralysis and placated tongue. The cases found in literature describe much more often the symptomatic forms of MRS. In our patient we found the classic form of the MRS, with the symptoms; lip edema, facial paralysis and plicated tongue(3,5). After the anti-inflammatory therapy, prednisone tablets 1mg/kg of the body weight, H2 receptor blockers, antibiotics, the inflammation of the lips improved significantly and esthetically. MRS is occasionally a manifestation of Crohn disease [5, 6] or sarcoidosis. Follow-up care is indicated particularly to exclude the development of Crohn disease or sarcoidosis in patients.

#### 43. IDENTITY IN LIGHT OF INTEGRATIVE THE-RAPY AS A DISPOSITION FOR THE CONSTRUC-TION OF NEW NEURAL PATHWAYS

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The aim of the poster is to present Integrative Therapy as Heraklitus' model, which represents 'Pantha rhei' in the sense of the idea of constant changes and permanent development of life, knowledge, and human society as well as an individual. Integrative therapy is an 'expanded bio-psychosocial model', which conceptualizes the human as a 'bodily subject' (body-soul-mind) in a social and ecological environment as well as in the temporary continuum (the past, present, future). IT (Integrative Therapy) is a modern approach of holistic and differential psychotherapy or 'humane therapy', belonging to new 'integrative paradigm' in psychotherapy (Petzold, 1992). It is oriented towards empirical research psychotherapy and clinical psychology, neurobiology and modern science theory (Petzold, 2003). IT was designed by prof. dr. multi Hilarion Petzold in the 1960s. IT is not designed as the final model, but it is rather changing according to new findings. It emerged out of various disciplines; practical procedure, based on the elements of active psychoanalysis (Ferenczi), Gestalt therapy, (Perls), psychodrama (Moreno), therapeutic theatre (Ilijne), as well as physical and movement therapy (Petzold) and behavioural modification (Kanfer). It is designed as a theoretical framework for a systematic integration of different methods, which is represented in the Three of Science, 1993. The goal of IT is to trigger healing processes in psychological, psychosomatic and psychosocial disorders and illnesses, to minimize mental suffering, as well as to encourage the development of potentials, social engagement and ecological awareness of individuals. The basic integrative rule is that a human becomes a human only in relation to other humans, through mutual social empathy. IT understands disease and health as a 'quality of human life processes'. This determination emphasizes that health is not an unchangeable state, but rather a development, created by means of cooperation with others (Cvetko, after Petzold 2011). We think and work with clients from the point of view of pathogenesis (together we investigate incriminating factors, critical life situations, pathogenic simulations, conflicts, disturbances, traumas). We give as much importance to salutogenesis by means of mutual discovery of our resources, protective factors, resistance, goals, coping strategies and individual creative styles. The process is designed through all life space development in the context and continuum. IT names 5 columns of identity: body, soul, spirit; social network; economic status, work and achievements; life philosophy and values. Knowing the whole picture enables us to work on the will.

IT methods originate in the holistic perception and treatment of the human. The concepts are as follows: correspondence, inter-subjectivity, embodiment, identity, system, context/continuum, shape/background, multiple prospects, socio-economic perception, cognitive, emotional and social learning, and creativity. Ex.: In different areas of action, IT employs different instruments. For the body, bodily therapy comes first, that is: dance therapy, breathing therapy, time practice and dietetics. The goal is balance, health and sensibility. For the soul, the area of action is psychotherapy, namely: active analysis, narrative, Gestalt therapy, psychodrama, intermedial art therapy. The goal is to acquire self-regulation, self-realization, spontaneity, empathy and emotional flexibility. For the spirit, there is neotherapy; meditative paths for finding meaning, understanding and absorption, dialogues of meaningfulness, creative media. For the social context, there exists socio-therapy; it is a therapeutic social network, family therapy, self-help groups. The goal is to acquire bearable social networks and reduction of alienation. IT encourages the involvement into volunteering organizations by means of volunteering work. In the ecological context, eco-therapy is a permanent learning for our lives and interventions at the micro, mezzo and macro levels (communities). Gardening is very popular. The goal is to preserve and create a healthy living environment. Results: As a multi-perspective therapy, IT is very useful at numerous levels of work, not only at the psychological one, but also at the sociological and ecological ones. It is not so classic, just an ordinary setting. This is the reason why it gets closer to clients in an easier way, especially when learning correspondence.

As a multi-perspective therapy, IT is very useful at numerous levels of work, not only at the psychological one, but also at the sociological and ecological ones. It is not so classic, just an ordinary setting. This is the reason why it gets closer to clients in an easier way, especially when learning correspondence.

I am personally familiar also with techniques of bilateral brain stimulation (EMDR for trauma healing) and Brain Gym exercises for an easier and faster learning. Those methods clearly demonstrate how new neural pathways are formed. I believe that, in the time of more and more stress, cancerous illnesses, brain and heart strokes, it is important to be well informed about the wider context for a good reintegration and establishment of new neural pathways.

#### 44. RESTLESS LEGS SYNDROME AND PERIODIC LIMB MOVEMENTS IN ACUTE STROKE PATIENTS WITH SLEEP APNEA

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The aim of this study was to analyze frequency of restless legs syndrome (RLS) and periodic limb movements (PLM) in acute stroke patients with sleep apnea.

It was analyzed 110 acute stroke patients with sleep apnea, treated at Department of Neurology, University Clinical Center Tuzla in the period December, 2009 - May, 2010. Acute stroke has been verified either by computerized tomography or magnetic resonance imaging of the brain. RLS and PLM were evaluated by questionnaire (International RLS Study Group Criteria) as well as information's taken by patients or family members. Average age was  $65.13 \pm 9.27$  years. Majority of patients were men (65/59%). The control group included the same number of acute stroke patients without sleep apnea. Average age was  $64 \pm 8.69$  years and sex ratio was the same as well. Statistical data was analyzed by Arcus Quickstat Biomedical statistical program with p<0.05 considered significant.

RLS has been verified in 18 (16.6 %) patients with apnea (10/22.2% women and 8/12.3% men), and in the control group in 12 (10.9%)(7/15.5% women and 5/7.7% men). PLM had 43 (40%) patients (25/38.5% men and 18/40% women) with apnea. PLM without apnea had 19 (17.3%) patients (12/18.5% men and 7/15.6 women). There is no significant differences in RLS in patients with or without sleep apnea, neither in men (X<sup>2</sup>=0.34, p=0.56) nor women (X<sup>2</sup>=0.29, p=0.59). Otherwise, there is significant difference in PLM in patients with sleep apnea both in men (X<sup>2</sup>=5.44, p=0.02) and women (X<sup>2</sup>=5.54, p=0.02).

Restless legs syndrome is presented in 16.6% acute stroke patients with and in 10.9% without sleep apnea (p>0.05). Periodic limb movements are significantly more frequent in

patients with (49%) then in patients without apnea (17.3%)(p<0.05).

### 45. INTIMA-MEDIA CAROTID MEASUREMENTS IN PATIENTS WITH BILATERAL DISEASE

Lila G., Koliqi R., Jashari F. University Clinical Centre of Kosovo, Prishtina, Kosovo

In patients with carotid atherosclerosis the future risk of stroke is mainly related to the degree of stenosis. Patients with bilateral carotid disease are at higher risk of stroke in the future. The aim of this study was to assess the relationship between common carotid artery (CCA) ultrasound markers of atherosclerosis and bilateral carotid disease. We analyzed 150 carotid arteries in 90 patients with known carotid disease (mean age 70±7 year, 39% females). Intima media thickness (IMT) and its grey scale median (IM-GSM) were measured at the CCA. Plaque textural features including grey scale median (GSM), juxtaluminal black area without a visible cap, and plaque coarseness, at bifurcation and ICA were also determined. CCA measurements and plaque measures were compared between patients with unilateral and bilateral disease.

Compared to patients with unilateral stenosis, those with bilateral stenosis had higher c-IMT ( $1.06\pm0.27$  vs.  $0.93\pm0.25$ , p=0.006) and lower IM-GSM ( $24\pm16.6$  vs.  $34\pm15.6$ , p<0.001). They also had more signs of vulnerable plaque features at the bifurcation and ICA segments, with lower GSM ( $31.2\pm21$  vs.  $37\pm15$ , p=0.016), lower median GSM of the JBA (4.1 vs.10.8, p=0.006), and higher JBA (3.9 vs. 1.6, p=0.005).

Patients with bilateral disease have more vulnerable features measured at carotid artery wall as well as more vulnerable features measured distally in the plaques located in bifurcation and ICA.

#### 46. WHITE MATTER MICROSTRUCTURE PREDICTS RESPONSE TO CHRONOTHERAPEUTIC TREATMENT IN BIPOLAR DEPRESSION

#### Mazza E., Bollettini I., Poletti S., Locatelli C., Benedetti F. Scientific Institute and University Vita-Salute San Raffaele, Milano, Italy

Changes of white matter (WM) microstructure have been proposed as structural biomarkers of bipolar disorder (BD). Chronotherapeutic treatments prompt a rapid and stable antidepressant response in bipolar depression by combining repeated total sleep deprivation and light therapy. The aim of the study is to investigate if baseline Diffusion Tensor Images (DTI) measures of WM integrity can predict response to chronotherapeutic treatment in a sample of depressed bipolar patients.

58 patients affected by a major depressive episode without psychotic features, with a diagnosis of BD were administered chronotherapeutic treatment. Patients were considered as responders to treatment if a 50% reduction of Hamilton Depression Rating Scale (HDRS) score was observed. Voxelwise DTI analyses were performed using Tract-Based Spatial Statistics. A t-test on DTI measures of WM integrity (axial, radial, and mean diffusivity, and fractional anisotropy) was performed between responders and non responders to chronotherapeutics. A correlation analysis between DTI measures and the delta of HDRS scores (difference between HDRS scores after treatment and HDRS scores at baseline) was then performed in the areas where a difference in WM integrity between responders and non responders was observed. We accounted for the effects of nuisance covariates which could influence WM structure: age, sex, age at onset of the illness, and lithium treatment.

In respect to responders, non responders showed increased mean diffusivity (MD) in several WM fiber tracts including corpus callosum, corona radiata, superior longitudinal fasciculus, inferior longitudinal fasciculus, cingulum bundle, thalamic radiation, and inferior fronto-occipital fasciculus, localized especially in the right hemisphere. Among these structures, the degree of clinical improvement negatively correlated with MD and radial diffusivity (RD) in several WM tracts.

We observed that increased MD and RD predict poor antidepressant response to sleep deprivation in core WM tracts which are crucial for the functional integrity of the brain. Increased RD reflects dysmyelination and demyelination without axonal loss, while increased MD suggests myelin degeneration. Myelin increases the speed of transmission of nerve signals, and damages on myelin sheaths cause a disrupted structural connectivity, leading to a reduction of the speed of signaling along the axon. These damages could affect the capability of neurons to communicate with each other efficiently, leading to a compromised functional connectivity. Our present findings reveal that the degree of reduction of WM integrity biases the efficacy of antidepressant treatments, suggesting that WM integrity may contribute to the efficacy of chronotherapeutic treatment.

#### 47. IS THE TEMPORAL STABILITY OF OBSESSIVE COMPULSIVE SYMPTOM DIMENSIONS INFLUEN-CED BY CLINICAL AND GENETIC CONTRIBU-TIONS? A LIFETIME RETROSPECTIVE STUDY

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Little is known about the temporal stability of symptom dimensions in adult patients with Obsessive-Compulsive

Disorder (OCD). Previous studies suggest that symptom dimensions might be stable, however longitudinal studies over longer periods of time are needed, considering that no dimensional study focused on a period longer than 10 years. The present study investigated retrospectively the lifetime OC symptom dimension stability in a large sample of adult patients. The impact of additional variables on temporal stability of OC symptom dimensions, such as age, age at onset, illness duration and familiar history of OCD was examined. Considering the role of glutamatergic dysfunction in OCD a possible effect of glutamate system gene SLC1A2 was also investigated.

We enrolled 178 subjects affected by OCD (DSM-IV criteria, SCID-I interview) aged between 17 and 70. OC symptomatology was assessed via YBOCS-SC: past OC symptoms, symptom at OCD onset and main symptom at the moment of the interview were collected and the entire symptomatology for each patient was categorized in symptom dimensions [5]. Finally, depending on temporal stability of OC symptom dimensions, the sample was divided into two groups: patients who showed more than one dimension during their clinical history (multidimensional disorder) and patients who showed the same dimension lifetime (monodimensional disorder). Patients were genotyped for SLCA1A2-181A>C.

Most patients (n=115; 64.7%) showed a multidimensional disorder. The main result of present study was that the multidimensional disorder was characterized by earlier age at onset (F=15.127; p=0.00014), higher rate of first degree relatives affected by OCD (2=6.408; p=0.011), lower rate of contamination symptom dimension (2=12.564; p=0.014) and higher frequency of G/G homozygotes for SLCA1A2-181A>C ( 2=10.505; p=0.005). Furthermore age at onset (p=0.0002) and SLCA1A2-181A>C (p=0.0063) were found to influence the temporal stability of symptom dimensions. According to lifetime stability of OC symptom dimensions we hypothesize that OCD can be dissected in two different subgroups, monodimensional and multidimensional disorder. This characteristic of the illness seems to be under genetic control with each subgroup characterized by specific and peculiar clinical features. These results should be taken as preliminary and should be confirmed by long follow-up studies. Future studies are needed in order to investigate if lifetime stability of symptom dimension could be used as a possible subtyping approach to reduce the OCD heterogeneity.

#### 48. INFLUENCE OF ADVERSE CHILDHOOD EXPE-RIENCE ON GRAY MATTER VOLUME IN MAJOR PSYCHOSIS COMPARED TO HEALTHY CONTROLS

Melloni Elisa M. T., Gallo M., Poletti S., Bollettini I., Vai B., Aggio V., Benedetti F. Scientific Institute and University Vita-Salute San Raffaele, Milano, Italy

For over two decades the neural correlates of major psychosis, such as schizophrenia and bipolar disorder, have been investigated by experts which found both function and structural abnormalities. The regions of reduced gray matter in schizophrenia are extensive and concern limbic (amygdala, hippocampus, thalamus), paralimbic (anterior cingulate, insula) and cortical areas (dorsolateral prefrontal and temporal) [1]. In bipolar disorder the gray matter loss, mainly present in paralimbic regions, is less extensive, but substantially comparable to those observed in schizophrenia, revealing a structural overlap between the two diseases [2]. Literature showed that adverse life events during childhood are correlated to the development of psychiatric disorders and that stress affect brain morphology modulating plasticity and neurogenesis [3]. Our study aims to investigate the effect of exposure to stressful family situations during childhood on gray matter in major psychoses and in healthy controls.

We recruited 426 subjects including 194 patients with bipolar disorder, 96 schizophrenic patients and 136 control subjects. All subjects underwent structural magnetic resonance imaging and were administered the Risky Families Questionnaire (RFQ) to assess the severity of adverse childhood experiences. We divided each diagnostic group into two subgroups (high and low RFQ). Voxel- based morphometry (VBM) analyses were performed to investigate 1) the effect of diagnosis on gray matter volume and 2) if this effect was different in subjects who experienced adverse childhood experiences compared to those who didn't lived these experiences.

Results identified an effect of diagnosis on gray matter volume in bilateral insula, in orbitofrontal cortex and in the left thalamus. The same differences were observed between controls, bipolar and schizophrenia patients, when considering only subjects who experienced a stressful family environment. No differences were observed in subjects with low levels of adverse childhood experiences.

This is the first study to show that differences in gray matter volumes observed between major psychoses and healthy controls are evident only in people who grew up in a stressful environment. These data could then indicate that growing up in a risky family play an important role in developing of these disorders, also affecting brain structure.

#### 49. STRUCTURAL CHANGES OF RAPHE NUCLEI IN DEPRESSION ASSOCIATED WITH PARKINSON'S DISEASE DETECTED BY TRANSCRANIAL SONO-GRAPHY AND DIFFUSION TENSOR IMAGING

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Transcranial brain parenchyma sonography (TCS) showed decreased echogenicity of the brainstem raphe (BR) in depression associated with Parkinson's disease (PD). Magnetic resonance imaging and histopathological studies confirmed the hypothesis of a structural changes of the BR in depression in PD. We compared fractional anisotropy (FA) values and apparent diffusion coefficients (ADC) of the BR in depressed and non-depressed PD patients, in comparison to TCS findings, to investigate possible structural disruption of the BR.

33 PD patients with depression (PD+ D+), 32 PD patients without depression (PD+ D-) and 34 healthy individuals (PD- D-) were included. PD patients with and without depression were matched for age and disease stage and duration. Echogenicity of BR was rated using TCS with a two point scale (grade 1:normal BR echogenicity same as red nuclei, grade 0: hypoechogenic, invisible or interrupted BR). ADC and FA values in various brain regions and white brain matter tracts were calculated using SPM5 and Matlab software.

Significant increase of mean ADC (t-test, each, P<0.0001) and significant decrease of mean FA values (t-test, each, P<0.0001) were found in patients with hypoechogenic BR compared with patients with normal raphe echogenicity. Mean FA values were significantly decreased in dorsal and ventral part of the BR in PD+ D+ patients but only in ventral part of the BR in PD+ without depression in comparison with healthy subjects (t-test, each, P<0.0001).Structural changes were detected in prefontal brain regions. Our findings depicted structural changes of the BR and certain brain regions in depression associated with PD which may reflect the pathogenic role of the basal limbic system and its projections in the pathogenesis of depression in PD that may have important therapeutic implications.

#### 50. COGNITIVE DYSFUNCTIONS IN ASEPTIC MENINGITIS CAUSED BY THE ECHO VIRUS – CASE REPORT

#### Petković D., Vuković B., Galić S., Andrić Z. The County Hospital in Požega, Croatia

Enteroviruses included in family Picornavirideae are separated into subgroup and serotypes: Polioviruses, Coxsackie viruses A and B serotypes, Echoviruses serotypes 1-24, Enteroviruses serotypes 68-75. Enteroviruses including poliovirus account for only 11-22% of all cases of encephalitis. Clinical spectrum of infection with ECHO viruses is extensive: asymptomatic infection, febrile illness with or without respiratory symptoms and CNS infections – aseptic meningitis, encephalitis, paralysis, Guillain–Barre syndrome. Objectives: Review of follow-ups during a one-year period of a female patient with aseptic meningitis, cognitive dysfunction and an electroencephalographic record showing abnormalities.

Previous psychiatric and neurological diseases were anamnestically excluded, in early childhood patient get over aseptic meningitis without aftermath .Physical and neurological examinations suggested the clinical diagnosis of aseptic meningitis characterized by fever, headache, meningismus with no focal neurological signs. The diagnosis was confirmed by CSF examination which revealed lymphocytic pleocytosis and negative bacteriological cultures. Etiologic diagnosis was confirmed by serological examination (ELISA) of paired serum samples (acute and convalescent phase disease) for enteroviruses performed at the Croatian National Institute of Public Health, Zagreb. EEG recordings were evaluated according to standards for the patient's age on a 21 channel Medelec apparatus. Cognitive functions assessed using psychological tests (Interview, WBII, AVLT, WMS, CFT, Bender Gestalt II, FAS, MMPI-2)

CSF contained 491 white cells/mm3 (90.2% lymphocytes), Glucosae level 2.8 mmol/L, Protein content 0,65g/L. Results of serologic examination in the acute disease phase showed positive specific IgM antibodies on Echoviruses, indicating recent infection. ECHO IgM 48, IgG 180 U/ml, Poliovirus IgG positive 1.18, Coxsackiae v. IgM negative <10, IgG positive 300 Convalescence phase: Echoviruses IgM 15 negative, IgG 140. EEG record in acute phase: diffused dysrhythmically changed predominantly in frontal region with paroxysmal tendency during hyperventilation. Control EEG record one year later: lighter irregularity in frontal region with paroxysmal tendency during hyperventilation. MRI brain scan was normal. Result of psychological testing: Average general intellectual functioning, memory disorders - mildly reduced verbal long term memory, verbal - logical long term and visual memory. Moderately reduced verbal fluency. This cognitive dysfunction indicates organic cerebral dysfunction.

After a one-year period, follow-up on a 30-year old female patient with aseptic meningitis caused by Echovirus and organic cerebral dysfunction development manifested by a symptomatology of memory disorders and diffuse abnormalities in electroencephalographic record showed spontaneous cognitive functions normalization, but EEG records still show localised irregularities in the frontal regions.

#### 51. ANTIDEPRESSANT TREATMENT WITH TOTAL SLEEP DEPRIVATION INDUCES CHANGES IN WHITE MATTER MICROSTRUCTURE IN BIPOLAR DISORDER

#### Poletti S., Bollettini I., Melloni E., Dallaspezia S., Benedetti F. Scientific Institute and University Vita-Salute San Raffaele, Milano, Italy

Bipolar disorder (BD) is characterised by changes of white matter (WM) microstructure and by a disruption of circadian rhythms. The chronotherapeutic combination of repeated total sleep deprivation and morning light therapy (TSD+LT) not only can acutely reverse depressive symptoms in approximately 60% of patients, but it also reduces the high percentage of relapses seen after the recovery night. Specific effects of sleep deprivation on the brain have been found by different brain imaging studies showing an association with functional and metabolic changes in specific brain areas of the corticolimbic circuit. Following this line of reasoning the aim of the study is to investigate the effect of chronoterapeutic treatment on WM microstructure in BD. Twenty-four patients affected by a major depressive episode without psychotic features, with a diagnosis of BD type I were administered one week of chronotherapeutic treatment through TSD+LT. On a 3.0 Tesla scanner (Gyroscan Intera, Philips, Netherlands) using a 6 channels SENSE head coil scanner were acquired diffusion tensor images (DTI) with 35 gradient directions. Voxelwise DTI analyses were performed using Tract-Based Spatial Statistics using TFCE correction (p=0.05). A paired t-test on DTI measures of WM integrity (axial, radial, and mean diffusivity, and fractional anisotropy) was performed between patients at baseline and after one week of TSD+LT treatment.

After chronotherapeutic treatment patients showed increased axial diffusivity (AD) and mean diffusivity (MD) in corpus callosum, corona radiata, superior longitudinal fasciculus, corticospinal tract and anterior thalamic radiation. All tracts were localized in the right hemisphere. The chronotherapeutic treatment is associated to increased AD and MD in several fibre tracts contributing to the functional integrity of the brain. The increase of MD was likely driven by the increase of AD. AD represents the water diffusivity parallel to the axonal fibers, reflecting the greater freedom of water to diffuse along the principal fiber axis rather than to travel across the surrounding myelin sheaths thus reflecting fiber integrity. The right lateralization of the effect is in agreement with a suggested dominant role of the right hemisphere in mood regulation. We suggest that chronotherapeutic treatment could counteract part of the detrimental influences of BD on WM structure, with specific benefits resulting for the patients from effects on WM tracts previously associated to BD and involving inter-hemispheric, and frontal connections.

#### 52. MISLEADING AND SUCCESSFUL PRESYMPTOMATIC DIAGNOSIS OF WILSON DISEASE

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Wilson's disease (WD) is an inherited autosomal recessive disorder of copper (Cu) transport resulting from mutations in the ATP7B gene encoding a P-type ATPase. WD is characterized by decreased biliary excretion of Cu and reduced Cu incorporation into apoceruloplasmin. The incidence ranges from 1:7,000 to 1:100,000 individuals. The onset of symptoms and clinical presentation are highly variable. Symptoms of liver disease and hemolysis tend to occur earlier in life than neurological and psychiatric dysfunction. The Kayser-Fleischer ring in addition to a low ceruloplasmin (<20 mg/dL) has been a major clue for diagnosis of WD which was further confirmed by a high liver Cu content  $(>250 \mu g/g dry wt)$ . In the absence of typical clinical symptoms, diagnosis becomes difficult, since no single biochemical test allows a secure confirmation. As an example a low ceruloplasmin may be present in subjects without WD or patients with WD can show a normal level of ceruloplasmin. Futhemore coincidence of another severe chronic diseases may delay the proper medical consultation. WD is a rare, but potentially treatable metabolic disorder and therefore should not be overlooked. However, it is not rare that patients go undiagnosed for years.

We report here 27 German and Turkish patients diagnosed by the molecular analysis at the age of 5 to 53 years. The ATP7B gene was investigated by direct sequencing of genomic DNA.

The most prevalent mutation among Germans was H1069Q accounting for about 42% of the mutant alleles. On the other hand among Turkish patients N1270S and R778G were most prevalent mutations with the frequency of 50 and 37.5% respectively. Our report will be also focused mainly onto presymptomatic adult patients whose diagnosis could only be made by a long difficult procedure. Wilson disease is a treatable inherited disease. Early treatment usually leads to favorable prognosis. Diagnosis and implementation of therapy at an asymptomatic stage of WD allows prevention of significant hepatic and neurologic morbidity. Mutation analysis is a crucial step for securing the presymptomatic diagnosis of WD.

#### 53. CLINICALLY ISOLATED SYNDROME -CASE REPORT

#### Serafimova K., Milosavljevik P., Petkovska-Boshkova T., Clinic of neurology, Skopje, Macedonia

A clinically isolated syndrome is the result of a single episode of demyelination in one area of the central nervous system (a monofocal episode) or several areas of the central nervous system (a multifocal episode) which lasts for at least 24 hours. Of the people who are eventually diagnosed with MS, 85% experience an initial onset of symptoms or a first attack that is referred to as a clinically isolated syndrome (CIS)1.

32 year old female patient Case history: 3 mounts ago-acute total loss of seeing (blindness) in the left eye After a consultation with ophthalmologist a diagnosis was made: Retrobulbar neuritis; with corticosteroid treatment... the condition got better Neurological status Lumbar puncture with electropherograme VEP SEP (n. medianus:n.tibialis) MRI

Neurological status: fine horizontal nystagmus in the left eye • Lumbar puncture with electropherograme: normal • VEP – normal • SEP (n. medianus:n.tibialis) – normal • Vitamin and analgesic therapy was applied MRI - In the white brain mass bilateral in T2 and in FLAIR pulse sequences nodular hypersignal changes are seen with different sizes, which are consistent with demyelination like MS. These changes are seen right in the distal segment of medulla oblongata Clinical Isolated syndrome: First attack of demyelination (clinical or MRI) • MRI control after 3 mounts – for new lesions.

### 54. SPEECH LANGUAGE THERAPY IN GLOBAL APHASIA WITHOUT HEMIPARESIS

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Global aphasia is the most severe type of aphasia often seen immediately after the patient has suffered a stroke. Approximately 20–40% of post stroke aphasia has been reported to be the global type, generally occurring after large perisylvian lesions in the left middle cerebral artery territory and is associated with contralateral hemiparesis. Global aphasia without hemiparesis (GAWH) is a rare stroke syndrome involving receptive and expressive language impairment, without the hemiparesis manifested by patients after large left perisylvian lesions. The role of Speech Language Therapy (SLT) in GAWH is still controversial in the literature. We enrolled six stroke patients with left hemisphere lesions admitted in our neurology clinic from 2011 to 2015, presented with global aphasia still one month after stroke onset and without hemiparesis or hemiplegia. These patients undertook Computed Tomography (CT) or/ brain MR imaging (MRI) exam and speech evaluation at the stroke onset, which revealed left hemisphere lesion and global aphasia according to the Western Aphasia Battery (WAB) test. Brain MRI showed that the lesion sites in the left hemisphere were temporal lobes, thalamus, basal ganglia and insula. Aphasia subtypes were confirmed after detailed language evaluation by a Speech-Language Pathologist using the western aphasia battery (WAB). The WAB aphasia quotient and subscales of fluency, comprehension, repetition, and naming were used to establish the subtypes of aphasia.

All the patients were treated with speech language therapy (SLT). The SLT sessions were performed every day with duration of 45 minutes each session. A follow-up examination, ten weeks later, showed marked improvement of global aphasia in some patients. The global aphasia evolved to Wernicke aphasia in two patients and, transcortical motor aphasia in one patient and transcortical sensory aphasia in two patients and, one patient recovered totally.

Our patients with global aphasia without hemiparesis evolved into different aphasia-subtypes after the treatment with SLT. Our results are in line with previous studies that establish SLT as an effective method for enhancing language recovery after stroke. SLT facilitate improvement in functional communication, expressive language and, receptive language and that social stimulation alone are not as effective as participation in formal SLT. We conclude that a critical objective analysis of the linguistic functions is necessary to point out the guidelines for a successful therapy and that, recovery could possibly be found in SLT, but the role of spontaneous recovery cannot be ignored.

#### 55. THE PREVALENCE OF COGNITIVE DISORDERS IN STROKE PATIENTS IN THE NEUROLOGY CLINIC OF REGIONAL HOSPITAL OF DURRES

Shehu E., Gjeci S., Shehu E. Regional hospital of Durres, Albania

We aim to describe the cognitive impairments in stroke patients hospitalized in our Neurology Department of Durres Hospital.

We conducted a cross- sectional study from January to December 2014. We enrolled in this study all the subjects with stroke hospitalized in our neurology department. We used for all patients a protocol to study the epidemiological, clinical, CT and/or MRI data, and cognitive function by psychometric tests.

The prevalence of stroke was estimated at 59 %. Ischemic stroke was more frequent with a prevalence of 71% of stroke. Atrial fibrillation, dyslipidemia, hypertension and diabetes were the strongest risk factors found. In 22,4% of cases, there was a previous diagnosis of stroke. The pre-

stroke cognitive impairments were found in 19% of patients. The frequency of cognitive impairments was estimated at 84.6%. Language impairments were found in 52,9 % of stroke patients. Aphasia was most frequent, approximately in 83% of stroke patients. Praxis disorders were found in 54.5% of cases and, memory impairment in 24 %. The MMSE performed in 80 patients sowed cognitive impairment in 72,3% of cases. More than half of patients had an IALD score at 4. Dementia was observed in 18,2% of all patients.

The cognitive impairments in stroke patients are very common. They should be assessed systematically by the most common psychometric tests.

#### 56. EFFECT OF COMT POLYMORPHISM ON SUBCORTICAL VOLUMES IN SCHIZOPHRENIA

#### Spangaro M., Bollettini I., Poletti S., Mazza E., Cavallaro R., Benedetti F.

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Abnormalities of subcortical structures have been consistently reported in schizophrenia and contemporary studies have focused on the identification of gene variants that could contribute to this endophenotype. One of the most studied polymorphism is the Val108/158Met (rs4680) of Catechol-O-methyltransferase (COMT) gene, a key regulator of dopamine (DA) availability, with Val allele associated with higher enzymatic activity and lower DA levels. rs4680 is associated with schizophrenia and implicated in different cognitive and neurofunctional alterations [1]. Moreover, COMT Met allele was associated with higher volume of amygdala and hippocampus in both schizophrenic and healthy subjects [2]. COMT Val108/158Met genotype influences neuronal growth, and its size in adults, via neurotrophic effects of DA during development. Functional genetic variations in COMT have been associated with sexually dimorphic effects in several neurocognitive aspects, suggesting that gender might be a critical factor to consider in interpreting COMT-dependent effects [3]. Based on these data, we hypothesized that a possible interaction between rs4680 and gender could modulate neurotrophic effects of DA, resulting in subcortical volume differences.

We examined rs4680 in 70 patients diagnosed with schizophrenia, according to DSM-IV criteria. All patients underwent 3T magnetic resonance imaging, volumetric segmentation was performed with the Freesurfer 5.3 image analysis suite. The Analysis of Covariance (ANCOVA) was used for the evaluation of the interaction between genotype and gender, considering subcortical volumes as dependent variable, COMT genotype and sex as categorical elements and age as covariate. The sample respected the Hardy–Weinberg equilibrium. ANCOVA revealed a significant interaction between rs4680 and gender on volumes of Left Amygdala (F=4.50, p=0.014), Right Thalamus (F=3.33, p=0.042) and Left Nucelus Accumbens (F=3,153, p=0.049), with Met carriers female patients showing higher volumes than other groups. Moreover, we also reported an effect of rs4680 on Left Putamen (F=4.21,p=0.019) regardless of subject's gender, with higher volumes among Met carriers.

This is the first study to report a joint effect of COMT and gender on brain volume among patients with schizophrenia. Consistent with previous studies, we found that Met allele was associated with higher volumes probably due to DA neurotrophic effects during neuronal growth. Interestingly, Amygdala, Nucleus Accumbens, Thalamus, and Putamen are highly involved in dopaminergic pathways, known to be disrupted in schizophrenia. The differential results of rs4680 based on gender support the hypothesis of sexually dimorphic effect of COMT genetic variations on brain morphology. Finally, this study provide challenging evidence for future research on subcortical volumes in patients with schizophrenia.

#### 57. INTRATHECAL BACLOFEN PUMP THERAPY IN SPINAL CORD INJURY PATIENTS: LONG-TERM DOSAGE EVALUATION

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The aim of this study was to investigate the long-term dosage evolution in spinal cord injury patients who received intrathecal baclofen drug therapy by programmable pump, exclusively focusing on the course and progress of the dosage and independently from any other clinical data. Data on dosage evolution were recorded from twenty patients with a minimum follow-up of 5 years. Daily baclofen dosage of the entire follow up period was analysed. In our patients group the period required to achieve a stable dose was twice as long when compared to the majority of studies available in the literature. No difference in terms of daily stable dose between our study and the literature was found. None of the patients met the widely agreed tolerance criteria. Patients with cervical level of injury showed that they required higher daily dose than patients with thoracic spinal cord injury (SCI). Thoracic SCI patients required longer titration before reaching a stable daily dose than the cervical patients. Patients who had the pump implanted after 24 months from initial injury tend to require less than the mean stable daily dose.

The long-term dosage evolution analysis of the intrathecal baclofen therapy is a useful tool in evaluating several important clinical aspects of the treatment of spasticity in spinal cord injury patients. The most signifcant are : loss of ITB efficacy, dosage titration, onset of secondary complications, timing of insertion of the baclofen pump, role of the intrathecal baclofen therapy in the multimodal strategies approach to treatment of spasticity secondary to spinal cord injury.

#### 58. PERSISTENT SOMATOFORM PAIN DISORDER VS CHRONIC POSTOPERATIVE HEADACHE

#### Šumski I., Knez Turčinović M., Marinić R., Cigrovski A. Neuropsychiatric hospital "Dr. I. Barbot", Popovača, Croatia

The ICD-10 defines persistent somatoform pain disorder as a persistent (at least six months, continuously on most days) severe and distressing pain, in any part of the body, which cannot be explained adequately by evidence of a physiological process or a physical disorder, and which is consistently the main focus of the patient's attention. Chronic postoperative headache can be defined as pain that has developed after a surgical procedure, is present for at least 2 months, and that other causes have been excluded. In psychiatry it is sometimes difficult to distinguish between these two entities, as was the case with our patient. Diagnosed with a meningeoma in 2013., she underwent a surgical procedure which was successful in removing the tumor. After the craniotomy however, she began experiencing constant, debilitating headaches, localised in the forehead, that have significantly lowered her quality of life. In adittion she developed a mood disorder manifesting with symptoms of anxiety and depression, irregular sleeping patterns, and cognitive deterioration. Our patient tried a gamut of pain managing treatments and procedures, all of which so far have failed to alleviate her symptoms. Her case presented to us a dilemma: is she suffering from a chronic postoperative headache or from a persistent somatoform pain disorder?

### 59. STROKE POST ARTERITIS TB OR BRAIN INFECTION?

#### Trifan F., Vatu M., Stemate C. University of Medicine and Pharmacy, Neurology Clinical Hospital, Craiova, Romania

Tuberculosis (TB) remains one of the world's deadliest communicable diseases. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease. Globally, 3.5% of new and 20.5% of previously treated TB cases, were estimated to have had MDR-TB in 2013 and an estimated 9.0% of patients with MDR- TB had extensively drug resistant TB (XDR-TB). In Romania, the TB incidence is 168cases/100.000 people, the biggest in Europa.(world health organisation- global tuberculosis report 2014 We are presenting the case of a diabetic patient, treated with oral antidiabetic, hospitalized for paretic right limb deficit, language disorders post arteritis TB Stroke, confirmed with cerebral MRI and thoracic CT(multiple homogeneous bilateral disseminated micronodular lesions for pulmonary TB),to whom is was initiated anti-tuberculosis and post stroke therapy. In evolution, the patient's condition worsens with impaired general condition, altered consciousness and the presence of a febrile syndrome. After the sputum examination (BK Negative), the pulmonologist decides that the patient is drug resistant and changes the anti-tuberculosis therapy, but he doesn't recommend bronchoscopy, arguing that brain lesions are a contraindication. Subsequently the patient's condition improves but after about 3 weeks he develops altered consciousness with comatose state, aphasia, right hemiplegia, hemodynamic instability. A cerebral MRI is performed (intracerebral miliary tuberculosis with leptomeningitis changes at left front-temporal and at pontinemesencephalic level ) bringing up the suspicion of fungal or bacterial brain superinfection, invalidating the diagnosis of acute stroke secondary TB arteritis. It was initiated antifungal and antibacterial treatment, the patient being transferred in the intensive care unit for life support, but again the bronchoscopy examination is considered incompatible with his multiple brain lesions.

Initially the patient's condition improves with antifungal, antibacterial and anti-tuberculosis therapy, but after about 2weeks from the elimination of the combined therapy and keeping only the anti-tuberculosis pills, the patient dies. Discussion 1. Was the bronchoscopy indicated despite the risk of the brain injury? 2. Was the TBdiagnosiscorrect,given thenegativesputumanalysisandimprovement of the patient condition after antifungal/antibacterial/ anti-tuberculosis combination therapy? 3. Based on the patient evolution and imagistic investigation was this a Stroke?

#### 60. FRONTO-LIMBIC NEURAL RESPONSE AND CONNECTIVITY PREDICT THE ANTIDEPRESSANT EFFECT OF CHRONOTHERAPEUTICS IN BIPOLAR DEPRESSION

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The identification of possible biomarkers of antidepressant response in depression may provide novel approaches for treatment selection. Several authors suggested that abnormalities within fronto-limbic structures might provide a neurobiological basis for the pathophysiology and maintenance of the bipolar disorder [1,2]. Depression recovery has been consistently associated with activity of fronto-limbic structures such as anterior cingulate cortex (ACC), and amygdala, both in terms of predictor and correlate of depression recovery. The combination of repeated total sleep deprivation and light therapy (TSD+LT) has been demonstrated to acutely reverse depressive symptoms in approximately 60% of bipolar depressed patients. Due of its rapidity and its multi-target mechanism of action, chronotherapeutics have been proposed as a reliable model for antidepressant treatments[3]. No study evaluated the effect of antidepressant response on cortico-limbic connectivity in bipolar depression during emotional processing. By combining fMRI with a technique that allows to investigate the connectivity in terms of causal relationships between regions (Dynamic Causal Modeling, DCM), we explored the effect of TSD+LT on neural responses to negative faces in a homogeneous sample of bipolar depressed patients.

We combined fMRI and DCM to study the effect of chronotherapeutics on neural responses and effective connectivity to emotional faces in healthy controls (HC, n=35) and bipolar depressed patients either responder (RBD, n=26), or non responder (nRBD, n=11) to 3 consecutive TSD+LT. DCM models, exploring connectivity between ACC, dorsolatelar prefrontal cortex (DLPFC), Amygdala, fusiform gyrus, and visual cortex were constructed. Bayesian Model Averaging provided DCM parameters, subsequently entered into statistical analyses.

After treatment, patients significantly increased their neural responses in DLPFC, ACC and insula, but nRBD had lower baseline and endpoint neural responses than RBD (pFWE<0.05). The increase in ACC was significantly correlated to symptomatological improvement. DCM showed that only RBD patients significantly increased intrinsic connectivity from DLPFC to ACC(t=2.74; p=0.011), and reduced the modulatory effect of the task on the connection Amy-DLPFC(t=2.2; p=0.037).

The clinical antidepressant response to chronotherapeutics is associated with an increase of neural responses and effective connectivity within prefrontal cortico-limbic networks during the implicit regulation of affective states. A rebalancing of neurotransmitters and a recover of the homeostasis between neural systems may underlie these changes. Furthermore, the functional activity seems to differentiate RBD from nRBD at the baseline, thus suggesting that fMRI might provide biomarkers for treatment selection, and in monitoring its efficacy in BD.

#### 61. PREGNANCY AND LABOR IN MULTIPLE SCLEROSIS: EXPERIENCES FROM TUZLA CANTON (BOSNIA AND HERZEGOVINA)

Vidović M., Burina A., Sinanović O., Zukić S. University Clinical Center Tuzla, School of Medicine of University Tuzla, Bosnia and Herzegovina Multiple sclerosis (MS) is autoimmune disease of central nerve system which is twice more often in women than in men. Therefore, in this population family planning and the impact of pregnancy on disease might be very important for the patients as well as physicians. The aim of this study was to evaluate pregnancy, way of labor and frequency of relapses after the labor in women with MS in Tuzla Canton (Bosnia and Herzegovina).

It was retrospectively analyzed medical records of female patients with MS from Tuzla Canton (Bosnia and Herzegovina) which have been pregnant in period January 1, 2002 - December 31, 2014.

In analyzed period 23 female patients with MS were pregnant. Average labor ratio was 1.7 per year. Average time period passed from definitive diagnose until labor was 4.6 years. Natural labor was performed in 65.2% of female-patients and there were no patients with complications during the pregnancy and labor as well. Due to lack of medication at that moment, Intravenous Immunoglobulin (IVIG) therapy was administered in 43.3% of female-patients. In first postpartum trimester were no relapses. In second it was in 4.3% and in third in 8.6% of patients. IVIG administration made no significant differences in relapse rate in women which have received this medication compared to women which have not.

In period of thirteen years 23 female patients from Tuzla Canton (Bosnia and Herzegovina) with multiple sclerosis were pregnant and have labored. Average labor ratio is 1.7 per year. During the pregnancy and in the first postpartum trimester were no relapses. In the second was in 4.3% and third in 8.6% of patients. Intravenous immunoglobulin administration has no impact on relapse rate.

## 62. DEPRESSIVE SYNDROME IN PATIENTS WITH CHRONIC BACK PAIN

#### Vidović V., Časar Rovazdi M., Kraml O., Rendulić Slivar S. Special hospital for medical rehabilitation Lipik, Croatia

The aim of this study was to determine the prevalence of depressive syndrome in patients with chronic low back pain (LBP) with or without propagation in the legs.

The subjects were patients from the neurological polyclinic at the Lipik Special Hospital, in the period from 1/11/2014– 15/2/2015 with a duration of pain spanning 3 months. For the purpose of evaluating and quantifying depressive syndrome, the Patient Health Questionnaire-9 (PHQ-9) was used. It comprised 9 questions that indicate the presence of symptoms of depression. A combination of a total score and the frequency of the three key symptoms can be used to establish a diagnosis of depressive syndrome and its division into "major" or "other" depressive syndromes. The intensity of pain was measured using the visual analogue scale (VAS). Exclusion criteria were the presence of any previously diagnosed psychiatric disorders and other diseases with reduced life expectancy or a threatening disability. Also excluded were patients with painful syndromes of another localisation with an intensity of pain conforming to VAS  $\geq$ 2 and those for whom a diagnosis of chronic LBP syndrome could lead to a secondary benefit.

In all, 61 patients were tested, 32 (52.5%) women and 29 (47.5%) men. The average age was 49.9 years (29-76), the average duration of pain was 9.39 years (SD 7.68), and the average intensity of pain on the VAS during the previous month was 6.03 (SD 2.07). The PHQ-9 criteria for a diagnosis of depressive syndrome were met by 30 (49.2%) of respondents.Of these, 17 (56.7%) had a "major" and 13 (43.3%) had "other" depressive syndromes. A group of respondents with depressive syndrome had a significantly higher intensity of pain compared to the group of patients without depression (t = 4.19, p < 0.001), without statistically significant differences in terms of age (t = 0.717, p > 0.05), sex (t = 0.647, p > 0.05), duration of pain (t = 1.85, p > 0.05) and their employment status ( $\chi$ 2 = 0.983; p > 0.05).

Nearly half of the respondents (49.2%) had a coexisting depressive syndrome. The intensity of pain is the most important risk factor for the onset of a depressive syndrome amongst the respondents, given that the study was designed to minimise the likelihood of the inclusion of those with other possible causes of depression.

### 63. SELF-PERCEIVED COGNITIVE DYSFUNCTION IN MULTIPLE SCLEROSIS PATIENTS

#### Vidović V., Časar Rovazdi M., Kraml O., Bašić Kes V. Special Hospital for Medical Rehabilitation Lipik, Croatia

The aim of the study was to assess the relationship of selfperceived cognitive dysfunction in patients with multiple sclerosis (MS) with respect to gender, age, duration of disease, disease course, level of incapacity and fatigue. The respondents were 60 patients older than 18 years of age with a confirmed multiple sclerosis diagnosis who in the period from 1 September to 31 December 2014 underwent inpatient rehabilitation in the Lipik Special Hospital for Medical Rehabilitation. Exclusion criteria were serious cognitive damage, any acute complication in the previous 3 months, and an established dementia diagnosis. Measurement of selfperceived cognitive dysfunction was performed using the 5items version of Perceived Deficits Questionnaire (PDQ). The PDQ-5 provides a self-report measurement of several domains of cognitive functioning: attention, retrospective memory, prospective memory, planning and organization. The total PDQ-5 score can range from 0-20. Higher scores indicate a greater self- perceived level of cognitive dysfunction. There is a positive correlation between self-perceived cognitive dysfunction and depression, while no consistent relationship was observed in regard to a measured cognitive deficit in neuropsychological testing. The assessment of fatigue was done using the Modified Fatigue Impact Scale (MFIS) questionnaire. The total MFIS score can range from 0-84, with higher scores indicating a greater impact of fatigue on daily activities.

The number of subjects totalled 60, of which 37 were women (61.7%) and 23 were men (38.3%). The average age was 49.5 years (29-71). The average time that had elapsed since patients were diagnosed with MS was 12.2 years (0.5-32 years). The average score obtained from the Expanded Disability Status Scale (EDSS) was 4.9 (1.5-9). Of the total number of patients, 30 (50%) patients had the relapsingremitting course of the disease (RRMS), and 30 (50%) the secondary progressive course (SPMS). The average PDQ-5 score for women was 8.0 (SD 4.68), and 7.3 (SD 5.58) for men. A positive correlation between the PDQ-5 score and the higher MFIS score (P<0.001) was found. There was no significant correlation in the PDQ-5 score with respect to gender (P=0.569), age (P=0.600), level of incapacity (P=0.204), the time that had elapsed since MS was diagnosed (P=0.413) and disease course (P=0.919).

There is a positive correlation between self-perceived cognitive dysfunction and the impact of fatigue on daily activities. Patients who complain on fatigue require attention due to a possible co-existence of a depressive disorder or cognitive impairment.

#### 64. OSTEOPONTIN GENE AND CLINICAL COURSE OF MULTIPLE SCLEROSIS IN A POLISH POPULATION

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Osteopontin (OPN) is a key cytokine involved in T-cell activation in multiple sclerosis (MS), and is therefore called an early T-cell activation gene. Studies performed in various geographical regions have demonstrated significant differences. In this study we analysed whether the OPN gene has an effect on MS occurence and clinical course in a Polish population.

Our study material consisted of 100 MS patients compared with control material. The clinical course was evaluated by the EDSS score. After extraction of DNA form peripheral blood cells, genotype and allele frequencies in exon 6 and 7 were examined using specific primers by a standard PCR reaction. The distribution of variables was tested with the D'Agostino-Pearson test. Then the statistical analysis based on one-way ANOVA, Mann-Whitney test and logistic regression was performed using a licensed version of MedCalc software.

The genotype distribution and allele frequencies were not similar between patients and controls but differences were not statistically significant. The heterozygous C/T genotype in position 8090 was detected in 21.6% of patients and in 10% control material. Based on one-way ANOVA testing, the clinically significant genotypes were identified. The EDSS score was higher in 8090 T/T+9250 C/C patients than in 8090 C/C +925 C/C MS patients. The disability in 8090 C/C+9250 C/T MS patients was higher than in 8090 C/C+9250 C/C MS patients.

Our results are negative with respect to the impact of the osteopontin gene on susceptibility to MS in Poland. Genetic polymorphism of OPN was established to be associated with MS in Japanese patients. It seems therefore that the haplotype structure may differ from one population to another. However, we have identified the 8090 T/T 9250 C/C osteopontin genotype associated with higher levels of disability in MS patients. No differences in age between genotype categories were found.

#### 65. FREQUENCY AND TYPE OF SLEEP DISTURBANCES IN PARKINSON´S DISEASE PATIENTS

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Sleep disturbances are important and often underestimated non – motor features in Parkinson's disease (PD). The causes of sleep disturbances are multifactorial and include nocturnal motor disturbances, nocturia, depressive symptoms, and medication use. The aim of this study was to analyze the frequency and type of sleep disturbances in PD.

The study was prospective and included 60 of PD patients. These patients were included in the study regardless of age, gender, disease duration and the type of used drugs. Control group included 30 of reumathology patients with approximately the same age. For the sleep disorders assessment was used Parkinson's diseases sleep scale (PDSS), and Hoehn and Yahr scale (HYS) for the assessment of the stage of the PD.

Among the 60 PD analyzed patients, mean age was 59.6  $\pm$  8.99 (28/46.67% female, and 32/53.33% male). In control group mean age was 60.3  $\pm$ 8.03 (16/53.33% female and 14/46.67% male). Out of all 60 PD patients, 26 (43.33%) of them had sleep distrubances on PDS scale. Most of the patients (43/71.67%) have difficulties staying asleep, while the smallest number of them (4/6.67%) suffered from distressing hallucinations at night. Those with severe form of

PB, (HYS of 4-5 stage), had a high severity of sleep disturbances on PDSS.

Sleep disturbances are the common non-motor symptoms in Parkinson's disease patients (43.33% of the analyzed patients). The most prevalent problem is difficulties staying asleep during the night. Sleep disorders geting worse as the disease progresses.

#### 66. SENSORY FIBERS IN MARTIN-GRUBER ANASTOMOSIS: A CASE REPORT

Zukić S., Sinanović O., Pirić N., Hodžić R., Burina A. University Clinical Center Tuzla, School of Medicine of University Tuzla, Bosnia and Herzegovina

Anatomical variations in the inervation of intrinsic hand muscle are well known, as Martin Gruber anastomosis (MGA). The incidence of MGAs ranges from 5% to 40%, with an average of 17%. Electrophysiological studies demonstrated that anastomosis involves only motor fibers, and that the sensory anastomosis between the median and ulnar nerve in the forearm is a rare occurrence.

We present three cases (two female and one male) of sensory Martin Gruber anastomosis. All three cases were detected during an ongoing study wich included patients with confimed Martin Gruber anastomosis for motor fibers. We performed electroneurographic examinations with surface recording electrodes wich were placed on the right hand thenar and hypothenar. The median and ulnar nerves were stimulated supramaximally at the wrist and at the elbow and compound muscle action potentials (CMAPs) were recorded. When MGA for motor fibers was detected, we also recorded clear sensory responce (SNAP) in the ulnar nerve while stimulating the second digit (wich is inervated by the n. medianus) of the hand. All three cases were of type 3 MGA for motor fibers. Two females had the sensory MGA on the right arm. The male patient had sensory MGA in both arms which would be considered extremely rare.

This study may highlighting the frequency of sensory Martin Gruber anastomosis and its clinical significance. We wish to express our gratitude to the following companies and institutions, who, through their generosity, have helped to make this congress possible:



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