ABSTRACT BOOK

TEACHING COURSES

13th May, Wednesday

Electroencephalography (EEG) in Epilepsy: A Practical Course

USE & ABUSE of EEG

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For Diagnosis and Management of Epilepsy the EEG is indispensable, being the single most specific and reliable clinical test, apart from the clinical history of the patient.

Nevertheless, the EEG is at the same time often underrated as well as overrated as to its true value and clinical significance. Its sensitivity and specificity have been questioned, it's reliability appears insufficient in this era of evidenced based medicine and as a localising test it is by far surpassed by modern Imaging techniques.

At the same time incorrect interpretation of apparent epileptiform EEG phenomena is a frequent cause of incorrect diagnosis of epilepsy with deleterious consequences for the subjects, so diagnosed while insufficient familiarity with non epileptiform EEG phenomena, both interictal and ictal, often results in non-recognition of real epileptic conditions and thus improper withholding of treatment or even misdiagnosis as psychogenic disorders.

The present course is not intended to teach the practical clinical use of the EEG, which takes time and experience, but to stimulate awareness to the intrinsic and extrinsic limitations of EEG in the assessment of epilepsy, to provide insight in how the possibilities of digital EEG can help to overcome some of these and to provide guidance in the way how a proper and orderly approach to the description and analysis of the EEG will help to prevent some of the frequent errors, still associated with the (ab)use of this essentially excellent clinical test.

ADVANTAGES OF DIGITAL EEG. COMPUTED MONTAGES. SOURCE ANALYSIS

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Digital EEG makes it possible to visualise the same event / discharge in different ways, providing complementary information about it. Changing the montages, paper-speed, filters and sensitivity aids in a better, in-depth analysis of the recordings. Computation of the digital data allows construction of montages specifically designed to enhance certain aspects of the recordings. However, these techniques have several draw-backs, and a theoretical knowledge of the used computations is necessary for a correct interpretation of the displayed signals. These topics, in addition to basic aspects of computer-assisted source analysis are covered in the lecture.

EEG INTERPRETATION AND THE EEG REPORT

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EEG represents huge set of data with high complexity. Its evaluation consists of visual interpretation of the recordings by trained specialists. Results of the interpretation are registered as free text in the "EEG report". This should not be exhaustive in describing irrelevant details but should include all the features that may have clinical significance. The free text format has several disadvantages: it leads to huge inter-observer variability, gives way to suboptimal assessment of the recordings and makes it impossible to transfer the results from one laboratory to another and building of multinational database. The structured EEG description format we propose covers all the clinically relevant features of the EEG recordings. It contains pre-defined, internationally accepted terms in choice-menus for the features to be described. It would provide quality-control, and it would help the less experienced clinicians by guiding them through the steps of EEG interpretation. In addition it would make possible the build-up of multinational database.

The important aspects of EEG interpretation and the structured description of the findings will be covered in the lecture.

Electroneuromyography (ENMG): From the Request to the Report

NEUROGRAPHY: SENSORY AND MOTOR CONDUCTION STUDIES

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Electroneurography – techniques and the interpretation of the tests that examine nerve conduction and generation of nerve impulses. The first measurements of motor nerve conduction velocity were done in 1850 by Herman von Helmholtz. Electroneurography is performed by stimulating a sensory, motor or mixed nerve with an electrical impulse while recording electrical activity from nerve or muscle. Sensory and motor conduction studies are essential for the diagnosis of peripheral nervous system diseases. By performing neurography is possible to measure the conduction velocity and record the nerve response in case the sensory neurography and the muscle response in case the motor neurography.

The main purpose of electrophysiological studies are (1) to diagnose diffuse polyneuropathy, (2) to determine whether motor or sensory fibers or both are affected, (3) to localize a focal lesion, (4) to evaluate the severity of a nerve injury, (5) to characterize the underlying pathophysiology – to determine the most likely primary pathological changes (such as axonal degeneration or demyelination). In early stages of neuropathy reduced amplitudes of muscle action potentials and sensory nerve action potentials are sensitive indicators of axonal loss. At later stages of the neuropathy, if the type of neuropathy allows for regeneration of the axons, collateral and/or terminal reinervation may have taken place.

The distinction between axonal loss and demyelination is based on the relationship between conduction velocity and amplitude of the compoud responses. Demyelination is characterized by reduced conduction velocities that cannot be explained by loss of fast conducting fibers – typical for hereditary and aquired polyneuropathies. Demyelination in acute neuropathy may be associated with conduction block too. There are typical patterns of abnormalities in nerve conduction studies in peripheral neuromuscular disorders.

Nerve conduction studies could not give the clinical diagnosis, it provides the essential diagnostic information only together with the history and clinical findings should only be performed if the clinical hypothesis exists.

ELECTROMYOGRAPHY: CONVENTIONAL NEEDLE STUDIES

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Needle electromiography (EMG) is an important stage of patient investigation after clinical examination and electroneurography. Clinical symptoms and ENG findings guide the optimal selection of specific muscles groups and the course of investigation. Needle EMG has three main steps of investigation:

– search of spontaneous activity;

– analysis of motor unit potentials (MUP) evoked by isolated discharges of motor neurons during mild voluntary contraction of the muscle;

– analysis of interference pattern (IP) during maximal contraction of the muscle.

In clinical EMG investigation, activity at rest is usually the first to be assessed. The non-voluntary activity is called spontaneous activity. Some spontaneous discharges may be observed in normal muscle (insertional activity, positive giant potentials, end-plate noise and spikes, "benign" fasciculation potentials, muscle cramps), other are abnormal spontaneous discharges (fibrillation potentials, positive sharp waves, myotonic, myokymic discharges, complex repetitive discharges, fasciculation potentials). Spontaneus activity can be classified also according to site of generation – in the muscle fiber, the nerve or the neuron.

The voluntary activity at low effort is single or small numbers of MUP that can be isolated and assessed individually by measuring a number of distinct parameters. While automated measurements can precisely quantitate many parameters during this investigation, the electromyographer is able to assess that subjectively and can make reliable estimates of findings. A combination of subjective and automated analysis is the most effective approach to clinical EMG.

A strong effort it is large numbers of MUP firing together, called an interference pattern (IP). Assessment of IP is an important part of the electromyographic evaluation. It contains information about recruitment, number and firing rates of MUs, fullness of the pattern and other. In myopathies there is early recruitment, full pattern at full effort and low amplitude. In neuropathy there is late recruitment, reduced pattern at full effort and high amplitude.

Needle EMG findings are interpreted in the light of the patient's history, physical examination, electroneurography and other tests. Three steps of electromyography help categorize motor dysfunction into upper and lower motor neuron disorders and myogenic lesions.

ELECTROMYOGRAPHY: QUANTITATIVE NEEDLE AND SURFACE STUDIES

A. Labarre-Vila
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Quantitative needle and surface EMG have been widely studied but surprisingly are still underused in routine laboratory ENMG laboratories. We have been personally involved in this field for many years, convinced by Buchthal and his school, then Willison, Stalberg, Guiheneuc and other famous EMGers interested in this field who contributed to the development and application of these techniques. Clinical use of those had been allowed by implementation of signal analysis in our EMG equipment. Then, we had been able to evaluate, compare and validate their potential improvement for diagnosis and follow-up studies in neuromuscular diseases. Quantitative needle and surface EMG techniques will be presented, and clinical use discussed.

INVESTIGATION OF THE NEUROMUSCULAR JUNCTION

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Investigation of the neuromuscular junction (NMJ) relies on "repetitive nerve stimulation" (RNS) and "single fiber electromyography" (SFEMG).

These tests are performed in patients who have clinical symptoms and signs suggestive of a NMJ disorder (myasthenia gravis, Lambert-Eaton myasthenic syndrome, botulism, etc.).

RNS studies the changes in size of the compound muscle action potential to repeated stimuli; i. e. the responses of all NMJs of the muscle recorded. In disorders of the NMJ a decrement of the size of the successive responses occurs to low frequencies of stimulation (around 3 Hz) due to failure of transmission of the impulse (blocking) occurring at the level of a number of NMJs. Sensitivity of RNS to disclose myasthenia gravis is around 50%. RNS performed after a short tetanic contraction increases the sensitivity of the test and discloses a marked increment of the CMAP in Lambert-Eaton myasthenic syndrome.

SFEMG studies the variation of the time (jitter) required for NMJ transmission and occurrence of blockings at the level of single NMJs. It is useful to confirm or exclude abnormal NMJ transmission when RNS is normal or equivocal. Sensitivity of SFEMG to disclose a NMJ disorder is close to 100%. However, an increased jitter is not specific of a NMJ disorder, it may also be observed in disorders of the motor nerves and muscle fibers.

LATE NEUROGRAPHIC RESPONSES F, H AND OTHERS

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The late responses F-wave and H-reflex are well known, thus they will just be alluded to.

Late responses, other than F and H, are frequently observed during routine neurographic studies, using surface or needle recordings (Table I). These responses have recently been called "A-waves" by some authors. To understand their origin and meaning simple maneuvers should be performed. Late

neurographic responses are characterized by their: 1) **origin**, proximal or distal to the stimulation site; 2) **position** on the recording, between the M and spinal responses (intermediate latency responses) or later; 3) **latency**, stable or with a jitter; 4) **constancy of occurrence,** evoked by all stimuli (constant), or not (inconstant); 5) **behavior in response to strong stimuli**, remains unchanged, or disappears into the M-wave; 6) **threshold**, evoked for normal, low or high intensities of stimulation; 7) **behavior in response to double stimuli**, disappears, or is evoked twice.

Table I. Late neurographic responses

Indirect responses	Direct responses
H and F-waves	Late potential
Axon reflex	Myo-axonal ephaptic response
Indirect double discharge	Direct double discharge

Determining the origin along the axon defines responses generated proximally to the stimulation site =**indirect responses**, and those generated distally =**direct responses**. Other criteria characterize the responses further (Table II).

Table II. Characteristics of the most frequent late neurographic responses other than F and H

	Late potential (collateral i-m r.)	Late potential (terminal r.)	Motor axon reflex	Indirect double discharge
1) origin	distal = direct		proximal = indirect	
2) position	intermediate	intermediate or >	intermediate or >	intermediate
3) stable latency	+	+	+	– (75%) + (25%)
4) constant occurrence	+	+	+	– (50%) + (50%)
5) strong stimulus shortens latency	–	–	+	–
6) threshold	normal	high	high	low
7) response to S1 **response to S2**	+ +	+ +	+ +	– – / +

r = reinnervation; intermediate = between M and spinal responses; > = longer than spinal latency; S1 and S2 = stimuli of the double stimulation; + = Yes; – = No

Three responses will be discussed in more detail: the **late potential**, the **motor axon reflex** and the **indirect double discharge.** These responses, observed frequently, are interesting in daily routine studies.

The **late potential** relates either to collateral or terminal reinnervation. The **motor axon reflex** relates to terminal reinnervation. Observation of these responses is demonstrative of a prior **axonal disorder**.

The **indirect double discharge** is observed in acute ongoing **myelinic disorder**. They may be observed in a number of normal subjects on the tibial nerve.

The other responses (listed in Table I) are observed less frequently. Their practical interest is limited. They should mainly be distinguished from the four types of responses discussed above.

The study of late responses other than F and H is of daily practical significance, it yields information on single axons and could be called “Single Motor Axon Conduction Studies”.

How to Examine Neurological Patient?

NEUROLOGICAL EXAMINATION: FUNDAMENTALS, GAIT AND PSYCHOLOGICALLY DETERMINED ABNORMALITIES

M. Donaghy
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1. A basic neurological examination

A quick and simple examination will be demonstrated which is sufficient for examining patients with disorders such as uncomplicated headache or epilepsy, or as part of a general medical examination. This basic examination concentrates on manoeuvres that give unequivocal evidence of pathology and avoids repetitive or impressive ways of detecting pathology.

Other tests should be added to this basic examination if the patient’s symptoms suggest a particular disorder, if abnormalities requiring further evaluation are detected during the basic examination, or if one is diagnosing specific abnormalities, such as visual disturbances or a weak limb.

The basic examination should be performed in four stages:

A basic neurological examination

i) During history taking, examine

Speech and cognition
Facial expression
Involuntary movements

ii) Stand the patient up and examine

Gait
Heel-toe walking
Romberg’s Test

iii) With the patient sitting facing you, examine

Cranial Nerves
- Fundoscopy
- Visual fields
- Horizontal Eye movements
- Pupil-Light responses
- Facial sensation
- Facial movements
- Hearing
- Palatal movement
- Tongue movement

The Arms
- Inspection
- Tone
- Power (Shoulder abduction and finger spreading)
- Finger-nose coordination

iv) Lie patient down and examine

Arm reflexes (biceps & triceps)
The Legs
- Inspection
- Ankle clonus
- Power (hip flexion and ankle dorsiflexion)
- Reflexes (knee and ankle)
- Plantar responses

and) Finally, examine additional features suggest by the history or by abnormalities on the basic examination

2. Psychologically determined disorders

Psychologically determined symptoms are common in neurological practice, and may be generated either consciously or unconsciously. In general, it is the severe, disabling and refractory minority of such symptoms and signs which are referred to psychiatrists. The first clue that a patient may be manufacturing their symptoms and signs psychologically comes from noting a discordance in the manner whereby patients describe their symptoms. Relatively trivial symptoms such as tingling may be described in a vivid, florid and exaggerated manner. The physical signs on formal neurological examination of such patients characteristically show fluctuation, or patterns of nervous system involvement which cannot be explained on anatomical grounds. The physical sign complexes most usually determined psychologically are:

• Muscle weakness in which the muscle bulk and reflexes are normal, but there is a markedly fluctuating pattern of power production.

• Sensation. Psychologically determined patches of sensory loss often have implausibly sharply defined boundaries, which shift and do not obey anatomical territories.

• Gait disorders often demonstrate marked fluctuation in severity and may have extremely athletic, or even balletic components.

• Visual loss with tubular or spiralling field abnormalities which do not respect the geometric basis of visual field angle.

• Cognitive impairment, of which the patients seem unusually aware, and with disproportionately affected digit span memory compared to other cognitive tasks.

3. Gait disorders

Inability to walk is a major cause of disability, often leading to falls. Practical analysis of normal gait will be demonstrated with particular attention to the separation of the feet, stride length, foot drop, waddling gait, arm swing, and rising and standing up.

Neurological gait disorders can be considered hierarchically. *Low level gait disorders* are caused by disorders of the skeleton, muscle, peripheral neuropathy or ataxia. Generally patients can compensate for these and remain ambulant.

Middle level disorders are due to disease of the pyramidal tract, basal ganglia, or severe cerebellar ataxia. Except when severe, patients can usually compensate for these disorders and remain ambulant.

High level gait disorders are poorly understood, often referred to as gait apraxias, and are due to damaged frontal lobe mechanisms leading to poorly organised posture, stepping, and gait ignition.

PLENARY LECTURES ORAL PRESENTATIONS

14th May, Thursday

Cerebrovascular disorders (Plenary Lectures)

THROMBOLYSIS: HOW HAS IT CHANGED ACUTE STROKE CARE?

Markku Kaste
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Size Of The Problem

One of three people will suffer a stroke, become demented, or both. About one million Europeans suffer stroke annually and stroke causes a greater loss of quality-adjusted life years than any other disease. It incurs a heavy economic burden to health care and social welfare. Due to the change in the age structure of populations the number of new strokes is predicted to double in the next few decades. The majority of patients who have suffered a stroke have trouble in speaking, walking, using a hand or seeing. Increasing number of strokes will cause both human and economic nightmare if we are not able to treat stroke patients better in the future than we do today.

Nihilism, An Old Obstacle For Good Care Of All Stroke Patients

One major reason for the size of the problems incurred by stroke being so huge is nihilism that nothing can be done in acute stroke, so why even try. Only a few other ideas in medicine are so inappropriate. How can this nihilism be eliminated; is there evidence such as thrombolysis in acute ischaemic stroke that will make a difference?

Stroke Thrombolysis

Thrombolysis with recombinant tissue plasminogen activator (rt-PA, alteplase) is safe and effective treatment for selected patients with acute ischaemic stroke within a 4.5-hour time window. Thrombolysis in stroke is more effective than thrombolysis in acute myocardial infarction when inclusion and exclusion criteria of the treatment are followed. The Safety Implementation of Thrombolysis in Stroke - MOnitoring STudy (SITS-MOST) verified that alteplase has the same safety and efficacy profile in clinical routine as in randomised clinical trials (RCTs). ECASS III verified that thrombolysis is safe and effective up to 4.5 hours. The results of the Safe Implementation of Thrombolysis in Stroke – International Stroke Thrombolysis Register (SITS-ISTR) revealed that thrombolysis as a part of routine clinical care is as safe and effective up to 4.5 hours as ECASS III and also the pooled analysis of RCTs had suggested. Based on the SITS registers the neurological emergency room of Helsinki University Central Hospital provides more stroke thrombolysis than any other European hospital and has the shortest door to needle time. According to the SITS registers more stroke patients per million inhabitants receive thrombolysis in Finland than in any other EU member country. This example shows that it is possible to provide thrombolysis for stroke patients nationwide. However, stroke thrombolysis asks for a well-organised service, which is widely missing.

Organisation Of Stroke Services

Stroke occurs acutely, is time-sensitive and requires well-organised services. A well-organised multidisciplinary ap-

proach to stroke care, the chain of recovery, includes emergency call centre (112), stroke triages, emergency medical services (EMS), emergency rooms (ER), stroke units (SU), rehabilitation hospitals and community health care. The chain is only as strong as its weakest part. All parts of such a chain must fit and work seamlessly together.

Emergency Medical Services (Ems)

Emergency call centre identifies a potential stroke patient and dispatches an ambulance staffed by personnel trained to identify and treat stroke patients. The ambulance personnel (paramedics) identify the stroke patient, ensure his/her vital functions and transport the patient quickly to the nearest hospital with appropriate resources for acute stroke management. The medical history of the patient determines whether he/she is eligible for thrombolysis in which case the patient must be transferred to an ER or to a SU where thrombolysis is available. The paramedics send a pre-hospital notification to the ER or SU to ensure rapid evaluation of the patient.

Emergency Room (Er)

Clinical assessment to establish the diagnosis of stroke must take place immediately after admission. Acute emergency management of stroke patients requires parallel processes at different levels including further stabilisation of vital functions, diagnostic work-up, treatment of acute life-threatening conditions, concomitant diseases and severe abnormalities of basic physiological functions, and specific treatments including thrombolysis when appropriate. Symptoms and signs, which may predict complications such as space occupying infarction or bleeding, co-existing acute myocardial infarction, aspiration pneumonia, and renal and liver failure, must be recognised early. All patients with suspected stroke require immediate brain imaging to distinguish between ischaemic brain infarction, spontaneous intracerebral haemorrhage and subarachnoid haemorrhage, and to identify diagnoses other than stroke.

Stroke Unit (SU)

Thrombolysis suits for selected patients. In well-organised services 15–16% of all acute ischaemic stroke patients and 30–40% of those arriving within a 3-hour time window receive it while stroke unit care suits for all stroke patients.

Stroke unit care is the only type of stroke management besides thrombolysis which has been shown to improve the outcome of acute stroke patients. Stroke unit treatment reduces death, dependency and need for institutional care. According to the Stroke Unit Trialists Collaboration stroke unit care reduces short-term relative risk of death and dependency by 18% when compared to care at a general medical ward. Elderly patients and those with severe stroke benefit most of stroke unit care and the beneficial effects are present at 10-year follow-up. In spite of its effectiveness stroke unit care has been underused throughout Europe. Only 13–14% of patients with acute stroke in Europe are treated in stroke units while 42% are treated in hospitals without expertise and facilities for acute stroke care. After thrombolysis became available, a growing number of European hospitals have started to organise their services and establish stroke units. In this respect thrombolysis made a difference for all stroke patients. A Finnish database, which covers all strokes in the whole population of Finland, reveals that stroke unit care reduces case fatality and need for institutional care. More patients can continue to live in their own homes and suffer less often recurrent strokes or myocardial infarctions. Accordingly, it is best for the patients and for the society.

Conclusions

Stroke thrombolysis has changed the way stroke is viewed and treated. Old nihilism that nothing can be done has been replaced by optimism that stroke can be treated and that it is possible to recover from stroke back to independent life at home.

PROGRESS WITH REPERFUSION THERAPIES FOR STROKE

A. V. Alexandrov

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Systemic tissue plasminogen activator (tPA) remains the only approved therapy and the fastest way to initiate treatment for acute ischemic stroke. ECASS 3 and STR-SITS-MOST data now provide evidence that tPA can be safely and effectively given in up to 4.5 hours from symptom onset and within conventional 3 hour window by centers novel to thrombolytic therapy. European and US regulatory decision are pending for tPA approval in 3–4.5 hour extended window.

The presence of a proximal arterial occlusion should not be viewed as an un-surmountable predictor of tPA failure, and early augmentation of fibrinolysis to improve recanalization can be safely achieved at bedside with diagnostic Doppler ultrasound. In CLOTBUST trial, 83% of patients achieved any recanalization (46% complete, 27% partial) with tPA+transcranial Doppler vs 50% (17% complete, 33% partial) with tPA alone within 2 hours of treatment, $p<0.001$. Sustained complete recanalization at 2 hours was 38% vs 13% respectively, $p=0.03$.

Catheter-based ultrasound delivery to arterial thrombi and intra-ventricular clots is subject of ongoing clinical trials. Addition of gaseous perflutren-lipid microspheres to tPA and transcranial Doppler can further facilitate early flow improvement with >50% rate of early complete recanalization and the recently completed multi-center international TUCSON trial showed a safe dose of micro-spheres that can be combined with systemic t-PA (data will be shown at the conference). Transcranial ultrasound delivery in an operator-independent and dose-controlled manner is being tested in a clinical trial.

INTRACRANIAL FLOW AUGMENTATION IN PATIENTS WITH PERSISTING OCCLUSIONS

Anne W. Alexandrov

Acute treatment is not available for ischemic strokes that arrive outside the window for intravenous tPA and/or intra-arterial rescue procedures. Methods capable of improving perfusion may be beneficial in these patients when brain tissue is still viable. External counterpulsation (ECP) is a system consisting of cuffs that are wrapped around the lower extremities and connected to an inflation system. The unit is triggered by the patient's ECG to inflate in ventricular diastole and deflate just prior to the next ventricular contraction. ECP is approved for use in patients with multi-vessel coronary artery disease and congestive heart failure, and has been shown to increase functional status, myocardial perfusion, nitric oxide release and angiogenesis. Use of ECP may hold promise as a therapy to improve brain perfusion in patients unable to receive reperfusion therapies. Our team has studied transcranial Doppler (TCD) waveform morphology in patients receiving ECP to enable measurement of real-time changes in blood flow velocities induced by the device. Peak diastolic augmented velocity increased on average by almost 200% in normal controls receiving ECP, with an overall increase in mean flow velocity averaging 125% above baseline. We have also shown that ECP is feasible, and appears to be safe as a potential treatment for ischemic stroke. Even when performed in patients that were on average 14 days out from the index stroke event, ECP was capable of producing a reduction of neurological deficits measured by the National Institutes of Health Stroke Scale (NIHSS). Our current work focuses on determining the optimal "dose" of ECP in the acute treatment of ischemic stroke, and examining feasibility and safety of ECP treatment in patients with transient ischemic attack (TIA) due to extensive

intracranial atherosclerosis. This session will review our methods and findings, as well as contrast ECP use to other existing methods available for augmentation of intracranial blood flow.

STROKE REHABILITATION AND TRANSLATIONAL NEUROSCIENCE

M. Nilsson

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Experimental and clinical studies have demonstrated that the central nervous system (CNS) has the potential to structurally and functionally recover after stroke and other types of acquired brain injury. A key challenge for the future is to elucidate the underlying mechanisms of spontaneous and stimulated functional recovery and to use them in novel neurorehabilitation strategies in the clinical settings. Animal studies have so far provided some important information about the cellular mechanisms involved in the recovery processes. Human studies based on e.g. brain mapping have demonstrated strong mechanistic similarities with the experimental studies. Functional recovery after stroke is dependent on the plasticity of both the cerebral cortex and unaffected parts of functional neuronal and astrocyte network. Neural plasticity is an intrinsic property that enables the mammalian brain to adapt to environmental changes during development and adulthood. The brain is responsive to environmental stimuli, physiological modifications, and experiences and its structure can be altered by experience in several measurable ways. To maximize the effectiveness of rehabilitation therapies after stroke, it is critical to determine how the brain responds to different types of stimuli. Extensive research in recent years has demonstrated that various forms of multimodal stimulation (stimulation of different senses), or environmental enrichment, promote brain plasticity. Enriched environment involves various types of stimulation, including social interactions and physical activities, and could therefore be a powerful tool to prevent cognitive decline during normal aging as well as to facilitate brain tissue repair and functional recovery following brain injury and malfunction. Sensory stimulation through various cultural activities, such as music and dancing, is an important component of enriched environment for humans. Through experience, we know that influence from culture is profound, although sometimes not well understood or even fully perceived. Despite experimental achievements and increasing amount of clinical experience in this area, the overall knowledge on this subject is still limited. The current presentation will include a discussion around the underlying mechanisms through which enriched environment and cultural stimulation induce brain plasticity and possible implications for stroke rehabilitation.

Cerebrovascular disorders (Oral Presentations)

KNOWLEDGE OF RISK FACTORS AND SYMPTOMS OF STROKE IN ESTONIA

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Background: Due to high mortality and chronic disability, the global burden of stroke is greater than that of heart disease. The outcome of stroke can be improved by effective therapies, including intravenous (iv) thrombolysis within 4.5 hours of onset of ischemic stroke. One of the most important reasons that patients are not treated with iv thrombolysis is that they do not attend hospital within the treatment time window. Late arrival to the hospital could be the result of poor appreciation of stroke warning signs by the patient and relatives. The current study was undertaken to assess the knowledge of stroke risk factors and symptoms among the Estonian population.

Methods: The study was conducted from October 2008 to February 2009 as face-to-face interview in streets, shopping malls, at schools or other public places in Estonia by first-year medical students. A simple closed-ended questionnaire was used. The items of the multiple-choice questionnaire were: what kind of disease is stroke?, what are the warning signs of stroke?, what are the stroke risk factors?, which action need to be taken at onset of stroke symptoms?.

Results: Three hundred and fifty five persons filled in the questionnaire, 31% of them were men and 69% were women. The mean age of respondents was 39.6 (±21.2) years for men and 40.6 (±19.7) years for women. The study was conducted in two big cities (Tallinn, n=122 and Tartu, n=228, missing place of residence n=5). Eighty five percent of respondents answered correctly that stroke is an acute disease. However, 41.7% of respondents thought that dyspnea is a stroke symptom and 44.8% that drinking coffee is a stroke risk factor. Most of the respondents (99%) knew that one should call the ambulance at onset of stroke, although 32.7% would also call to a friend or a relative.

The knowledge about stroke was without differences between the sexes. Higher level of education was related to higher and younger age with lower level of stroke awareness. The best results were obtained by persons around 40–60 years.

Conclusion: Knowledge about stroke symptoms and risk factors was better among middle-aged persons and for those with higher education. Although most of the respondents were aware that ambulance must be called immediately at onset of stroke, several questions about stroke were answered incorrectly both by the younger and older respondents. Therefore, stroke awareness campaigns are still needed to address this knowledge gap in Estonia.

INTRAVENOUS THROMBOLYSIS WITHIN 3–4.5 HOURS FOR ACUTE ISCHEMIC STROKE IN LITHUANIA

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Background: The recent studies showed that intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator (rt-PA) is safe and still effective for patients with acute ischemic stroke within 3–4.5 hours, but it has not yet been approved in daily clinical practice. The aim of the study is to evaluate the efficacy and safety of rt-PA IVT within 3–4.5 hours for acute ischemic stroke patients in Lithuania.

Materials, methods: This is an observational open study. The consecutive patients with acute ischemic stroke who received IVT in Vilnius University Emergency Hospital and Vilnius University Hospital Santariškių Clinics during 2002–2008 were included. According to time from onset of stroke to start of

thrombolysis all patients were divided into 2 groups: 0–180 and 181–270 min. The primary end-point was disability at day 90 by modified Rankin scale (favourable outcome: 0–1 point, unfavourable outcome: 2–6 points). Safety endpoints included the mortality and symptomatic intracerebral hemorrhage (sICH). sICH was defined as parenchimal hemorrhage type 2 associated with neurological deterioration 4 points by NIHSS scale.

Results: We reviewed data of 111 patients who received rt-PA IVT for acute ischemic stroke since 2002. Results of follow-up and clinical outcome after 3 months were available for 88 patients. They were selected for final analysis of efficacy. 72 patients (81.8%) received IVT within 0–180 min, and 16 patients (18.2%) – within 181–270 min. The baseline characteristics and clinical signs were similar in both groups. At day 90 after IVT favourable outcome was documented for 23 patients in the 0–180 group, and for 16 patients – in 181–270 group (31.9% vs. 37.5%, p=0.67, respectively). Safety analysis included mortality and sICH of all 111 patients. The mortality was higher in the first group, but it was not statistically significant (18.1% vs. 0%, p=0.11). The sICH rate was similar in both groups (1.4% vs. 0%, p=1).

Conclusions: The IVT is still effective and safe treatment option within 3–4.5 h after onset of ischemic stroke. The extension of time-window for rt-PA thrombolysis in selected patients may help to implement IVT for urgent therapy of acute ischemic stroke in Lithuania.

OUTCOME PREDICTORS OF DECOMPRESSIVE SURGERY IN MALIGNANT INFARCTION

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Background: Malignant infarction of the middle cerebral artery (MCA) is characterised by a severe course and extremely high mortality rate. Randomised controlled trials (DECIMAL, DESTINY) proved mortality reduction and increase of favourable functional outcome in early decompressive surgery. However, factors predicting functional outcome are not well defined.

Objective: To identify prognostic factors on outcome of decompressive surgery in malignant MCA infarction.

Methods: It was the retrospective hospital based study, including 18 patients treated with decompressive surgery due to the malignant MCA infarction. There were 10 female and 8 male patients, mean age 62.2 ± 8.2 years. Information about patient's survival and functional state was collected from telephone conversation with patient's relatives. Functional outcome, assessed by modified Rankin Scale (mRS) on discharge, half-year and 1 year after operation, was divided between favourable (scores 0–4) and unfavourable (5 and death). To compare means of clinical and laboratory variables between two groups we used: Student t, x^2 Fisher's test. To find out association between some variables we used Pearson's correlation coefficient (r).

Results: 1 year survival after decompressive surgery in patients with malignant infarction of the MCA is 50%. According to 1 year mRS evaluation the mean time from stroke onset to malignant manifestation was 63.6 h in favourable and 24.9 h in unfavourable group (p=0.001); post-operative (24 h) Glasgow Coma Scale (GCS) score was higher in favourable group (p=0.033). Patients with malignant manifestation after 48 hours from stroke onset had statistically longer 1 year survival and better functional outcome (p<0.003). A significant correlation was noted between preoperative fibrinogen concentration and mRS on discharge (r=-0.522, p=0.031).

Conclusions: Slower malignant manifestation (>48 hours), higher post-operative GCS score on 24th hour and higher preoperative fibrinogen concentration suggest the better outcome in patients after decompressive surgery for malignant infarction of MCA. These factors may be important in predicting the outcome of these patients.

ADAPTATION AND TESTING OF THE LITHUANIAN MIGRAINE DISABILITY ASSESSMENT QUESTIONNAIRE

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Background: Migraine is a common neurological disorder with high levels of pain and disability, but it remains under-diagnosed and under-treated. Original Migraine Disability Assessment (MIDAS) questionnaire is reliable and valid instrument to determine the degree of migraine-related disability, to improve patient-physician communication, and to identify patients with high treatment needs.

Objective: To perform cross-cultural adaptation of the MIDAS and to test reliability and validity of the Lithuanian version (MIDAS-LT). To assess migraine disability using MIDAS-LT in two separate groups of patients: migraine without (M0) and with aura (MA).

Materials and methods: Cross-cultural adaptation of questionnaire for Lithuanian speaking population was performed following International Society for Pharmacoeconomics and Outcomes Research recommendations. Psychometric properties were tested on Vilnius university hospital Santariškių clinics out-patients with one or more migraine attacks during the year. Internal consistency and test-retest reliability was assessed in two weeks after initial evaluation. Construct validity was evaluated using 90-day headache diary and validated Lithuanian SF-36v2.

Results: 145 participants (mean age 36.04±10.02; 80.7% females and 19.3% males; 82 M0 and 63 MA patients) were involved in the study. 55.2% of them had migraine diagnosis in their medical records. 33.1% migraineurs used specific abortive treatment for their attacks, 16.5% patients were taking prophylactic medications. MIDAS-LT demonstrated acceptable internal consistency (Cronbach alpha 0.81 [95% CI; 0.76 – 0.85], item total correlations 0.36 – 0.83), and test-retest reliability (interclass correlation coefficient 0.90 [95% CI; 0.82 – 0.94]). Correlations for all constructed hypothesis according headache diary data and SF-36v2 assessment were significant (p < 0.001). Total MIDAS-LT scores were higher in M0 group (23.21 vs. 13.43, p = 0.007) though there were no significant differences of age, headache frequency (MIDAS A), intensity (MIDAS B), acute and prophylactic medication use between M0 and MA patients. 65.8% M0 and 49.2% MA patients had high level of disability (MIDAS-LT grade III and IV).

Conclusions: MIDAS-LT can be used as instrument for migraine disability assessment in Lithuanian speaking population. Questionnaire provides valuable subjective information about migraine impact and severity.

CHRONIC PAIN IN LATVIA

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Chronic pain is common worldwide in Europe seriously affecting daily activities, social and working life of sufferers. It is problem in Latvia too, but was not studied previously.

The computer-assisted telephone survey was undertaken during March–April 2008 to explore the prevalence, severity, treatment and impact of chronic pain on the quality of life of sufferers in Latvia. Screening interviews for representative sample of 2005 adult respondents assessed prevalence, demographics and characteristics of chronic pain. 207 respondents who fulfilled the screening criteria and who agreed to participate were then interviewed further.

19% from 2005 respondents had suffered from moderate to severe pain (> 5 on NRS) for > 6 months, had experienced it in the last month and several times during the last week. In-depth interviews showed: 68% respondents had moderate pain, 32% – severe; 62% were in pain for 5 to 20 years, on average – 10,5; 12% had been diagnosed with depression because of their pain; 25% had even suicidal thoughts; 63% were less able or unable to work outside the home; 13% had lost and 15% changed their jobs. 39% visited doctor 2–9 times in the last six months, only 1% of respondents were evaluated using pain scales. 29% of chronic pain sufferers were currently not being treated, 77% used non-medication treatment, e. g., ointments, gels (38%), massage (23%), vitamins (14%), physical therapy (13%). 58% were taking non-prescription analgesics (ibuprofen 68%, combined medications 17%, paracetamol 16%) and 81% – prescription medicines, e. g., NSAID (72%), nenarcotic analgesics (15%), antiepileptics (10%), weak opioids (9%). 47% showed inadequate pain management.

Chronic pain is widespread in Latvia, seriously affecting the quality of life. The obtained results demonstrate quite alike situation as in Europe, dominance of more negative aspects is higher in Latvia. Overall results demonstrate that despite the pain and inadequate mangement chronic pain sufferers have accepted their pain as a part of their life.

DEEP PRESSURE PAIN THRESHOLD EVALUATION FOR DEEP PAIN DIFFERENTIATION

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This study aimed to compare and evaluate affordable and easy to use diagnostic tools for quantitative evaluation and differentiation of deep pressure pain, and to determine the differences of life quality among patient groups with diabetic neuropathy.

Methods: Altogether, 25 patients with DM were included into this study. Of all patients, 14 (56%) were men and 11 (44%) – women. Mean age of the patients was 46.16 ± 14.06 years. Three patient groups were formed: patients with painful diabetic neuropathy (PDN, n = 9), patients with painful diabetic neuropathy and intermittent vascular claudication (PDNIC, n = 7), and patients with non-painful diabetic neuropathy (NPDN, n = 9). Deep pressure pain threshold was evaluated with hand-held algometer and with sphygmomanometer. The blood flow was evaluated by calculating toe-brachial and ankle-brachial pressure indexes. Neuropathy was evaluated by sensory tests (brush, cotton, 10 g monofilament for superficial senses; 125 Hz camertone for deep senses) and motor function (strength, reflexes). The quality of life was evaluated using SF – 36 scale, depression and anxiety – using HAD scale. Neuropathic pain properties were evaluated by neuropathic pain questionnaire (NPQ) and by neuropathic pain symptom inventory (NPSI). Patient groups were compared using nonparametric Mann- Whitey criteria. Data were processed using SPSS – 8.

Results: No statistically significant differences were detected in deep pressure pain threshold assessed both by sphygmomanometer and hand held algometer between three patient groups. In patients with PDNIC, physical activity was significantly more bound and deep pressure pain was more severe compared to patients with PDN (0.017). In patient groups with pain, neuropathy symptoms were more expressed, and physical health and social functioning were more constraint compared to NPDN patients. Depression symptoms were more pronounced in patients with PDN as well as emotional functioning was worse compared to NPDN patients.

Conclusion: Deep pressure pain threshold assessment using both sphygmomanometer and hand held algometer did not allow differentiate between patients with PDN, PDNIC and NPDN. Quality of life was worse in patients with painful neuropathy compared to those without pain.

Headache / Pain (Plenary Lectures)

THE IMPACT AND COMORBIDITY OF HEADACHE

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In most societies, the impact of headache disorders on the public health is usually underestimated, and headache patients and health-care providers have felt that there is a stark discrepancy between the need of headache sufferers and the resources provided for treatment and research. To correct this inequity, several initiatives have been launched to collect scientific evidence on the burden and cost of headache disorders.

"Lifting The Burden (LTB): The global campaign to reduce the burden of headache worldwide" is supported by the World Health Organisation, the International Headache Society, the European Headache Federation, and the World Headache Alliance. In 2007, LTB published a report showing that almost 50% of the world's population suffered from headache during one year, 40% from tension-type headache (TTH), 11% from migraine, and 3–4% from "chronic headache". Although migraine is definitely most incapacitating for the individual, it appeared that on a societal level TTH was more burdensome because of the much higher prevalence.

In 2005, a report by the European Brain Council showed that there were 46 million migraine patients in Europe (25 EU members and Switzerland, Norway and Iceland), costing around 46 billion € in 2004. Cost estimates for TTH could not be made due to lack of scientific studies, but migraine alone

proved to be the most costly of all the Neurological disorders, more than stroke, parkinsonism and multiple sclerosis. Most of the costs were indirect costs, i. e. due to work absence. Even relatively expensive migraine drugs are hugely cost effective if they can reduce work absence.

"Eurolight" is a project supported by the EU, aiming to fill in gaps in the knowledge about the headache prevalence and burden in Europe, and to raise awareness that headache is an important public health issue, in order to promote a beneficial change for all headache patients.

Headache, and migraine in particular, has been found to be comorbid with pain in other parts of the body, and also psychiatric disorders like depression and anxiety. There is also comorbidity to gastrointestinal complaints, stroke, obesity, and asthma. The nature of the association between these disorders and headaches is probably complex and varied, and in general, it is difficult to establish causal relations between the disorders. Comorbidities may contribute to the burden of headaches, they are important for an optimal handling of headache patients, and ultimately they may shed light on the pathophysiology of headaches.

IS MIGRAINE A PROGRESSIVE BRAIN DISORDER?

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By definition, progressive brain disorders are characterised by an irreversible increase over time, and thus with age, of the clinical disability and/or the lesion load due to the disorder in all or subgroups of affected subjects. It is, for instance, undisputable, that neurodegenerative disorders like Alzheimer or Parkinson disease belong to this category and that lesion load as well as disability steadily increase with time in the progressive forms of MS, and that lesion load in the brain may increase in uncontrolled hypertension for some time before occurrence of neurological symptoms.

It suffices to examine the prevalence rates of migraine with increasing age to be convinced that, globally taken, migraine is a self-limiting disorder of which prevalence decreases markedly after the age of 50. The reassuring finding that migraine has no negative impact on cognitive functions in the elderly (Gaist et al. 2005; Kalaydjian et al. 2007) also suggests that overall does not induce clinically significant brain lesions even after a long disease course. In recent years, however, it has become clear in subgroups of migraineurs that the disorder can transform from an episodic form into a chronic one, that brain lesions appear on MRI scans and that the risk for ischemic stroke is increased. We will examine the facts and fancies of these 3 findings.

Risk factors for transformation into chronic migraine (15 headache days per month with 8 headache days fulfilling the criteria for migraine) are high attack frequency, psychiatric co-morbidity, obesity, caffeine overuse and, for up to 80% of subjects, acute medication overuse (Bigal & Lipton 2008). The latter is a well known chronifying factor for most headache types and gives rise to so-called "medication overuse headache". It is reversible by withdrawal of the acute drugs and adequate preventive treatment, but not in all patients (Zeeberg et al. 2006). Medication overuse headache is likely to occur in genetically predisposed subjects (Radat et al. 2007; Cevoli et al. 2009) and may have as a brain correlate hypofunction of the medial orbito-frontal cortex (Fumal et al. 2006). Chronic migraine is not irreversible (Scher et al. 2003).

An increased incidence of deep white matter lesions has been found on MRI in migraineurs (Swartz et al. 2004). The Dutch CAMERA study where thin MRI slices were analysed found no difference in the number of white matter lesions between migraineurs and controls, but the "load" of lesions (thus their size) was increased in migraine patients, especially in females (n=7) with >1 attack/month (Kruit et al. 2004, 2005). In the same study, small T1 hypo-intense lesions, supposed to be infarcts, were found in greater numbers in the cerebellum. However, such lesions were present in only 13 migraine with aura patients out of 161, compared to 3/134 migraine without aura and 1/140 controls. Moreover, these findings have not been replicated yet and similar MRI lesions were found to reversible in a case report (Rozen 2007). Analyzing a subgroup of migraine subjects from the previous studies, Kruit et al (2009) recently reported that iron content of putamen, periaqueductal gray matter and red nucleus was not different from controls in the total cohort of migraineurs, but that it was increased in subjects younger than 50 in proportion to the duration of the disease. Whether this is an epiphenomenon of repeated activation of centres involved in head pain processing or eventually a causally related factor in migraine remains to be determined. The fact that iron deposition does not differ significantly between episodic and chronic migraineurs (Welch et al. 2001) is not in favour of the latter assumption. Both increased (sensorimotor cortex – Da Silva et al. 2007; visual areas – Granziera et al. 2007) and decreased (cingulate gyrus – Valfré et al. 2007, Schmidt-Wilcke et al. 2008) gray matter densities have been reported with VBM in migraine. Most of these changes are likely to be secondary to repeated activation of cortical areas and possibly reversible.

Finally, several large epidemiological surveys have confirmed that migraine with aura is an independent risk factor for ischemic stroke, but only in females below the age of 55 in whom migraine also increases the risk for myocardial infarct (see review by Kurth et al. 2007). The role of persistent foramen ovale in migraine with aura, where it is clearly more prevalent, remains to be determined. PFO does not account for the increase in white matter lesions (Shalchian et al. 2009).

In conclusion, migraine is overall a benign self-limiting disorder. It may become chronic because of various factors among which acute medication overuse is the most prevalent. Migraine with aura is associated with a slightly increased risk for brain MRI lesions which seemingly do not favour cognitive decline and the precise nature of which remains to be determined. Migraine with aura is undoubtedly a risk factor for ischemic stroke in young women in whom estrogen-containing contraceptive pills should be avoided and smoking forbidden.

FINDING NEW DRUG TARGETS FOR THE TREATMENT OF MIGRAINE

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No new preventive drugs specific to migraine have appeared for the last 20 years and existing acute therapies need improvement. Unfortunately, no animal models can predict the efficacy of new therapies for migraine. Because migraine attacks are fully reversible and can be aborted by therapy, the headache or migraine provoking property of naturally occurring signalling molecules can be tested in a human model. This model has predicted efficacy of nitric oxide synthase inhibition and calcitonin gene-related peptide receptor blockade. The pharmaceutical industry should pay more attention to human models although methods are different from normal target validation.

NEUROPATHIC PAIN: ITS MANIFESTATIONS AND MANAGEMENT

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Neuronal hyperexcitability is a key feature in neuropathic pain conditions. The manifestations of such hyperexcitability include spontaneous discharges in nociceptors, sensitisation of second order neurons in the dorsal horn of the spinal cord, recruitment of silent nociceptors, expansion of receptive fields, and reorganisation of central projections in the brain. The clinical translation of this array of neuronal events is only partly understood. Pain within a damaged nerve territory, lowered pain threshold, pain induced by non-noxious stimuli, extraterritorial spread of pain, and sensory abnormalities are presumed reflections of such neuronal hyperexcitability after nerve injury. The clinical presentation of patients with peripheral and central neuropathic pain will be described.

The neuronal hyperexcitability has either a peripheral or central component or a combination of such mechanisms. In certain conditions it is possible to demonstrate sensitisation of nociceptors, and in other conditions the sensitisation is more likely to be central. The use of various blocks or a combination of quantitative sensory testing with pharmacological modulation of neuropathic pain may in some cases be useful and aid in distinguishing between peripheral and central sensitisation. Treatment of neuropathic pain is difficult, but the discovery of new molecular targets involved in the development and maintenance of hyperexcitability has created new optimism in new and more specific treatments for pain. The classical targets for neuropathic pain are the mu opioid receptor, sodium channels, calcium channels, and the monoaminergic transport systems. A review of the existing treatment for neuropathic pain will be provided. More recently, this list has been expanded with selective sodium channel blockers, K channel openers, growth factors, BH4 synthesis modifiers, signal transduction and transcription factors acting peripherally. Central use-dependent calcium channel blockers, substances inhibiting signal transduction, microglial activation or prevent apoptosis are also potential candidates to reduce neuropathic pain.

COMPLEX REGIONAL PAIN SYNDROMES

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Formerly known by many names, such as reflex sympathetic dystrophy and causalgia, the new diagnostic entity, complex regional pain syndrome (CRPS), was first introduced in 1994. The diagnostic criteria of this painful disorder were codified by the International Association for the Study of Pain (IASP) in the same year. The original criteria have since been revised and other proposals at consensus meetings have been proposed. The difficulties in classification reflect the challenges which are met in treatment and management of this disabling condition.

According to the current, IASP-approved criteria CRPS can be diagnosed based on the presence of the following symptoms and signs:

1) Continuing pain, which is disproportionate to any inciting event

2) Patient must report at least one symptom in three of the four following categories

hyperalgesia, hyperesthesia
skin temperature asymmetry, skin color change or asymmetry
sweating asymmetry, edema
decreased range of motion, dystonia, tremor, weakness, trophic changes of hairs or nails

3) Patient must display at least one sign at time of evaluation in two of the four following categories

pinprick hyperalgesia, brush-evoked pain, hyperalgesia/allodynia to deep somatic pressure
skin temperature asymmetry, skin color change or asymmetry
sweating asymmetry, edema
decreased range of motion, dystonia, tremor, weakness, trophic changes of hairs or nails

4) There is no other diagnosis that better explains the signs and symptoms

CRPS is traditionally differentiated into two groups, CRPS I and CRPS II. The diagnosis of CRPS II requires presence of evidence of peripheral nerve injury, whereas CRPS I does not. Both types look clinically very similar. Dutch CRPS researchers have suggested another kind of classification, which reflects differences in skin temperature and pathophysiology. The two clinical subgroups in this classification are “primarily warm” type and “primarily cold” type.

The list of inciting events associated with development of CRPS is long. The most common causes are fractures, sprains, arthritis and soft tissue injuries. Severity of the physical injury is not related to the risk of CRPS; even minor traumas have been reported to incite this condition. CRPS can also be provoked by disease states such as stroke, vasculitis, myocardial infarction, herpes zoster and deep venous thrombosis. Spontaneous CRPS is rare, but does occur.

According to the current view, several distinct pathogenic mechanisms underlying CRPS are of importance. In CRPS, both autonomic and somatic nervous systems are affected, and in addition, inflammation, hypoxia, genetic and psychological factors each give their contribution to the cascade of events and development of chronic pain state.

Management of CRPS is challenging and most of the current treatment strategies are still lacking efficacy. Combining drug therapy with physiotherapy (especially mirror therapy) and in selected cases with invasive procedures (spinal cord stimulation) and multi-professional team approach usually brings the best results.

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15 May, Friday

Movement Disorders / Dementia (Plenary Lectures)

TREATMENT OF ADVANCED LATE STAGE PD.

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L-dopa combined with a dopa decarboxylase inhibitor is a highly efficacious symptomatic treatment for Parkinson's disease, which improves motor handicap, quality of life and increases life expectancy by about 5 years. Orally active dopamine agonists, selective type B monoamine oxidase, COMT inhibitors, amantidine and anticholinergic drugs are also useful adjuvant medications which may help to augment the therapeutic response and counteract l-dopa provoked motor fluctuations and dyskinesias. Despite these advances many patients start to escape from optimum control after 5–15 years of sustained therapy with the emergence of the on-off syndrome, speech and swallowing difficulties and motor freezing with falls. There is also a five-fold increase in cognitive impairment in elderly patients with Parkinson's disease and many of these individuals also have visual hallucinations, daytime somnolence and delirium presenting major therapeutic challenges.

Three effective options are now available for the management of refractory motor fluctuations but these are not yet available in all countries. The cheapest and least invasive is the use of the waking day subcutaneous apomorphine pump, which can reduce off period disability by more than 50% and reduce dyskinesias. About half the patients on this treatment are able to withdraw gradually all oral anti-Parkinsonian medication except for a nocturnal and early morning dose of l-dopa. Similar results can be achieved by enteral dopa administration (Duodopa) administered through a gastro- jejunostomy. Deep brain stimulation of the subthalamic nuclei is a further highly effective approach for the long-term levodopa syndrome and may also permit a marked reduction in oral anti Parkinsonian medication. Each of these treatments has its advantages and draw backs which in centres where all three options are available should be discussed fully with the patient in order to inform decision making. Clozapine is the most effective anti-psychotic drug available but it should be used sparingly and in low doses to control paranoid psychoses and behavioural disorders. Cholinomimetics can be very effective in some patients with daytime sleepiness, visual hallucinations and amnesia but are ineffective in others.

Physical therapies can be of great help in minimising falls and alleviating start hesitation and motor blocking and pedunculopontine nucleus stimulation is undergoing evaluation in severe cases. Cell based therapies and gene therapy using viral vectors remain valid research strategies and it is hoped that our greater understanding of the cell biology of the proteins linked with genetic mutations in monogenetic Parkinsonism will lead to better early treatments for Parkinson's disease.

GENETICS OF PARKINSON'S DISEASE: RECENT ADVANCES

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Parkinson disease is the second most common neurodegenerative disorder with an overall prevalence of approximately 1.8% of the population over the age of 65 years. Most cases of Parkinson disease are thought to result from the effects of multiple genes as well as environmental risk factors. The genetic cause for some forms of Parkinson disease has been identified using linkage analysis followed by positional cloning in families having earlier age of disease onset and either autosomal dominant or autosomal recessive inheritance. Twelve loci are now associated with highly penetrant autosomal dominant or recessive Parkinson disease, and causative mutations have been identified in many genes including SNCA, UCHL1, LRRK2, PARK2, DJ-1 PINK1 and other genes. In addition, several susceptibility genes including Gaucher disease-causing GBA gene have been identified.

In families with a non-mendelian form of Parkinson disease, first-degree relatives of an affected individual are between 2.7–3.5 times more likely to develop the disease than individuals without a family history of Parkinson disease. Genetic counseling of affected individuals and their family members must be done on a family-by-family basis. Understanding how genetic mutations cause familial Parkinson disease is likely to clarify molecular mechanisms underlying this condition and will provide a guide for the development of novel therapies.

EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE

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With the availability of symptomatic drug treatment in Alzheimer's disease (AD), and with novel disease-modifying drugs in clinical trials, there is an increasing demand to diagnose AD in the early phase. An early diagnosis also facilitates tailored and goal-oriented social care and counselling for the patient and the caregivers. However, in the early phase of the disease the diagnostic process may be complex, as patients with other transient or progressive disorders may present with similar symptoms.

In the current clinical criteria (NINCDS-ADRDA), the diagnosis of AD is based on characteristic symptoms and signs, and the exclusion of other causes [1]. New research criteria [2] based on positive findings in supplemental brain imaging with MRI and PET (or SPECT) and in biofluid markers have been proposed, and are particularly important in patients with mild to moderate symptoms and when there is doubt about the diagnosis.

The European Federation of Neurological Societies (EFNS) scientist panel on dementia recently published its second, revised international guideline on the diagnosis and management of AD and other disorders associated with dementia [3]. This guideline presents a peer-reviewed evidence-based statement for the guidance of practice for clinical neurologists, geriatricians, psychiatrists, and other specialist physicians responsible for the care of patients with dementia. It covers major aspects of diagnostic evaluation and treatment, with particular emphasis on the type of patient often referred

to the specialist physician. The main focus is AD, but many of the recommendations apply to dementia disorders in general.

This review will focus on current clinical practice and early biomarkers in the diagnosis of AD.

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ALZHEIMER'S DISEASE AND CEREBROVASCULAR DISEASE – THE SECRET PARTNERS

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Alzheimer's disease (AD) as the most frequent progressive memory disease is recognized as a stage-concurrent disorder. AD core pathology has a site specific evolution over time, and AD symptoms and their progression is understood by the location of the lesions; from early AD to more severe stages. The old AD research criteria by exclusion have been replaced by the phenotype approach.

Risk factors of AD and cognitive impairment include cerebrovascular disease (CVD, Stroke), silent infarcts and white matter lesions as a surrogate of small vessel disease (WMLs). Increased AD risk relates to arterial hypertension, high cholesterol, obesity, diabetes, atherosclerosis, major depression and head trauma. Lower AD risk factors include high education, physical activity, social activity, antioxidants, fish oil, treatment of arterial hypertension and use of statins. Probability of late-life AD can be related to a midlife Risk Score.

Vascular Cognitive Impairment (VCI) concept covers spectrum of vascular aetiologies including AD+CVD and a spectrum of severity from impairment in one or two cognitive domains to a more global syndrome. VCI is shifting old "dementia thinking" from thresholds (as the old Alzheimerized dementia) to a continuum of cognitive impairment, from the late to early stages and from effects to causes.

VCI relate to complex interactions between vascular aetiologies (different types of CVD, vascular risk factors), changes in the brain (infarcts, ischemic WMLs, atrophy, but also AD type changes) and host factors (age, education, genetics). One category is post-stroke cognitive impairment and dementia; cognitive impairment post-stroke is seen in 60% and dementia in 25% of patients with ischemic stroke aged 55 to 85 years. The two major forms of VCI relate to "the stroke brain" i. e. large vessel disease and cardiac embolic events, and "the network brain" i. e. small vessel disease.

Brain as end-organ approach focuses especially on the executive small vessel anterior network- brain, which is known to be the largest endothelial organ of the human economy. Subcortical vascular disease and dementia (SIVD) is the main subtype of VCI, the small vessel prototype.

Confluent WMLs seen on magnetic resonance imaging are surrogate of small vessel disease. The European LADIS-study showed how confluent WMLs relate even in short term to bad clinical outcomes: disability, death, cognitive decline, depression, impaired ADLs, impaired gait and stability, urinary problems and stroke.

AD+CVD. In unselected neuropathology series prevalence of AD+CVD is high (50 to 70%). Already Alzheimer (1906) and Tomlinsson et al. (1070) recognized AD+CVD, which long has been underestimated CVD, especially small vessel disease, relate to an earlier expression of clinical AD syndrome, as do the independent vascular risk factors.

The secret partners AD and CVD (Stroke) are challenging our brain health. In persons aged 65 years of age, every 1 of 3 men and 1 of 2 female have a lifetime risk to have AD, CVD or AD+CVD; which is the main challenge of independent life style in the coming years.

Where to invest. The general stock market has disappointed many of us. However, to invest on brain health; treatment of risk factors (CVD primary and secondary prevention) and promotion of protective factors is know to give secure growth to our investments in long run. Why not start today.

Movement Disorders / Dementia (Oral Presentations)

RELATIONSHIP BETWEEN COGNITIVE DYSFUNCTION, P300 EVENT-RELATED POTENTIAL AND CHOLINERGIC TREATMENT IN ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is the most common cause of dementia in the elderly people. AD is a neurodegenerative disorder that typically presents with continuous decline in memory and other cognitive functions. The early and accurate diagnosis of AD is essential to improve the patients' management. Cognitive event-related potentials, in particular the P300 potential (a late positive wave of the brain electrical activity associated with the detection of target stimulus), have been used in clinical practice as an objective marker of the cognitive functions.

The aims of our study were to compare the P300 event-related potential profile in patients with AD and in healthy elderly controls, to assess a correlation between various cognitive tests and the P300 potential profile in patients with AD and also to assess the electrophysiological differences of P300 potential profile in two groups of patients with AD – either treated with a stable dose of donepezil or treatment-naïve. 71 patients older than 65 years with mild to moderate AD and 50 healthy controls were included into the study. The diagnosis of AD was based on NINCDS–ADRDA criteria for Probable AD. The selected cognitive tests and P300 event-related potential evaluation (using standard auditory stimulation and "odd-ball paradigm") were performed for all subjects.

Results: The P300 potential latency and P300 response time have been found to be significantly longer and the P300 potential amplitude lower in patients with AD compared with healthy controls.

In AD patients, a significant relationship has been found between P300 potential latency and results of overall cognitive dysfunction assessment (as expressed in MMSE and ADAS-

Cog total scores), as well as working memory, attention and language functions evaluation data.

The change in P300 potential latency correlated with improved cognitive functions in patients treated with donepezil. Cholinergic stimulation reduced the recognition time of the target stimulus (the interpeak P300–N200 latency shortened) and enhanced neural activity (the P300 amplitude became significantly higher). Donepezil has been found to influence the patients' behaviour: it accelerated some neurophysiological processes and reduced the response time to a target stimulus.

The study results show that the P300 potential is important in clinical practice for the diagnosis of AD, its differential diagnosis and patients' follow-up during the treatment with cholinergic medicines.

NEUROTOXICITY OF EPHEDRONE-MANGANESE IN ADDICTS AND IN ANIMAL EXPERIMENTS

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During the recent years, in several countries including Estonia, Latvia, Ukraine and Russia, the progressive syndrome of hypokinesia, dysarthria, dystonia and postural dysfunction has been reported in drug addicts, who have intravenously injected self-prepared mixture from pseudoephedrine (Sudafed tablets), potassium permanganate, and acetic acid, containing ephedrone and manganese. Since 2006, 35 cases have been examined and videotaped in Estonia. Evaluation included MMSE (results range from 24 to 30), UPDRS (19 to 79), H&Y (1 to 5), and PDQ-39 (16 to 71). The chemical analysis showed the ephedrone yield of the non optimized reaction approximately 44%, and the mixture was found to contain 595 ppm Mn.

In 123I-IBZM SPECT and MRI imaging, two patients had slightly decreased tracer uptake bilaterally in striatum. In all other cases, normal postsynaptic dopaminergic function in striatum was found. MRI showed symmetrical hyperintense T1-weighted signals in the globus pallidus of active users but no abnormalities in former users.

In animal study, four groups (100% drug, 50% dilution, 20% dilution, and the control group, 15 animals in each group) of C57B6 mice were injected with 0.3 ml solution intraperitoneally once a day for a period of seven months. One dose with the highest concentration contained 19.2 mg of manganese and estimated 0.15 mg of ephedrone. Motility box testing showed a strong acute stimulating effect of the drug appearing immediately after the injection: the distance covered by the toxin treated mouse (average 343.1 m) was significantly longer as compared to the control mice (215.1 m). The mice did not express the signs of parkinsonism or dystonias. The biodistribution data shows that in 11C-labelled DTBZ (vmat2) ex vivo brain PET autoradiography, and whole brain radioactive tracer accumulation, there was a significantly lower whole brain accumulation of the radioactive tracer in the treated animals. PET autoradiography showed no significant difference in tracer uptake in striatum. 9.4T MRI showed no significant change or manganese accumulation in the brain. The manganese levels in blood of the toxin treated mice were remarkably high: 528–660 μg/L.

The syndrome is similar to manganism but it is presently unknown, whether it is mainly manganese induced or partly related to long-term effect of ephedrone. The animal experiments are aimed to clarify the mechanisms of toxic parkinsonism described in the drug abusers.

APPLICATION OF SPECT FOR DIFFERENTIAL DIAGNOSTICS OF PD AND ET

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Introduction: Parkinson's disease (PS) is a chronic, progressive, neurodegenerative disease of multifactoral aetiology, which is manifest by tremor at rest, rigidity, bradykinesis and postural instability. Essential tremor (ET) is the most common type of movement disorders, which is seen 10 to 20 times more commonly than PS. The differential diagnostics of both of these diseases at an early stage may cause difficulties. The clinical manifestation of Parkinson's disease is determined by slow, progressing dopaminergic neuron loss of subcortical nuclei. Examination by SPECT with joflupan ^{123}I (DaTSCAN) allows to state the degree and localization of the damage of subcortical nuclei.

Aim of study: By means of SPECT to assess the functionality of dopaminergic neurons of subcortical nuclei in patients with Parkinson's disease and the diagnoses of essential tremor, and to study the correlation of SPECT examination results with clinical symptoms.

Material and methods: From 2004 till 2008 examinations by SPECT were made in Pauls Stradins Clinical University Hospital on 85 patients (33 males, 52 females). Patients' mean age was 56 years (SD±10.8), the mean length of the disease 6,4 years (SD±7.1).

Results: Clinically Parkinson's disease was diagnosed in 59 patients (69.4%). The mean patient age was 58 years (SD±9.9), the mean length of the disease 3.9 years (SD±3.07). In SPECT examination 58 patients (98.3%) were diagnosed unilateral (49.15%) or bilateral (49.15%) subcortical structure damage. One patient (1.7%) was not seen any structural changes in SPECT examination. The diagnosis of essential tremor was clinically made in 26 patients (30.6%). The mean patient age was 53 years (SD±12.4), the mean length of the disease 12,4 years (SD±10.1). According to SPECT data – 18 patients (69.2%) were not diagnosed changes in subcortical structures, which would confirm ET diagnosis. 8 patients (30.8%) were diagnosed unilateral or bilateral loss of dopaminergic neurons, which suggested the neurodegenerative process and the need to undertake a specific therapy.

Conclusions: Clinical application of SPECT examination is significant for the differential diagnosis of essential tremor and Parkinson's disease. Early diagnostics of Parkinson's disease is essential in order to help start the therapy earlier, thus slowing the rate of symptom development and to preserve patients' ability for self-care for a longer period of time.

EARLY DIAGNOSTICS OF COGNITIVE IMPAIRMENT USING 6CIT TEST

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Background: The 6 Item Cognitive Impairment Test (6CIT) was developed in 1983 by regression analysis of the Blessed Information Memory Concentration Scale. It was revalidated in UK and the format was altered (6CIT-Kingshill Version 2000©) so that it is considerably more user friendly. It consists of six questions that are simple, non-cultural, and don't require any complex interpretation. As 6CIT is easy linguistically and culturally translatable and only takes less than 5 minutes

to perform, we decided to compare it with the MMSE test which appears to be the most widely used cognitive assessment tool in Lithuania.

Aim: To evaluate the validity and reliability of the 6CIT Lithuanian version as a screening tool for the diagnosis of cognitive impairment comparing it with MMSE.

Methods: Testing was carried out in the Department of Neurology of Kaunas Medical University Hospital. Two groups of patients were tested using the 6CIT and the MMSE tets. The main group consisted of patients (n=30, mean age 74.07±7.46 yrs), who were diagnosed as demented (Alzheimer's disease (AD) or vascular type of dementia) or had mild cognitive impairment (MMSE 26). A control group (n=49, mean age 70.04±12.11 yrs) consisted of patients with no cognitive disturbance (MMSE > 26).

Results: Altogether, 79 persons were tested. Cronbach of 6CIT was 0.76. A good correlation was found between 6CIT and MMSE, both in dementia (r = -0.786, p<0.01) and in control (r = -0.458, p<0.01) groups. When patients were stratified into two groups according to the age (first group 70 yrs, second – >70 yrs), 6CIT and MMSE scores were found to be significantly worse in the second group comparing to the first one (p<0.01). The 6CIT scores differed according to the level of dementia: in those with mild dementia (n=11) 6CIT score was 13.67±7.4, in those with moderate (n=11) – 16.27±5.7, and in those with severe (n=6) – 25.20±1.64 (^{2} = 16.596, df = 3, p<0.05).

Conclusion: 6CIT Lithuanian version has sufficient validity and reliability for diagnostics of cognitive impairment. This brief and easy to use test benefits to evaluate the severity of cognitive impairment and may be used as a screening tool for an early detection of cognitive impairment especially at the primary care level.

GENETIC PARKINSONISM: 10 YEARS OF NATURAL HISTORY

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Genetic parkinsonism represents a relatively new entity within our understanding of Parkinson's disease (PD). The shift towards the younger age of onset is the clinical hallmark of this disorder. Several PD genes and gene loci have been identified due to the recent progress in the field of molecular neurogenetics. When clinically present, the syndrome of PD, consisting of bradykinesia, muscle rigidity, tremor with or without other additional signs, is influenced by certain medications, like levodopa preparations, dopamine agonists etc. Hence our knowledge about the natural course of the genetic parkinsonism is limited nowadays.

We present the case of 42 year-old woman with genetically proved PARK4 genetic parkinsonism, whose clinical course of the disease remained uninfluenced by antiparkinsonian medications for approximately 10 years. Patient was initially investigated repeatedly with MRI, which proved to be normal and her previous diagnoses included posttraumatic stress-disorder, conversion disorder and depression. Only about 10 years after the onset of the disease performed SPECT showed marked dopaminergic degeneration and effective treatment was started. Although it is very regrettable, that patient's disease remained undiagnosed and untreatable, this situation gives us the rare opportunity to observe retrospectively the natural course of PARK4 related genetic parkinsonism. To our knowledge the natural course of this disorder for such a long period was never described in literature so far.

Epilepsy I (Plenary Lectures)

ADVANTAGES OF DIGITAL EEG. COMPUTED MONTAGES. SOURCE ANALYSIS

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Digital EEG makes it possible to visualise the same event/discharge in different ways, providing complementary information about it. Changing the montages, paper-speed, filters and sensitivity aids in a better, in-depth analysis of the recordings. Computation of the digital data allows construction of montages specifically designed to enhance certain aspects of the recordings. However, these techniques have several draw-backs, and a theoretical knowledge of the used computations is necessary for a correct interpretation of the displayed signals. These topics, in addition to basic aspects of computer-assisted source analysis are covered in the lecture.

DIFFERENTIAL DIAGNOSIS OF EPILEPSY

P. Wolf

Epilepsy has more and more become a treatable disorder; therefore it is important that the diagnosis is not missed and the patient can be treated. Also, therapy resistance is a challenge in every individual case, and a frequent reason of resistance is wrong diagnosis, i. e. the condition treated is not epilepsy. The most important diagnostic procedure is taking a good case history. Whenever possible, the information given by the patient and that given by witnesses of seizures should both be taken, ideally together.

The most important ancillary investigation is the EEG but it cannot decide the diagnosis, only support or contradict a clinically-based diagnostic hypothesis. Both false negative and false positive findings are possible, but the rate of false negatives can be reduced by including sleep in the EEG recording and by provocation methods. Co-registration of seizures by video and EEG may be required to decide the diagnosis in difficult cases. But sometimes already a video registration of a seizure may suffice to decide the diagnosis and that could be taken by the family at home on digital camera. Neuroimaging with MRI, though highly important for discovering etiologies of (symptomatic) epilepsies, does not contribute to the differential diagnosis.

Frequent differential diagnoses are vasovagal and cardiac syncope, and psychogenic non-epileptic seizures. Migraine and narcolepsy can pose problems of differential diagnosis especially in atypical cases. Nocturnal seizures need to be distinguished from REM and NREM sleep behaviour disorders. Less frequent but often misdiagnosed as epilepsy are paroxysmal choreoathetosis, episodic ataxias and similar episodic movement disorders.

PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES): DIFFERENTIAL DIAGNOSIS, CLINICAL FEATURES, MANAGEMENT AND TREATMENT

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Psychogenic non-epileptic seizures (PNES) is a heterogeneous functional disorder with a complex psychosocial and cultural background. There is a female preponderance in occurence. The patients may have other concomittant symptoms such as functional movement disorder or functional paresis. Depression or personality disorder are common. It is a common diffential diagnosis in specialized epilepsy centers where about 20% of the patients have PNES with or without epilesy. Occurence In the epilepsy population is estimated to about 4%. Diagnosis of PNES is a constant challenge in clinical practice. Nessesary are re-evaluation of the anamnesis, valid description of seizures and in some cases video electroencephalograhpic (EEG) recordings. No single clinical clue can solve diagnostic problem as well as no single paramedical procedure can, although advances i video EEG monitoring have contributed substantially to improve possibilities of accurate diagnosis.

The background for PNES is very heterogeneous and often difficult to ascertain. The seizures may be precipitated by somatic illness or other stressfull experiences and most of the patients have experienced emotional neglect and / or psychological, physical or sexual abuse in childhood.

Management and treatment requires a multidisciplinary team including psychiatrist and psychologist, but there is no golden standard of treatment, as there is a lack of conclusive results from randomised controlled studies. However, Cognitive Behavioural Therapy may be the choice of treatment as it is recognized as the treatment of choice for similar types of conditions as somatoform disorders.

NON CONVULSIVE STATUS EPILEPTICUS

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Nonconvulsive status epilepticus (NCSE) is a term used to denote a range of conditions in which electrographic seizure activity is prolonged and results in nonconvulsive clinical symptoms. It can take many forms. In this presentation, a classification scheme will be presented and the clinical features of the common forms will be discussed. The treatment and outcome of the condition depends on the clinical form and the aetiology and can vary widely. There are also a number of fascinating epileptic 'boundary syndromes' which may be forms of NCSE and these will also be described and discussed.

Epilepsy II

TREATMENT ISSUES FOR WOMEN WITH EPILEPSY OF CHILDBEARING POTENTIAL

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Most women with epilepsy have uncomplicated pregnancies and give birth to normal children. Nevertheless, the risk that seizures and antiepileptic drugs may harm the unborn child is a matter of concern. Adverse effects of the treatment need to be balanced against fetal and maternal risks with uncontrolled seizures. The strategy has been to use the appropriate drug for the type of epilepsy in monotherapy at lowest effective dosage to maintain seizure control throughout pregnancy. Epilepsy and pregnancy registries have been established to advance our understanding of the teratogenic potential of different antiepileptic drug regimens. Emerging data indicate a particularly high risk of congenital malformations in association with use of valproic acid. Recent data also suggests that compared to carbamazepine and phenytoin, exposure to valproic acid in utero is associated with lower verbal IQ in the offspring. These potential adverse effects appear to be dose-related with higher risks above 800–1000 mg/day. A conservative approach to the use of valproc acid is recommended in women of child-bearing potential whereby alternative antiepileptics should be proposed to those planning pregnancies wherever satisfactory seizure control can be thereby maintained. The importance of seizure control during pregnancy must not be neglected and attempts to major changes in treatment should be accomplished before conception. Additionally, preliminary data suggest that there might be differences between antiepileptic drugs with respect to seizure control during pregnancy with a higher risk for seizures with lamotrigine and oxcarbazepine. This might be related to pharmacokinetic alterations and regular monitoring of serum concentrations is therefore recommended for these drugs. In cases where valproic acid is used during pregnancy, either because the pregnancy was unplanned or because alternative treatment options of equivalent efficacy are unavailable, appropriate counselling, precautionary measures and monitoring should be provided.

TREATMENT OF REFRACTORY EPILEPSY

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The majority of the patients with newly-diagnosed epilepsy respond well to antiepileptic drugs (AEDs). Long term trials have suggested that about 50% of patients with newly-diagnosed epilepsy become seizure-free with the first AED. Failure to do so may be due to several reasons not related to treatment itself, like incorrect diagnosis of epilepsy. Also the choice of AED might be inappropriate for the epilepsy syndrome or the patient fails to take prescribed drug as needed.

Given a correct diagnosis of epilepsy, failure to respond to the first drug (lack of efficacy) is known to be associated with poor subsequent outcome and with the likelihood for the patient to have drug-resistant epilepsy. Drug-resistant (refractory) epilepsy is defined as continuation of seizures despite optimal monotherapy with two successive first-line (AEDs) or with one monotherapy and one combination regimen.

Choice of AED combinations should be guided by side effect profile and drug interactions. Synergistic (supra-additive) effects have been demonstrated for specific combinations in comparative trials, in particular sodium valproate and lamotrigine. The argument against add-on therapy traditionally has been its propensity to cause more toxicity with no additional substantial improvement in treatment efficacy. Still there is evidence that not so many patients given combination therapy do suffer from remarkable side effects. The aim of the treatment should be seizure-freedom. However after initial treatment failure and after establishing drug-refractoriness this probability will be quite low. Thus the patient and the doctor should discuss the adequacy of seizure control, existing side effects of the treatment and resulting loss of quality of life to determine best balanced treatment options with maximized seizure control and low level of side effects.

SURGICALLY REMEDIABLE EPILEPSY SYNDROMES IN ADULTS

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Around 30% of patients with epilepsy continue to have seizures that are not adequately controlled by pharmacotherapy. There are surgically remediable syndromes that have a poor prognosis with purely medical treatment but that respond well to surgical treatment. It has been suggested that around 3% of patients with intractable epilepsy might benefit from epilepsy surgery. A multidisciplinary team dedicated to epilepsy is necessary in order to develop a surgical programme. A comprehensive epilepsy surgery evaluation of surgical candidates involves a combination of clinical, electrophysiological, neuroimaging, neuropsychological, psychiatric and psychosocial evaluations. Recent advances in neuroimaging techniques have improved the prospects of finding lesions that might be related to the seizure focus. It should, however, be remembered that a structural lesion does not necessarily equal the seizure focus. Concordance of results from different investigations, especially EEG and imaging data, is necessary for the decision to perform surgery. Complications related to epilepsy surgery are few and age related. Specific epilepsy syndromes that are surgically remediable have been identified. Especially in these cases epilepsy surgery should not be considered a last resort, but the treatment of choice and should be considered early. In adults these syndromes include the mesial temporal lobe syndrome and localisation-related epilepsies due to specific lesions.

Lack of or underutilisation of epilepsy surgery is considered one of the main problems of epilepsy care all across Europe. Even in Western Europe epilepsy surgery is a clearly underutilised treatment. One reason for this underutilisation of the resource of epilepsy surgery might be lack of knowledge about epilepsy within the medical profession or lack of knowledge about the favourable results of surgical treatment of epilepsy within the neurological community. It is important to emphasize that individuals with pharmacoresistant epilepsy can be identified within a few years of the onset of their epilepsy, if adequate antiepileptic medication is pursued. The implication of this is that after failure of two first-line antiepileptic drugs patients with medically intractable epilepsy should be referred for evaluation to tertiary referral centres, where epileptological expertise will then diagnose their epilepsy syndrome and identify suitable candidates for presurgical evaluation.

Epilepsy (Oral presentations)

PROSPECTIVE MULTICENTER STUDY OF OUTPATIENT APPOINTMENTS FOR PATIENTS WITH EPILEPSY WITHIN ONE-YEAR (2006) OBSERVATION IN POLAND. PRELIMINARY REPORT.

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Aim: To determine frequency and distribution by specialty of outpatient appointments and usage of diagnostic and therapeutic evaluations and laboratory tests in patients with chronic epilepsy within one-year study.

Material and method: This paper is a part of multicenter study estimating global costs of epilepsy in Poland in 2006. A prospective questionnaire survey was conducted in 18-antiepileptic/neurological centers in Poland, including 969 consecutive patients with epilepsy (mean age – 27.8 yrs). Ultimately, 772 patients underwent 12-month observations (5 appointments conducted every 3 months).

Results: In 12 months 772 patients with epilepsy attended 6509 times outpatient services (mean number of appointments – 8.43 per person). Among all specialties most frequently they attended neurologist office (65.3%), then GP's, gynecologist, dentist, psychiatrist and other offices. Diagnostic evaluations were mostly epilepsy related (84.4%), while other consisted of 15.6%. Mean number of EEG/video-EEG was 1.0 per person and MRI/CT – 0.2 per person. Among laboratory blood examinations most frequently liver enzyme (34%), morphology (18%) and electrolytes (15%) were performed; AED concentration examination constitute 3.8% of all blood exams. Mean number of laboratory examination was 7.2 per person/year.

Conclusions: Patients with chronic epilepsy are high users of healthcare resources which comprise outpatients visits, diagnostic and therapeutic evaluations and laboratory exams. Mean number of outpatient attendances was 8.43 per person in one year. More than 2/3 of them were epilepsy related.

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PROGNOSIS OF EPILEPSY: LONG-TERM OUTCOME IN AN ESTONIAN POPULATION

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There are two main questions regarding prognosis of epilepsy in the patients with newly diagnosed epileptic seizures: the chance of achieving seizure freedom and the risk of premature death. There is general agreement that overall prognosis of newly diagnosed epilepsy is good. During long term follow-up about half to 2/3 of patients achieve 5-year seizure remission. It is also widely accepted that the risk of death for people with epilepsy is increaced two to three times compared with the risk for the general population. There are no population-based studies on prognosis of epilepsy from cen-

tral and eastern Europe, where major socioeconomic changes occurred over last decades.

Aim: To evaluate the remission rate and mortality risk in adult epilepsy patients who were identified earlier in a population-based incidence study carried out in Tartu, a city of about 100000 inhabitants in Estonia.

Methods: 81 persons aged 20 years and older (55 men, 26 woman) were identified as epilepsy incidence cohort in 1994–1996. The patients were revisited twelve years later. We analyzed mortality, seizure remission rate and risk factors in relation to remission of seizures.

Results: After 12.5 years 56% of patients had achieved 5-year seizure remission. The whole cohort standard mortality ratio (SMR) was significantly increased (SMR 2.6; 95% CI, 1.8–3.5). Mortality risk was elevated among patients with remote symptomatic (SMR 3.6; CI 95% 2.3–5.2) and cryptogenic (SMR 2.1; CI 95% 1.1–3.6), bud not idiopathic epilepsy. Considering specific risk factors for epilepsy, mortality risk was the greatest in patients with cerebrovascular diseases (SMR 5.3; 95% CI 2.7–9.5), followed by head injures (SMR 2.5; 95% CI 0.9–5.3) and neoplasms (SMR 2.2; 95% CI 0.5–6.4).

Conclusions: There are no significant differences in main epilepsy prognosis figures in Estonia compared with published results from other developed countries.

EPILEPSY AND DRIVING LICENSING IN LITHUANIA

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Purpose: In Lithuania driving was prohibited for patients with current diagnosis or history of epilepsy despite seizure activity for many years. From 2009 driving is allowed for those patients who do not have seizures 2 years or more, or are seizure-free 10 years or more (professional drivers).

Aim of the study was to estimate: 1) the attitude of doctors and patients towards the legalization of driving; 2) the impact of driving restrictions to quality of life (QoL) of patients, 3) the frequency of illegal driving by patients with epilepsy, 4) the incidence of traffic accidents because of epileptic seizure.

Methods: 503 patients with epilepsy were given a questionnaire regarding clinical and social issues, and impact of inability to drive to their QoL. 156 doctors completed a questionnaire regarding legal permission to get the driver's license for patients with current or past epilepsy.

Results: 64.1% of patients indicated that driving restrictions have negative impact to their QoL. 28.4% of patients, despite prohibition, held driver's license, and 31.2% of patients were driving a car (18.0% women vs. 43.2% men). Current driving was declared by 47.6% of working patients. 60.0% of patients drive despite having generalized seizures (1–5/month). 6.17% of driving patients experienced an accident because of the seizure.

73.2% of patients with epilepsy supported legal permission to drive for seizure-free patients. 94.5% of doctors supported driving permission for driving of clearly defined subgroup of epileptics. 87.8% of them considered the eligibility of patient to drive only if patient is seizure-free without medications; 39.7% – with medication. 19.8% of doctors would allow driving if only night seizures occur, 14.4% – if seizures are focal. 45.2% considered permission to drive after 5 years seizure-free period, 43.2 % – after 2 years. 26.7% wouldn't withheld driving license after first seizure. 94.5% would use EEG in the assessment of driving fitness.

Conclusions: Most of patients and neurologists supported legal permission to drive for seizure-free patients. One third of patients with active epilepsy drive a car despite inflexible rules. The rate of accidents because of seizure is relatively low. We are going to extend our study for the next few years to evaluate a rate of accidents during driving.

LONG-TERM EEG MONITORING: ESTONIAN EXPERIENCE

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Long-term EEG monitoring (LTM) is a useful tool in the diagnosis and treatment of epilepsy expanding the possibilities for differential diagnosis of seizures, semiologic description, syndromic diagnosis of epilepsies, and is also used in the presurgical evaluation of epilepsy patients.

Since the end of 2005 LTM has been available in the Department of Neurology and Neurosurgery of University of Tartu, Estonia. 64-channel Grass Telefactor EEG machine in a special ward with 24-hour EEG nurse monitoring is used to perform studies lasting up to one week. Fast drug withdrawal is used for patients on antiepileptic drug treatment.

This 3 years experience has given 88 long-term monitoring studies with 6495 recording hours.

370 seizures have been recorded. Main diagnostic question has been the nature of seizures with 36 patients out of 88. In case of 12 patients non-epileptic attacks were diagnosed. In 4 patients previously considered having non-epileptic attacks epileptic seizures were seen.

One third of patients (33) were investigated with the indication of specification of epileptic syndrome, and in one patient monitoring with the suspicion for non-convulsive status epilepticus due to disturbances of consciousness was performed. 5 patients with previous diagnosis of focal onset seizures were proven to have a generalized syndrome.

18 patients with temporal lobe epilepsy were investigated as a part of pre-surgical evaluation. 8 out of these patients have been operated consecutively and 3 of them are completely seizure free.

Regarding safety the frequency of generalized tonic-clonic seizures has possibly increased during the study due to fast drug withdrawal. There have been no cases of status epilepticus. Possibly dangerous situations for the patient and staff with ictal aggressiveness and unexpected falls during monitoring have been witnessed without any serious consequences and safety measures have been enhanced.

It can be concluded that LTM has provided better conditions for diagnosis of epilepsy by improving differential diagnosis of seizures, answering some of previously unanswered questions, helping to differentiate syndromes of epilepsy, localizing possible seizure onset and is hopefully influencing the quality of epilepsy management in general.

16 May, Saturday

Multiple Sclerosis (Plenary Lectures)

EARLY TREATMENT ON MULTIPLE SCLEROSIS

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Numerous findings about early events in multiple sclerosis (MS) demonstrate how seriously the onset of MS has to be taken and that early treatment initiation is in the patients' best interest.

From a pathological angle, one can argue that axonal damage starts very early in the course of the disease. Likewise, inflammatory activity in relapsing-remitting MS is not restricted to episodes of clinical impairment, but typically starts before an initial clinical relapse which has let to the concept of "clinically absent syndrome" and generally continuous during remission. Moreover, the immune-mediated processes that underlie MS becomes more compartmentalised in the CNS and thus more difficult to control as the disease progress.

Patients with a first event suggestive of MS (also called: clinically isolated syndrome (CIS)) and an abnormal MRI scan have a high risk of developing MS. According to findings from CHAMPS and ETOMS clinical trials and epidemiological studies, the risk depends on the number of lesions on the initial MRI. Patients with a high number of lesions at first presentation have a very high risk of developing a second attack shortly after the first attack. Baseline MRI features in patients with a first event seem not only to determine the risk of conversion to definite MS but also correlate with disability at 5 years.

Further evidence for the importance of early treatment derives from the demonstration that vast majority of patients with CIS and positive brain MRI develop new brain MRI lesions allowing the diagnosis of MS according to the McDonald criteria (McDonald 2001). For example in the BENEFIT clinical trial it has been shown that 85% of patients on placebo developed McDonald MS within 2 years, the majority of them within one year (Kappos et al., 2006). The 2005 revision of the criteria might even have allowed for a quicker diagnosis in many of these patients.

All three clinical trials conducted in patients with CIS – BENEFIT, CHAMPS and ETOMS (Kappos et al., 2006, Jacobs et al., 2000, Comi et al., 2001) – have shown that treatment with IFNB can slow down the rate of conversion to clinically definite MS (CDMS), prolong the time to CDMS and reduce MRI activity. The three years extension of the BENEFIT trials shows that IFNB-1b treatment right after a first clinical event suggestive of MS can significantly reduce the risk of permanent increase of disability as measured by the Expanded Disability Status Scale (EDSS) compared to delayed treatment. Delayed treatment is treatment initiation after the second clinical event of after 2 years whichever came first. This is a truly novel finding and another convincing argument in favour of a paradigm shift towards earlier treatment initiation.

From studies in relapsing-remitting MS, we already have evidence that late treatment initiation or low-dose regimens do not seem to match the benefit of early, high-dose therapy, at least over an observation period of four years (PRISMS Study, 2001). However, now it has been shown that this concept is already applicable at the stage when patients display the first signs of MS, which underscore the urgent need to treat patients rather early than wait for further MS signs to develop.

In summary, all these findings convincingly indicate that treatment with IFNB should be started as early as possible in the course of MS. Clearly, what is lost in delaying MS treatment is not regained, and with the BENEFIT 3-year data we see that time lost means loss of brain function, even in the early stages. Physicians and patients should carefully consider these observations in deciding when to initiate treatment.

COMBINATION THERAPIES IN MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is an example of a neurological disease that was considered untreatable until relatively recently. However, since 1995 beeta interferons and later glatiramer acetate (GA) have been widely accepted as first line therapy for relapsing remitting (RR) MS. In addition to first line treatments historically mitoxantrone and cyclophosphamide and recently natalizumab are usually considered as second line treatments. With the advent of these new possibilities in management of MS defining responders and non-responders to treatments has become increasing important. Approximately 80% of patients demonstrate at least 30% more decrease in relapse rate in comparison with pre-treatment. However, only about 50% of patients show excellent treatment response with no relapses and no progression of disability on treatment. The patient groups usually considered as non-responders are PwMS who develop relapses and disabilty progression on first line treatments and PwMS with very aggressive MS from onset. The first group includes PwMS who are non-responders already during the first year on treatment. The second group are PwMS on interferons who develop neutralising antibodies during 1–2 years having clinically excellent response to therapy. During following 3–4th year they start to experience disease activity. The important issue for the third group of PwMS with active MS from onset, is the question whether to start with induction treatments or to switch to rescue medication or combinations when first line treatment fails. There is increasing number of papers describing these patient populations with switching therapies and using combination therapies. Also, recently some clinical trials addressing the issue of combination therapies are emerging. We have mostly limited data on combinations of interferons with azathioprine, cyclophosphamide, methotrexate, natalizumab and GA. Also, efficiency and safety of combinations of GA with mitoxantrone, natalizumab, methylprednisolone (MP) have been described. Current studies have shown that if the reason for suboptimal treatment response is related to the development of neutralizing antibodies the attempts to increase the efficacy of interferon treatment with add on with methylprednisolone or azathioprine are unsuccessful. New data on combinations with interferons and GA is emerging. Also, the question whether to use present second line treatments and combinations as rescue or induction therapy for PwMS who have agressive MS remains unanswered.

LONG-TERM EFFECTS OF INTERFERON – BETA THERAPY AND THE ROLE OF NEUTRALIZING ANTIBODIES

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Treatment of multiple sclerosis (MS) with interferon-beta (IFN-beta) is frequently associated with the development of neutralizing antibodies (NAbs) against IFN-beta. NAbs gener-

ally appear after 12–24 months of IFN-beta therapy. Patients who have remained NAbs negative during the first 24 months of IFN-beta therapy only rarely develop NAbs.

Although NAbs may disappear during continuing therapy with IFN-beta, particularly with IFN-beta 1b, the majority of patients, who become NAb-positive, remain NAb-positive for several years.

The presence of NAbs prevents IFN-beta from reaching its specific receptor, which is a prerequisite for a biologic response to IFN-beta.

Several studies have concordantly shown that NAbs reduce the effect on relapse rate and on MRI measures of disease activity. Patients with NAbs have approximately 50% higher relapse rate than patients without NAbs. In placebo-controlled trials patients with NAbs had disease activity measured as relapse rate and MRI changes similar to placebo treated patients. Long-term studies suggest that NAbs may interfere with the effect of IFN-beta on disease progression.

NAbs occur in significantly fewer patients treated with IFN-beta 1a (Avonex) intramuscularly compared to patients treated with IFN-beta 1a (Rebif) subcutanously or an most frequent with IFN-beta 1b (Betaferon), whereas there is no difference between occurrence of NAbs in patients treated with IFN-beta 1a (Rebif) subcutanously and patients treated with IFN-beta 1b (Betaferon) subcutanously.

NAbs should be measured in all patients treated with an IFN-beta preparation, at least during the first 24 months. In patients who have remained NAb-negative during 24 months measurements of NAbs may be discontinued, as such patients only rarely develop NAbs during prolonged IFN-beta therapy. Change of therapy should be considered in patients with continuous presence of NAbs. The frequency of NAbs is one factor among others to take into consideration when choosing an IFN-beta product.

FUTURE THERAPIES IN MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is the prototype inflammatory autoimmune disorder of the central nervous system and the most common cause of neurological disability in young adults exhibiting considerable clinical, radiological and pathological heterogeneity. Novel insights in the immunopathological processes, advances in biotechnology, development of powerful MRI technologies together with improvements in clinical trial design led to a variety of evaluable therapeutical approaches. Therapy has changed dramatically over the past decade yielding significant progress for the treatment of relapsing remitting and secondary progressive MS. A substantial number of pivotal and preliminary reports continue to demonstrate encouraging new evidence that advances are being made in the care of MS patients. The majority of these strategies more or less specifically target subsets of the immune response in MS involving activation and expansion of T cells, their circulation and transmigration over the blood brain barrier, but also other cell types like B cells and probably also natural killer cells. In this presentation available data on the presently most promising new therapeutic approaches will be discussed. These involve the orally available compounds cladribine, FTY720, fumaric acid esters as well as the monoclonal antibodies alemtuzumab, natalizumab and rituximab. After successful completion of phase III studies, these compounds may have the potential to add to the current therapeutic armenterium especially for relapsing remitting disease courses in the near future, possibly opening the way to a more individualized treatment.

Multiple Sclerosis (Oral presentations)

CLINICAL AND RADIOLOGICAL DIFFICULTIES OF THE DIAGNOSIS IN PATIENTS WITH UNUSUAL CNS DEMYELINATING DISEASES, CASE ANALYSIS

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Background: diagnostic criteria of multiple sclerosis, is based on typical MS compatible clinical history and established MRI findings. Sometimes in cases of typical MS clinical presentation MRI findings can mimic neoplasm (tumefactive MS) or MRI findings typical for MS can be found in patients with ADEM. In cases of Devic disease – neuromyelitis optica characteristic presentation is simultaneous optic and spinal demyelination with variable MRI appearance of spinal cord lesions.

Purpose: to analyze 3 clinical cases of CNS demielinating diseases – 1) Devic neuromyelitis optica, 2) MS with tumefactive cerebral lesion, 3) ADEM presenting clinical and radiological findings, possible differential diagnosis.

Materials and methods: case histories, neurological examination results, results of immunological tests, MRI examination findings on initial and follow-up series were analyzed in all 3 patients.

Results: 1. patient A-B presented with clinical symptoms of the left retro bulbar neuritis and was successfully treated. Clinical symptoms of retro bulbar neuritis relapse and mild spinal cord symptoms were observed after 1 year, with conformation of optical nerve demyelination on MRI. After 3 years period progressive spinal cord clinical and radiological damage without stable remission were found.

2. patient L-P presented with clinical symptoms of acute and progressive weakness and pain in the right leg, in two week period symptoms of the lower limb paraparesis and urine incontinence developed. MRI examination showed tumour like lesion in the left frontal lobe, one periventricular lesion and multiple confluent lesion in spinal cord, all lesions were enhancing after administration of contrast. Bilateral retro bulbar optic nerves non-enhancing demyelination and retrospective clinical history of neuritis allows exact conformation of MS.

3. patient I-P presented with subacute symptoms of cognitive impairment without clinical or laboratory findings of acute or subacute infection. MRI examination showed multiple demyelinating lesion in brain and spinal cord. After specific treatment clinical improvement were obvious, but radiological changes of the lesions were slow. No symptoms of relapses were observed in 4 years period and diagnosis of ADEM were established.

Conclusion: Precise evaluation of clinical, anamnestic and radiological data in atypical cases of multiple sclerosis or rare demyelinating diseases can allow to estimate precise diagnosis of underlying disease.

CORRELATION OF COGNITIVE DYSFUNCTION AND MRI FINDINGS IN MULTIPLE SCLEROSIS

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Background: Most patients with multiple sclerosis (MS) experience a decline in cognitive function, even in the early stages of the disease and it is typically progressive. Neuropsychological studies in MS show a prevalence rate of cognitive dysfunction (CD) up to 65%. Correlations of cognitive disability exist with MRI findings of brain atrophy. Studies shows associations between impaired information processing speed and the bicaudate ratio, T2 hypointensty of deep gray matter nuclei, enlargement of the lateral ventricles, enlargement of the third ventricle and thalamus atrophy.

Objectives: To describe CD, to assess the relationship with MRI linear measurements and to select MRI sensitive markers of linear atrophy influencing cognitive processes in MS.

Methods and results: 60 patients with MS who underwent brain MRI were investigated. Expanded Disability Status Scale (EDSS) was performed and cognitive tests battery was applied. Working memory was tested by Digit Span Forwards Test (DSf), speed of psychomotor reactions – by Digital Symbol Substitution Test (DSST), Trail Making Test A (TMT A), frontal functions – by Trail Making Test B (TMT B), Five Point Test (FPT). To evaluate anxiety and depression, HAD scale we applied. Width of third ventricle, bicaudatus index, bifrontal index, Hucmann index, index of frontal atrophy, Evans index and index of corpus callosum were measured to determine atrophy in relation of CD. Correlations were determined: DSST, TMA, TMB, FPT correlated with age; DSST, FPT – with duration of MS; DSb, DSST, TMA, TMB – with education; DSb, DSST, TMA, TMB, FPT – with MS clinical course. CD also depends on MRI markers of brain atrophy: results of all cognitive tests, except DSf, correlated with index of corpus callosum, width of third ventricle and bicaudatus index. We established that depression in MS correlated with CD: DSST, TMA, TMB, FPT; weak correlation between depression and width of third ventricle was found.

Conclusions: Cognitive functions in MS are mostly affected for the older patients with lower education, with longer duration of MS disease and for secondary progressive MS course. Depression is weakly explainable by linear MRI markers. Cognitive disability of MS patients is reflected by MRI findings describing brain atrophy. MRI linear measurements: index of corpus callosum, width of third ventricle, bicaudatus index could be used as sensitive markers of brain atrophy, leading to cognitive dysfunction in MS.

COMPARISON OF IMMUNOMODULATORY THERAPIES FOR TREATMENT OF RELAPSING- REMITTING MULTIPLE SCLEROSIS: CLINICAL EXPERIENCE IN HOSPITAL OF KAUNAS UNIVERSITY OF MEDICINE

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Background: Multiple sclerosis (MS) is an immune mediated disease of young adults that requires lifelong treatment. Evidence support immunomodulatory therapies with either recombinant interferon-beta (INFb) or glatiramer acetate (GA) as the first-line for relapsing-remitting clinical course MS (RRMS), and positive results from phase III trials encourage start of treatment even in patients with clinically isolated syndromes to diminish the risk for permanent disability.

Aim: To compare the relative efficacies of INFb formulations and GA for the treatment of RRMS.

Patients and methods: It was a retrospective study of 206 patients (women 138 (66.9%), men 68 (33.1%) with RRMS. All the patients, who have been treated with basic immunomodulatory therapies in Hospital of Kaunas Medical University in-patient and out-patient neurological departments, were evaluated for their relapse rates and Kurtzke's Expanded Disability Status Scale (EDSS) scores. Mean age of the patients was 40.19 ± SD 9.37 (CI 95% 38.91–41.48 years). Estimated disease duration ranged from 5 to 20 years in one third of the patients. Of all RRMS patients, 39 (18.9%) were treated with INFb-1b 250 mcg SC (group A), 82 (39.8%) with INFb-1a 44 mcg SC (group B), 28 (13.6%) with INFb-1a 30 mcg IM (group C) and 57 (26.7%) with GA 20 mcg SC (group D). The data of clinical status (EDSS scores), which has been re-evaluated every 3 months, and relapse rate were collected in a specially prepared electronic table. The multivariate analysis (ANOVA) was performed using statistical package STATISTICA for Windows.

Results: The number of relapses reduced in every group after specific treatment has been initiated. No statistically significant differences were observed between the treatment groups A, B, C and D, regarding relapse rate per year ($F=1.67$, $p=0.23$), as well EDSS scores ($F=1.66$, $p=0.21$). Both optimal control of the disease (relapse rate per year < 1) was achieved, and the EDSS scores in the range of 0–2 points were consistent for more than a half of the patients.

Conclusions: All of the INFb formulations and GA were effective in reducing the number of relapses and preventing progression of the disability for RRMS patients. The choice of basic immunomodulating therapy must be based individually on an informed decision about the risk/benefit ratios and evidence.

MINI-AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN MS

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During the last decade immunosuppressive therapy with autologous haematopoietic stem cell transplantation (AHSCT) has been used as a therapeutic option for multiple sclerosis (MS) patients. The question of the optimal conditioning regimen, myeloablative or non-myeloablative, is still unclear. The goal of our research was to study safety and efficacy of mini-AHSCT in MS patients.

Eighty four patients with MS (secondary progressive – 26, primary progressive – 16, progressive-relapsing – 5 and relapsing-remitting – 37) were included in this study (mean age – 33.0, range: 17–54; male/female – 30/54). The conditioning regimen included reduced or modified BEAM. Median EDSS at base-line was 4.0 (range 1.5–7.0). The median follow-up duration was 9 months (range 6–24 months). Neurological evaluation was performed at baseline, at discharge, at 3, 6, 9, 12 months, and every 6 months thereafter AHSCT. MRI examinations were performed at baseline, at 6, 12 months, and at the end of follow-up.

Notably, no transplant-related deaths were observed. Transplantation procedure was well tolerated by the patients. Among 49 patients included in the efficacy analysis 24 patients (49%) experienced clinical stabilization and 25 (51%) – improvement 6 months post-transplant. Two patients experienced relapse after 6 and 12 months stabilization, while other patients remained stable or improved. Sixteen (33%) patients had active lesions at base-line, and all turned to inactive 6 months post-transplant. In two patients who relapsed active lesions appeared. No active, new or enlarging lesions were registered in all other patients. The latter patients were off therapy throughout the post-transplant period.

In conclusion, mini-AHSCT may be considered as a safe and effective treatment for MS. The collection of long-term follow-up data is worthwhile to confirm these findings.

Miscellaneous (Plenary Lectures)

SMALL FIBRE NEUROPATHIES – CLINICAL CHARACTERISTICS AND MANAGEMENT

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Small fibre neuropathies (SFN) are a subtype of peripheral neuropathies characterized by the impairment of small diameter myelinated A and unmyelinated C-fibres. In addition to sensory fibres also autonomic fibres may be involved. Diagnosis of SFN is based on abnormal findings of small-fiber function in at least one of the following: neurological examination, specialized electrodiagnostic testing (quantitative sensory testing, tests of sudomotor function and cardiovascular autonomic function tests), and pathologic studies (measurement of intraepidermal nerve fiber density).

Clinical characteristics of SFN include persisting neuropathic pain, abnormal sensations of numbness or tightness, symptoms of restless legs, cramps affecting distal parts of the lower extremities, and a number of autonomic symptoms. In clinical examination, reduction in thermal and pain sensitivity is very often noticed, but otherwise the findings of neurological examination are unremarkable. ENMG is usually normal, but may reveal mild axonal neuropathy. There are also some unusual clinical presentations of SFN, which include non-length dependent small fiber ganglionopathy, characterized by early involvement of face, trunk or proximal limbs. It has been suggested that some localized pain syndromes, such as burning mouth syndrome and vulvodynia, are associated with small fibre pathology.

SFN is very often a disease of the elderly, running a benign course. Idiopathic SFN can safely be considered to represent at least 30% of all small fiber neuropathies. Diabetes mellitus and impaired glucose tolerance are important causes to rule out underlying SFN. Other known causes are some autoimmune, inflammatory and infectious diseases, alcohol and toxins, amyloidosis, hypothyroidism, and Fabry's disease.

Causative treatment should be given wherever possible. Symptomatic treatment should be given along the guidelines for treatment of neuropathic pain. Both gabapentin and tramadole have been shown to be effective in treatment of painful SFN, but there are also patients in whom drug treatment is not bringing enough relief for pain.

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NEW CONCEPT AND NEW DIAGNOSTIC CRITERIA FOR ALZHEIMER'S DISEASE

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The criteria of the NINCDS-ADRDA and the DSM-IV-TR for Alzheimer's disease (AD) represent the prevailing diagnostic standards in research. While these sets of criteria represented an important step forward following their publication, they have now fallen behind the unprecedented growth of scientific knowledge of the disease from its earliest clinical manifestations through postmortem histopathology. Distinctive and reliable biomarkers of AD are now available through structural brain imaging with Magnetic Resonance Imaging (MRI), molecular neuroimaging with Positron Emission Tomography (PET) and cerebrospinal fluid (CSF) analyses. This progress provides the impetus for the revised research diagnostic criteria for AD. Our proposed diagnostic framework was developed through an international working group 2005, who determined by consensus that a set of revised AD criteria could be developed to capture both the earliest stages, prior to full-blown dementia, as well as the full spectrum of the illness. These new criteria are centered around a clinical core of early and significant episodic memory impairment. They stipulate

that in addition there must also be at least one or more abnormal biomarkers amongst structural neuroimaging with MRI, molecular neuroimaging with PET and CSF analysis of amyloid / tau proteins. The timeliness of these criteria is underscored by the myriad of drugs currently under development that are directed at altering the disease pathogenesis, particularly at the production and clearance of amyloid as well as at the hyperphosphorylation state of tau. Validation studies within both existing and prospective cohort studies will be needed to advance these criteria and optimize their sensitivity, specificity and accuracy.

The strength of these proposed research criteria is the introduction of neurobiological measures onto the clinically based criteria. Their usefulness will be determined in the future as investigators apply the criteria in a variety of research studies and as key issues in their application are resolved.

EPILEPTIC NETWORK INTERACTIONS IN VITRO: WHAT CAN ELECTROPHYSIOLOGY AND IMAGING TELL US?

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Cell networks involved in epileptic activity generation are heterogenous and comprised of distinct subtypes of inhibitory (I) and excitatory (E) neurons. Thus, we believe that the macroscopic phenomena of epileptic activity 'hypersynchrony' need to be characterized in terms of the interactions between the relevant neuronal subtypes taking part in this process. In vitro brain slice preparations and variety of experimental seizure models allow to study local (individual cell) or global (entire slice) network interactions. We study the role of distinct cell subtypes in the epileptiform events using electrophysiology and voltage-sensitive dye (VSD) imaging. This way we investigate local and global network interactions simultaneously. We employ two common in vitro seizure models (4-AP and high K+) to study synchrony in two subtypes of rat hippocampal interneurons (OLM and basket cells, BC) and excitatory pyramidal (P) cells. Dual and triple whole-cell recordings in OLM, BC, and P cells exhibit complex cell-specific synchronizations that help us subdivide typically perceived monolithic seizures into tri-partite initiation, body, and termination stages. Analysis of synaptic currents in OLM and P cells suggests that these stages can be characterized by dynamically shifting ratios in excitatory and inhibitory conductances. Global activity of the epileptiform events measured with VSD and fast digital cameras shows that interictal burst propagation in hippocampus is faster yet anatomically confined compared to the neocortex. Using fast sampling imaging rates and dual extracellular or whole-cell recordings simultaneously we describe spatiotemporal dynamics of epileptiform 'fast ripples' (oscillations above 200Hz). We show that the fast ripples initiate as stationary activity 'hubs' and propagate as alternating E-I wave-like bands at speeds three times faster than the interictal bursts. Ripple amplitude and frequency is greatly reduced by the gap junction blocker mefloquine. Additionally, evoked and spontaneous interictal burst spatiotemporal propagation patterns can be confined by beta adrenergic receptor agonist isoproterenol. Simultaneous studies of the local and global dynamics extend our knowledge of the basic spatiotemporal mechanisms of epileptiform activity and hold significant clinical relevance, yet it remains a challenge to identify and control the relevant cellular mechanisms that underlie the evolution of endogenous seizure stages in vivo.

Miscellaneous (Oral presentations)

CNN PROJECTS IN FRAMEWORK PROGAMME FP7: OPPORTUNITIES AND EXPERIENCES

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One of the five FP7 specific programmes "Cooperation" supports all types of research activities. Health is a major theme in this Programme with a total budget of 6.1 billion for the period 2007–2013. European funded human health research is focusing on three pillars:

1) Biotechnology, generic tools and medical technologies;

2) Translating research;

3) Optimising the delivery of health care to European citizens.

International cooperation is an integral part of the Health theme and project consortia.

CNN projects are mainly funded through the pillar "Translating research for human health" in the area: "Research on the brain and related diseases, human development and ageing". This activity has a particular emphasis on translational research, meaning translation of basic discoveries into clinical application.

There are 3 general principals for the successful application: consulting and carefully following the instructions of annual Health Work Programme, following the guide for applicants and submission of the proposal before deadline. After the submission a proposal will have to pass the evaluation process to be retained for funding. Only eligible proposals will go to a scientific evaluation which is a peer review and will be carried out by a panel of external independent experts. The evaluation criteria are:

1) Scientific and/or technological excellence;

2) The quality and efficiency of the implementation and management;

3) The potential impact through the development, dissemination and use of project results. Only applicants with highly ranked proposals will be invited by the European Commission to negotiate a grant agreement providing an EU financial contribution.

There have been 3 calls opened in the FP7. The first call for the area "Research topics on the brain and related disease" covering 6 topics: Stroke and mechanisms underlying ischemic brain damage; Coding in neuronal assemblies; Neurobiology and anxiety disorders; Memory loss: underlying mechanisms and therapy; From basic spinal mechanisms to spinal cord disease and trauma; Neuron-glia interactions in health and disease. The 2nd call topics were: Restorative approaches for therapy of neurodegenerative diseases; From mood disorders to experimental models; Neuronal mechanisms of vision and related diseases. In the first two calls 23 projects were funded for a total of 91.5 mln EUR. Twenty

brain-related research projects were funded under other activities of the Theme 'Health' for an additional 100 mln EUR. For the 3d call in 2009 were opened such topics as: Synaptopathies: genesis, mechanisms and therapy; Identifying genetic and environmental interactions in schizophrenia; Optimising current therapeutic approaches in schizophrenia; Understanding the blood brain barrier to improve drug delivery to the brain; Psycho-social factors of brain disorders and rare neurological diseases.

Brain research is still one of less investigated and one of the main focuses of health research in EU; therefore, for this area projects is assigned approximately 1/3 part of European health research grants.

BACTERIAL MENINGITIS: TRENDS AND DEVELOPMENTS IN ESTONIA

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Objective: This study aimed to survey prospectively all cases of community acquired bacterial meningitis in Estonia in all age groups during the period from the 31st of December 2007 until the 30th of December 2008.

Methods: Case identification of bacterial meningitis was based on clinical symptoms and examination of CSF. For every patient, case report form was filled which included data of medical history, initial symptoms, time of administration antibiotics, cerebrospinal fluid and blood culture results. Before leaving the hospital, neurological, neuropsychological and auditory status was evaluated. In case of unfavorable outcome, the autopsy records were reviewed. RNA was extracted from the blood of patients.

Results: Among the patients were 28 men and 23 women, 14 children (<15 years old) and 37 adults, with mean age of 39.4 years.

First signs at home were febrile temperature (95%), altered mental state (68%), headache (66%), vomiting (63%), epileptic seizures (12%), rash (12%). In hospitalisation, nuchal rigidity (82%) in adults and headache (100%) in children, was the most common symptom. Among all the patients, 17% had epileptic seizures.

Cerebrospinal fluid culture was positive in 29 cases (59%) and blood culture was positive in 21 (49%) cases. The probable reason for relatively low number of positive values is antibiotic therapy before lumbal puncture or blood sampling.

In cerebrospinal fluid, the mean pleocytosis was 2124×10^6/l (ranged 6–13440×10^6/l), mean protein level 3.2 g/l (ranged 0.2–10.1 g/l).

Mechanical ventilation was needed in 43% of patients with the mean duration 8.8 days.

Without any neurological sequela left the hospital 55% of the patients. Seven patients died, the mortality rate in the sample was 14%.

In genechip analysis of this RNA, substantial differences in gene expression profiling have been found compared to controls.

Conclusions: The survey on community acquired bacterial meningitis in Estonia gives knowledge on the epidemiology and outcome of this life-threatening infectious disease in a country where Hib vaccination was recently introduced and the rate of penicillin non-susceptible Streptococcus pneumoniae is still low. Since similar conditions apply to all Baltic countries, it enables to make extrapolations for entire region.

WHAT IS NEW IN TB MENINGITIS?

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We report a suspected case of TB meningitis, a six year old boy, who initially presented to a local district hospital with three weeks history of headache and vomiting and a day history of confusion and he was found to have Papilloedema.

He was known to have poly articular idiopathic juvenile arthritis since age of 15 months and he had received varies immunosuppressant drugs and steroids in the past.

He was initially put on IV antibiotic and acyclovir, during his admission at our hospital, he was extensively screened for infections, and under went LP, he had abnormal CSF results high protein and low glucose, Therefore, antituberculous therapy and steroid were initiated prior to establishment of the diagnosis of TBM

After 10 days of starting anti TB therapy he was discharged home in a stable condition.

Tuberculous meningitis is a lethal disease that is often diagnosed late due to the insidious nature of its symptoms and hard to make a diagnosis. Delayed treatment of TBM is associated with a high mortality rate and irreversible neurological deficits; therefore, the option of a rapid and accurate diagnostic procedure is required.

There are many important unanswered questions about TB meningitis; we review the available evidence to answer some of these questions.

POSTER PRESENTATIONS

CEREBROVASCULAR DISORDERS

PLASMA CONCENTRATION OF HEAT SHOCK PROTEIN AND RISK OF ISCHEMIC BRAIN STROKE

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Heat shock protein (HSP) has been hypothesized to be a potential biomarker of atherosclerosis. However, no prospective studies have yet been performed to investigate the association between HSP plasma concentration and risk of ischemic brain stroke. We have tested it using methylenetetrahydrofoliate reductase (MTHFR), one of the main enzyme involved in the metabolism of homocysteine. Hyperhomocysteinemia (HHY) is considered an independent risk factor for stroke and is affected by genetics and dietary factors. Prevalence of vascular risk factors was assessed; fasting homocysteine (Hcy) and vitamin B6 (in co-factor form as pyridoxal phosphate (PLP) were assayed in all patient. The plasma Hcy and PLP levels were measured using a self-modified and validated high pressure liquid chromatography (HPLC). We have measured the level of antibodies against certain HSPs in vitro, in serum of ischemic stroke patients and control group using ELISA. The level of antibodies against one of the bacterial HSPs, GroEL, correlates with the level of homocysteine in serum. It points at the possible significance of autoimmune reactions contributing to atherosclerosis. We have also purified MTHFR and tested the influence of HSPs of the KJEB system in vitro, using spectrophotometric test for MTHFR activity. We found that MTHFR is partially protectet from the effect of heat shock by KJEB system and that KJEB proteins can restore that activity of the enzyme when it is lost due to thermal denaturation. Our findings show that HSPs can be involved both in the development of atherosclerosis, as well as protection against ischemic brain stroke. Futher studies need to be done.

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HIPEROMOCYSTEINEMIA AS A RISK FACTOR OF STROKE

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Introduction: Some clinical and experimental studies suggest that hight homocysteine concentrations may cause the atherogenic and trombotic events. Atherogenic propensity associated with hyperhomocysteinemia results from endotelial dysfunction and injury followed by platelet activation and thrombus formation. The prevalence of hyperhomocysteinemia has been estimated to be about 5% in the general population, and 13–47% among patient with symptomatic atherosclerotic vascular disease as a stroke (Auer J et al., 2006). Stroke in these patients is accompanied by a higher rate of cerebral microangiopathy and multiple infarctions than in other stroke patients. Vitamin supplementation decreases or even normalizes plazma homocysteine concentrations in most cases.

Objective: The objective of this study is to determine plasma total homocystein level is associated with risk of ischemic stroke and correlated with other risk factor of stroke.

Materials and methods: A population-based study performed in a hospital population. Cases (n=92) had ischemic stroke, and control (n=46) matched for age, sex were derived through random – digit dialing.

Results: 1. Elevated tHcy were more commonly found in cases (cases 54 of 92 or 58,7%) than control (16 cases of 48 or 33%). 2. Hiperhomocysteimenia is the second more common risk factor of stroke after hypertension. 3. In this study were not found correlation between hiperhomocysteinemia and other risk factors of stroke.

Conclusion: 1. Serologic evidence of hipehomocysteiemia is associated with ischemic stroke. 2. Elevated homocystein level is more common associated with atherotrombotic and undetermined stroke subtype. 3. Homocystein is independent risk factor of stroke.

C. PNEUMONIAE CHRONIC INFECTION AS A RISK FACTOR OF STROKE

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Introduction: Serologic studies over the past several years have renewed interest in the role of infectious agent in the causation of stroke. Among a variety of agents, Helicobacter pylory, cytomegalovirus, and Chlamydia pneumoniae have received the greatest attention. Direct and indirect effects of infectious agent on the vascular wall may modulate atherogenesis, that is a cause of stroke in 50%. C. Pneumoniae is a gram-negative intacellular bacterium that is distributed worldwide. Serologic evidence of infection with Chlamidia pneumoniae has been associated with cardiovascular disease, but relationship with stroke risk remains uncertain.

Background: The objective of this study is to determine whether serological evidence of C. Pneumoniae infection is associated with risk of ischemic stroke and correlated with stroke subtype.

Materials and methods: A population-based study performed in a hospital population. Cases (n=92) had ischemic stroke, and control (n=46) matched for age, sex were derived through random – digit dialing. Titers of C pneumoniae- specific Ig G were measured using microimmunofluorescence.

Results: 1. Elevated Ig G titers were more commonly found in cases (57 cases of 92 or 62%) than control (18 cases of 48 or 39%). 2. Elevated Ig G titers were found in 13 cases of 25 (52%) atherotrombotic stroke, 13 cases of 19 (68%) undeterminated stroke and 31 cases of 48 (65%) cardioembolic stroke.

Conclusion: 1. Serologic evidence of C pneumoniae infection is associated with ischemic stroke. 2. Elevated C pneumoniae Ig G titers were more associated with cardioembolic and undeterminated stroke subtype. 3. Ig G may be a marker of risk of stroke. 4. Future studies of the effect of C pnemoniae on stroke risk are warranted.

STROKE RISK FACTOR WITH LETHAL OUTCOME

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Introduction: Stroke occupies the second place in structure of death rate among the population of Ukraine.

Purpose: To study the influence of stroke risk factor on lethal outcome by the method of hospital registry. Methods. Retrospective analysis of data for 1534 patients with stroke, 236 events with lethal outcomes was conducted.

Results: Lethal outcomes of stroke prevailed among women: 53%, and 47% at men. Patients at the age of up to 50 years made 5.08%, 50–59 years – 13.5%, 60–69 years – 25.0%, over 70 years – 123 (52.1%). Average age of patients made 68.6 years. Ischemic stroke (IS) was diagnosed at 116 (49.1%) patients, while hemorrhagic stroke (HS) – at 112 (47.5%). Lethality at acute period of stroke made 15.34%. Correlation amount events of IS and HS has formed 1:1. Major risk factors were: arterial hypertensia – at 219 patients (92.7%), diabetes – at 40 (16.9%), fibrillation – at 24 (10.1%), smoking – at 29 (12.2%), alcohol abuse – at 14 (5.9%), stroke in the anamnesis – at 59 (25.0%) and old myocardial infarction – at 75 (31.7%). Arterial pressure was checked regularly only at 8.9% of patients, episodic – only 44.5%, no check – 46.6%.

Conclusions: High percent of such risk factors as arterial hypertensia and vascular events in the past signals absence of adequate treatment and preventive measures. It is necessary to increase educational level among doctors who are connected with vascular pathologies and among the population.

DETECTION OF CEREBRAL ISCHEMIC LESIONS USING MRI AFTER CAROTID STENTING WITH EMBOLIC PROTECTION DEVICES

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Introduction: Recent evidence indicates that the use of embolic protection devices (EPD) increases the safety of carotid artery angioplasty and stent placement (CAS) that may be associated with clinically silent cerebral lesions. The detection of acute cerebral ischemia is the most important and clinically useful application of diffusion-weighted MR imaging (DWI). We prospectively evaluated the occurence of cerebral emboli, as represented by new lesions on DWI, in patients treated with protected CAS.

Objective: To assess by DWI the efficacy of cerebral protection devices in avoiding embolization, and to describe radiological findings of new ischemic lesions and their association with neurologic deficits in patients with severe carotid artery stenosis undergoing CAS with EPD (MO.MA and Defender systems).

Methods and Materials: From December 2008 to March 2009 we performed 12 CAS procedures in 12 patients (age 58–83 years) using EPD. MRI with DWI was performed prior and 2 days after CAS procedure for all 12 patients using 1,5T Siemens Avanto scanner. 2 scanning planes (axial and coronal) were used for more detailed visualization of lesions. New ischemic lesions were evaluated from DWI (b=1000) and from apparent diffusion coefficient (ADC) images. Ischemic findings by shape and size were classified into focal (<10 mm) and linear (>10 mm).

Results: DWI revealed that all patients had radiological signs of acute ischemical lesions, possibly except 1 patient (minimal changes, present only in 1 scanning plane). Postprocedural MR images showed new ipsilateral DWI lesions on the side of stent for all 12 patients. 8 patients had bilateral foci, 3 patients had cerebellar lesions, and 1 patient had single lesion in brainstem. Linear (>10 mm) cortical damage was present in 3 patients. Clinically none of the patients had minor or major stroke, 1 patient had hemispheric TIA, attributable to the side of stenting.

Conclusions: Small cerebral ischemic foci are common findings on DWI after carotid stenting. EPD has not fully protected patients from peri-procedural microembolism. Distal protection devices resulted (possibly due to new filters) in visually larger DWI foci, compared to proximal EPD. The majority of new lesions are clinically silent. Further investigations should be performed comparing embolism related to CAS with EPD versus endarterectomy.

TRENDS IN ANTICOAGULATION FOR PATIENTS WITH ACUTE STROKE AND ATRIAL FIBRILLATION

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Background: Atrial fibrillation (AF) is a strong stroke risk factor. Majority of patients with AF should be given anticoagulation for stroke prevention in the absence of contraindications, according to international and local algorithms for stroke prevention. However, adherence to accepted guidelines in clinical practice may be inadequate.

Objective: To examine actual trends in treatment with anticoagulation for secondary stroke prevention administered for patients with AF in tertiary care university hospital in Lithuania.

Materials and methods: Retrospective study was performed in Department of Neurology, Vilnius University Hospital Santariškių klinikos (VUHSK). 104 patients with cerebral infarction and AF who were treated in VUHSK during 2007 were included. According to administration of indirect oral anticoagulants (OAC) at discharge patients were categorized into 2 groups: OAC given (OAC+) and OAC not given (OAC-). Demographic data, type of AF, stroke risk factors, severity of neurological deficit and physical condition, demand of OAC estimated by CHADS2 score, reasons for rejection of anticoagulation were evaluated and compared between the groups.

Results: Mean age of patients was 75.6 ± 7.8 years. 20 patients (19.2%) had paroxysmal, 77 (74.0%) – chronic, and 7 (6.7%) – undetermined AF. At discharge OAC were prescribed for 41 (39.4%) patients. Analysis disclosed some significant differences between OAC+ and OAC- groups: 1) age: OAC+ patients were younger than OAC- (72.3 vs. 77.8 years, respectively; $p < 0.001$); 2) severity of neurological and somatic condition: OAC+ patients had milder impairment and were rarely transferred to palliative care hospitals (14.6% vs.

31.7%; p = 0.049); 3) use of OAC before the onset of stroke was much more frequent in OAC+ group (39.0% vs. 6.3%; p<0.001). No differences in gender, type of AF, stroke risk factors and demand of OAC by CHADS2 were observed. Only younger age of patient was associated with administration of OAC according to logistic regression analysis (OR 0.94 [95% CI; 0.85–0.95]; p = 0.001). Most prevalent reasons for rejection of OAC were severe neurological deficit (17.7%); impaired balance and coordination (11.3%); lack of possibilities for regular INR control (11.3%); delirium state (8.1%); other reasons (16.3%); unexplained reasons (35.5%).

Conclusions: OAC is more frequently administered for younger patients with milder impairment. Older and severely ill patients with atrial fibrillation who may really benefit from anticoagulation for secondary stroke prevention often do not receive it despite strong indications and accepted guidelines.

THE ACCESSIBILITY OF INTRAVENOUS THROMBOLYSIS IN LITHUANIA

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Background: Intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator is recommended as the first line treatment within 3 hours of onset of ischemic stroke. Only small part of stroke patients receives it due to late arrival to the treating hospital. In Lithuania IVT is currently available for the large cities' inhabitants mainly. The aim of study is to estimate the current possibility to perform IVT in Lithuania and give the recommendations to improve the accessibility of the treatment.

Materials, methods: The questionnaire was used for evaluation of Lithuanian hospitals' facilities to treat acute stroke patients in the beginning of 2009. According to international SITS-ISTR registry and our own data we presumed the mean "door to needle" time 60 min, the mean time from stroke onset to emergency call 15 min, and the time for primary evaluation of the patient 20 min. Then the estimated time for ambulance arrival and transportation of stroke patient to the nearest suitable hospital was calculated for various Lithuanian regions. Our estimations were compared to actual accessibility of IVT in Lithuania according to completed questionnaires.

Results: 25 hospitals out of 41 where stroke patients are treated (61%) responded to our survey. 16 hospitals have necessary facilities and services to perform the IVT for the stroke patients. At least one IVT was performed in only 9 of them. According to our estimations, current IVT therapeutic window implies that time "stroke onset to door of nearest stroke center" cannot exceed 42 min. Therefore, the maximal distance from the patient to the stroke center should not exceed 45 km. The current stroke centers with IVT availability do not fully cover the territory of Lithuania, and at least 2 additional IVT sites are necessary for optimal IVT accessibility.

Conclusions: The number of hospitals, where IVT is performed in Lithuania, is not adequate at present. The additional evaluation of facilities for IVT in other hospitals and multiple educational activities are needed in order to optimize the stroke center network in Lithuania and to improve prompt accessibility of IVT for patients with acute stroke.

THROMBOLYSIS AND STROKE. WHERE ARE WE LOSING TIME (BRAIN)?

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Introduction: Thrombolysis with alteplase is the most efficient method in treating acute stroke. However, it could be performed only during first 3 hours after symptom onset until the publication of the paper by Hacke at al in September 2008. The per cent of patients who arrive in hospital in time to get this treatment is only about 5% in most countries.

The aim of this single centre study was to describe the loss of time before thrombolysis of patients who received thrombolysis in West-Tallinn Central Hospital from 2005–2008.

Results: During 4 years 50 stroke patients received thrombolysis with alteplase. All patients were thrombolysed in 3 hour window. In 2005 thombolysed patients comprised 16/600 (2.6%), 10/654 (1.5%) in 2006, 7/603 (1.2%) in 2007 and 17/528 (3.2%) 2008 of ischaemic stroke patients. The mean age of thrombolysed patients was 70.7 years (min 51, max 93 years). The mean time from symptom onset to the call to 112 was 60.9 minutes (min 25, max 143 min; 0 minutes for few patients who got stroke at the hospital). Only 42% per cent of patients calls were coded for ambulance accurately as C or D (lights and sirens) the rest were given lower priority by 112 dispatcher. The time ambulance spent from receiving the call until the patient reached emergency department (ED) varied from 11 to 81 minutes (mean time 29 min). The mean time from ED to thrombolysis was 84.8 minutes (min 46, max 142), from onset to thrombolysis 145.4 minutes (min 63, max 230). Mean time spent at the ED was 29 minutes (min 13, max 80), from ER to CT of the brain 46 min.

Conclusions: Although only those patients were analysed who were succcessfully treated – they received thrombolysis, massive loss of time was present during all steps of the pathway. The problems why so much time is lost and strategies for improvement are discussed.

STROKE MORTALITY TRENDS IN KLAIPEDA'S POPULATION FROM 1994 TO 2008

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The objective of the study was to evaluate stroke mortality trends in Klaipėda's population during the period of 1994–2008.

Methods: The official mortality statistical data were used to evaluate stroke (WHO stroke definition) mortality rates per 100,000 of Klaipėda population. The age-adjusted mortality rates were calculated by using the Segi's world population for direct standardization. Data for men and women were observed separately. Trends were analysed using the method of linear regression on logarithms of the age-standardized annual rates. Yearly percentage changes in stroke mortality were calculated for the entire study period, from 1994 to 2008, with this period divided into 2 parts: from 1994 to 2000, and from 2001 to 2008.

Results: The data analysis of the two periods showed that from 1994 to 2000, the overall stroke mortality rates in both men and women were decreasing by 11%/yr, while during the

second period (2001–2008) the mortality rates tended to increase by 10%/yr. (p=.010) in men, and by 1.4%/yr. (p=.696) in women. The study revealed that during the period of 1994–2000 mortality rates from stroke were decreasing among both men (-17.52%/yr; 95% confidence interval (CI) -30.0 to -4.5%/yr; p=.018) and women (-17.3%/yr; -28.8 to -5.8%/yr; p=.002) aged 35–64 years. The tendency of decreasing mortality trend was also observed in men (-11.1%/yr; -25.0 to +2.8%/yr; p=.095) aged 65–79 years, while in women of the same age this decreasing trend was not statistically significant (-8.8%/yr; -21.3 to +3.8%/yr; p=.13).

During the period of 2001–2008, mortality from stroke was increasing among men (+19.3%/yr; 95% CI +10.0 to 28.5%/yr; p=.002) aged 35–64 years, while among women of the same age this increasing trend was not statistically significant (+4.5%/yr; -7.4 to +16.4%/yr; p=.391). In both men and women aged 65–79 years increasing mortality trend was not statistically significant (respectively +5.7%/yr; -1.5 to +12.9%/yr; p=.099 and +0.2%/yr; -8.3 to +8.7%/yr; p=.956).

Conclusion: From 1994 to 2000, mortality from stroke was decreasing among both Klaipėda men and women aged 35–64, while in the elderly population (65–79) this decreasing trend was not statistically significant. During the period of 2001–2008 mortality from stroke increased in younger or middle age men (35–64), while among women (aged 35–64 and 65–79) and elderly men (65–79) the age-adjusted mortality rate remained relatively unchanged.

FACTORS INFLUENCING LONG-TERM SURVIVAL AMONG STROKE SURVIVORS OVER 65

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The goal was to evaluate the impact of age on long-term survival of stroke survivors and an analysis of risk factors.

Contingent and Methods: We performed a prospective hospital-based study of 1045 stroke survivors who had discharged from the index hospitalization in Klaipėda in 1995–2000 (5 years of follow-up).

We have reported mortality rates and patterns in patients who survived their index hospitalization, and our mortality results are taken from the point of discharge from the index hospitalization. Therefore, comparisons with other studies need to be made with the knowledge that most other studies report mortality from the time of stroke symptom onset. We conducted a case-comparison study on 1045 stroke survivors divided into 4 subgroups according to age: <65; 65–74; 75–84; and 85 and older.

We analyzed the following leading pathology: arterial hypertension, diabetes mellitus, atrial fibrillation, history of myocardial infarction, angina pectoris, congestive heart failure, and prior physical activity (mobility). Univariately the mortality rates for all patients were studied by Kaplan-Meier survival curves stratified according to age. The independent association between each variable and either death was estimated by means of the Cox proportional hazard model.

Results: Long-term mortality among stroke survivors during five years after stroke was 15.9%. At the multivariate analysis, the risk of death in patients aged 65–74 was significantly and independently associated with age, male sex, and medical history of atrial fibrillation (relative risk RR=1.9), myocardial infarction (RR=2.0), diabetes (RR=2.4), and prior physical activity (mobility) (RR=2.0); in the group aged 75 to 84 – cognistive heart failure (RR=1.7); in the group aged 85 and older – diabetes mellitus (RR=5.5). Hypertension was not significantly associated with increased long-term mortality.

Conclusion: The major modifiable predictors of poor long-term outcome in stroke survivors aged over 65 years were a low level of activity before the stroke and leading pathology: history of myocardial infarction, atrial fibrillation, cognistive heart failure and diabetes mellitus. These data highlight the importance of long-term secondary prevention of vascular events in stroke patients, targeted as much at the cardiovascular as at the cerebrovascular circulation. Prestroke level of function may play an important role in predicting stroke outcome in the elderly.

CHRONIC BRAIN ISCHAEMIA. ATTEMPT TO CLASSIFY AND TO TREAT

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Lack of interest in a quite indefinite form of pathology – chronic brain ischaemia (CBI) – enabled us to classify and place it into a quite particular frame. The purpose of rubrification is both theoretical, classificational and purely practical, as it enables dynamically observe various manifestations of the disease. We tried to group all syndromes of CBI into permanent and paroxysmic ones. Permanent syndromes were stated for the patients with dominant clinical picture of cephalgic, vestibular-ataxic, pyramidal syndrome, light cognitive disorder, symptoms of Parkinson's syndrome, bulbar syndrome and organic psychosyndrome. Paroxysmic syndromes were divided into transient global amnesia, drop attack, syncope, late onset epilepsy and falls by elderly people. All these syndromes could simulate stroke, but their visualisational and prognostical course is much better.

We examined 241 patients, 143 women and 93 men, the patients' age was from 56 to 84. Cerebral CT and MRT were performed for all patients and stroke was excluded. The concomitant pathology was hardly expressed and did not dominate in their clinical picture. In 198 patients permanent syndromes of CBI were found and they were classified in such way: cephalgic syndrome (73 patients), vestibular syndrome (43 patients), pyramid syndrome (8 patients), light cognitive disorder (20 patients), Parkinson's syndrome (2 patients), bulbar syndrome (1 patient), organic psychosyndrome (51 patients). In the group of paroxysmic syndromes (43 patients) such kind of classification was received: transient global amnesia (13 patients), drop attack (8 patients), syncope (4 patients), late onset epilepsy (10 patients), falls by elderly people (8 patients).

For all these manifestations of CBI, we applied special treatment: anticonvulsants for late onset epilepsy, nootropes, cerebral metabolytes and cholinesterasis inhibitors for a light cognitive disorder, analgetics for a cephalgical syndrome and so on, however, we administered medicaments to improve cerebrovascular circulation, i. e., vinpocetin, pentoxifillin, cinnarizin, ginkgo biloba preparations, for all our patients. Our purpose was to improve cerebral perfusion, stimulate metabolic processes in the brain tissue after improving blood circulation by decreasing pathological manifestations and clinical expressions simultaneously. We recorded these results by observing a patient's clinical status and registering his/her subjective state. In the group of permanent syndromes 80% of the patients felt much better, subjective symptoms, such as headache, dizziness, decreased or disappeared, memory improved. In the group of organic psychosyndromes, decrease in the intensity of dysphorical, depressed, hypochondrical syndromes was stated, the mood of the patients improved. It was noticed that objective symptomatics of the patients with

Parkinson's syndrome, a bulbar syndrome and other also improved as a result of the treatment. Even better results were received in the group with paroxysmic syndromes. During our observation period (120 days), episodes of transient global amnesia did not repeated, there were only 2 drop attacks for the patients with expressed cerebrovascular atherosclerosis and rough neck spinal osteochondrosis, we noticed much fewer falls by elderly people and better postural stability.

We observed 44 patients with CBI stated according to our conception as a control group, however, vasoactive treatment was not administered to them. In the group of the patients with permanent and paroxysmic syndromes of CBI who were administered vasoactive treatment, clinical manifestations of the disease were slightly, subjective symptoms were milder.

It could be concluded, what vasoactive treatment for patients with CBI is necessary and must be administered along with medicaments and other means of treatment according to the dominant symptom.

THE REACT STUDY – BEHAVIOURAL MAPPING OF PATIENTS' ACTIVITY IN STROKE REHABILITATION

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It is known that comprehensive stroke unit care in close collaboration with rehabilitation facilities results in decreased mortality and better functional outcome. The concept is strongly recommended in international guidelines of stroke treatment and rehabilitation. However, we lack knowledge on what components of stroke unit care are attributable to the effects, strong candidates being incresed staff skills and earlier/more physical activity. There are strong indications that early mobilisation decreases complications as pneumonia and thrombosis, increases the cerebral blood flow and promotes neurogenesis and repair. Large studies have been launched to map these factors in the acute stage of stroke, but still we lack initiatives for mapping which dose of physical activity is optimal for stroke rehabilitation. It has been shown that even in stroke units patients' level of activity is relatively low. There are also concerns that too large an activity level would be decremental for the patient. A randomised controlled trial is therefore warranted and we are launching a pilot study as a preparation for that.

The aims of this study is to map activity patterns and levels in stroke patients in four rehabilitation hospitals in the Swedish West Gothia region. We will also test the feasability of registering activity using an electronic device.

Eighty patients aged 40–70 years will be included in the study 2–5 weeks after acute stroke, equally divided by the participating clinics and by both sexes. Sixty of these will be registered with a behavioural mapping technique. A trained rater will follow five patients a day and every 10 minutes register activity level, company and dwelling within the clinic. Twenty patients will be mapped using the device. Data will be analysed accumulated for all clinics and over the span of the study. Factors for analysis are activity in total, variations in activity over the day and week and in relation to the patient's sex and stroke severity, time in different activity levels and with different professionals.

The optimal timing and dosing of physical activity in stroke rehabilitation is not supported by scientific evidence. Neither do we know what level of activity today's practice actually comprises. This study will answer the latter question and constitute a necessary pilot study for a randomised controlled trial that will yield an evidence-base for increasing efficacy in stroke rehabilitation.

PHYSICAL AND MENTAL HEALTH OF STROKE SURVIVORS, AND THEIR DAILY ACTIVITIES

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The aim of the study was to compare the quality of life between stroke survivors and controls with respect to their health, daily activities, and mental health.

Contingent and methods of the study: The studied group consisted of 508 25–84 year-old inhabitants of Kaunas city who have survived first-onset stroke. The control group consisted of 508 age- and sex-matched randomly selected inhabitants of Kaunas city who had not experienced stroke. The SF - 12 Quality of life questionnaire was used for the study. Logistic regression was used to compare quality of life with respect to health, daily activities, and mental health.

Results. Only 1.0% of stroke survivors evaluated their health as excellent or very good, compared to 24.4% of the controls ($p=0.0005$); the respective percentages of those who evaluated their health as poor or fair were 78.9% and 26.4% ($p=0.0005$). Health significantly limited moderate activities in 35.2% of stroke survivors and 3.5% of controls ($p=0.0005$). During the last 4 weeks, health status or emotional problems most of the time or a little of the time impeded social activities in 19.3% of stroke survivors and 1.6% of controls ($p<0.05$). Comparing according to age, sex, and diseases (arterial hypertension/myocardial infarction/atrial fibrillation/diabetes mellitus/transient ischemic attack), stroke had the greatest negative effect on social activities (odds ratio – 36.7), caused sadness (odds ratio – 16.0), and significantly limited home activities (odds ratio – 15.5).

Conclusions: 28.2% of stroke survivors evaluated their health as poor, and 50.7% as fair, compared to, respectively, 1.8% and 24.6% of controls. Stroke significantly impaired the subjects mental health and limited their daily activities.

CORRELATION OF THE OUTCOMES OF MIDDLE CEREBRAL ARTERY ATHEROTHROMBOTIC AND CARDIOEMBOLIC CEREBRAL INFARCTION WITH INDICES OF CAROTID ARTERY PLAQUE STABILITY

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Aim: To determine the correlation between the Middle Cerebral Artery (MCA) infarction outcomes with the Cerebral Infarction subtype and the stability of the Carotid Artery atherosclerotic plaques.

Materials and methods: We examined 585 MCA infarction patients treated in the Stroke Unit; 73.2% had a Atherothrombotic cerebral infarction (ATCI) and 26.8% had a Cardioembolic cerebral infarction (CECI). The patients were divided into 6 groups with a mean age of 67.1 ± 11 years. The stability of the atherosclerotic plaques of the extracranial part of the Carotid Artery was assessed by US PHILIPS IU 22 equipment. The modified Rankin (mRS) scale was used to characterize the stroke outcomes.

Results: It was established that 54.5% patients with ATCI had stable Carotid Artery plaques, while instability occurred in 45,5%. Unstable plaques were 3.2% less common in patients with CECI compared to the ATCI group ($p<0.1$). MCA infarc-

tion outcome findings in both groups appeared to be almost the same; the only difference was 18% more complications for patients with ATCI than CECI. There was a significant correlation between the stability of plaques and the outcome of MCA infarction among the patients examined. In the group with stable plaques, 76% were able to walk (0–3 degrees mRS), 21% were bedridden (4–5 degrees mRS) at the time of discharge, 3% died. In the group of patients with unstable plaques 62% were consistent with 0–3 degrees mRS, 27% were bedridden (4–5 degrees mRS), 11% died. The number of bedridden patients and those who died was significantly greater in the group of patients with unstable Carotid Artery plaques ($p<0,001$).

Conclusions: The outcome of MCA infarction was similar in the ATCI and CECI groups but complications were more often found in patients with ATCI than CECI. Carotid Artery plaque instability was found to increase notably among bedridden patients as well as the mortality rate.

PROGNOSTIC FACTORS OF THE BRAIN ANEURYSMS RUPTURES

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Objective: to estimate prognostic factors of the brain aneurysms ruptures by brain vessels angiography.

Methods: the work is based on complex examination of 324 patients with brain aneurysms, treated in 5th Minsk clinic. Primary hemorrhage were revealed in 218 patients (67.3%), repeated hemorrhage – in 92 (28.4%) and in 9 patients etiology of hemorrhage were not clear. By the sex dividing was following: men – 224 (69%), women – 99 (31%). The age was in range from 16 to 78 years. The most common place where aneurysms were revealed was anterior communicated artery – in 217 (67.9%) patients. In 45 (14%) patients aneurysms were located at internal carotid artery and in 1 (0.3%) patient it was located at the vertebral artery. Intraarterial digital subtraction angiography (DSA) was performed on specialized angiographic complex "NEUROSTAR S" by Siemens. We used non-ionic X-ray contrast medium, such as ultravist-300, ultravist-350, omnipaq-300, omnipaq-350, visipaq-320. Injection was made by automatic injector ANGIOMAT 6000. Injection speed was 3–8 ml per second.

Results: by using DSA, was spent an estimation of aneurysmal size which were a source of intracranial hemorrhage. The greatest size estimated towards it maximal diameter. For estimation an authentic data about influence of aneurismal size on cases of repeated intracranial hemorrhage, maximal diameters of aneurysms were compared in groups with primary and repeated hemorrhages. In group with primary intracranial hemorrhage the range of aneurismal size was 3.2–4 mm. In group with repeated intracranial hemorrhage the range of aneurismal size was 3.9–6 mm. The average size was compared by non-parametric methods (Kolmogov-Smirnov, Mann-Witney). Statistical methods showed authentic differences between sizes of aneurisms in groups with primary and repeated hemorrhages. Mathematical model of repeated hemorrhage development risk depended of aneurismal size was constructed which based on obtained data (for calculations had been used the method of ROC curves). Also a formal threshold of predictive force was revealed. It was 11 mm (sensitivity – 58%, specificity – 80.1%). But ROC curve is smoothed after sensitivity 0.6. At close value 10 mm the sum of sensitivity and specificity is maximal. Max K was 0.1.

Conclusion: being based on received data, increasing size of arterial aneurysms is one of prognostic factor of it rupture.

OPTIMAL PROJECTIONS IN DIAGNOSIS ARTERIAL ANEURYSMS OF INTERNAL CAROTID ARTERY BY THE METHOD OF DIGITAL SUBTRACTION ANGIOGRAPHY

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Objective of the research: to reveal an optimal projections in diagnostic arterial aneurysms (AA) of internal carotid artery (ICA) by using digital subtraction angiography (DSA).

Materials and methods: 91 patients were examined and diagnostic angiographic procedures were performed in 5th Minsk clinic from 1998 to 2009. 91 AA of the ICA were revealed. Frequency of revealing AA of the ICA in additional straight projections in dependence from cranial or caudal angulations C-arm gantry were analyzed. Angiographic examination was considered as a positive (optimal) when the body, bottom and neck of the aneurism were visualized. On the other side, when were visible only a part of body or we didn't saw a neck of aneurysm, examination was considered as a negative.

Results: for visualization AA of the ICA were used two position of the C-arm gantry in relation to a horizontal axis – standard straight projection with cranial angulation from 0° to -30° and with caudal angulation from 0° to +30°. DSA in straight projection with cranial angulation were performed in 31 patients with S-shaped tortuosity of internal carotid artery syphon and positive results were established only in 10 (32.3%). DSA with caudal angulation at the same group revealed 25 (80.6%) positive results. Informativity of the second method is authentically above: Chi2- test = 3.37, $p<0,05$.

Analysis of dependence frequency reviling AA of the ICA with S-shaped tortuosity of ICA syphon and normal ICA from motion range of C-arm's gantry had shown that the most frequently AA of the ICA revealed in straight projection with cranial angulation from 0° to -30° (in 48 patients – 80.0%, from 60 examined). At the caudal gantry rotation (from 0° to -30°) detection indicator was appeared authentically lower (in 10 patients – 32.3%, from 31 examined)): Chi2- test 4,22, $p<0,04$.

Conclusion: the offered method of diagnostic AA of the supraclinoid part of ICA consists of contrast injection through catheter introduced in initial part of the common carotid artery and simultaneous angiography in straight projection with cranial angulation 15° and in lateral projection without angulation. The method differs from other that in it performs an additional angiography in straight projection with caudal angulation 25°–30°. It allows to recieve an additional information about arterial aneurysms of the ICA and raises accuracy and effectivness of DSA because of deriving additional data about ICA aneurysm (size and location).

PREDICTION OF PROGRESSIVE COURSE AT ACUTE CARDIOEMBOLIC ISCHEMIC STROKE: THE ANALYSIS OF CLINICAL CHARACTERISTICS

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The aim of this study is to reveal prognostic clinical factors of progressive clinical course at acute cardioembolic ischemic stroke.

Methods: The prospective clinical observation study was performed on the basis of neurological department in hospital of medical emergency service in 2007–2009. There were examined 76 patients with acute cardioembolic ischemic stroke (IS) provoked by chronic or paroxysmal atrial fibrillation (AF). Stroke subtypes was classified according to TOAST criteria. According to IS clinical course all patients were divided into 2 groups: 39 patients with progressive IS and 37 patients with regressive IS. The complete diagnostic investigation included clinical examination, neurovisualization (CT or MRI), Doppler sonography, chest radiography, ECG, laboratory tests. Statistical analysis was performed by odds ratio calculation (OR), 95% confidence interval (95% CI). Statistical significance was achieved at $p < 0.05$.

Results. Patients were taken basic neuroprotective, antiaggregation or anticoagulation treatment. Clinical characteristics of patients with progressive and regressive cardioembolic IS are presented in the table. Progressive clinical course of cerebral ischemia led to severe neurological deterioration. Patients condition with progressive and regressive IS by modified Rankin Scale on outcomes > or = 3 pt. was marked at 35 (89.7%) and 11 (29.7%) cases accordingly; $p<0.001$.

Conclusion. As a result of observation cohort study it were revealed the following prognostic factors of progressive clinical course at acute cardioembolic ischemic stroke with AF: age ($p = 0.025$), female sex ($p = 0.048$); carotid stroke ($p = 0.004$), right carotid stroke ($p = 0.001$); NIH stroke scale score on admission > or = 12 pt. ($p < 0.001$), arterial hypertension ($p = 0.044$), congestive heart failure ($p = 0.04$), gastroenterological pathology ($p = 0.039$), urological pathology ($p = 0.019$).

NON-LINEAR ANALYSIS OF HEART RATE VARIABILITY IN PATIENTS WITH ISCHEMIC STROKE AND ATRIAL FIBRILLATION

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The purpose is to estimate autonomic dysfunction in patients with ischemic stroke (IS) and atrial fibrillation (AF) by non-linear analysis of heart rate variability (HRV).

Methods: Prospective study of 76 patients with acute cardioembolic IS was performed in 2007–2008. Patients were divided into 2 groups according to clinical course of IS: group with progressive IS and neurological deterioration (n=39) aged 75 [12] (Median [Range]) yrs and group with regressive IS (n=37) aged 70 [15] yrs; $z = -2.24$; $p = 0.025$.

HRV investigation was performed by using program-technical complex "Bries-M" in due electrocardiogram course records of 5 minutes in stationary conditions according to international standards. Time domain (SDNN, MxdMn, Mo, AMo, RMSSD, NN50, pNN50, SI), frequency domain (HF, LF, VLF, LF/HF), geometric (TI) and non-linear (chaos-gramm, approximate entropy – ApEn) HRV parameters were measured.

HRV parameters at IS were compared with control group (19 subjects aged 35 [14] yrs) from the data base of Belarusian Research-Clinical Center "Cardiology". Statistical analysis was made with Mann-Whitney U test (significant level of $p < 0.05$), Chi2- test for qualitative data and in case of small-expected frequencies Fisher's exact test.

Results: Chronic AF was diagnosed at 18 (46.2%) patients with progressive IS and at 20 (54.1%) ones with regressive IS ($p>0.05$); paroxysmal AF – at 21 (53.8%) and 17 (45.9%) cases accordingly ($p>0.05$). In control group SDNN was 51.3 [29.5] msec, ApEn – 0.022 [0.049]. SDNN in patients with progressive IS was 129.6 [123.6] msec and exceeded control level in 2.5 times; $z= -4.34$; $p < 0.0001$). SDNN at regressive IS exceeded controls in 2.6 times (131.9 [119.2] msec vs 51.3 [29.5] msec accordingly; $z=-4.36$; $p < 0.0001$). Approximate entropy at stroke with atrial fibrillation exceeded significantly control level of ApEn what characterized difficulty and abruptness of non-stationary processes of heart rate management at atrial fibrillation. So ApEn level at progressive IS was 0.756 [0.767] ($z= -4.24$; $p < 0.0001$ in comparison with controls), at regressive stroke – 0.744 [0.903] ($z = -3.55$; $p = 0.0004$ accordingly).

Conclusion: HRV investigation at acute cardioembolic IS demonstrated severe dysfunction of central and vegetative neural control of heart rate management. Traditional linear (SDNN) and non-linear HRV parameters (ApEn) at progressive IS with atrial fibrillation exceeded the same indices of control group.

HEADACHE / PAIN

COMPLEX TREATMENT FOR AGEING PATIENTS WITH COITAL CEPHALGIA

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Introduction: Coital cephalgia (CC) is a headache related to sexual activity and is classified within the group of thunderclap headache. Research achievements in European countries for patients with CC show positive results of complex treatment: necessary medication (MT) and cognitive hypnotherapy (CH).

Aim of the study was to investigate the benefits of the CH and MT in the complex 4 weeks treatment course for working ageing patients with CC.

Material and Methods: During 2006–2008 years period 41 ageing female and male patients was consulted with coital and post-coital headache (CC) during sexual activity: intercourse, masturbatory orgasms. 34 patients of them were treated and observed. A group (females = 17, males = 9) 4 weeks received complex treatment: CH twice a week, MT – anxiolytic NoofenR 250 mg twice a day. Control or B group (females = 4, males = 4) received 4 weeks only NoofenR, 250 mg twice a day. Before starting CH course Clarc J. C. &

Jackson J. A. hypnotic susceptibility test was performed, a stage of anxiety and intensity of pain was measured by Rosenberg Self-Esteem Scale and Visual Analogue Scale. Treatment efficacy was re-evaluated in follow-up visit after 5 months.

Results: 34 female and male patients, aged between 60 and 67, white collar workers, suffering one-six months from severe, throbbing orgasmic headache, were treated. Patients had also anxiety, sleep disruption after psychotraumatic events in their workplace and family life. Before treatment course in all cases was done neurological and another necessary clinical examination.

At the conclusion of the complex treatment course there was significant headache reduction in 26 A group's patients, high hypnotizable patients achieved a greater reduction. In CH sessions patients received hypnotherapeutic imagery with muscular and mental relaxation, analgesia during sexual intercourse. There were no side effects by using NoofenR, CH allowed decreasing the dose of anxiolytic. Catamnesis data showed that there were no any medication in 19 A group's patients, they used regularly self-relaxation. Only 2 patients of control (B) group after 4 weeks therapy had improvement of health state.

Conclusion: Complex 4 weeks treatment – cognitive hypnotherapy and anxiolytic NoofenR is just an optional short-term therapy for working ageing individuals suffering from psychogenic, stress related coital cephalgia and anxiety.

RIGHT-TO-LEFT SHUNT AND CLINICAL FEATURES OF MIGRAINE WITH AURA

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Background: Migraine with aura (MA) is associated with high frequency and larger size of right-to-left shunts (RLS). Clinical studies reported that in some families the dominant inheritance of small intracardiac RLS is linked to inheritance of MA. There are suggestions that embolization through RLS may give rise to aura.

Objective: To assess if clinical characteristics of migraine and aura are different in patients without and with RLS.

Materials and methods: The participants of the study were MA patients of Vilnius university hospital Santariskiu clinics with one or more attacks during the year. Migraine characteristics (age of onset, family history, number and pain intensity of attacks, disability, duration and symptoms of aura), demographic data, use of abortive and prophylactic medication were collected using a special questionnaire. RLS was assessed using contrast transcranial Doppler sonography (c-TCD) according to the Venice Consensus Conference. According to c-TCD findings RLS was categorized into 4 groups: 0) no microembolic signals (MES), 1) 1–10 MES, 2) > 10 MES and no curtain, and 3) MES shower or curtain, when a single microembolic signal cannot be identified. The results were documented separately for rest condition and Valsalva maneuver (VM) testing. Large RLS was considered when >10 MES were registered at rest or shower/curtain was registered after VM. Clinical features of MA were compared between patients with or without RLS, and between patients with or without large RLS.

Results: We enrolled 72 MA patients (mean age 36.17 10.40; 70.8% females). RLS was confirmed in 46 (64.8%) cases, 29 patients (40.8%) had large shunt. Patients with RLS had longer duration of aura (39.24 min vs. 23.40 min, p=0.020) and higher attack frequency per month (2.83 vs. 1.35), but this difference did not reached the level of significance (p=0.053). There were no clinical differences between MA patients with or without large RLS.

Conclusions: Longer duration of migraine aura may predict presence, but not the size of RLS. Other clinical features of MA have no association with presence or size of RLS.

HEADACHE IN A PEDIATRIC EMERGENCY DEPARTMENT

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Goals: our work wanted to prove the importance and usefulness of Pediatric Emergency Department (PED) for a disease increasingly emerging in Italy. That's why there is the need to set guidelines for proper diagnosis and follow-up.

Headache, a very frequent symptom in pediatrics, can severely affect the child and his family's life quality, representing an important reason of access in PED.

From the clinical point of view, it proves very handy to subdivide headaches in primary and secondary ones. As far as the primary ones are concerned, the common migraine without aura is recognized as the most frequent in the child, while the most recurrent among the secondary ones are due to infective processes and they represent the 57% of the patients admitted to first aid access with headache with acute onset.

Our work analyses the data collected from June 2000 to December 2006, at Pediatric Emergency Department of Institute "G. Gaslini", concerning the admissions of patients affected by headache, with particular attention to the necessity of coming up with a clinical and diagnostic path.

During the study there have been 228.255 admissions, of which have been discharged or admitted 2214 patients with diagnosis of headache of which 55% are male, and 45% female.

After triage, 14.3% has been evaluated as white code, 74.3% as green one, 10.8% as yellow one and 0.6% as red one. Final destination of these patients has been hospitalization for 38%, OBI for 8%, home or ambulatory control for 54%.

Conclusions: The accesses to ED for headache are increasing. It needs better information of the family, coordination among territorial structures and clinic management in ED.

SURVEY OF PATIENTS AFTER LOW BACK SURGERY

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Objectives: The main target of each spine operation is to diminish pain syndrome and to improve physical functioning of the patient. The result of spine surgery depends on many factors and in part of cases the improvement was not achieved, pain continued to persist for years. Failed back surgery syndrome has been reported from different centers and countries in different figures particularly in cases of degenerative disorders. The aim of this study was to evaluate the long term results of low back surgery in Latvia.

Methods: 72 patients (42 or 58% females, 30 or 42% males; mean age 53 years) who have undergone spine surgery on

average 5.9 years ago were interviewed from November 2008 using written inquiry forms of 16 questions. Respondents were selected on basis of refereed data from general practitioners.

Results: The majority of interviewed 78% have undergone the operation because of intervertebral disc herniation and protrusion, in other cases indications for surgery were spondylolistesis, scoliosis, spine injury. 73% of respondents had one operation, 21% two, 6% 3–7 operations. Only 29% of patients were free of pain one month after surgery, 25% were without pain six month after surgery, but at the moment of the interview (3 months to 10 years after surgery) only 13% of patients. 15% of patients had severe pain one month after back operation, 16% after 6 months, but at present time (on average after 5.9 years) 32% have severe pain. At the same time periods 22% of interviewed showed mild pain (at 1 month), 19% at six month and 19% in nowadays. In total sufficient pain relief was succeed in 44% of operated patients after half a year and in nearly one third (32%) up to now but chronic pain continued in others (68% of patients). Residual functional restrictions were registrated at the moment of study: 9% of patients had different pareses, 3% experienced episodes of neurogenic claudication, but 1% were narcotic analgesics addicted. 84% of patients were overall satisfied with the results of the operations, but 16% recognized the operation as non-effective or low-effective.

Conclusions: There is reasonable number of patients after lumbar spine operations who have continued to experience and report pain afterwards in Latvia. It could depend on the follow-on criteria and carefully selection of patients for spine surgery but rehabilitation activities, progression of degenerative disease are of importance as well.

THERMAL PERCEPTION IN POLYNEUROPATHY PATIENTS

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Objectives: In spite of variable complains, polyneuropathy is often clinically clear syndrome, but not all types of nerve fibers involvement can be proved by nerve conduction studies. Quantitative sensory testing (QST) can be used to evaluate small C and A-delta fibers, thereby could have value in small fibers neuropathy diagnosis. The aim of present study was to find possibly changed thermal perception thresholds in polyneuropathy patients compared to healthy individuals.

Methods and material: 23 patients (6 males, 17 females, mean age 45.3) with proved diagnosis of polyneuropathy (clinically and by nerve conduction studies and/or changed sympathetic skin reactions) were referred for study by neurologists in Paul Stradins Clinical University Hospital in Riga. Predominant were sensory symptoms in 10 patients, motor- in 2 patients, sensorimotor in 3 patients, autonomic in 8 patients. All patients were tested by Medoc TSA-II Neurosensory analyzer to measure perception and pain thresholds. The following series of the tests were performed: perception threshold for warmth and cold, pain threshold for heat and cold for both feet and arms. Results were compared to 12 healthy controls (9 females and 3 males, mean age 28.4 years).

Results: Most of polyneuropathy patients (21) had changed thermal-QST thresholds. No notable changes were found in 2 patients only. Most frequent threshold changes were: warmth hypoesthesia 17, cold hypoalgesia 17, cold hypoesthesia 15, heat hypoalgesia 12, cold allodynia 7, heat allodynia 3. Paradox reactions were found in 3 patients. We found that 5 patients were allodynic to both heat and cold. Hypoesthetic and allodynic patients were analyzed separately to exclude that summing positive and negative threshold changes give normal results. We propose this for further data analyses. The following threshold values were found in polyneuropathy patients: warmth perception 27.5 compared to 30.1 in control group, cold perception 38.2 compared to 33.8 in control group, cold pain 5.4 compared to 11.2 in control group, heat pain 47.27 compared to 44.00 in control group.

Conclusions: Polyneuropathy patients have changed thermal perception and pain thresholds compared to healthy individuals. The usefulness of QST in polyneuropathy patients should be estimated. We propose to analyze allodynic and hypoesthetic patients separately.

RADICULAR AND LOW-BACK PAIN – CHANGES IN PAIN AND PERCEPTION THRESHOLDS

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Low-back (LBP) and radicular (RP) pain is most common chronic pain syndromes worldwide, 37% of chronic pain sufferers in Latvia as well. RP is recognized as neuropathic, also LBP has neuropathic pain (NeP) component in more than third of patients. These components require different pain management strategies and correct pain diagnosis is of great importance.

The aim of study: To determine the changes in thermal perception and pain thresholds as small nerve fibers' dysfunction in patients with chronic LBP and RP, and to detect its' correlations with clinical manifestations.

Methods and material: 17 patients with LBP (age 60±13 y), 19 patients with RP due to lumbal radiculopathy (55±13 y) and 9 control group without pain (52±12) underwent quantitative sensory testing (QST) using Medoc TSA-II Neurosensory analyzer. Thermal perception and pain thresholds were detected on both sides of back and in regions of one or two lumbal dermatomes. Pain was evaluated by VRS, McGill Pain Questionnaire and Brief Pain Inventory.

Results: Changes in thermal perception and pain detection thresholds were detected in LBP patients over the painful sites of back and also over the distal dermatomes in legs indicating of NeP component. In patients with RP decreased thermal and pain perception were found not only over the affected side but over dermatomes on contralateral side too, where radiculopathy was not diagnosed by clinical examination. Hyperalgesia was more pronounced over the back in LBP while in patients with lumbal radiculopathy over the distal dermatomes.

Conclusions: Chronic LBP without clinical manifestations of radiculopathy can include neuropathic pain mechanisms what could be considered in diagnostic and therapeutic strategies.

TREATMENT OF THORACIC OUTLET SYNDROME: CASE REPORT

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Purpose: Neurogenic thoracic outlet syndrome refers to compression of brachial plexus at the thoracic outlet area. It is one of the most controversial nerve compression syndromes

ever. Nobody doubts symptoms of TOS arising from cervical rib or elongated transverse process of C7, but what if same symptoms arise, but there is no evidence of any anatomical impediments? These patients usually deteriorate over the time despite professional help by pain clinics.

In this study we present patient manifesting thoracic outlet syndrome with positive result from surgical treatment.

Method and results: A 41 year old storage house worker without previous trauma or surgery has 5 years history of progressive weakness and severe intolerant deep pain in the shoulder and left upper extremity, visual analogue scale – up to 10/10 most time of day. No night rest was available. In the neurological examination – "guarding hand" position, hyperalgesia, allodynia, stiffness, edema, abnormal sweating and cyanosis in left upper extremity, motor strength 2/5. Tinel was radiating from supra- and infraclavicular areas to hand. Trapezius muscle was extremely painful with distinct trigger points. MRI of the neck and brachial plexus shows no abnormality. Neck X – ray was negative. Electrodiagnostic studies unperformed because of pain, but previous studies did not reveal particular abnormalities. Medical treatment, continuous epidural injections, stellate ganglion blocks and surgical sympatectomy had no effect.

There was performed surgical transaxillary first rib resection that was followed by scalenus anterior 90% removal and scalenus medius 50% removal. During surgery very narrow costo-clavicular angle with impinged subclavian vein was noted. At the same time very broad scalenus medius muscle insertion at the first rib was seen with scarred and thick fascia. Patient was seen 10 weeks postoperatively with pain 6/10 in the upper extremity, no hypersensitivity, almost normal 2 point discrimination in the fingers (7–8 mm) and fair range of motion in the hand. Grip was 7 kg as opposed to none before the surgery.

Conclusion: Thoracic outlet syndrome is one of the causes of complex regional pain syndrome and in case of ineffective conservative treatment requires surgical intervention. We believe that even if improvement was not 100%, any improvement in case of intractable and debilitating pain is justification for thoracic outlet decompression surgery.

MOVEMENT DISORDERS / DEMENTIA

TREATMENT OF PARKINSON'S DISEASE IN ESTONIA

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The purpose of this clinical study was to assess the treatment patterns and the prevalence of motor complications compared in 1996 and 2008 in patients with Parkinson's disease.

Methods: The sample of the patients with Parkinson's disease studied in Tartu University Clinics, included 134 cases in 1996, and 160 cases in 2008.

Results: All the patients in the survey used the antiparkinsonian medication. In 1996, levodopa was administered for 76% of the patients, with mean daily dose of 584 mg (mostly regular levodopa), and mean duration of 4.6 years. In 52%, levodopa was used as monotherapy. Motor complications were described in 43% of levodopa users: on-off fluctuations in 26%, and dyskinesias in 39%. In 2008, the percentage of levodopa users is somewhat higher – 88%, with mean daily dose of 524 mg (mostly prolonged release formation, or with COMT-inhibitor), and mean duration of 4.5 years. The proportion of levodopa monotherapy has decreased to 27%. Motor complications were present in 31% levodopa users: on-off fluctuations in 24%, and dyskinesias in 22%. The treatment strategies have changed remarkably during 12 years: the proportions of users have increased for dopamine agonists (from 13% to 47%), amantadine (from 19% to 39%), and MAO-B inhibitors (from 7% to 13%) but dramatically decreased for anticholinergics (from 26% to 1%).

Conclusions: Treatment strategies have changed through 12 years in Estonia: though the percentage of levodopa users has increased, there are less motor complications. Usually, levodopa is used as a controlled release formulation in combination therapy now. All antiparkinsonian medications are reimbursed 100% by the Health Insurance Fund in Estonia, including non-ergoline dopamine agonists, new generation MAO-B inhibitors and levodopa combination with COMT-inhibitors.

PREVENTING STROKE AND DELAYING ALZHEIMER DISEASE: CAN WE DO BETTER?

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The growing menace

We need to start preventing early, because 8% of individuals over the age of 65 years have had a stroke, 8% are demented and 17% have some cognitive impairment short of dementia. Cognitive impairment and stroke represent risks for each other. 25% of those who have cognitive impairment have had a stroke and 64% of stroke patients have some cognitive impairment. One in four individuals aged 65 years or older will suffer a stroke, cognitive impairment or both, unless we do something about it.

Limitations of current approaches

Currently attention focuses on the extremes, patients with problems severe enough to come to medical attention, typically with a stroke or dementia. In between, lie the neglected majority of patients who may have silent cerebral infarcts, leukoaraiosis, subclinical or incipient Alzheimer's disease, and various combinations thereof. Only 13% of patients who suffer a stroke ever get a warning in the form of a TIA. When these patients are examined they often have cognitive impairment of the executive type. Stroke specialists evince little interest in cognitive disorders and those interested in cognitive disorders largely focus on Alzheimer's disease, showing little interest or expertise in cerebrovascular disorders. Current criteria for diagnosing cognitive disorders are woefully inadequate, and put the emphasis on the late stages at which time little can be done. We have suggested the term "vascular cognitive impairment" to identify any cognitive disorder caused by or associated with vascular factors, which in principle are treatable and preventable.

Can we do better?

Physical inactivity, obesity, hypertension and hyperlipidemia represent risk factors for stroke and also for so-called Alzheimer's disease. We need to develop a common vocabulary of understanding and focus on disease mechanisms rather than nosological descriptions, identify common therapeutic targets and speed up the pace of preventive trials, particularly those beginning at the asymptomatic stage. Fortunately, the accelerating pace of scientific discovery, the power of electronic communication and growing awareness, offer opportunities to stem the tide of stroke and cognitive disorders. The wellbeing of millions depends on it.

CRANIAL CT FEATURES IN DEMENTIAS

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Learning Objectives: Demonstrating CT Features in Dementia clinical/radiologic correlation. To determine the predictive capacity of CT in suggesting this diagnosis.

Background: Dementia has a constellation of features based on its aetiology/localization, affecting the frontal/temporal lobes in a 1:10 ratio. A vascular insult could be a common cause of dementia through arteriosclerotic encephalopathy. CT could offer an initial reliable imaging option.

Method/Technique: This review concerned 20 cases (14 males, 6 females: 2 <40 years, 5 between 40 to 60 years, 5 between 60 to 80 years, 1>80 years). Clinical features: hypertension 2 new onset behavioral abnormality 3 disorientation 1 mood changes 1 headaches 2 inability to walk 1 truncal ataxia 2 progressive dementia 4 extrapyramidal signs 1 paraplegia 1 obstipation 1 deteriorating mental state 1 remote symptomatic convulsive seizures 2 slurred speech 1 polydispsia 1 polyuria 1 diabetes insipidus 1 neurodegenerative disease 1 cerebral tumour 1 memory deficit 1 agnosia 1 cerebral degenerative condition 1 hallucinations 1 acute confusional state 1 nocturnal monoparesis, compatible Alzheimer's 2 disadochokinesia 1 antegrade/retrograde amnesia 1 cerebellar ataxia 1.

CT features normal 9, calcification: left ocular globe 1/ pineal gland 1, choroids plexus 4 occipital lobe hypo density 1 Ventricular dilatation: lateral ventricle 1 right anterior ventricular limb 9 right anterior temporal limb 9 right posterior ventricular limb 8 left anterior ventricular limb 8 left temporal ventricular limb 8,left posterior ventricular limb 8, 3rd 8 4th 3, hypo dense lesions: right 4, left 4, left ocular globe 1hyper dense lesions: right4, left 3, brain infarctions 5, brain tumour 3, poroencephaly, senile atrophy, markedly increased subarchnoid 13 supratentorial sign of brain atrophy 1, l sub cortical/parenchymal cerebral atrophy 11, frontal cortical cerebral atrophy 10, parietal cortical cerebral atrophy 10, Temporal cortical cerebral atrophy 9, localized brain oedema to the right frontal lobe 1, left frontal cerebral atrophy 1, blunting of the subarchnoid frontally 1, occipital cerebral atrophy 5, neurodegenerative disease 2, hyperdense shadows on both parietal lobes without oedema 1, poor white grey matter differentiation 1.

Conclusion: In appropriate clinical settings HR CT applied by experienced personnel is very informative in the nomenclature / diagnosis of dementias. Indeterminate cases could be evaluated/clarified at MRS/MRA / SPECT.

EPILEPSY

EPILEPSY IN ELDERLY PERSONS (HOSPITAL DATA ANALYSIS)

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Introduction: The incidence of acquired epilepsy increases at the age of 60+, especially in cerebrovascular disease (CVD) (Anneger, 2001). The aim of our investigation was to estimate the frequency and peculiarities for patients in neurological department of clinical hospital "Gailezers" of Riga city.

Methods: Retrospective analysis of medical histories of 237 patients with epilepsy at the age of 45 to 69 years, 130 males and 107 females, for period 2001–2007, was done.

Results: CVD was the main cause of epilepsy in 161 patient (68%), the highest frequency in the group 60–69 years.

In CVD patients epilepsy developed due to ischemic stroke (66%), haemorhage (11%), malformation (8%), encephalophathy (15%). The second cause of epileptic fits (13%) was sequel of cerebral trauma, often after alcohol consumption. 2% of epileptic cases were due to cerebral tumours and infections.

In 58% of cases was diagnosed generalized epilepsy, in 42% – partial seizures.

Conclusions: 1. In elderly persons of Latvia the main cause of late onset epilepsy is CVD, especially ischemic events. 2. Remarkable part of patients suffer epilepsy after craniocerebral injury, often joined with alcohol consumption; it is factor to consider the prevention of symptomatic epilepsy.

POSTICTAL PSYCHOSIS IN TEMPORAL LOBE EPILEPSY: 2 CASE REPORTS

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Postictal psychosis (PIP) typically follows an exacerbation in seizure frequency or intensity, and emerges after a lucid interval. It has been reported in up to 6% of all patients undergoing video-EEG monitoring. Postictal psychosis complicates both primary generalized and partial epilepsy, being more frequent in partial epilepsy specially in temporal lobe epilepsy (TLE). Diagnostic criteria are: (1) episode of psychosis within 1 week after a seizure(s); (2) psychosis >15 h and <3 months; (3) delusions, hallucinations in clear consciousness, bizarre, or disorganized behavior, formal thought disorder, or affective changes; and (4) no evidence AED toxicity, nonconvulsive status epilepticus, recent head trauma, alcohol, or drug intoxication or withdrawal, prior chronic psychotic disorder. Risk factors for PIP include: age above 30 years, localization-related epilepsy, bilateral seizure, or interictal foci, clustering of seizures, secondary generalization. PIP typically arises after >10 years of seizures and is most common in equally in right and left temporal lobe epilepsy.

We describe two female patients aged 43 and 48 with refractory temporal lobe epilepsy who underwent video-EEG monitoring at our hospital. During EEG monitoring they had numerous complex partial seizures and after about 24 h lucid period developed episodes of postictal psychosis with agitation, delusions, visual and auditory hallucinations. Both patients had intractable temporal lobe epilepsy, one of them had left mesial temporal sclerosis.

Conclusion: PIP could often be observed in TLE patients undergoing video-EEG monitoring.

EVOLUTION AND PROGNOSIS OF THE CHILDHOOD ABSENCE EPILEPSY

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Purpose: studying of the effectiveness of antiepileptic therapy in child absence epilepsy, variant of transformation of childhood absence epilepsy into another forms of idiopathic generalized epilepsies and estimation of prognosis.

Methods: Were investigated 30 children with child absence epilepsy (17 boys and 13 girls) in the age rate from 4 till

18 years in the period of 2003–2008 years. Video-EEG monitoring was done with the systems BMS1 5000 and BMS1 6000 (Nicolet, USA), Beehive-Millenium 32 (Grass Telefactor, USA) and system of portable video-EEG monitoring Encephalan-Video on the basis of mobile EEG register RM-19/26 Encephalan-RM (Medicom MTD, Taganrog, Russia).

Results: Having observed in dynamic population of 30 patients with childhood absence epilepsy (CAE), we have revealed, that at 5 patients (16.7%) was marked transformation into juvenile absence epilepsy (JAE) with addition of generalised tonic-clonic seizures and 2 patients (6.7%) were transformed into juvenile myoclonic epilepsy (JME) with addition of myoclonic and generalized tonic-clonic seizures. Achievement of clinical-electroencephalographic remission was possible at 26 patients (86.7%): at 23 patients (76.7%) at the stage of CAE, and at 3 patients (10%) after transformation into JAE. Achievement of remission in 17 cases (56.7%) was noted on a background of valproate monotherapy, in 5 cases (16.7%) – on a background of ethosuximide monotherapy, on combination of valproates with ethosuximide – in 3 cases (10%), and on combination of valproates with benzodiazepines – in 1 case (3.3%). In 2 cases of CAE transformation into JAE and in all 2 cases of transformation in JME was noted partial pharmacoresistance on the background of valproates, ethosuximide, benzodiazepines, levetiracetam and topiramate treatment in monotherapy and various combinations. In cases of JME impossibility of clinical remission achievement has been caused by catamenial course of seizures and occurrence of photosensitivity.

Conclusions: Prognosis of the childhood absence epilepsy is favorable with achievement of complete clinical-electroencephalographic remission in 86.7% cases. The least favorable variant of currention of disease is transformation into JME with partial pharmacoresistance in all this cases (6.7%), while in more than a half of cases of transformation into JAE is possible to achieve proof remission.

COMPUTED TOMOGRAPHIC FEATURES IN SYMPTOMATIC SEIZURES

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Background: Remote symptomatic childhood convulsive seizures is considered a high yield epileptic phenomenon making undertaking an initial easily applicable high definition resolution performance imaging such as cranial CT worthwhile. It offers clues that direct further imaging, electrophysiological studies, neurosurgical intervention, vagal nerve stimulation and novel chemical chaperone therapy.

Imaging Findings: This review concerns the Cranial CT of 51 children with childhood remote symptomatic seizures undertaken with a Somita Siemens CT scan at 3 mm slices and interpreted in a standardized manner by the Radiologist/Neurologist. 26 females, 25 males The seizure types were subtle seizures 3, atypical absences 5, focal seizures 7, atypical myoclonic seizures 4, generalized tonic- clonic seizures 32. Associated features were consanguinity/endogamy 17, positive family history of epilepsy 5, deaf mutism 2, history of hypoxic-ischaemic encephalopathy 3, neurodevelopmental delay 13, defect of self regulation 5, post meningoencephalitis 11, globally impaired executive functions 3, dysmorphisim 3, mental retardation 13, trauma 4, hemiplegia left 3, right 2, organic cerebral dysfunction syndromes 3, cerebral palsy 5, globally neurodevelopmentally delayed 3, syncopal attacks 1, left retrotorticollis 1. Hallucintions 1. The CT features demonstrated were Normal CT features 7, compatible intracranial tumour 1, basal ganglia calcifications 1, intracranial suppuration 2, intracranial haematoma 1, plagiocephaly 1, cerebral cortical atrophy 7, cerebral subcortical atrophy 9, atrophic ventriculomegaly 3, large cisterna magna 3, periventricular hypodense image 1, right hypodense lesion 1, right temporal horn dilatation 1, temporal labial mesial sclerosis 1, post infective destructive calcification 1, frontal lobe calcification 1, dilated subarachnoid spaces 10, frontal lobe atrophy 6, dilated posterior horn of the lateral ventricle 3, asymmetry of the cranial vault 1, calcification of the choroids plexus 1, right frontal lobe proencephalic cyst 1, panventriculomegaly 2, midline structural collapse 1.

Conclusion: Compared to CT in childhood idiopathic seizures abnormal CT in childhood remote symptomatic seizures correlated with aetio-clinico-pathologic features. These figures and the normal CT features could be evaluated further, corrected, remodified or confirmed at MRS/MRA/SPECT with chromatographic metabolic screen.

DEPRESSION AND ANXIETY IN ADULTS WITH EPILEPSY

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Purpose: to determine frequency of depression and anxiety in patients with epilepsy; to analyze relation of depression and anxiety with clinical characteristics of epilepsy, patients' demographics and social characteristics; to compare the depressiveness in epilepsy and other neurological disorders.

Methods: 193 patients with epilepsy and 168 without epilepsy were given a questionnaire regarding social and demographical issues. Depression and anxiety were measured by the Lithuanian version of Hospital Anxiety and Depression Scale (HAD Scale). A score of 11 or higher indicates the probable presence of the mood disorder. Patients with epilepsy were investigated regarding the fear of a recurrence of seizures.

Results: 97 men and 95 women with epilepsy and 80 men and 88 women without epilepsy answered questionnaires up to date. The mean age in epilepsy group was 39.65±13.52 years, in control group – 42.14±15.27. Duration of epilepsy – 14.1±12.34 years. Symptoms of depression were determined in 19.7% of patients with epilepsy compared to 11.2% of patients without epilepsy ($p<0.05$); anxiety – in 39.9% patients with epilepsy vs. 25.0% of patients without epilepsy ($p<0.05$). 84.2% of epileptics and 85.0% of patients without epilepsy with depressive symptoms had clear-cut defined anxiety symptoms. 57.0% of patients with epilepsy shoved neither depressive no anxiety symptoms (compared to 73.8% of patients without epilepsy). We didn't find statistically significant difference of depression and anxiety between sex in epilepsy group, however women without epilepsy had more severe anxiety than men ($p<0.01$). 45.1% of patients with epilepsy notified about frequent or permanent fear of seizures. The fear of seizures, older age (>45 years), unemployment and low background were associated with more severe depression and anxiety ($p<0.01$). Patients with generalized epilepsy or secondary generalized seizures had more severe anxiety than patients with partial seizures without secondary generalization ($p<0.01$).

Conclusions: Depression and anxiety are common and important problems in patients with epilepsy. Patients with epilepsy have higher rate of anxiety and depression, compare to other neurological disorders. Severity of depression and anxiety is associated with older age, unemployment, shorter education and type of epilepsy. These symptoms are highly related to the fear of a recurrence of seizures.

EPILEPSY AND FAMILY LIFE IN LITHUANIA

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Purpose: to evaluate the influence of epilepsy on familial status and sexual functioning in patients with epilepsy.

Method: 198 patients with active epilepsy were provided with questionnaire regarding epilepsy characteristics, family life and sexuality.

Results: 73 men and 125 women (mean age 35.83±13.56 y) were examined. Familial status: 87 (43.5%) (39.7% men and 46.4% women) – were married, 38% (49.3% men and 32.0% women) – unmarried, 8.5% – divorsed and 5.5% – widowers'. 63.2% unmarried patients pointed out dificulty in communication with other people due to epilepsy. 26.1% of divorced patients noted epilepsy as the main reason of divorce. 1/3 of patients (70% of them – women) concealed their epilepsy at the beginning of relationship with partner. 27.7% of patients believe their family life would be better without epilepsy. 36.1% of responders stressed the community impact on family life of patient with epilepsy. 98 (49.7%) of responders are childless: 11.6% pointed physical reasons; 23.3% voluntary refrained from having children; 14.8% (84% of them – women).had fear to transmit epilepsy to offspring. 45.0% of patients have sexual problems: diminished sexual desire – 28.2%; fear of seizure during sexual intercourse – 18.9%; sexual arousal problems – 21.7%, fear of conception – 31.2%. Only 46.2% of patients with sexual dysfunction sought for professional advice.

Conclusions: 1. Less than a half of the patients with epilepsy go to family life. 2. Patients with epilepsy avoid communication with other people and tend to conceal epilepsy. 3. The main reason for childless between men – sexual arousal problems, between women – fear of heredity. 4. Patients with epilepsy rarely seek for help due to sexual disturbances.

THE RENIN-ANGIOTENSIN SYSTEM AND ANTIEPILEPTIC DRUGS IN THE MES TEST

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Drugs affecting the renin-angiotensin system, angiotensin-converting enzyme (ACE) inhibitors and angiotensin-II (AII) receptor antagonists, are widely used in the treatment of hypertension, congestive heart failure or diabetic nephropathy. However, very limited evidence exists on the potential influence of these drugs on the anticonvulsant activity of second-generation antiepileptics (AEDs) in epileptic patients with hypertension. To assess that, the mouse maximal electroshock seizure (MES) model was used, which is regarded as an experimental model of tonic-clonic seizures and, to a certain extent, of partial convulsions with or without secondary generalization. In the current study, the effects of ACE inhibitors (enalapril and cilazapril) and AII receptor antagonists (losartan and telmisartan) on the protective activity of oxcarbazepine (OXC), lamotrigine (LTG) and topiramate (TPM) were examined. Electroconvulsions were produced by an alternating current (25 mA, 50 Hz, 500 V, 0.2 s stimulus duration) delivered via ear-clip electrodes. The ACE inhibitors and AII receptor antagonists were tested in the MES model at doses that did not influence the threshold for electroconvulsions.

Enalapril (30 mg/kg i.p.) and losartan (30 and 50 mg/kg i.p.) potentiated the protective activity of LTG, while cilazapril and telmisartan were ineffective. Telmisartan (30 mg/kg i.p.) was the only hypertensive drug which enhanced the anticonvulsant action of TPM. None of tested ACE inhibitors and AII receptor antagonists affected the antiseizure action of OXC. These results indicate interactions between drugs affecting the renin-angiotensin system and LTG or TPM, which may have some clinical importance.

CLINICAL CHARACTERISTICS OF THE CHILDHOOD ABSENCE EPILEPSY

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Purpose: studying of clinical characteristics of epileptic seizures in childhood absence epilepsy.

Methods: Were investigated 30 children with childhood absence epilepsy (17 boys and 13 girls) in the age rate from 4 till 18 years in the period of 2003–2008 years. Video-EEG monitoring was done with the systems BMS1 5000 and BMS1 6000 (Nicolet, USA), Beehive-Millenium 32 (Grass Telefactor, USA) and system of portable video-EEG monitoring Encephalan-Video on the basis of mobile EEG register RM-19/26 Encephalan-RM (Medicom MTD, Taganrog, Russia).

Results: The age of debut of seizures varies from 2 till 9 years. Typical absences are obligate type of seizures (100%). Predominantly (at 25 patients – 83.3%) were observed complex absences: absences with tonic component (deviation of eyes upward, probable retropulsion of the head) – at 8 patients (26.7%), absences with eyelid myoclonus – at 7 patients (23.3%), absences with pharyngo-oral automatisms – at 6 (20%), absences with encopresis – at 2 (6.7%), absences with gesture automatisms – at 1 (3.3%) and absences with vegetative component (hyperemia of the face) – at 1 patient (3.3%). Simple type of absences was fixed at 5 patients (16.7%). Absence seizures were unique type of seizures at 23 patients (76.6%), but at 5 patients (16.7%) was observed addition of generalized tonic-clonic seizures and 2 girls (6.7%) had transformation into juvenile myoclonic epilepsy with addition of myoclonic and generalized tonic-clonic seizures.

Conclusions: Childhood absence epilepsy is characterized by typical absences, predominantly complex type (83,3%), more often - absences with tonic component, absences with eyelid myoclonus and absences with pharyngo-oral automatisms. Addition of generalized tonic-clonic seizures was seen at 16,7% of cases and addition of myoclonic seizures in 6,7% testified transformation into juvenile myoclonic epilepsy.

ETIOLOGY OF EPILEPSY

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Epilepsy is caused by excessive excitability of cortical neurons and its spread via the networks within the brain. This process is determined by the abnormal activity of neurotransmitters and ion channels, or synaptic derangements, which may be genetically predisposed or occur due to stuctural brain damage at any age.

The inheritance of epilepsy is multifactorial and complex. Monogenetically inherited epilepsies may have different phenotypes. On the other hand, identical phenotypes may be the result of different genotypes. Genetically determined epilepsies, although most starting in childhood, may extend into adulthood, like autosomal dominant nocturnal frontal lobe epilepsy, juvenile myoclonic epilepsy, or progressive myoclonic epilepsy.

Structural brain damage as a cause for epilepsy may be identified in around 35% of cases. In adults, symptomatic epilepsies are often of partial type. Mesial temporal sclerosis is the most common cause for temporal lobe epilepsy. Sometimes it is accompanied by an extratemporal lesion (dual pathology). Brain tumours cause epileptic seizures in 8–16% of adult epilepsy cases, being the most comon cause for newly-onset seizures at the age between 35 and 55 years. Arteriovenous malformations manifest with seizures in 17–40% of cases, and cavernous hemangiomas in 40–70%. The risk of late post-traumatic epilepsy is around 12% within the first year and in fact depends on certain risk factors. Cortical malformations may cause up to 3% of all epilepsies and around 20% of the drug-resistant ones. Epilepsy occurs in 60% of patients with tuberous sclerosis, other neurocutaneous disorders being related to epilepsy as well.

Modern imaging techniques and molecular genetic studies have improved our understanding of the etiology of epilepsy. However, the precise etiology-related mechanisms and the correlations among the etiological, pathogenetic, clinical and prognostic factors needs further research.

THE PECULIARITIES OF PREGNANCY AND DELIVERY IN WOMEN WITH EPILEPSY AND ANTIEPILEPTIC DRUG THERAPY IN LITHUANIA

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Introduction: Most pregnant women with epilepsy require antiepileptic drug (AED) therapy. There are several international pregnancy registries for studying of AED teratogenicity. Despite the thousands of women in these registries around the world, there is not enough information about impact on pregnancy of AEDs.

Objective: To analyze pregnancy-related complications in women with AED and rate of fetal malformations; frequency of seizures during pregnancy related to different AED therapy.

Materials and methods: 100 pregnancies of women with active epilepsy and AED treatment in Lithuania were prospectively evaluated according to EURAP (International Registry of Antiepileptic Drugs and Pregnancy) protocol, including data on AED therapy, frequency of seizures, course of pregnancy and delivery, incidence of fetal malformations.

Results: The mean age of pregnant women was 25.7 (16–45) years. 69 of them had 1st, 19 – 2nd, 10 – 3rd and 2 – 4th pregnancy. 9 of pregnant women had primary, 72 – secondary, and 19 – high level of education. During pregnancy 65 women used 1 AED, 29 – 2 AEDs, and 6 – 3 AEDs. Aetiology of epilepsy: 14 – symptomatic, 26 – cryptogenic, 53 – idiopathic and 7 – unknown. There were 4 premature terminations of pregnancy: 1 due to of medical reasons, 1 spontaneous abortion and 2 interruptions of pregnancy (because of woman's villing). 80 (84.2%) of women has natural labour delivery, and caesarean section was performed in 15 (15.8%). 34 women didn't experienced seizures during first trimester of pregnancy, 50 (52.1%) – during the second trimester, and 68 (70.8%) – during the third trimester. 40 women were on VPA, 32 – CBZ, 31 – LTG, 20 – OXC, 8 – CZP, 6 – TPM, 2 – GBP, 1 – BZD, and 1 – on ZSM. One fetal malformation was diagnosed for newborn of woman with VPA, and another pregnancy was interrupted because of fetal malformations in woman on VPA and OXC. Overall incidence in malformation rates were 2.1%.

Conclusions: Most women with epilepsy and AED treatment do not have obstetric and delivery complications. Increase in seizure frequency during pregnancy is rare and more frequent in women treated with lamotrigine and oxcarbazepine. Our findings suggest that overall rate of malformations is relatively low and mostly related to VPA treatment during pregnancy.

MULTIPLE SCLEROSIS

ONE QUESTION AS A SCREENING INSTRUMENT FOR DEPRESSION IN PERSONS WITH MULTIPLE SCLEROSIS

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Introduction: Depression is the most described psychiatric condition accompanying multiple sclerosis (MS) with the lifetime prevalence rate up to 67%. The aim of the study evaluate how effectively one question "Are you depressed?" works as a screening tool for depression in persons with MS.

Results: During 2 weeks of in-patient stay the mood disorder was analysed in 134 consecutive in-patient persons with MS. The results from a single question were compared with formal clinical diagnosis and the classification from a standard questionnaire. On the basis of clinical interview and Beck Depression Inventory the diagnosis of depression was confirmed. 57% (77/134) persons with MS answered "Yes" to the question "Are you depressed?". The diagnosis of depression was confirmed in 94% (72/77) persons with MS and not confirmed in 6% (5/77) persons with MS. Hence, the screening test sensitivity was 91%. 43% (57/134) answered "No". 70% (40/57) did not have depression. In this case the sensitivity was 54%. 30% (17/57) of this group were actually depressed according to tests and clinical impression. The age, sex, duration of the disease, cognitive abilities and physical disability did not influence consistency of the answers with test results and clinical opinion.

Conclusions: one question interview is a useful tool screening of depression in persons with MS as it confirms existing depression (sensitivity 91%), but the results should be treated with caution if the person with MS denies mood problems.

CLINICO-MORPHOLOGIC DISSOCIATIONS OF THE ONSET OF A MULTIPLE SCLEROSIS

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Introduction: The idea of heterogeneity of the disease, stated by the ancestor of the doctrine about multiple sclerosis (MS) Jean-Martin Charcot (1872) and periodically confirmed with the subsequent researchers (O. A. Hondkarian, 1983; Lassman, 2000), is particularly actual for timely prescription of adequate treatment in a onset of this disease. Objectives. Purpose is to try to reveal some clinico-morphological features of onset of multiple sclerosis, using modern methods of neurovisualization and the data of clinical examination of patients. Materials and methods.10 patients with a multiple sclerosis (6 women and 4 men) aged from 19 to 24 years were examined during their initial visit to the expert neurologist. The diagnosis was established according to McDonald's (2001) and Kurtske's (1983) criteria. For neurovisualization of brain tissue condition magnetic resonance imaging (MRI) with 1.5 T field tension and proton magnetic resonance spectroscopy (PMRS) in STEAM&PRESS method were used. Results. The one-focal onset of multiple sclerosis in form of a retrobulbar neuritis (3 persons), multifocal onset MS with minimum pyramidal cerebellar symptomatology (4 persons), afferent disturbance and increased motiveless fatigability with minimum active complaints of patients (3 persons) were clinically registered. On MRI morphological changes of brain were not revealed in two cases, but the large foci of demyelination with edema (5 cases) and in three patients the hyperintensive on Ò2 and heavily weighed T1 images were found out in corpus collosum and paraventricular zones of white substance. In 8 from 10 cases either clinico-morphologic or morpho-clinical dissociations were recorded. The PMRS which, in essence, is a method of functional research of tissue is presented in our observations by changes of three peaks of a resonant curve: rise of inositol concentration (in 8 from 10 cases), reduction of choline peak (in 6 from 10 cases) and reduction of creatine peak (in 4 from 10 cases). In all 10 cases of PMRS use changes of brain metabolism were observed both in foci of demyelination determined by means of MRI and in the points of a brain investigated outside MR foci demyelination.

Conclusion: Initial clinical and morphologic signs of multiple sclerosis are heterogeneous in space and time that indicates a prescription of differential therapy.

THE CONDITION OF BRAIN METABOLISM ACCORDING TO THE DATA OF PROTON MAGNETIC RESONANCE SPECTROSCOPY AS THERAPY PREDICTION OF MULTIPLE SCLEROSIS

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Introduction: The number of patients with mild forms of multiple sclerosis (MS) (clinically isolated syndrome, afferent disturbances in the onset of the disease, moderate cognitive disturbances in remittent course of the disease, etc.) increased in connection with the success of diagnosis and treatment of MS. "The drugs changing multiple sclerosis course" created on the basis of immunological link of MS pathogenesis, do not cover all peculiarities of demyelination, and have the marked side effects, causing depression and insomnia.

Objectives: The aim is to study perculiarities of myelin metabolism disturbances in the presence of MS and to use these data for the therapy prediction of MS by means of high fild proton magnetic resonance spectroscopy (PMRS) of the brain.

Materials and methods: 36 patients with different duration of the disease were examined: the onset of MS (1–2 years of the disease) – 8 patients; remittent MS (3–5 years of the disease) – 12 patients; secondary progressive MS (7–12 years of the disease) – 16 patients. Examinations were made using magnetic resonance imager (MRI) Siemens according to programs of the Center of radiation diagnosis and treatment of oncological patients in Saint Petersburg.

Results: Outwardly identical foci of demyelination, visualized on MRI, gave various spectra of metabolic disorders, what corroborated their heterogeneity. At the onset of disease in 7 of 8 patients the increase of inositol peak, approximately 2 times more the norm, and appearance of lipid peak in 5 of 8 patients, which became high in MS progression, were registered. During the exacerbation of remittent MS and its secondary progressive course in new foci the reduction of NAA/Cho ratio up to 1.35–1.45 and NAA/Cr ratio up to 1.20–1.30 was recorded. In the old foci zone the increase of signal intensity of creatine and choline with reduction of NAA/Cho+Cr ratio up to 0.47–0.62 was observed. In 5 from 7 cases the increase of inositol peaks appeared earlier than perifocal edema and accumulation of intravenously injected gadolinium. In severe course of the disease in 3 of 12 patients with remittent MS and in 10 of 16 patients with progressive course of the disease the sharp NAA decrease about 2–3 times less the norm was recorded. It corroborated the axonal damage with the development of neurotransmitters conduction block.

Conclusion: It is expedient to use more extensively obtained data for the secondary prophylaxis of MS progression.

THE IMPORTANCE OF THE BINDING ANTIBODIES AGAINST INTERFERON-BETA FOR THE EFFECTIVENESS OF INTERFERON-BETA TREATMENT IN MULTIPLE SCLEROSIS

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Background: Binding antibodies (BAbs) to Interferon-beta (IFN) develop during the treatment of multiple sclerosis (MS) with IFN . BAbs are regarded as one of factors that may diminish the treatment efficacy.

Objectives: To compare the titres of BAbs in the blood sera of the patients treated with various IFN preparations; to evaluate the impact of BAbs on the efficacy of the treatment with IFN .

Methods: The research was performed at Vilnius University Hospital Santariškių Clinics. 114 blood sera of the MS patients treated with IFN were analysed. BAbs titres were determined with the BÜHLMANN anti-IFN EIA kit. Determination of BAbs

titres was repeated in 22 patients after 6 months. Demographic data were collected and the impact on MS progress during the treatment with IFN was recorded. 102 patients were selected for the final analysis.

Results: 11 patients were treated with AVONEX® (group A), 64 patients – with REBIF® (group R), and 27 patients – with BETAFERON® (group B). Average duration of the treatment was 22.51 ± 17.26 months. The groups did not differ in age and the duration of the illness ($p>0.05$). BAbs titres were: Group A – 25% quantile (Q1) = 18.3; 75% quantile (Q3) = 30.2; Group R – Q1 = 22.325; Q3 = 79.675; Group B – Q1 = 240.3; Q3 = 1541.0. BAbs titres in Group B were statistically significantly greater compared to those of Groups A and R ($p<0.001$). Annual rate of exacerbations and the change in the disability degree during the period of the treatment with IFN did not differed significantly between the groups ($p>0.05$). Annual rate of exacerbations correlated with the BAbs titre within the Group R ($p = 0.003$). Reliable connection between the BAbs titre and the change in the disability degree during the treatment period was not obtained ($p>0.05$). While assessing BAbs dynamics during the 6 months period ($N=22$), the changes in the BAbs titre were not statistically significant ($p>0.05$).

Conclusions: The titres of BAbs in the BETAFERON treated group are greater compared to the AVONEX and REBIF treated groups. Greater titres of BAbs are related to more frequent exacerbations of MS. This relation was statistically proved only in the largest (62.7%) REBIF (IFN- -1a) group. The titres of BAbs are not related to the changes in the disability degree during the treatment period.

AVONEX IMMUNOMODULATING EFFECTS IN MS PATIENTS

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Introduction: Multiple sclerosis (MS) is an autoimmune disease which is related to T celll activation in periphery and results in CNS damage. Therefore there are many immunomodulating agents used in therapy reducing immune activity.

Aim: To analyse Avonex effects on immune answer during immunomodulating therapy in MS patients.

Patients and Methods: 49 patients (39 woman, 10 man) with verified diagnosis of MS received Avonex.

13 patients had cerebral form, 36 – cerebrospinal remiting/relapsing form of MS. To evaluate Immune answer lymphocyte subpopulations – CD3, CD4, CD8, CD16, CD19, CD95, CD38 were determined by using laser flow cytofluorimeter method Becton Dickenson wth coresponding monoclonal antibodies. Humoral immune answer was controled by determination of IgG, IgM, IgA level in patients serum (Dade Behring, Nephelometer). BAB antibodies were determined using Buhlmann ELISA test system, Swithzerland.

Results: Lymphopenia was observed in 25%, leucopenia in 6%, neutropenia in 4%. Before therapy was started 35% of patients had immunoglobulin syntesis interference. IgM was increased in 16%, during the course of therapy, % of patients with humoral immunity changes increasis, moustly affecting IgM, IgG synthesis.Cellular immune answer was decreased in 16%, it decreasis during therapy course and in 14% CD16 absolute count was reduced. Positive BAB antibodies were detected in 9%.

Conclusions: Lymphopenia is more frequent penia if Avonex is used in therapy of Ms patients. BAB antibodies positivity is not stable during the course of therapy. MS patients before the immunomodulating therapy had cellular and humoral immune answer problems. Avonex influenced to cellular CD4, CD16 absolute count level and more frequently increases Ig G,I IgM levels. Avonex immunomodulating effect is due to cellular and humoral immunity.

CARDIAC MYXOMA PRESENTING AS MULTIPLE SCLEROSIS: 2 CLINICAL CASES

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We observed two patients with cardiac myxoma, who initially presented with neurological signs and symptoms, mimicking multiple sclerosis. Both cases were middle aged women (51 and 43 years), who had various neurological complaints (speech disorders, disorders of coordination, limb weakness and numbness) and neurological signs (pyramidal signs, asymmetrical reflexes, various patterns of hypoesthesia and weakness, cerebellar ataxia). In both cases we noted recurrent neurological symptoms as in relapsing-remitting multiple sclerosis (RRMS). In brain MRI multiple lesions (T2 weighted hypointense) were observed – both gadolinium enhancing and none-enhancing. In both cases lumbar puncture and cerebrospinal fluid analysis was performed (no oligoclonal bands detected). Somatosensory evoked potentials were normal. No other abnormalities were noted in routine blood analyses, except elevated erythrocyte sedimentation rate – 57 and 83 mm/h. In both cases RRMS was diagnosed (fulfilling revised McDonald criteria). As neurological symptoms and complaints progressed, echocardiography was performed and final diagnosis of left ventricle myxoma was established. Heart tumours were resected, and the neurological symptoms regressed with some sequelae.

Myxoma is the most common primary tumour of the heart. It can present with constitutional, cardiac and embolic symptoms. One third of patients can have brain embolism symptoms. Nearly all patients have asymptomatic vascular lesions in brain white matter on MRI, which can complicate the correct diagnosis. In young patients with clinical relapses and multiple white matter lesions on brain MRI it might be difficult to differentiate cardiac myxoma from demyelinating disorders.

We propose properly evaluate patients' complaints, history, objective findings making diagnosis of stroke or MS, and do not forget the possibility of cardiac myxoma. Correct diagnosis can prevent from irreversible and possibly lethal complications. In case of stroke in young patient it is advisable to perform echocardiography and rule out cardiac myxoma. Before establishing diagnosis of MS it is necessary exclude other pathology – echocardiography would be recommended in case of atypical course of the disease or in presence of atypical symptoms.

Keywords: cardiac myxoma, relapsing-remitting multiple sclerosis, echocardiography, brain white matter lesions.

RELAPSE OF PATIENTS WITH MULTIPLE SCLEROSIS AND CERVICAL SPONDILOSIS: CASE REPORTS

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Background: Multiple sclerosis (MS) is most common chronic inflammatory demyelinating disease of the central nervous system among young adults. Cervical spondilosis generally has its onset in the fifth or later decades whereas MS occurs in younger age group. But a few patients will have both MS and cervical spondilosis. However myelopathy syndrome has occured less than five persent of cervical spondilosis patients.

The vast majority of patients with MS (80–85%) start with a patern marked by exacerbtions-also reffered to as relapses. A relapse is usually conventionally defined as the development of new symptoms lasting at least 24 hours and separated from a previous attack by at least a month.

Goals: The purpose of this study was to evaluate the relapse which may be relate with MS or cervical spondilosis.

Methods: Case histories, neurological examination results, MRI examination findings in 3 patients. Patients were identified through the Latvian multiple sclerosis centre. Disability was measured with the use of Kurtzke's espanded disability status scale (EDSS). Patients according MRI evidence were divided into three groups: 1) cerebrospinal MS and new developing cervical spondilosis with impact on spinal cord; 2) cervical spondilosis and new developing spinal cord lesion; 3) patients have both MS lesions and cervical spondilosis.

Results: The evaluated MS patients were on average 36.0 years old, mean disease duration 7.3 years, median EDSS 3.0. All patients (3) were received IV methylprednisoloni, but in one case we didn't see a normalisation of the symptoms.

Conclusions: Cervical spondilosis, disk disease can produce MS-like symptoms. Spinal cord symptoms are often, but not always, explained by spinal cord lesions.

CLEAN INTERMITTENT SELF CATHETERIZATION IN PERSONS WITH MULTIPLE SCLEROSIS: THE INFLUENCE OF COGNITIVE DYSFUNCTION

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Introduction: Bladder problems are very common in persons with multiple sclerosis (PwMS). The aim of this study was to investigate the ability of persons with multiple sclerosis to learn clean intermittent self-catheterization (CISC).

Intervention: The physical disability of 23 PwMS was evaluated with the expanded disability status scale (EDSS), and cognitive status was evaluated with the Brief Repeatable Battery of Neuropsychological Tests (BRB-N). CISC was taught by the same continence advisor, who was blinded to the cognitive test results. The ability to learn CISC was evaluated immediately after sessions and three months later. Twenty-three consecutive PwMS participated in the study.

Results: 87% (20/23) of the PwMS successfully finished CISC training. The number of lessons needed to acquire CISC skills differed significantly depending on the EDSS (Spearman r=0.682, p=0.0003), but the total cognitive decline subscore did not influence the ability to learn CISC. Only 13% (3/23) of the PwMS failed to learn CISC. The ability to learn CISC depended on the number of lessons needed to acquire CISC (r=–0.499, p=0.0313) and the EDSS score (r=–0.433, p=0.0390), but not on the course of the disease (r=0.125, p=0.5696) or on cognitive decline (r=–0.311, p=0.1480). After 3 months of follow-up, 30% (6/20) of the PwMS had ceased performing CISC. A follow-up indicated no statistically significant correlations among any of the subscores of the cognitive test battery, the EDSS score, the course of the disease, and the time required to learn CISC and effective bladder management.

Conclusions: Our study thus confirmed that most (87%) PwMS were able to learn CISC in spite of cognitive dysfunction and therefore to improve their quality of life.

MISCELLANEOUS

A STUDY OF PATIENTS WITH POLYNEUROPATHIES USING THE CUSP

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The cutaneous silent period (CuSP) is a transient suppression of the electromyographic activity of a voluntarily contracting muscle that follows a strong electrical stimulus applied to a cutaneous nerve. The CuSP is evoked by the excitation of the small A delta nerve fibers.

We compared the CuSP of 140 patients with polyneuropathies (PNPs) to that of 50 healthy controls. PNPs were divided into myelinic PNP (41 patients), axono-myelinic PNP (54 patients) and axonal PNP (45 patients). In the PNP patient groups we performed sensory and motor nerves conduction studies on the upper and lower limbs, and CuSP was recorded from abductor pollicis brevis (digit II stimulation), abductor digiti minimi (digit V stimulation), tibialis anterior (superficial peroneal nerve stimulation) muscles. The PNP patients required stronger stimuli than healthy subjects to obtain a CuSP. Unless atrophic muscles prevented their recording, in most patients with PNP a CuSP could be recorded. This demonstrates that small A delta fibers are at least in part preserved in most PNPs, even when the PNP is severe. In all PNP patient groups CuSP had a prolonged latency. A reduction of CuSP duration is observed in the axonal PNP group, whereas CuSP duration is increased in the myelinic and axono-myelinic PNP groups. In 4 patients (from the axonal PNP group) with sensory neuronopathies, CuSP was usually absent (10/12 nerves).

To conclude, the CuSP which allows an indirect study of the A delta fibers, is usually preserved, although altered in most PNP patients. The sensation allowed by these small fibers probably represents the ultimate protection when the function of large myelinic fibers is lost. Absence of CuSP in sensory neuronopathies may help distinguishing ganglionopathies from sensory axonopathies.

SYMPTOMS IN ACUTE STAGE AND SEQUELAE AFTER TICK-BORNE ENCEPHALITIS

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Introduction: Tick-borne encephalitis (TBE) plays a significant role in neuroinfection group in Europe. Since the end of 80's Latvia has become an endemic region of tick-borne encephalitis; the rate of morbidity is the highest one in the world having reached its peak in 1994 (53 cases per 100 000 inhabitants).

Aim of study: To estimate TBE sequelae in Latvia analyzing clinical symptoms and complains in acute stage and their effect on further patients' life quality and functional abilities.

Materials and methods: The research was performed by retrospective analysis using inquiry of patients who have had TBE. There were 100 TBE patients from Riga Eastern Clinical University Hospital 'Gailezers' and Paul Stradins Clinical University Hospital, who were treated for TBE from 1994 to 2004. Sequelae after TBE were compared with symptoms in acute stage of TBE from the hospital records for the same patients.

Results: The total number of respondents (n=100) included 43 male and 57 female. The average age of respondents was 54.73 years (22–82). After discharge from the hospital 6.45 years had passed on average (range 1–13). The most frequent complaint after TBE was increased fatigue: 61% patients noted it, compared to 44% (p=0.023) in the acute period. 58% of patients with chronic TBE complained of headaches in comparison with 84% in acute stage (p=0.001). Half of respondents noticed memory impairments, 42% – sleep disturbances, and 36% had concentration difficulties. 27% of patients noted pareses in the stage of sequelae, though in the acute stage of TBE 40 (40%) patients presented pareses (p=0.072). In the acute stage muscular hypotrophy/atrophy was in 20 (20%) cases, however, 23 (23%) patients observed them as sequelae (p=0.731). Total 39 (39%) patients noted balance and coordination disturbances, and 40 (40%) patients noted vertigo (p=0.884).

Conclusions: The most of patients had health disorders after TBE, observed worsened life quality and altered work capacity, some patients became disabled as well as experienced need for continuous rehabilitation and social assistance. Statistical significant difference was only between some symptoms in acute stage of TBE and sequelae (headache, fatigue).

GUILLAIN-BARRE SYNDROME: 142 CASES

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Objective: To evaluate etiology, clinical symptoms and forms of Guillain-Barre syndrome (GBS) of patients, treated in Vilnius University Hospital Santariskiu Clinics from 1994 till 2008.

Methods: Medical charts and case histories of patients, diagnosed with GBS, were reviewed.

Results: During 1994–2008 in Vilnius University Hospital Santariškių Clinics 142 patients with GBS were treated. 88 patients (62%) were male, 55 patients (38%) were female. Most patients (68%) were above 41 years of age. There was obvious season prevalence – 33.3% of cases manifested from September to November, the second peak was in January (13% of cases). History of infection was determined for 88 patients (62%), viral and bacterial causes were equally distributed. In most cases disease reached maximum in 1 weak (50 patients). Most commonly disease started with paraesthesias (78% of cases). Most prominent pain was in legs (48%). All patients developed limb weakness; in 82% of cases tendon reflexes were lost. Cranial nerve involvement was noticed 86% of patients – most prevalent was abducent nerve palsy. Autonomic disturbances were observed in 44% of cases. Most common clinical form is sensory-motor (96 patients, 67.6%), pure motor (37 patients, 26%), ataxic (8 patients, 5.6%). We observed 1 patient with Miller-Fisher syndrome. For 5 patients GBS relapsed. Cerebrospinal fluid analysis showed elevated protein amount in 120 cases (84.5%), for 7 patients (5%) lumbar puncture was not performed. In most cases (55.6%) complete blood count analysis did not reveal any abnormalities, although for 41 patient leukocytosis was detected, in 39 cases – elevated erythrocyte sedimentation rate. Nerve conduction studies in 44.4% of cases showed demyelinating lesion, in 26.8% cases – mixed axonal and demyelinating lesion, although 16 patients (11.3%) showed no abnormalities. 91 patient (64.1%) was treated with plasmapheresis, only 3 patients received intravenous immunoglobulin. Mortality from GBS is 1%.

Conclusions: GBS is common acute neurological condition, increasingly diagnosed in our hospital. The most common clinical form is sensory-motor demyelinating polyneuropathy. Diagnosis and treatment of GBS is adequate. Our data correspond with other reports from various countries.

CLINICAL AND ELECTROPHYSIOLOGICAL SIGNS OF CRITICAL ILLNESS NEUROPATHY

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Objective: The aim of the study was to evaluate clinical and electrophysiological signs and symptoms of critical illness neuropathy.

Methods: 50 patients, treated in Vilnius University Hospital Santariškių klinikos 1st Department of Reanimation and Intensive Therapy seven days or longer, were evaluated for critical illness neuropathy. 28 of them had definite neuropathy or high likelihood of neuropathy. They were included in the study. The diagnosis of neuropathy was made based on distal symmetric neuropathy diagnostic criteria (2005). Clinical neurological exam, nerve conduction studies (NCS) and needle electromyography (EMG) examination was performed for all patients.

Results: 28 patients, 20 males (71%) and 8 females (29%), who had a definite neuropathy and high likelihood of neuropathy (according used criteria) were included in the study in the period between May and December, 2008. Mean age +/- SD was 59.28 years +/- 15.34. Mean duration of treatment in ICU was 20.43 days +/- 14.62. 17 patients (60.7%) had complaints, suggesting neuropathy – pain, numbness or weakness in the limbs. 24 patients (85.7%) had decreased or absent ankle reflexes. 12 patients (42.9%) showed distal limb muscle atrophy. 13 patients (46.4%) had objective sensory disturbances, mainly impaired vibratory sense – 14 patients (50%) had vibratory sense impairment in arms, 24 patients (85.7%) – in legs. Position sense in leg was abnormal in 53% of cases. On NCS examination for all patients most consistent abnormal finding was decreased peroneal nerve motor response amplitude – in 49 nerve examinations (87.5%), sural nerve conduction velocity was decreased in 48 nerve examinations (85.7%). Frequent abnormality was reduced peroneal nerve conduction velocity (in 76.8% cases) and decreased sural nerve amplitude (71.4% of patients). 19 patients (79.2%) had decreased sensory ulnar nerve amplitude, although this finding maybe biased due to too small population. There was no statistically significant difference in treatment duration between patients with distal muscle atrophy and without ($p=0.75$).

Conclusions: Patients with critical illness neuropathy most frequently clinically present with reduced or absent ankle reflexes and sensory disturbances, most consistent of which is vibratory sense impairment. Most common neurophysiological signs include reduced peroneal motor amplitude and decreased sural nerve conduction velocity.

PERIPHERAL NERVE DAMAGE AFTER TREATMENT IN INTENSIVE CARE UNIT

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Objective: The aim of the study was to evaluate the peripheral nervous system damage in patients after long-term treatment in intensive care unit (ICU).

Methods: 50 patients, 35 (70%) male and 15 (30%) female, treated in ICU seven days or longer, were included. All patients were evaluated for the signs and symptoms of neuropathy and myopathy. Clinical neurological exam, nerve conduction studies and needle electromyography examination was performed. The diagnosis of neuropathy was made based on distal symmetric neuropathy diagnostic criteria (2005).

Results: Mean +/- SD duration of treatment in ICU was 17.66 days +/- 12.28. 28 patients (56%) were diagnosed with neuropathy including definite neuropathy for 21 patient (42%) and 7 patients (14%) with high likelihood of neuropathy. 10 patients (20%) had no signs neither symptoms of neuropathy. Abnormal nerve conduction studies were in 35 patients (70%), seven of them did not meet criteria of neuropathy. Spontaneous activity on needle examination was noticed in 9 patients (18%). Ulnar nerve injury was diagnosed for 5 patients (10%). 7 patients (14%) had median nerve compression in carpal tunnel. Myopathy was diagnosed for no patients. 8 patients (29%) of those diagnosed with neuropathy may have had old neuropathy, but it was not diagnosed previously. In 20 cases (71%) neuropathy affected arms and legs, in 8 cases (29%) neuropathy manifested only in legs. Out of those with neuropathy 20 were males (71%) and 8 were females (29%). In 22 patients (79%) neuropathy was sensory-motor, only 6 patients (21%) had pure motor involvement. All patients had predominantly axonal nerve damage; no pure demyelinisating lesion was detected. In 17 cases (61%) neuropathy was severe; in 11 cases (39%) it was mild. There was no statistically significant difference in age between patients with neuropathy and without neuropathy ($p=0.115$). Patients with neuropathy were treated in ICU 6 days longer, but the difference was not statistically significant, only the tendency was noticed ($p=0.072$).

Conclusions: Peripheral nervous system damage is common after long-term treatment in ICU. Severe sensory-motor axonal neuropathy, more prominent in legs, is the most common clinical syndrome. Damage of individual peripheral nerves may also occur. Myopathy is rare and has not been diagnosed in this study. There is no difference in age and treatment duration between patients with neuropathy and without.

MAGNETIC RESONANCE IMAGING AFTER CONCUSSION. CASE-CONTROL STUDY

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Background: Until now there is a lack of carefully controlled studies with conventional MR imaging performed exclusively in concussion with short lasting loss of consciousness (LOC).

Methods: A MR investigation was performed within 24 hours and after 3 months in 20 patients who had suffered a concussion with a verified loss of consciousness of maximally 5 minutes. As a control group, 20 age- and gender matched patients with minor orthopaedic injuries had a MR investigation using the same protocol.

Results: In a concussion population with an average LOC duration of 1. 4 minutes no case with unequivocal intracranial traumatic pathology was detected.

Conclusions: An ordinary concussion with short lasting LOC does not or only seldom result in a degree of diffuse axonal injury (DAI) that is visualized by conventional MR with field strength of 1.0 Tesla (T). Analysis of earlier MR studies in concussion using field strength of 1.5 T as well as of studies with diffusion tensor MR imaging (DTI) reveal methodological shortcomings, in particular use of inadequate control groups. There is, therefore, a need for carefully controlled studies using MR of higher field strength and studies with DTI MR exclusively in common concussion with LOC of maximally 5 minutes.

PROGNOSTIC VALUE OF EEG AND BAEP EVALUATION IN CHILDRENS COMA

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The aim of our investigation was: to determine the prognosis of consciousness recovery in traumatic coma of pediatric patients evaluating and comparing clinical examination combined with EEG and BAEP studies.

Material and methods: 42 children with severe acute head trauma were investigated in intensive care unit (ICU) using standard treatment. Evaluation of coma was performed using Glasgow coma scale (GCS). Functional state of central nervous system, their changes and prognosis of recovery were analyzed by following methods: CT scan, spectral topographical analysis of EEG and brainstem auditory evoked potentials (BAEP) during income period and in time of first week.

Results: In CT scan supratentorial injury was established as the most frequent type of injury, affecting in 43% (27) of cases, brain edema in 81% of cases, diffuse neuroaxonal damage in 21, 4% (9) of patients. Recovery was significantly later in cases with supratentorial injury. In 17 cases EP were abnormal due to impairment of the auditory pathway at the level of pontine region; consciousness recovered after 76 days or not recovered. In 22 cases EP were normal, consciousness recovered in 30 days. Visual EEG analysis showed prevalence of delta activity in 33 cases, 3 cases of "alfa coma", EEG desynchronisation in 5 cases, burst-suppression in 1 case. Significantly faster recovery was in patients with basic delta activity. Permanent or variating slow wave activity was monitored during follow-up of brain bioelectric activity in coma; locally slowered activity waves were monitored that reflected brain injury localisation, found in CT scanning. Quantitative EEG analysis as topographical evaluation of spectral bands showed maximal delta frequency alternation in vertex electrode positions in survived patients in time of first monitoring of EEG. In acute period of coma a pronounced fluctuation of delta activity was found in sensomotor cortex projections, which reflect thalamus-cortical relations activity. It is thought that these connections are related with consciousness recovery possibilities.

Conclusion: Evaluation of neurophysiological parameters in coma has meaning in prognosing coma outcome. Normal patterns of BAEP are predictor of good outcome. EEG delta spectral bands reactivity is valuable indicator of positive outcome in ICU in coma with preferable points for EEG monitoring in vertex projections.

INCIDENCE OF TRAUMATIC SPINAL CORD INJURIES IN ESTONIA FROM 2003 TO 2007

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Background: Traumatic spinal cord injury (TSCI) is a disabling and extremely costly condition. Persons with TSCI may experience a wide range of activity limitations and participation restriction as well as psychological disorders. Most epidemiological studies are from developed countries, and information about epidemiology of TSCI from the Eastern part of European Union countries as well as Estonia is missing. However, information on incidence of TSCI would provide a valuable material for planning the needs for rehabilitation and primary prevention.

The aim of the study was to provide data on the incidence and causes of traumatic TSCI in Estonia from 2003–2007.

Patients and Methods: The medical records for all patients having diagnosed TSCI in Tartu University Hospital and in North Estonia Medical Centre from 2003–2007 were retrospectively analyzed. As a rule, all patients surviving the initial trauma are treated in these hospitals in Estonia. Demographical data, causes of trauma and medical data were registered. The incidence of TSCI was expressed per 1 000 000 Estonian population (census 2000).

Results: A total of 191 patients with TSCI (32 women and 159 men) were registered. The mean age at onset of injury was 38.7 years (SD 17.3) for all patients, 37.8 (SD 16.9) for men and 43.3 years (SD 19.0) for women. The annual incidence rate was 34.1 (95% CI 29.4–39.3) for both sexes, 63.1 (95% CI 53.7–73.7) for men and 10.4 (95% CI 7.1–14.6) for women. The rate for men was significantly higher than that for women. Most of the cases were from the age group 15–24 years among men (27%) and 35–44 years among women (28%). The most frequent causes of TSCI were fall (42%), followed by traffic accidents (27%) and swimming/diving (15%). Violence was recorded as a cause of TSCI in 4% and suicide in 1% of cases. For patients 65 years the most frequent cause of TSCI was fall (58%). Alcohol preceded TSCI in 50% of cases. Incomplete paraplegia occurred in 28% of cases.

Conclusions: Compared to other studies the incidence rate of TSCI in Estonia is high, particularly in men. The sex distribution (men/women) of TSCI was 5/1. TSCI occurred earlier in Estonia (in mid-twenties) and were related to alcohol in half of the cases. Falling was the main cause of TSCI and the most prevalent cause in the elderly. Like in other studies incomplete paraplegia was the most frequent outcome of TSCI.

BOTULINUM TOXIN A TREATMENT OF WRITER'S CRAMP

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Objective: To assess the outcome of arm action dystonia in patients treated with botulinum toxin type A (Dysport®).

Background: Writer's cramp is an arm action dystonia that locks the wrist and fingers, twisting them into abnormal postures, and interfering with handwriting. For many patients this is incompatible with their jobs. The estimated prevalence of writer's cramp is 69/million (Nutt et al., 1988). Standard medications for dystonia, such as trihexyphenidyl and benzodiazepines, have poor response rate in this task-specific condition.

Methods: There was the retrospective analysis of patients who received Dysport® treatment of writer's cramp at Clinical University Hospital 'Gailezers' over the period of years 2005–2008.

Results: There were 3 female patients included in the study. The age of patients at the onset of dystonia ranged from 24 to 53 years. The number of mouse units injected per session ranged from 70 to 200. The number of injection sites ranged from 2 to 4. The overactive muscles that were chiefly responsible were revealed by observation and palpation. Injections into the muscles were given without EMG recording. Follow-up was available in two cases. Writing was impaired by abnormal flexion of wrist in one case, and by abnormal extension of wrist in another one. Both patients improved on writing after the treatment.

Conclusions: The botulinum toxin A treatment of writer's cramp can be effective even without EMG recording.

ALGORITHM OF DIZZINESS PATIENTS' CARE AT EMERGENCY MEDICAL CENTRE

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Problem of dizziness is multidisciplinary, therefore it is very important to determine its type tactically correctly, and already at the Emergency Medical Centre (EMC) to undertake the necessary examinations, to involve the appropriate specialists in order the patient is transferred to the specific ward where the timely etiopathogenic therapy could be started.

Patients get into EMC with different diagnoses – acute vestibular syndrome, otitis media, a.vetrebralis syndrome, cerebral infarction VBB, transitory ischaemic attack VBB, hypertensive crisis, etc., illnesses, with dizziness being the main symptom. At this stage the algorithm of dizziness diagnostics is applied, which has been elaborated at Pauls Stradiņš Clinical University hospital. At the EMC the doctor evaluates the patient's objective status, clinical and biochemical tests are done, TA, temperature, ECG and CT for the brain are performed. On the basis of the patient's complaints, objective findings and examination results, the specific profile specialists get involved (ENT, neurologist, internist, etc.). Specifying the cause of dizziness, specialists make the diagnosis and the patient is taken to a special ward. Half of patients transferred to EMC were found to experience a non-vestibular dizziness, one third of patients continued the therapy ambulatory.

On the basis of the algorithm patients are admitted in the department of neurology mostly with central vestibular syndrome, most common diagnoses are cerebral infarction or TIA VBB, much rarer – multiple sclerosis, neuroinfections, degenerative CNS diseases.

In order one could timely make a diagnosis and improve the treatment outcome, it is important to solve the problem of dizziness jointly in cooperation with EMC doctors, radiologists, ENT specialists, neurologists, internists and family doctors.

TYPES OF DIZZINESS, BASED ON SURVEY OF PATIENTS' QUESTIONNAIRES

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Dizziness is one of the most common patients' complaints both in ambulatory and hospital practice. In cases of dizziness the perceived impulses by vestibular, visual and deep proprioreceptive system are discoordinated, causing discomfortable and unpleasant sensations in patients.

In order one could assess the pathogenetic mechanism of dizziness (vertigo or pseudovertigo), in January 2008, special patients' dizziness cards were designed. Within the period from II–IV, 99 hospital and ambulatory patients from 20–82 years of age (73 women and 26 men) were surveyed. The analysis was carried out to understand the character of dizziness, intensity, hearing symptoms, course of dizziness (sudden fit or chronic, persisting), provocative factors, accompanying factors (nausea, vomiting, sweating, headache, anxiety), data of the case history (injuries, medicines, hearing disorders), as well as the assessment of neurological symptoms, status objectivus (pulse, ECG, TA), tests. Patients were examined by the ENT or neurologist ENT, extracranial brachiocephalic blood vessel duplex scanning, EEG, CT, MRI, MRA.

By surveying the results, they showed: peripheral vestibular syndrome 16% patients (otitis, Meniere's syndrome – 11 women and 5 men), BPPV 15% patients (13 women and 2 men). Central vestibular syndrome 20% patients – acute cerebral infarction VBB (4 women and 7 men), TIA VBB (3 women and 2 men), cortical vertigo (temporal epilepsy – 3 women and 1 man). A.vertebralis syndrome 11% patients (9 women and 2 men), of them 12% psychogenous (in the age group from 20–46 years), but 24% being related to somatic diseases – arterial hypertension with crises, anaemia, diabetes mellitus.

From the patients questioned the prevalence of complaints were 3 times more common in women. Vertigo was 53% – mostly peripheral (31%), but pseudovertigo and compose made in total 47% of all cases.

CHRONIC FATIGUE SYNDROME: NEUROLOGICAL SYMPTOMS AND HERPETIC INFECTION

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Objectives: Chronic fatigue syndrome (CFS) is an illness characterized by profound disabling fatigue accompanied by combination of non-specific symptoms. The etiology and pathogenesis of CFS remains unknown, until diagnosis of the disease is symptom-based clinical diagnosis. The major hypothesis of CFS pathogenesis is that infectious agents such as viruses, HHV-6 and HHV-7 in particular, that possess immunomodulating properties including the ability to alert the expression of immune activation molecules, to modulate of several cytokines and chemokines and to induce apoptosis in lymphocytes, also may trigger and lead to chronic activation of the immune system and CFS development. The aim of this study was to evaluate objective and subjective neurological symptoms to determine HHV-6 and HHV-7 activation in the CFS patients and potential interrelation between viruses' activation and CFS development.

Methods: Blood samples from randomly selected and neurologically examined 64 patients (41 females, 23 males; mean age 37 years) with clinically diagnosed CFS according to the 1994 CDC case definition criteria and randomly selected 50 (30 females, 20 males; mean age 38 years) healthy blood donors (BD) were investigated for evidence of active HHV-6 and HHV-7 infection.

Results: In CFS group 38.9% of patients were complaining on diffuse weakness, 17.3% – on headaches, 13.5% – myalgias, 14.9% – joint pain, 10.7% – sleeping disorders, 9.3% – vision problems, 6.7% – nausea, 5.3% of patients – profuse sweating. Almost a half of patients in this group (40%) have subfebril body temperature. Pharingitis was diagnosed in 14.7%, hepatomegaly – in 14.5% of patients with CFS. After neurological examination of cranial nerves, motor and sensory systems, no focal symptoms were found. Active HHV-6 infection (plasma viremia) was detected only in CFS patients (in 11/64 or 17.2%). The rate of active HHV-7 infection was significantly higher in CFS patients in comparison with BD (36/64, 56.3% and 2/50, 4.0% respectively, p=0.00002).

Conclusion: No focal symptoms of damages of central nervous system was found in patients with CFS, all complains are more subjective. Active infection with both HHV-6 and HHV-7 is more frequent in patients with CFS than in healthy blood donors suggesting that these two viruses, alone or in concert, may be involved in the etiopathogenesis of CFS.

MOBILIZATION OF STEM CELL WITH GRANULOCYTE-COLONY STIMULATING FACTTOR

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Objective: This study was designed to investigate the effects of Granulocyte colony-stimulating factor (G-CSF) administration in rats for 6 week after traumatic brain injury (TBI).

Methods: Adult male Wistar rats (n = 30) were injured with controlled cortical impact device and divided into four groups. The treatment groups (n = 10 each) were injected subcutaneously with recombinant human G-CSF. whicle group (n=10) received phosphate buffered saline (PBS) and only Brdu intraperitoneally. Bromodeoxyuridine (BrdU) was used for mitotic labeling. Experimental rats were injected intraperitoneally with BrdU. Rats were killed at 6 week traumatic brain injury. Neurological functional evaluation of animals was performed before and after injury using Neurological Severity Scores (NSS). Animals were sacrificed 42 days after TBI and brain sections were stained by Brdu immunohistochemistry.

Results: Statistically significant improvement in functional outcome was observed in treatment groups when compared with control ($p < 0.01$). This benefit was visible 7 days after TBI and persisted until 42 days (end of trial). Histological analysis showed that Brdu cell positive was more in the lesion boundary zone at treatment animal group than all injected animal.

Keyword: stem cell mobilization-G-CSF-Traumatic brain injury.

NEUROLOGICAL COMPLICATIONS OF UREMIA AND HEMODIALYSIS

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Objective: To analyse neurological complications of uremia and hemodialysis.

Material and methods: During the period of January 2000 – December 2007 in the Department of Nephrology and Hemodialysis of Vilnius City University Hospital we examined 85 patients (45 women and 40 men) with failure of renal function who sustained lesion of nervous system. Their age varied from 26–85 years (in average – 65.6 years). All patients went through neurological examination, general blood and urine testing, biochemical blood testing (urea, kreatine, electrolytes, acid-alkali balance), in presence of indications – head (spine) radiography, cerebral (spinal) CT, CT angiography and MRI. Results. Presence of dialyzed patients – 41 (48.2%). Average duration of hemodialysis – 2.4 years (28.77 months). Neurological complications of uremia occurred in 34 (40.0%) dialyzed patients: acute and chronic uremic encephalopathy, polyneuropathy, hydrocephaly, lacunar infarctions, parkinsonism, hyperkalemic paralysis and other. Uremic encephalopathy was diagnosed in 11 (12.9%) patients. Neurological complications of uremia was present in 44 (51.8%) non-dialyzed uremic patients. Most frequent: uremic encephalopathy – in 19 (22.4%) patients, uremic polyneuropathy – in 7 (8.2%) patients, restless legs syndrome – in 6 (7.1%) patients. Neurological complications of hemodialysis occurred in 7 (8.2%) patients: hemorrhagic stroke – in 4 (4.7%), dialysis disequilibrium syndrome – in 1 (1.2%), dialytic headaches – in 2 (2.3%) patients. Clinical cases were presented. Hyperkalemic paralysis, uremic restless legs syndrome, uremic chorea were described in Lithuania for the first time. The newest scientific literature about neurological complications of uremia and dialysis was reviewed, obtained own data were compared with data of the literature.

Conclusions: Uremia causes impairment of central and peripheral nervous system. Uremic encephalopathy is the most frequent neurological complication of uremia. Characteristic neurological complications of uremia are dyskalemic paralysis, restless legs syndrome and chorea. Neurological complications of hemodialysis – hemorrhagic stroke, dialysis disequilibrium syndrome, dialytic headaches. Lacunar infarction and hydrocephaly in dialyzed patients are more frequent. Treatment of neurological complications of uremia depends on their clinical manifestation and course of failure of renal function.

ANTICOAGULANT UNDERUSE IN STROKE PATIENTS WITH ATRIAL FIBRILLATION

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Background. Atrial fibrillation (AF) is a frequent heart disorder and a risk factor for stroke. Although it is known, that use of anticoagulation in AF reduces the risk of stroke by 62–66% (3–8%/year), underuse of anticoagulation (mainly due to the fear of haemorrhagic complications) is a world-wide problem. The present study assesses the use of anticoagulation in patients with ischemic stroke and analyses the probable causes for anticoagulation underuse.

Methods. All patients admitted to our department with the diagnosis of ischemic stroke (either first-ever or recurrent) and AF from January 2004 to December 2005, were included. We registered the type and duration of AF, details of anticoagulation use and stroke severity according to Scandinavian Stroke scale (SSS). The indication for the need for anticoagulation was determined using CHAD2 (Congestive heart failure, Hypertension, Age >75 years, Diabetes, previous stroke) score.

Results. A total of 155 (129 first-ever and 26 recurrent) stroke patients (95 women and 60 men) were included in the study, with mean age of 76 (±10) years. Fourteen patients had paroxysmal AF, 8 had persistent and 133 patients had permanent AF. The CHAD2 score before and after the index stroke was greater than 2 in 75% and 100% of patients, respectively. Fourteen (9%) patients were on anticoagulation before the stroke and was continued in 13 patients, the treatment was started during the hospital stay in 6 (4%) and was recommended to start later in 15 (10%) patients. The main reasons for not prescribing anticoagulation were severe stroke (19%) and advanced age (7%), the reason was not known in 49 patients (32%). Patients in whom anticoagulation was either continued, prescribed or recommended, had less severe stroke according to SSS score ($p<0.0001$). Patients with paroxysmal AF had less severe stroke compared to patients with persistent or permanent AF ($p=0.02$). Case-fatality rate at 30-days was 28%, 33% for women and 20% for men ($p=0.08$).

Conclusion. Although according to the CHAD2 score, anticoagulation was indicated for all patients, only 21% of patients received this treatment or it was recommended to start later. In 1/3 of patients, the reason for not prescribing anticoagulation was not discussed in the case history. It can be concluded, that anticoagulation is probably underused in stroke patients with AF in Tartu and more attention should be paid on this important issue in primary and secondary prevention of stroke.

PLASMA CONCENTRATION OF HEAT SHOCK PROTEIN AND RISK OF ISCHEMIC BRAIN STROKE

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Heat shock protein (HSP) has been hypothesized to be a potential biomarker of atherosclerosis. However, no prospective studies have yet been performed to investigate the association between HSP plasma concentration and risk of ischemic brain stroke. We have tested it using methylenetetrahydrofoliate reductase (MTHFR), one of the main enzyme involved in the metabolism of homocysteine. Hyperhomocysteinemia (HHY) is considered an independent risk factor for stroke and is affected by genetics and dietary factors. Prevalence of vascular risk factors was assessed; fasting homocysteine (Hcy) and vitamin B6 (in co-factor form as pyridoxal phosphate (PLP) were assayed in all patient. The plasma Hcy and PLP levels were measured using a self–modified and validated high pressure liquid chromatography (HPLC). We have measured the level of antibodies against certain HSPs in vitro, in serum of ischemic stroke patients and control group using ELISA. The level of antibodies against one of the bacterial HSPs, GroEL, correlates with the level of homocysteine in serum. It points at the possible significance of autoimmune reactions contributing to atherosclerosis. We have also purified MTHFR and tested the influence of HSPs of the KJEB system in vitro, using spectrophotometric test for MTHFR activity. We found that MTHFR is partially protectet from the effect of heat shock by KJEB system and that KJEB proteins can restore that activity of the enzyme when it is lost due to thermal denaturation. Our findings show that HSPs can be involved both in the development of atherosclerosis, as well as protection against ischemic brain stroke. Futher studies need to be done.

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HYPERHOMOCYSTEINEMIA AND RISK OF ISCHEMIC STROKE; THE INFLUENCE OF GENETICS AND ENVIRONMENTAL DETERMINANTS

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Hyperhomocysteinemia is emerging as possible risk factor for cardiovascular disease, but it's role in stroke remains controversial. Both, genetics and environmental factors affects homocysteine levels. One of the most common genetics defects of homocysteine metabolism is a mutation in the enzyme methylenetetrahydro folate reductase (MTHFR) and cystationine beta syntase (CBS). In patients in acute phase of ischemic stroke we studied the prevalence of MTHFR–genotype and compared with the plasma homocysteine levels. We have also determined the plasme concentration of vitamin B6 (measured as PLP- pyridoxal 5'-phosphate)

Methods. We have studied 195 persons, 130 of whom were in acute phase of ischemic stroke Prevalence of vascular risk factors was assessed. Fasting tHcy, pyridoxal 5'-phosphate (PLP), the frequency of occurrence of two polymorphisms of the MTHFR gene (C677T and A1298C) and CBS gene (Ä22/493-514 and T833C) were measured. Stroke severity was evaluated with the NIHSS, outcome by modified Rankin scale.

Results: The mean age of the patients was 68.05±13.4 years and it was statistically significantly higher in women (72.05±12.4) than in men (65.9±13.4). The prevalence of

conventional risk factors such as diabetes mellitus, hypertension and hyperlipidemia were significantly higher in patients compared with controls but the group didn't differ in homocysteine levels accordingly to other vascular risk factors. Thcy differed significantly ($p<0.005$) between patients and controls. Hcy levels were higher in male and older (>70 y) patients compare to controls. Mean hcy levels were significantly higher in large artery strokes. Heterozy gotic genotype C677T of MTHFR was detected in 24% of patients. In 60% of patients at least one heterozygotic mutation was detected. Hyperhcy was correlated with mutations in either gene ($p=0.04$).

Conclusions: Hyperhomocysteinemia seems to be an independent risk factor for ischemic stroke. High level of homocysteine in large-artery strokes may suggests the possible role of hyperhomocysteine as an independent atherogenic factor. We found an association between mutation in either MTHFR or CBS gene and raised plasma homocysteine. The low level of PLP may showed that enzyme deficiency should be balanced by other factors, so treatment with vitamin B may be beneficial in reducing plasma homocysteine level.

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