V. PhD Symposium

of

Doctoral School of Neuroscience

PROGRAM
&
ABSTRACTS

University of Debrecen

November 29, 2014

.

V. PhD Symposium
of Doctoral School of Neuroscience

University of Debrecen

2014

Head of Doctoral School of Neuroscience
Prof. Dr. Miklós Antal, DSc

Secretary of Doctoral School of Neuroscience
Dr. Zoltán Kisvárday, DSc

Board of members:

Miklós Antal
Ervin Berényi
András Birinyi
László Bognár
László Csiba
István Fekete
Ede Frecska
Béla Fülesdi
Tibor Hortobágyi
Zoltán Kisvárday
Álmos Péter Klekner
Péter Pál Molnár
György Székely
István Sziklai

Supervisors and tutors:

Miklós Antal
Roland Berecz
Ervin Berényi
András Birinyi
László Bognár
Béla Clemens
Tünde Csépány
László Csiba
Anikó Égerházi
István Fekete
Ede Frecska
Béla Fülesdi
Judit Hallay
Hortobágyi Tibor
Zoltán Kisvárday
Álmos Péter Klekner
Mária Tünde Magyar
Klára Matesz
Csilla Molnár
Péter Molnár
Péter Pál Molnár
László Novák
László Oláh
Sándor Szabó
Zoltán Szekanecz
György Székely
Holló Krisztína Szentesiné
István Sziklai
Péter Szűcs
Zsuzsanna Vekerdy-Nagy
Ervin Wolf
János Zatik

V. PhD Symposium of Doctoral School of Neuroscience

November 29, 2014

09:30-10:00	**Arrival** (coffee & tea)	
10:00-10:05	**Welcome Address** – Miklós Antal	Head of Doctoral School of Neuroscience
10:05-10:55	Plenary Lecture – **László Acsády (MTA-KOKI)**	
	Thalamus in other color	

Part I. Chairman: Péter Pál Molnár

11:10-11:20 **Judit Gál** (3rd year PhD student)
Supervisor: Csilla Molnár
ASSESSMENT OF MORTALITY AND OUTCOME OF PATIENTS WITH SAH USING DIFFERENT VOLUME THERAPY

11:20-11:30 **Aletta Andrea Harman** (3rd year PhD student)
Supervisors: István Fekete, Ferenc Mechler
FREQUENCY OF PERIPHERAL NEUROPATHY AND MYOGEN LESION IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED (ANCA) SMALL VESSEL VASCULITIS

11:30-11:40 **Pálóczi Balázs** (2nd year PhD student)
Supervisor: Béla Fülesdi
DICLOFENAC PREMEDICATION, AS THE EFFECT OF PRE-EMPTIVE ANELGESIA AFTER POST THORACOTOMY CHEST AND SHOULDER PAIN, AS WELL AS THE CHANGES OF THE POST OPERATIVE BREATHING FUNCTION VALUES

11:40-11:50 **Adrienn Pongrácz** (2nd year PhD student)
Supervisor: Béla Fülesdi
REVERSAL OF NEUROMUSCULAR BLOCKADE WITH SUGAMMADEX AT THE REAPPEARANCE OF FOUR TWITCHES TO TRAIN-OF-FOUR STIMULATION

11:50-12:00 **Ágnes Fekete** (2nd year PhD student)
Supervisor: Béla Fülesdi
COMPARING PREMEDICATION STRATEGIES IN DENTAL CARE OF DISABLED PATIENTS

12:00-12:10 **Gyöngyösi Zoltán** (2nd year PhD student)
Supervisor: Béla Fülesdi
FIRST CLINICAL EXPERIENCES WITH THE FRONT FORMULA FOR PRE-OPERATIVE AIRWAY ASSESSMENT AND DOCUMENTATION

12:10-12:20 Coffee break

Part II. Chairman: István Fekete

12:20-12:30 **Szilvia Kecskés** (3rd year PhD student)
Supervisor: András Birinyi
NEURAL NETWORKS UNDERLYING THE SWALLOWING PHASE AND VISCEROMOTOR RESPONSES OF PREY CATCHING BEHAVIOR OF THE FROG

12:30-12:40 **Noémi Zsuzsanna Kovács** (2nd year PhD student)
Supervisors: Béla Clemens
EEG-BASED FUNCTIONAL NETWORKS IN PATIENTS WITH TYPICAL ABSENCE SEIZURE

12:40-12:50 **Laczkóné Réka Majer** (3rd year PhD student)
Supervisors: Ede Frecska, Tibor Hortobágyi
RESEARCH OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS IN NEURODEGENERATIV AND VASCULAR DEMENTIAS

12:50-13:00 **Balázs Murnyák** (3rd year PhD student)
Supervisor : Tibor Hortobágyi
THE IMPACT OF SOMATIC *TP53* MUTATIONS ON THE IMMUNOHISTOCHEMICAL EXPRESSION OF P53 PROTEIN IN GLIOMAS

13:00-13:10 **Dániel Tamás Nagy** (2nd year PhD student)
Supervisor: Judit Hallay
THE PROGNOSTIC AND DIAGNOSTIC RULE OF URINARY N-ACETYL-ß-D-GLUCOSAMINIDASE ON SURGICAL ICU

13:10-13:20	Coffee break

Part III.	Chairman: Zoltán Kisvárday
13:20-13:30	**Rita Varga** (2nd year PhD student) Supervisor: Zoltán Mészár MIGRATION AND DIFFERENTIATION OF NEURONS IN THE SPINAL DORSAL HORN DURING EMBRYOGENESIS
13:30-13:40	**Klaudia Dócs** (2nd year PhD student) Supervisor: Miklós Antal NEURONAL AND GLIAL EXPRESSION OF MONOACYLGLYEROL LIPASE IN THE SUPERFICIAL SPINAL DORSAL HORN OF RODENTS
13:40-13:50	**Fariba Javdani** (2nd year PhD student) Supervisor: Miklós Antal DIFFERENTIAL EXPRESSION PATTERNS OF K^+/CL^- CO-TRANSPORTER (KCC2) IN NEURONS WITHIN THE SUPERFICIAL SPINAL DORSAL HORN OF RATS
13:50-14:00	**Kázmér Kovács** (2nd year PhD student) Supervisor: Ervin Berényi NEUROSURGICAL PLANNING AND NEURONAVIGATION
14:00-14:10	**Attila Somogyi** (2nd year PhD student) Supervisor: Ervin Wolf COMPLEX CHARACTERIZATION OF NEURONAL DENDRITES: THE METHOD OF MORPHOFUNCTIONAL MATRICES AND ITS POSSIBLE APPLICATION TO IDENTIFY PATHOLOGICAL PRINCIPAL CELLS IN ALZHEIMER'S DISEASE

Conclusion	Miklós Antal

End of Symposium

.

ABSTRACTS

Assessment of mortality and outcome of patients with SAH using different volume therapy

Judit Gál (3rd year PhD student)
Éva Simon
Levente Molnár

Supervisor: Csilla Molnár

Department of Anesthesiology and Intensive Care, University of Debrecen, 4032 Debrecen, Hungary;

Introduction: Vasospasm and secondary ischemia following subarachnoideal hemorrhage considerably affect the clinical outcome. The effectiveness of crystalloid- (Lactated Ringer's solution) and colloid-based (Voluven) one-H therapies were compared in a prospective, randomized, single-blind study. We assumed that vasospasm will occur less frequently in patients treated with Voluven, therefore mid-term outcomes of this group would be more favorable.
Patients and methods: Patients with Hunt-Hess grade I-III. were involved in the study. After diagnostic neuroradiology imaging and defining the value of target blood pressure envelope randomization took place to specify fluid therapy. TCCD, GCS, arterial blood gas values, pulse rate, blood pressure, NIH Stroke Scale and the amount of vasoactive agents administered were recorded in every 24 hours. GOS and Barthel Index (BI) were also written down. The primary endpoint was defined as the incidence rate of vasospasm in both groups, while 30-days survival rates and the severity of the condition were secondary endpoints of the study.
Results: 96 patients were enrolled in the study. Silent group: vasospasm occurred in 0/10 cases in the R-L group and 1/14 cases in the Voluven group. No significant differences were registered between the two groups regarding the incidence of vasospasm, NIHSS, GOS and BI values. Ruptured group: vasospasm developed in 29/38 cases in the R-L and 25/34 cases in the Voluven group, which is a non-significant difference. No statistically significant difference was found in terms of NIHSS and BI values, while GOS values were significantly better when crystalloid-based therapy was used.
Conclusion: Based on the endpoints of the study our results indicate that there is no difference in the effectiveness of preventive Lactated-Ringer's- and Voluven-based one-H therapy.

Frequency of peripheral neuropathy and myogen lesion in antineutrophil cytoplasmic antibody associated (ANCA) small vessel vasculitis

Aletta Harman (3rd year PhD student)

Supervisor: István Fekete, Ferenc Mechler

Department of Neurology, University of Debrecen, 4032 Debrecen, Hungary;

Introduction: In systemic vasculitis the peripheral nerves are affected in 60-70%, but myogen involvement is less known.
Methods: We tested the frequency of neuropathy and muscle damage in a homogenous ANCA small vessel vasculitis patient group. Fifteen patients were recruited. Time since verifying ANCA positivity in average was 4 years. Neurological and neurophysiological examination (electroneurography, electromyography) were performed. Currently we present the preliminary data and results of our long-term prospective study.
Results: The peripheral nerves were affected in the majority of the examined patients. The detailed electroneurography results were the following: 2 patients suffered from mononeuropathy multiplex affecting the lower limbs, 1 of them the sensory and motor nerves and in the other only the sensory part have been affected. Eight patients had neuropathy in the lower limbs, in 2 patients only the sensory nerves were affected and the other 6 patients suffered from sensoro-motor neuropathy. Polyneuropathy was detected in 3 patients. The electroneurography were normal in 2 cases, who had been diagnosed two weeks and one month ago. Interestingly high percent of the patients had myogen lesion (53%). But electromyography revealed abnormality in all patients (8 patients neurogen lesion, 1 patient both).
Conclusion: We found that in most of the ANCA positive patients not only the peripheral nerve lesion is characteristic but the myogenic lesion as well. Follow up of the patients is necessary to detect the progression of the clinical neurophysiological conditions.

Diclofenac premedication, as the effect of pre-emptive anelgesia after post thoracotomy chest and shoulder pain, as well as the changes of the post operative breathing function values

Balázs Pálóczi[1](2nd year Phd student)
Tamás Végh[1]
Ágota Kazup[1]
Farkas Orsolya[1]
Parham Choromi[2]

Supervisor: Béla Fülesdi[1]

[1]*Department of Anesthesiology and Intensive Care, University of Debrecen, 4032 Debrecen, Hungary*
[2]*Department of Anesthesiology and Intensive Care, Hetényi Géza County Hospital, 5004 Szolnok, Hungary*

*Introduction:*Thoracotomies are thought to be one of the most difficult surgical incisions to deal with post-operatively, because they are extremely painful and the pain can prevent the patient from breathing effectively. Currently the surgical and post-operative anelgesia are managed by the combination of local anesthetics and opioid pain killers through an epidural cannula. In addition we give intravenously diclofenac as well as intravenous nalbuphin as necesserary.
By definition pre-emptive analgesia means that the treatment of pain is initiated before the surgical procedure by analgetics or nerve blockade techniques. As a result of the pre-emptive antinociceptive treatment, the quantity of post-operative medications can be decreased, the analgesia has less complications and the patients are more satisfied.
In our study we intend to examine the pre-emptive analgetic effect of diclofenac. This abstract summarizes the preliminary results.
Goals: Our goals are to achieve 10% reduction of the thoracotomy pain recorded by VAS score, and to achieve 10% reduction of the shoulder pain recorded by VAS score, compared to the non-diclofenac control group.
Patients and methods: Patients underwent thoracotomy will be divided into two groups.:
Group 1: 100mg diclofenac per os (n=50)
Group2 /control: patients do not given diclofenac premedication (n=50)
We examine every patient for seven days: we record the patients' pain with the help of the Visual Analogue Scale (VAS).
Results: There were no significant differences in cumulative morphine equivalent dose (cMED) values of epiduraly administered drugs, neither in cMED of intravenously administered drugs ($cMED_{epidural}$ DICLO Group: 121±118 vs $cMED_{epidural}$ CONTR Group: 148±125, p=0.4; $cMED_{iv}$ DICLO Group: 772±1231 vs $cMED_{iv}$ CONTR Group: 1106±1482, p=0.4;). There were no significant differences in cumulative VAS values in terms of thoracotomy pain ($cVAS_{th}$ DICLO Group: 24±12 vs $cVAS_{th}$ CONTR Group: 23±9, p=0.7), neither in cVAS values measured for shoulder pain ($cVAS_{sh}$ DICLO Group: 7±8 vs $cVAS_{sh}$ CONTR Group: 9±7, p=0.5).
Our results are preliminary. Further investigations are needed to drawn correct conclusions.

Reversal of Neuromuscular Blockade with Sugammadex at the Reappearance of Four Twitches to Train-of-four Stimulation

Adrienn Pongrácz, (2nd year PhD student)

Supervisor: Béla Fülesdi

Department of Anesthesiology and Intensive Care, University of Debrecen, Debrecen, Hungary.

Background: Sugammadex is a new reversal agent, a specific encapsulator of steroidal muscle relaxants, such as rocuronium. Doses of sugammadex required to reverse deep, moderate and shallow rocuronium-induced neuromuscular blockade have been established. However, no adequate doses for the reversal on reappearance of four twitches of train-of-four (TOF) stimulation have been established.
Methods: This single center, randomized, controlled, double-blind, four groups parallel-arm study included 80 patients undergoing general anesthesia. Neuromuscular monitoring was performed with calibrated acceleromyography. Once rocuronium-induced neuromuscular blockade recovered spontaneously to TOF-count-four, patients randomly received 0.5, 1.0, 2.0 mg/kg of sugammadex or 0.05 mg/kg of neostigmine. The time between study drug injection and reversal of TOF ratios to 1.0 was measured. Rapid reversal (≤ 2.0 min average upper limit 5.0 min) was the primary endpoint and slower reversal (≤ 5.0 min average upper limit 10 min) was the secondary endpoint of the study.
Results: Sugammadex in doses of 1.0 and 2.0 mg/kg reversed threshold TOF-count-four to TOF ratios of 1.0 in 2.1 ± 0.8 min (mean ± SD) and 1.8 ± 0.9 min, respectively. Sugammadex, 0.5 mg/kg induced a similar degree of reversal in 4.1 ± 1.9 min ($p < 0.001$ *vs.* 1.0 and 2.0 mg/kg). Neostigmine, 0.05 mg/kg reversed TOF ratios to 1.0 in 8.5 ± 3.5 min ($p < 0.001$ *vs*. sugammadex groups).
Conclusion: Sugammadex 1.0 mg/kg rapidly and effectively reverses rocuronium-induced block that has recovered spontaneously to a threshold TOF-count-four. A dose of 0.5 mg/kg was equally effective but satisfactory antagonism took as long as 8 minutes to take place.

Comparing premedication strategies in dental care of disabled patients

Ágnes Fekete (2nd year PhD student)

Supervisor: Béla Fülesdi

Department of Anesthesiology and Intensive Care, University of Debrecen

Background: Dental care of disabled patients in general anesthesia started in 2013 at our University. These patients are difficult to handle, often react aggressively to environmental changes, anesthetic/dental interventions, therefore may be dangerous to medical staff. Thus premedication is crucial for them. We decided to find the best preanesthetic agent for our patients. In our double-blind study we use orally applied midazolam or a new sedative drug, dexmedetomidine (Dex.) delivered intranasally (IN). The former has been used for premedication for decades, the latter has mainly been used for intravenous sedation, but recently performed studies reported the safe use of it for IN premedication. Dex. used intranasally has not been yet tested in disabled patients.
Methods, end-points: As the study started in summer 2014, here I set down the principles and aims of our work. We randomize 150 dental patients into 3 groups. We use general anesthesia in all patients, the difference is in premedication. In group A we use oral midazolam, in group B IN Dex., in group C also IN Dex. in higher dose. After premedication we observe the patients, record their vital parameters and sedation-agitation status regularly. After dental treatment we continue our observation for 2 hours with same parameters being monitored. As this kind of dental care is performed within frames of one-day surgery, it is crucial for us that our patients be transported back safe and early to their everyday life. Thus we are interested how these agents influence the length of postoperative period and recovery of vital functions. Evaluating our data, comparing different ways of premedication may help us to choose the best agent or way of delivery in a difficult-to-handle patient.

First clinical experiences with the FRONT formula for pre-operative airway assessment and documentation

Zoltán Gyöngyösi [1] (2nd year PhD student)
Peter Biro[2]

Supervisor: Béla Fülesdi[1]

[1]*Department of Anesthesiology and Intensive care, University of Debrecen, 4032 Debrecen, Hungary;*
[2]*Institute of Anesthesiology, University Hospital Zurich, Raemi Str. 100, CH-8091 Zurich, Switzerland.*

Background: Prediction and documentation of a difficult airway is essential for the safety of anesthesia. Simple onedimensional scoring systems for preoperative airway assessment have limited predictive value. Composite scoring systems are considered more sensitive. The aim of the present work was to test the clinical usefulness of the FRONT score, a newly developed composite scoring system.
Methods: This multi-center, inter-observer, prospective and double-blind investigation included 250 patients from the University of Cluj-Napoca, Romania and 726 from the University of Debrecen, Hungary. The preoperative evaluation of the patients' airways was performed by a preoperative team (team A) who obtained a predicted FRONT score. A different intraoperative team (team B) involved into the actual instrumentation of the airway scored the actual findings by using the FRONT scoring as well. The intraoperative scores were compared with the predicted ones.
Results: Our results show a fair relationship between the preoperative FRONT score and the one observed at the induction phase (r = 0.47). Among its components the best correlation was observed for F (facial) and R (dental row) features (r = 0.46 and 0.44 respectively) while the weakest correlation was observed for the O (oral) feature (r = 0.29) followed by the T (tracheal) component (r = 0.36).
Conclusion: We found that the FRONT scoring system is a simple and effective method for assessing and defining airway management difficulties. Further prospective studies are needed to quantify the sensitivity and specificity of the method.

Neural networks underlying the swallowing phase and visceromotor responses of prey catching behavior of the frog

Szilvia Kecskés (3rd year PhD student)
Klara Matesz
Andras Birinyi

Supervisors: András Birinyi

Department of Anatomy, Histology and Embryology, University of Debrecen, 4032 Debrecen, Hungary

Prey-catching behavior (PCB) of the frog consists of a sequence of coordinated activity of different muscles which is modified by various sensory signals. One of the important efferents is the nucleus ambiguus, containing the motoneurons of the glossopharyngeal and vagus nerves which controls the movement of the laryngeal and pharyngeal muscles.
The activity of the neuronal network is modified by various inputs. Snapping of prey object stimulates the trigeminal afferent terminals in the oral mucosa, which initiate contraction of muscles innervated by the glossopharyngeal and vagus nerves, however the neuroanatomical background is not yet examined. The aim of this study was to study the involvement of the trigeminal afferents in the swallowing phase of PCB.
Experiments were performed on *Rana esculenta,* where the trigeminal and glossopharyngeal (IX)-vagal (X) nerves were labeled simultaneously with different fluorescent dyes. Using confocal laser scanning microscope, close appositions were detected between the trigeminal afferent terminals and somatodendritic components of the IX-X motoneurons of the ambiguus nucleus (NA). Neurolucida reconstruction revealed the spatial distribution of the trigeminal afferents in the functionally different parts of the NA. Thus, the visceromotor neurons supplying the stomach, heart and lung received about two third of the trigeminal contacts followed by the pharyngomotor and then by the laryngomotor neurons. On the other hand, individual motoneurons responsible for innervation of the viscera received less trigeminal terminals than the neurons supplying the muscles of the pharynx.
The results presented here suggest that the direct contacts between the trigeminal afferents and IX-X motoneurons may be one of the morphological substrate of a very quick response during the swallowing phase of PCB. Combination of direct and indirect trigeminal inputs may contribute to optimize the ongoing motor execution.
This work was supported by MTA-TKI 11008 and a TÁMOP 4.2.4.A/2-11-1-2012-0001.

EEG-based functional networks in patients with typical absence seizure

Noémi Zsuzsanna Kovács[1] (2nd year PhD student)
S. Puskás[2]
M. Besenyei[3]
T. Spisák[4]
G. Opposits[4]
K. Hollódy[5]
A. Fogarasi[6]
I. Fekete[2]
M. Emri[4]

Supervisor: Béla Clemens[1]

[1] *Kenézy Hospital Ltd., Department of Neurology, Debrecen, Hungary*
[2] *University of Debrecen, Faculty of Medicine, Department of Neurology, Debrecen, Hungary*
[3] *University of Debrecen, Faculty of Medicine, Department of Pediatrics, Debrecen, Hungary*
[4] *University of Debrecen, Department of Nuclear Medicine, Debrecen, Hungary*
[5] *University of Pécs, Department of Pediatrics, Pécs, Hungary*
[6] *Epilepsy Center, Bethesda Children's Hospital, Budapest,Hungary*

Introduction: We investigated neuronal mechanisms of seizure predisposition, seizure precipitation and therapeutic drug effects of absence epilepsy (ABS). Our goal was to explore statistically significant differences between neural networks with characterizing epileptic network activity determined by extracranial EEG functional connectivity (EEGfc).
Methods: A total of 120 seconds, artifact-free, paroxysm-free, eyes-closed, resting state EEG background activity was analyzed for each person.
Design1: Twenty-four, medication free ABS patients were compared with age- and sex-matched normal control persons (NC) to specify absence network.
Design2: From the same ABS patients' interictal and immediate preictal periods were compared, in order to explore network rearrangement before seizure.
Design3: Fifteen seizure free ABS patients' interictal activity before and after medication were compared to explore the effect of the treatment on network dynamics.
Main results:
Design1: we found increased bifrontal cortical delta and theta EEGfc in the ABS group as compared to the NC group as "absence specificity" of the network.
Design2: we found increased delta EEGfc in temporal, parietal and occipital areas in the preictal state as compared to the interictal state which facilitates the emergence of absence seizures.
Design3: we found treatment related increased alpha EEGfc in biparietal cortical regions which reflects on network rearrangement inhibiting the emergence of absence seizures.
Discussion: Increased EEGfC indicates hypercoupled state among those cortical areas, which were previously demonstrated by MEG and fMRI based network studies playing role in seizure predisposition and precipitation.
Significance: On the basis of our results, EEGfc is a competent method to describe neuronal dysfunction and for the judgment of the treatment effect in terms of network dynamics and topography in ABS patients.

Research of Behavioral and psychological symptoms in neurodegenerativ and vascular dementias

Laczkóné Réka Majer[1] (3rd year PhD student)
Ede Frecska[1]
Tibor Hortobágyi[2]

Supervisors: Ede Frecska[1], Tibor Hortobágyi[2]

[1]*Psychiatry Clinic*
[2]*Institute of Pathology, Division of Neuropathology, Clinical Center University of Debrecen, 4032 Debrecen, Hungary*

Backgrounds and aim: The behavioural and psychological symptoms of dementia (BPSD) represent a clinical challenge and largely contribute to caregivers' burden. The behavioural symptoms include aggressive behaviour, agitation, disinhibition, divagation whereas the psychological symptoms include hallucinations, delusions, irritability, sleep and appetite changes. In our project we prospectively study BPSDs in a patient cohort. Behavioural and assess their relationship to cognitive decline and quality of life of patients. The associated caregivers' burden is also analysed. Our aim is to see whether i) there is a dementia and dementia-subtype specific cognitive symptom pattern, ii) is there a dementia and dementia subtype (vascular vs neurodegenerative) specific BPSD symptom pattern, and iii) whether the patients and caregivers' subjective and self-reported quality of life has a relationship or not to the severity of symptoms.
Methods: The following neuropsychological tests are performed on patients with dementia at the Neurology Clinic and Psychiatry Clinics of the University: SCID-I, HIS, GDS, MMSE, MMMS+C, ADAS-Cog, BEHAVE-AD, NPI, WBI-5, IIRS, ADL I-II. Patients are regularly assessed at follow-up visits. Patients were classified as having predominantly vascular or neurodegenerative dementia, respectively, according to the clinical assessment and diagnosis. Standard statisctical assessment was performed using T-test and ANOVA tests.
Results: Until now 72 patients have participated in the study (mean age: 74 years): 36 were classified as having vascular dementia and 36 with neurodegenerative dementia. Regarding cognitive functions there was no significant difference between the vascular and neurodegenerative dementia groups (mean MMSE:19,6 vs 19,4). BPSD symptomps were different in between neurodegenerative and vascular dementia groups with similar cognitive function. In addition, several correlations were demonstrated between quality of life, burden of disease and BPSD, and between severity of cognitive deficit and BPSD.
Findings: The behavioural and psychological symptoms of dementia are important factors in determining the patients' quality of life and contribute to the caregivers' burden. It seems that there is a difference in frequency and severity of behavioural and psychological symptoms between vascular and neurodegenerative dementias. This supports the initial hypothesis that dementia-specific symptom patterns exist. In further studies a more exact subtyping of dementias is planned with special emphasis on 'mixed dementias'.

The impact of somatic *TP53* mutations on the immunohistochemical expression of p53 protein in gliomas

Balázs Murnyák (3rd year PhD student)
Tamás Csonka

Supervisor: Tibor Hortobágyi

Department of Neuropathology, Institute of Pathology, Faculty of Medicine, University of Debrecen, 4032 Debrecen

Background and aims: Glial tumours represent the most frequent type of primary brain cancers. *TP53* mutations are early events in gliomagenesis, occuring mainly in astrocytic and oligoastrocytic lineages. Moreover, p53 pathway is also disturbed in the majority of the these tumours. Identification of *TP53* alterations is important in the neuropathological diagnosis, it helps the discrimination of astrocytomas from oligodendrogliomas and has prognostic and therapeutic relevance. The immunohistochemical detection of p53 protein can reflect its mutation status, because *TP53* alterations can result in p53 accumulation in the nuclei of tumour cells.
Matherials and methods: The aim of our study was to estimate the possible impact of somatic *TP53* mutations on the immunohistochemical expression of p53 protein in gliomas. Using the latest IARC TP53 Mutation Database (R17), we analysed the relationship between individual *TP53* alterations and immunohistochemical expression data in gliomas.
Results: The p53 immunohistochemical status was available in 21% (353 cases) of the total 1688 somatic *TP53* mutations. The majority of these alterations (84%) were p53 IHC positive. The most frequent *TP53* mutations were also p53 IHC positive: R273C (45 positive/2 negative), R175H (27/0), R248Q (11/4), R248W (12/1), R273H (12/1) R282W (8/0). Analysing 15 other tumour sides, we find that most of the R213* mutations are p53 IHC negative, but this mutation is relatively rare in gliomas.
Conclusion: Our findings indicate that p53 immunohistochemistry – a routinely used simple and cheap methodology in diagnostic (neuro)pathology – has good sensitivity and specificity regarding the presence or absence of p53 mutations in a tumour sample.
Acknowledgement: This study was supported by the Hungarian Brain Research Program – Grants No. KTIA_13_NAP-A-II/7 and KTIA_13_NAP-A-V/3.

The prognostic and diagnostic rule of urinary N-acetyl-ß-D-glucosaminidase on surgical ICU

Dániel Tamás Nagy[1] (2nd year PhD student)
Gergely Takács[1]
Anna V. Oláh[2]
István László[1]
Béla Fülesdi[1]
Zsolt Szentkereszty[3]

Supervisor: Judit Hallay

[1]*Department of Anesthesiology and Intensive Therapy, Univ. Debrecen, 4032 Debrecen, Hungary*
[2]*Department of Laboratory Medicine, Univ. Debrecen, 4032 Debrecen, Hungary*
[3]*Department of Surgery, Univ. Debrecen, 4032 Debrecen, Hungary*

The urinary N-acetyl-ß-D-glucosaminidase (NAG) is an early marker of tubular damage of the kidney caused by elevated proteolytic activity. It can be influenced by numerous nephrotoxic agents or effect, such as longterm use of sevoflurane or high intraabdominal pressure. In our experiment we are examining the changing of this marker in a tetanus patient sedated by sevoflurane, and in severe acut pancreatic patients combined with monitoring other prognostic and diagnostic values.
In the case report the management of a 82-year-old patient with intractable tetanic convulsions after forearm injury was demonstrated. The patient was sedated with midazolam, relaxed with cisatracurium, ventilated under control, but the convulsions persisted. Then sevoflurane was applied, ensuring muscle relaxation and sedation. Sevoflurane inhalation at elevated doses reversibly influenced kidney function and hepatic enzyme activities. Increased values of urinary NAG index showed temporary tubular damage. After 24 days ventilation the frequency of convulsions was mitigated, sevoflurane was gradually decreased and stopped. After the weaning process the patient was discharged. We succeded in sedating the patient for 19 days using the sevoflurane after 5 days using midazolam. Alterations in the laboratory parameters were reversible.
In acut pancreatitis there are different prognostic scores based on parameters measured especially in first 48 hours after admission. The Atalanta-classification, Bisap-score and Ranson-score have good prognostic results, and serum amyloid-A has also been shown as a sensitive and specific marker of acut pancreatitis. In our patients on the ICU we were monitoring intra abdominal pressure and NAG index in addition. In these severe cases we measured early elevated values, but we need more case to verify the real prognostic benefit of this simple and cheap additional method.
Acknowledgement: I would like to thank Orsolya Bozsó for the laboratory work.

Migration and differentiation of neurons in the spinal dorsal horn during embryogenesis

Rita Varga (2nd year PhD student)

Supervisor: Zoltán Mészár

Department of Anatomy, Histology and Embryology, University of Debrecen, 4032 Debrecen, Hungary

The superficial part of the spinal dorsal horn serves as the first relay station of nociceptive information in a highly organised laminated structure. Despite the large morpho-functional heterogeneity of neurons involved in the formation of these laminas, they originate from a single neuroprogenitor group called dP4 (or dPL). Daughter cells deriving from dP4 progenitors born later than the deep dorsal horn neurons and they are differentiating into excitatory (dILB) and inhibitory (dILA) neuron populations. Data however are scanty about the lamination of these neurons to form the superficial spinal dorsal horn and it is also not known how they differentiate further to assemble into nociceptive circuits. Our major was to understand better of these processes by investigating first the migratory routes of late born dILA and dILB neurons and then finding possible key molecules involved in these processes. For labelling migrating dILA and dILB neurons, we delivered constitutive GFP expressing DNA vector into embryos spinal cord at 12th days of gestation (E12) by in utero electroporation. Embryos were then collected after 1-4 days of the surgery and GFP labelled migrating neurons were identified with immunofluorescent double labelling. Majority of the labelled cells was found beside the ventricular zone after one day of in utero electroporation. We found labelled cells in the superficial spinal dorsal horn two days after electroporation that was these cells were positive for TUJ-1 showing their neuronal fate, while a group of neurons remained close to the central canal. Most of the GFP labelled cells were also Brn3a or Pax2 immunopositive with a non-overlapping manner that was characteristic for dILA (Pax2) and dILB (Brn3a). Our results indicate that late born neurons arise from a common pool born at the same time but because of some unknown reasons they segregate from each other immediately after their birth and show different developmental courses.

Acknowledgement: This work was supported by grants from TÁMOP 4.2.4.A/2-11-1-2012-0001 „National Excellence Program”, Hungarian Scientific Research Fund (OTKA PD 108467), MTA-JSPS and MTA-DE Neuroscience Research Group, Hungarian Academy of Sciences.

Neuronal and glial expression of monoacylglyerol lipase in the superficial spinal dorsal horn of rodents.

Klaudia Dócs (2nd year PhD student)

Supevisor: Prof. Dr. Antal Miklós

Department of Anatomy, Histology and Embryology, Faculty of Medicine, University of Debrecen, Debrecen 4032 Hungary

Endocannabinoids are key modulators of nociceptive information processing at various levels of the central nervous system including the spinal dorsal horn. Anandamide and 2-arachidonoylglycerol (2-AG) are the most relevant regulators of synaptic function. The molecular machinery responsible for the activity-dependent 2-AG biosynthesis have already been described in the spinal dorsal horn, but less is known about the expression and distribution of enzymes which are responsible for the degradation of 2-AG.
The main degrading enzyme of 2-AG is monoacylglyerol lipase (MGL) however its distribution in the spinal pain processing neural network remains largely unknown. Thus, here we investigated the cellular distribution of MGL in laminae I-II of the rodent spinal dorsal horn with immunocytochemical methods and revealed an abundant immunoreactivity for MGL in the superficial spinal dorsal horn. Investigating the co-localization of MGL with markers of peptidergic and non-peptidergic primary afferents, axon terminals of putative glutamatergic and GABAergic spinal neuron, as well as astrocytic and microglial profiles, we found that nearly 17 % of the peptidergic (immunoreactive for CGRP), a bit more than 10 % of the axon terminals of putative glutamatergic spinal neurons (immunoreactive for VGLUT2), and approximately 20 % of the astrocytic (immunoreactive for GFAP) profiles were immunolabeled for MGL. On the other hand, however, axon terminals of non-peptidergic (binding IB4) nociceptive primary afferents and putative inhibitory spinal neurons (immunoreactive for VGAT) as well as microglial (immunoreactive for CD11b) profiles showed negligible immunostaining for MGL. Both light and electronmicroscopic studies revealed a substantial immunostaining for MGL in perikarya of spinal neurons.
Our results suggest that in the superficial spinal dorsal horn 2-AG is broken down by astrocytes, and axon terminals of peptidergic primary afferents and excitatory neurons.

Differential expression patterns of K^+/Cl^- co-transporter (KCC2) in neurons within the superficial spinal dorsal horn of rats

Fariba Javdani (2nd year PhD student)

Supervisor: Miklós Antal

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical and Health Science Center, University of Debrecen, Debrecen 4012, Hungary

$GABA_A$ receptor mediated inhibition is associated with a chloride-influx that depends on inwardly directed chloride electrochemical gradient, which is regulated by potassium-chloride co-transporter, KCC2. Here, we investigated the cellular distribution of KCC2 in the superficial spinal dorsal horn of rats by using immunocytochemical methods. We demonstrated that perikarya and dendrites widely expressed KCC2, but axon terminals proved to be negative for KCC2. Studying the somato-dendritic distribution of KCC2, high and low levels of KCC2 expression were equally recovered. In single ultrathin sections we also observed dendritic segments that were negative for KCC2. Investigating KCC2 expression on neurons immunoreactive for NK1 receptor, which allowed us to study a large part of the somato-dendritic compartment of some neurons we found that KCC2 presented a quite heterogeneous distribution along the dendritic membrane. Measuring the distances between gephyrin-IR and KCC2-IR spots on NK1-R-IR dendrites we found that some putative inhibitory postsynaptic membranes keep larger distances from KCC2 than others. In addition, we found that postsynaptic membranes of putative inhibitory synaptic contacts establishing loose association with KCC2 transporters are arranged in clasters along the dendritic membrane. The results suggest that $GABA_A$ receptor mediated synaptic mechanisms may vary at different sites of the somato-dendritic membrane of neurons in the superficial spinal dorsal horn.

Neurosurgical planning and neuronavigation

Kázmér Kovács[1] (2nd year PhD student)
Gutema Emanuel[2]
Katona Péter[3]

Supervisor: Ervin Berényi

[1]*Department of Medical Laboratory and Imaging Sciences University of Debrecen*
[2]*Department of Neurosurgery, Clinical Centre, University of Debrecen*
[3]*Kenézy Gyula hospital and clinic*

Modern medical imaging techniques and data processing are essential for neurosurgical planning. Using well prepared information the neuronavigation system is an effective partner for localization and orientation in tumor suppressed regions. There are several challenging task to be solved during applying data processing pipeline to present precise subject specific information for neurosurgeons. This information can come from CT, MR or PET examinations. Considering the contrast enhanced 3DT1 MRI sequence as the reference image, the neurosurgical planner's task to registrate functional, diffusional and other landmarks from various functional (motor, sensor, speech or memory), diffusion MRI scans and other imaging methods.
Since 2006, in University of Debrecen multimodal medical images have been used for neurosurgical planning but the conditions of a real-time neuronavigation system only achieved in spring 2014. Therefore a new data processing pipeline has been developed. The presentation will show detailed steps of data processing of a free scientific software from University of Oxford called FMRIB Software Library. Neurosurgeons only asked for special image processing in problematic cases, some of them will be showed. In 2014 September and November, our research group faces another challenge: a 3T Philips Achieva TX MRI scanner and NordicNeuroLab MRI accessories are implemented into the imaging workflow thus data processing and surgical planning pipelines should be revised.
More refined imaging sequences and continuously maintained pipeline enhancing the accuracy of neurosurgical interventions. Applying this knowledge in the daily routine brings us closer to try new research techniques in computational neuroscience.
Acknowledgement: We gratefully acknowledge the financial support of NAP project KTIA_NAP_13-1-2013-0001 and HURO/1101/051/2.4.1 project for the NordicNeuroLab and the neuronavigation system.

Complex characterization of neuronal dendrites: The method of morphofunctional matrices and its possible application to identify pathological principal cells in Alzheimer's disease

Attila Somogyi (2nd year PhD student)

Supervisor: Ervin Wolf

Department of Anatomy, Histology and Embryology, University of Debrecen, 4032 Debrecen, Hungary;

Effects of one of the most frequent neurological disorders, the Alzheimer's disease, on dendritic impulse propagation were investigated. During the course of the illness, accumulations of amyloid-beta peptide appear in brain tissue in the form of insoluble extracellular plaques, and neurons and synapses show signs of degeneration. We examined layer II/III pyramidal neurons of the somatosensory cortex in Tg2576 transgenic mice overexpressing human amyloid precursor protein. Earlier studies reported morphological changes, but electrophysiological measurements could not differentiate between the mutant and control principal neurons based on their passive membrane properties and action potential generation as measured on the soma. Therefore, we investigated the differences in dendritic impulse propagation of control and mutant pyramidal cells by computer modelling and morphofunctional matrices (MFM).
Spatial reconstructions of these neurons were fed into a segmental cable model created by the NEURON simulator (Duke University, USA); current inputs (constant and sinusoidal f = 50 Hz) were modelled at thousands of dendritic sites per neuron to simulate local synaptic activities and map the whole dendritic surface. Log attenuation, voltage- and current transfers and propagation- and local delays (functional distances) of somatopetally propagating PSPs were computed between the dendritic model synapses and the soma. These functional distances and path distances of dendritic input sites from the soma were normalized in each neuron and percentages of dendritic surface areas with the same geometrical and functional distance ranges were summed up. These data were visualized as colour coded MFMs. Similarities of MFMs were measured and cluster analysis was performed on the MFMs. We found significant separation between transgenic and wild type principal cells based on their current transfer properties quantified by our new MFM method.
Acknowledgement: The authors are grateful to Dr. Alán Alpár for the files containing the reconstructed morphology of control and Tg2576 principal neurons and for the past financial support by TÁMOP 4.2.4. of the National Excellence Program.

ABSTRACTS OF STUDENTS WHO CANNOT ATTEND THE PHD SYMPOSIUM

PARP1 and p53 labelling index correlates with tumour grade in meningiomas

Tamás Csonka[1] (3rd year PhD student)
Balázs Murnyák[1]
Rita Szepesi[2]
Andrea Kurucz[1]
Álmos Klekner[3]

Supervisor: Tibor Hortobágyi[1]

[1] *Department of Neuropathology, Institute of Pathology, University of Debrecen Medical and Health Science Centre.*
[2] *Department of Neurology, University of Debrecen, Medical and Health Science Centre.*
[3] *Department of Neurosurgery, University of Debrecen, Medical and Health Science Centre*.

Meningiomas are one of the most frequent intracranial tumours, with 13 histological types and three grades according to the 2007 WHO Classification of Tumours of the Central Nervous System. p53, as one of the most potent tumour suppressor proteins, play a role in nearly 50% of human tumours. Poly ADP-ribose polymerase (PARP) is a DNA repair enzyme with high ATP demand. It plays a role in apoptosis by activating apoptosis inducing factor, and in necrosis by consuming NAD+ and ATP. Only PARP1 has been investigated in details in tumours out of the 17 members of the PARP superfamily; however, its role has not been studied in meningiomas yet. The aim of this study was to determine the role of p53 and PARP1 in meningiomas of different grade and to establish whether there is any correlation between the p53 and PARP1 expression. Both PARP1 and p53 has been expressed in all examined meningiomas. PARP1 labelled grade II tumours with higher intensity as compared to grade I and III neoplasms, respectively. Increased p53 expression was noted in grade III meningiomas. There was no statistical correlation between p53 and PARP1 expression. Our data indicate that both PARP1 and p53 activation is a feature in meningeomas of higher grade, PARP1 overexpression being an early whereas p53 a late event in tumour progression.

Study of the toxicity of gadolinium containing contrast agents on cell lines

Attila Laczovics[1] (2nd year Ph.D. student)
Gábor Szemán-Nagy[2]
Melina Tóth[2]
András Székely[1]

Supervisor: Ervin Berényi[1]

[1]*Faculty of Medicine, Department of Biomedical Laboratory and Imaging Science Faculty of Medicine, University of Debrecen 98. Nagyerdei Blvd. 4032 Debrecen*
[2]*Faculty of Natural Sciences, Department of Biotechnology and Microbiology, University of Debrecen 98. Nagyerdei Blvd. 4032 Debrecen*

The use of gadolinium containing contrast agents has been incorporated into the examination protocol of MRI studies. The fact that the different types and the different grades of tumors take up contrast material to a different degree, helps differential diagnostics. The extent and the nature of contrast enhancement is determined by the impairment of the blood brain barrier. For a long time gadolinium containing chelates have been deemed safe in the literature. Around the year 2000, these agents were linked to nephrogenic systemic fibrosis (NSF).
We set out to design a method with which we can determine the toxicity of commercially available gadolinium containing contrast agents to cell lines. It is well known that the different gadolinium containing chelates differ in their chemical structure to a great extent. For instance, some have a negative, while others have a positive charge. There are macrocyclic agents and there are open chain ligands (complex forming) of Gd(III) ion.
For our study we used two different cell lines, and four different gadolinium containing contrast agents.
A-172 glioblastoma cell lines from astrocytes and fibroblast cells were grown in a 96 hole plate. Four hours later we exchanged the medium, then we added the gadoterate meglumine, gadoversetamide, gadodiamid or gadopentetate dimeglumine in 1μmol/ml of concentration. Cells without the contrast agent were the controls. Cells were incubated in the presence of chelates for 24-, 48 hours at 37 degrees Celcius, and in the presence of 5% of CO_2. Then we exchanged the medium for MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] which could only be taken up and converted to formazan crystal by metabolically active cells via endocytosis. The colour intensity of the thus acquired solution is proportional to the viability of the cells and the numbers of cells within the system.
The MTT assay is suitable for the examination of the viability and proliferation of cells grown in the presence of contrast agents. Our method highlights the importance of the chemical structure of contrast agents which influences the uptake of gadolinium due to the different dissociative kinetics of the different complexes.

Significance of the Cupid's Bow deformity of the vertebral body

András Székely[1] (2nd year Ph.D. student)
Enikő Oláh[2]
Angéla Zvolenszki[2]
Ferenc Pusztai[2]

Supervisor: Ervin Berényi

[1]*Dept. Biomedical Laboratory and Imaging Science, Univ. Debrecen. 4032 Debrece,n Nagyerdei Blvd. 98*
[2]*Kenézy Gyula Kórház Központi Radiológiai Diagnosztika, 4026 Debrecen. Bartók Béla út 2-26.*

Background Information/Purpose: There are several known morphological variants of the vertebrae, which may be a result of pathological processes but can also be physiological. One of the normal variants is the so-called Cupid's Bow deformity, that is caused by paired parasagittal concavities within the body of the vertebra, and they may give the appearance of a bow in the frontal projection. In the lateral projection, the endplate deformities caused by these concavities are seen in the posterior portion of the vertebral body.
Educational Goals/Teaching Points: The aim of this study is to introduce this normal endplate variant, to highlight its importance through a clinical case, and to provide new knowledge that is the result of an incidence study.
Key Anatomic or Pathophysiologic Issues, Imaging Findings or Imaging Technique: Between the 1st of January, 2013 and the 31st of March, 2014 we retrospectively analyzed the thoracic and lumbar spine x-rays of 1466 patients performed at our institution to find out how common the Cupid's Bow deformity was. We initially identified 2011 patients who had both AP and lateral images taken of the thoracic and lumbar spine, but 545 were excluded due to either block vertebra, severe spondylarthrosis, scoliosis, or vertebral fractures. The Cupid's Bow deformity was most frequently seen on L.IV. (261), followed by L.V (107), L.III. (68), L.II. (11) and L.I. (7). We were also able to identify it on Th. XII (4), Th. XI. (4) and Th X. (1) . The bow shape was most commonly seen on the lower endplates, but in 10 instances the upper endplate was affected. The arms of the bow were mostly symmetric (89%). The deformity more commonly affected one vertebra (235), but in some cases we saw it on more than one consecutive vertebrae: in one case on five consecutive thoracic and lumbar vertebrae. It was more common in males (p=0,001) and in the 30-50 year age group.
Conclusion: Knowledge of the Cupid's Bow deformity is vital for the practicing radiologists since it may mimic pathological fracture or it may lead to the underdiagnosis of more ominous endplate deformities.