Clinical Neurosciences D221
The Leader of the Doctoral School: Dr. Komoly Sámuel

B-1/2005 Clinical neuroimmunology and stroke Program leader: Dr. Komoly, Sámuel

Dr. Czéh, Boldizsár czeh.boldizsar@pte.hu	Department of Laboratory Medicine	**The neurobiology of stress**
Stress appears to be increasingly present in our modern, and demanding, industrialized society. Virtually every aspect of our body and brain can be influenced by stress and although its effects are partly mediated by powerful corticosteroid hormones that target the nervous system, relatively little is known about when, and how, the effects of stress shift from being beneficial and protective to becoming deleterious. Decades of stress research have provided valuable insights into whether stress can directly induce dysfunction and/or pathological alterations, which elements of stress exposure are responsible, and which structural substrates are involved. Our aim is to understand the neuropathological and molacular changes in response to stress in different CNS structures.		

Dr. Horváth, Rita rita.horvath@newcastle.ac.uk	Department of Neurology	**Clinical and genetic characterisation of hereditary motor neuropathies**
Hereditary sensorimotor neuropathy, referred as Charcot-Marie-Tooth disease (CMT) is one of the most common inherited neuromuscular disorders. CMT and CMT related disorders are genetic neuropathies manifesting with a clinical continuum from predominantly motor through sensorimotor and predominantly sensory involvement. The pathophysiology based classification enables to differentiate between the demyelinating (CMT1) and axonal (CMT2) phenotype. The clinical diversity might be explained by an underlying genetic heterogeneity. As a result of the increasingly available diagnostic possibilities, such as panel screening of known causative genes and whole exome sequencing, more than 80 disease causing gene mutations have been already identified.		

Dr. Komoly, Sámuel komoly.samuel@pte.hu	Department of Neurology	**Assessment of cognitive functions in multiple sclerosis**
Multiple sclerosis (MS) is a chronic disease characterized by the demyelination of nerve fibers and axonal damage. Based on scientific data from the recent years, it is accepted that many of the patients are affected by cognitive decline and other psychological dysfunctions. These additional symptoms can influence the quality of life of patients as much like transitional physical symptoms in the early stage and permanent neurological deficit in the late stage of the disease. Our study aims to explore the neuropsychological status of MS patients from the MS Center in the Department of Neurology, University of Pécs. We plan to perform a long-term follow up of the patients. We also plan in a number of patients special MR ivestigations (tractrography, 31P spectroscopy etc.). Our additional goal is to explore possible predictive cognitive factors and the relationship between disease activity and psychological changes.		

Dr. Komoly, Sámuel **Dr. Illés Zsolt** komoly.samuel@pte.hu	Department of Neurology	**Population-based epidemiology of the neuromyelitis optica (NMO) spectrum in Hungary based on a national register; "head-to-head" comparison of NMO epidemiology between Hu**
The neuromyelitis optica (NMO) spectrum covers inflammatory demyelinating diseases of the CNS mediated by pathogenic antibodies against the water-channel AQP4 and myelin protein MOG. Despite of diagnostic criteria, the NMO spectrum may be difficult to distinguish from multiple sclerosis (MS). Misdiagnosis can result in flaring up of NMO due to incorrect medication, while NMO misdiagnosis leads to inappropriate treatment of MS. A recent study also indicated that overlapping entities may influence epidemiological data of MS. Recently, several European countries (Austria, France, Germany, and UK) have created a national NMO network, which conduct collaborative studies and set up guidelines. Considering these facts, here we plan (i) to examine the national epidemiology of NMO spectrum in Hungary: we will use an existing national database at Pécs, which is based on results of anti-AQP4 antibody testing provided for the whole country, and also on an existing collaborative national network. (ii) We will create a national database and registry. (iii) In international collaboration, we will compare the NMO epidemiology in Europe using the same database/registry criteria in Hungary and Denmark to establish population-based epidemiological data in both countries. The Danish part of the project has been already accepted in Denmark as a PhD project. We will address if NMO prevalence differs among European countries similar to MS. Using these national NMO databases and already available population-based MS epidemiology data in Hungary and Denmark, we will also examine, if higher prevalence of MS is associated with lower prevalence of NMO among European populations, a difference existing among Asian and European populations. (iv) Anti-MOG antibody testing will be established in Odense (University of Southern Denmark) using a cell-based assay, and will be provided for AQP4-seronegative Hungarian and Danish samples: both AQP4 and MOG-seropositive NMO epidemiology will be established and compared between the two countries. The project will contribute to create a national Hungarian NMO network similar to a few European countries. This may help in setting up collaborative international research and developing national guidelines. The study will tighten collaborative research between the University of Southern Denmark and the University of Pecs, and provide a basis for a number of future joint studies.		

Dr. Szapáry, László szapary.laszlo@pte.hu	Department of Neurology	**Investigation of PACAP in acute and chronic cerebrovascular diseases**
Pituitary adenylate cyclase-activating polypeptide (PACAP) was discovered as a member of the secretin/glucagon/ vasoactive intestinal peptide (VIP) family. PACAP is widely distributed in the central and peripheral nervous systems and acts as a neurotransmitter, neuromodulator, and neurotrophic. The neuroprotective role of PACAP using in vitro and in vivo models have been confirmed. We try to investigate the potential neuroprotective effects of PACAP in different cerebrovascular diseases particularly in acute phase and to evaluate of its role in stroke patho-physiology.		

B-2/2014 Neuromorphology and neuropathology Program leader: Dr. Ábrahám, Hajnalka

Dr. Ábrahám, Hajnalka hajnalka.abraham@aok.pte.hu	Central Electron Microscopic Laboratory	**Neuropathological examination of the tissue surgically removed due to temporal lobe epilepsy**
Regarding the etiology, temporal lobe epilepsy can be divided into three groups: mesial temporal sclerosis-, brain tumor- and cortical developmental malformation-related epilepsies. During our work, surgically removed neo- and archicortical (hippocampal formation, subiculum, entorhinal cortex)		

structures due to therapy of temporal lobe epilepsies will be examined. Examinations will be carried out with light and electron microscopic methods (immunohistochemistry, immunoelectron microscopy). Our aim is to study cell death, cell proliferation, synaptic reorganization and other morphological alterations that indicate abnormal neuronal migration. We search those common morphological changes in epilesies due to different etiologies which, independently of the cause of the epilepsy, is the consequence of the hyperexcitation. We aim to discover neuropathologoical changes that may clarify the cause of epilepsy.

Dr. Ábrahám, Hajnalka hajnalka.abraham@aok.pte.hu	Central Electron Microscopic Laboratory	**Morphological examination of the developing human cerebral cortex**
Our knowledge about the development of the central nervous system including the cerebral cortex is based mainly on results of studies on experimental animals. Less direct information is available about the development of the human cerebral cortex. Therefore, we plan examination of neuronal maturation, development of synaptic connections and myelination in normal human neo- and archicortex with immunohistochemitry and conventional histological methods. We also study morphological changes that occur during development in the cerebral cortex in aneuploidy. Our aim is to find morphological evidences that may explain the long-lasting cognitive development of healthy humans and the mental retardation found in aneuploidy.		

Dr. Pál, Endre pal.endre@pte.hu	Department of Neurology	**Investigation of the pathomechanism of myotonic dystrophy and complex care of patients**
Myotonic dystrophy is the most common aduthood hereditary muscle disease. It involves not only the skeletal muscles but other systems (such as heart, endocrine system, eyes) as well, therefore complex care is necessary for patients. The molecular mechanisms of the disease is only partly understood. It seems that the transcripted mRNAs have tri- or tetranucleotid repeats, and those abnormal RNAs sequestre RNA-binding spicing proteins (eg. MBNL1) in the nucleus inhibiting the mRNA development. This study involves histological technics (morphometry, immunohistochemistry, in situ hibridization) that support the diagnostic procedure and allow the differentiation of MD type 1 and type 2. For patient follow-up we use electrophysiologc tests and imaging (muscle MRI). Finally, we try to educe a physiotherapic program to improve patients physical condition and slow down the disease progression.		

Dr. Pál, Endre pal.endre@pte.hu	Department of Neurology	**Investigation of mitochondrial alterations in muscle diseases**
Beyond the primary mitochondrial diseases there are several muscle diseases and neurodegenerative diseases, whre mitochondrial damage was detected (decreased enzime activity, presence of abnormal mitochondria in tissues, mitochondrial DNA deletions). The puropes of this study to detect these alterations in different myopathies: quantification of mitochondrial pathology in autoimmune myositis (measuring enzyme activity, finding ragged red fibers /RRF/ and cytochome-c oxidase /COX/ negative fibers, long-range PCR). Same investigations is planned to be performed in muscle dystrophies and if possible in acquired myopathies pl. statin myopathy, ischemic muscle damage. We test mitochondrial biomarkers suitable for monitor the diseases (eg. FGF21).		

Dr. Pál, Endre pal.endre@pte.hu	Department of Neurology	**Investigation of the pathomechanism of muscle degeneration and regeneration**
In muscle fibers the atrophy/hypertrophy is determined by the balance of protein degradation and synthesis. The common basis of regulation is the insuline		

growth factor (IGF) receptor and the associated proteine kinase B (AKT). In active, phosphorilated form AKT inhibits the protein degradation via the inhibition of the ubiquitin-proteosome system (E3 ligases, atrogin-1). In the other patway AKT stimulates muscle fiber hypertrophy through mTOR activation. Investigation of these mechanisms in muscular dystrophies and acquired myopathies (eg. inactivity, steroid myopathy) is possible by histology (immunohistochermistry, in situ hibridisation) and molecular biology methods (mRNS measurement by RT-PCR). The degree of regeneration can be specified on histology samples (eg. satellite cell density). Ther results of above tests might be compared to clinical data, perhaps biochemical markers obtained from blood.

B-4/2014 Neurosurgery — Program leader: Dr. Büki, András

Dr. Dóczi, Tamás tamas.doczi@aok.pte.hu	Department of Neurosurgery	**From the doctrine of Monroe and Kellie towards the realisation of digital neurosurgery**
Monroe described the concept on the volume-regulation of intracranial compartments in 1824, and Kellie has tested it in clinical settings in 1873. The pressure-volume relationship between ICP, volume of CSF, blood, and brain tissue, and cerebral perfusion pressure (CPP) is known as the Monro-Kellie doctrine or the Monro-Kellie hypothesis. The original hypothesis states that the cranial compartment is incompressible, and the volume inside the cranium is a fixed volume. The cranium and its constituents (blood, CSF, and brain tissue) create a state of volume equilibrium, such that any increase in volume of one of the cranial constituents must be compensated by a decrease in volume of another as stated first by Burrows in 1846 and employed in clinical practice by Cushing since 1925. The principal buffers for increased volumes include both CSF and, to a lesser extent, blood volume. These buffers respond to increases in volume of the remaining intracranial constituents. In the initial era of modern neurosurgery macrosurgical techniques were employed. It was served by indirect diagnostics such as ventriculography, pneumo-encephalography and efficiency was measured by means of mortality rates. Micro-neurosurgery is the gold standard of neurosurgery of our days. It is served by direct diagnostic methods, such as CT, MRI and DSA. Microsurgical technique is based on 5-15 X magnification of the operation field described by microtopography. Surgical target is approached via non-invasive pathways, i.e. the CSF spaces. Operating microscope and specialized micro-instruments have been developed, and therapeutical efficiency has been measured by morbidity data. We have now the “digital era”: neuronavigation (like a GPS system), “key-hole” minimal-invasive craniotomy and techniques, functional neurosurgery, endovascular neurosurgery by means of DSA, stereotactic fractionated radiotherapy or radiosurgery. The program is presenting all of the physiological, anatomical, pathological, biochemical and molecular biological data necessary to the understanding of modern digital neurosurgery.		

Dr. Dóczi, Tamás tamas.doczi@aok.pte.hu	Department of Neurosurgery	**Volume regulation of the brain**
The precise adjustment of cerebral water content and brain volume is of critical importance for the normal functioning of the central nervous system (CNS). The brain, surrounded by the bony cranium is highly sensitive to any increase in intracranial volume. Failure of the compensatory mechanisms may result in decreased cerebral blood flow and mechanical tissue damages, the most dangerous of them being cerebral herniation. Although numerous investigations have been performed to elucidate intracranial volume buffering, little is known about the cellular and molecular mechanisms of the volume regulation of the nervous tissue. Constant volume of the nervous tissue is a requirement of action potentials and synaptic activities of neurons. The leader of this program has put forward the concept that brain water and electrolyte content is regulated by a central neuro-endocrine system that is independent of systemic regulation.		

It has been shown, that the endothelium of the brain vasculature is not freely permeable to water, in fact it exhibits similar water permeability properties as epithelial membranes known to regulate membrane water permeability (e.g. kidney collecting duct epithel. Arginine vasopressin (AVP) and atrial natriuretic peptide (ANP), peptide hormones important in the volume homeostasis of extracerebral tissues, have been suggested to play similar regulatory role in the CNS. These hormones and their receptors have been demonstrated in significant concentration in the brain and it has been shown, that they enter the CSF directly from the brain and not from the systemic circulation, thus plasma vasopressin and ANP levels may not actually reflect their central activity. Vasopressin antagonists and atriopeptin analogues may be useful in combatting raised intracranial pressure. Recent introduction of MRI and proton MR spectroscopy enabled the non-invasive investigation of physiological and also physical water compartments in the nervous tissue. Quantitative clinical measurements of brain water content and that of the free and bound tissue water fraction have opened a new world for the study of brain volume regulation. Participants will be well-worsed also in the theory and practice of MRI.

Dr. Dóczi, Tamás tamas.doczi@aok.pte.hu	Department of Neurosurgery	**Surgical treatment of vascular malformations of the nervous system**
The participanst of this program should get mastery of scientific evalutaion of the neurosurgical treatment of these complex malformations. They will be introduced to micro-neurosurgical, endovascular and radiosurgical methods. Indications for treatment, and operative techniques will be evaluated. Special attention is dedicated to the pathophysiological details of pressure and flow regulations within the arterial and venous tree. Theoretical program: anatomy and physiology of cerebral circulation; pathoanatomy and pathophysiology of malformations, treatment techniques. Practical program: participation in individual treatments, in operations, video-demonstrations. Participants can perform individual flow-dynamic studies.		

B-5/2014 Clinical and human neurosciences Program leader: Dr. Janszky, József

Dr. Fogarasi, András fog.andras@gmail.com	Department of Neurology	**Age dependent changes in epileptic seizures**
Although the frequency of childhood epilepsy is about 1%, our knowledge is low on this field. We have improved our experiences on seizures, interictal and ictal discharges and their age-depending changes since using long term video-EEG monitoring. Archive data of hundreds of children with epilepsy can help better assessment of ictal signs (motor, autonomic, emotional signs, automatisms and consciousness) and their agre dependency. These results can help to understand not only epilepsy but also physiology of the developing brain. Our studies include seizure semiology classification, epileptogenic lesions, structural and functional neuroimages as well as epilepsy surgery results and outcome in temporal and extratemporal lobe epilepsies.		

Dr. Hollódy, Katalin hollody.katalin@pte.hu	Department of Paediatrics	**Nutrition and growth in children with chronic neurological disability**
The recommended age-specific equations estimate energy requirements based on neurologically intact, physically active children, do not calculate on the inactivity or very vigorous dyskinetic movements. The equations are based mainly on body size and height to determine the predicted resting energy expenditure. To measure the height in children with spasticity and severe kyphoscoliosis requires special methods. Clinicians and dietitians have to tailor the optimal food intake (orally or via percutan gastrostomy) to the needs of the children with cronic neurological disability to avoid overweight and underweight.		

In our research 5-18 years children with chronic neurological diseases will be surveyed. The general health status, neurological condition, nutritional status, gross and fine motor development, speech and communication, mental status will be examined physically and with special tests. Psychosocial aspects of feeding children with cerebral palsy will also be studied. To identificate the factors which have effects on feeding ability is essential to promote adequate growth and nutrition.

Dr. Hollódy, Katalin hollody.katalin@pte.hu	Department of Paediatrics	**Differential diagnosis of movement phenomena during infancy with video-EEG monitoring**
The incidence of epilepsy in the infantile period is the highest of all age groups. The accurate diagnosis of infantile seizures is critically important. It is often very difficult to differentiate between benign, non-seizure related events and real, seizure-related movements in this age period. We will examine less than one year old infants with video-EEG monitoring and distinguish between the genuine epileptic seizures and pathologic and non-pathologic movement problems/disorders. With the precise observation of the movements and with the simultaneous EEG recordings more accurate diagnosis and earlier started treatment will be available.		

Dr. Kovács, Norbert kovacsnorbert06@gmail.com	Department of Neurology	**Deep brain stimulation in movement disorders**
Parkinson's disease, essential tremor and dystona are the most frequent movement disorders. These disorders can be treated by both pharmacological and neurosurgical procedures. In this topic we would like to focus on the evaluation of the pathomechanism, efficacy and safety of deep brain stimulation in movement disorders.		

Dr. Kovács, Norbert kovacsnorbert06@gmail.com	Department of Neurology	**The efficacy of repetitive transcranial magnetic stimulation int he treatment of various movement disorders**
Repetitive transcranial magnetic stimulation (rTMS) is a unique non-invasive technique capable of stimulating the brain tissue in vivo. Using various rTMS techniques, not only the experimental study of human brain function is feasible but rTMS may play an important role in the treatment of certain syndromes of neurodegenerative disorders (including Parkinson's disease and Alzheimer's disease) and psychiatric problems (e.g. depression). The aim of this research topic is to evaluate the efficacy of rTMS treatment on various movement disorders and to experimentally study the pathophysiological changes associated with neurodegeneration.		

B-1/2012 Psychiatry — Program leader: Dr. Tényi, Tamás

Dr. Herold, Róbert herold.robert@pte.hu	Department of Psychiatry and Psychotherapy	**Linguistic aspects of mentalization deficits in schizophrenia**
Mentalization is the ability to attribute mental states (intentions, desires, beliefs, emotions) to others and oneself. The development of mentalizing skills is strongly dependent on language competence. Primarily the pragmatic language skills show a significant association with the mentalization skills.		

Mentalization deficits are present in schizophrenia, however it is not clear in what extent this deficits are determined by the language abnormalities characteristic for schizophrenia. The aim of the PhD work is to assess the characteristics of language deficits in schizophrenia, and their effect on mentalizing skills.

Dr. Herold, Róbert herold.robert@pte.hu	Department of Psychiatry and Psychotherapy	**The treatment of mentalization deficits in schizophrenia**
Mentalization is the ability to attribute mental states (intentions, desires, beliefs, emotions) to others and oneself. This ability has a crucial role in social interactions, as it allows the understanding and prediction of social behaviour. Marked and stable mentalization deficits are present in schizophrenia that significantly influence the outcome of the disorder. Some preliminary data suggest that the mentalization performance can be improved by appropriate therapeutic approach. The aim of the PhD work is the study of therapeutic tools that result in an improvement in the mentalization performance in schizophrenia.		

Dr. Herold, Róbert herold.robert@pte.hu	Department of Psychiatry and Psychotherapy	**Mentalization deficits in schizophrenia**
Mentalization is the ability to attribute mental states (intentions, desires, beliefs, emotions) to others and oneself. This ability has a crucial role in social interactions, as it allows the understanding and prediction of social behaviour. According to the data of recent research now it is clear that mentalization is impaired in schizophrenia, and it fundamentally influences the long-term outcome of the disorder. However it is not exactly known in which way this ability is impaired, and how it is related to the other dimensions of social cognition in schizophrenia. The aim of the PhD work is to explore the nature of the mentalization deficits in schizophrenia in the context of other dimensions of social cognition.		

Dr. Herold, Róbert herold.robert@pte.hu	Department of Psychiatry and Psychotherapy	**Neurocognitive and mentalization deficits in schizophrenia**
Mentalization is the ability to attribute mental states (intentions, desires, beliefs, emotions) to others and oneself. The prerequisite of the development of the mentalization skills is the appropriate maturational process of the nervous system. It is generally accepted that neurodevelopmental abnormalities are present in schizophrenia resulting in marked neurocognitive deficits, which in turn may significantly affect the mentalization skills. The aim of the PhD work is to assess the neurocognitive deficits in schizophrenia, and their effect on mentalizing skills.		

Dr. Herold, Róbert herold.robert@pte.hu	Department of Psychiatry and Psychotherapy	**Imaging methods and mentalization deficits in schizophrenia**
Mentalization is the ability to attribute mental states (intentions, desires, beliefs, emotions) to others and oneself. According to the imaging studies of the recent years it seems clear which brain structures and neuronal networks are involved in mentalization. However, only few data are available on the connection of the pathological functioning of these brain networks and the appearance of the mentalization deficits. Schizophrenia is characterised by both neurodevelopmental and neurodegenerative processes resulting in brain abnormalities that could affect the proper functioning of mentalization skills. The aim of the PhD work is to study the structural and functional brain abnormalities responsible for the mentalization deficits in schizophrenia.		

Dr. Herold, Róbert herold.robert@pte.hu	Department of Psychiatry and Psychotherapy	**The neurobiology of mentalization**
Mentalization is the ability to attribute mental states (intentions, desires, beliefs, emotions) to others and oneself. Recently, significant efforts have been made to clarify the neurobiological background of mentalization. More and more data is available regarding the brain structures responsible for mentalization, but data is also increasing in respect of the underlying neurotransmission dysfunction. It is well known that significant neurobiological abnormalities are present in schizophrenia, and these abnormalities may play a role in the development of mentalization deficits, and later in the further deterioration of these skills. The aim of the PhD work is to study the neurobiological differences characteristic for schizophrenia in the light of the mentalization skills.		

Dr. Kelemen, Gábor kelemen.gabor@pte.hu	Department of Psychiatry and Psychotherapy	**Processes of recovery from substance abuse**
The approaches to primary prevention, therapy and rehabilitation are often rooted in non-reflected theories, what is one of the underlying issues in the recurrent debates on the effectiveness and efficiency of the given programs. The more we explore the processes of recovery the more the biological and psychosocial intervention might be well-grounded both in prevention and recovery. This PhD research plan is concerned with the role of subjectivation and "recovery capital" in the relationships of addict persons and its relation to the addictive processes including craving, representations and health learning that of are related to the brain system. Research questions includes as follows: What are the core processes of subjectivation in the service of one's recovery? How do recovering persons reconstruct their social environment to build their recovery capital?		