HuNDoC 2019

3rd HUNGARIAN NEUROSCIENCE MEETING FOR UNDERGRADUATE STUDENTS, GRADUATE STUDENTS AND JUNIOR POST-DOCS

HuNDoC 2019

16 JANUARY, 2019 Debrecen, Hungary

SPONSORS

The Organizing Committee of HuNDoC2019 Meeting is grateful for the support of its Sponsors:

Hungarian Neuroscience Society

University of Debrecen

BioTech Hungary Kft.

Biomedica Hungaria Kft.

Greiner Bio-One Hungary Kft.

INVITATION

Dear Colleagues and Fellow Students,

We kindly invite you to participate in the 3rd Hungarian Neuroscience Meeting for Undergraduate Students, Graduate Students and Junior Post-Docs in Debrecen 2019.

This symposium has been organized for 4 years as a satellite event of the meeting of Hungarian Neuroscience Society.

The PhD symposium aim is to create a fascinated atmosphere where students can present and discuss their data, share their ideas. This is a great opportunity to meet and help each other, improve your presentation skill and also to learn from each other.

Join us for the HuNDoC2019 organized by Debrecen and enjoy the neuroscience in a relaxed atmosphere! We hope to encourage many young researchers, junior post-docs and PhD students to showcase their research, stimulate fruitful conversations and meet scientists from diverse backgrounds to share ideas.

See you there!

the Organizers

GENERAL INFORMATION

Organising Committee of the HuNDoC2019:

Angelika Varga; Zoltán Mészár; Miklós Sivadó; Klaudia Dócs; Rita Varga

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

E-mail: hundocdebrecen2019@gmail.com

Facebook: HunDoc_Debrecen_2019

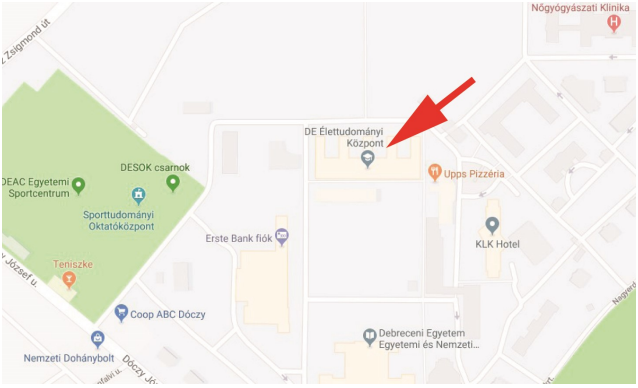
Free Wifi will be available at the conference venue.

Network: HunDoc

Password: hu2019do

Venue: Life Science Building, University of Debrecen, Egyetem tér 1.

Lecture hall: F008-009



Registration Desk:

Opening hours: 16th January 08.30-16.00

Oral Presentations: The programme committee selected 12 abstracts for oral presentation. Oral presentations are limited to a 10 minutes presentation with 5 minutes for discussion. Presentations must be prepared in Powerpoint, other formats will not be supported. Use of personal computers will not be permitted. Prior to your session, please upload your presentation in the lecture room.

Poster Presentations: 16th January 12:20-13:20 and 15:05-16:00. All poster presenters are required to prepare a mini poster (size: 28 cm x 46 cm).

Language: The official language is English. This means that all abstracts, mini posters and talks should be prepared and presented in English.

Liability and Insurance: The organizer is not able to take any responsibility whatsoever for injury or damage involving persons and property during the congress.

Public Transportation: You will find a tram stop, line 1 outside the University of Debrecen. You can take the tram 1 or bus 10 at the Railway Station to get to the hotels or conference venue.

Taxis:

Főnix Taxi, Phone: +36 52/444-444 www.fonixtaxi.hu

Citytaxi Debrecen, Phone: +36 52/555-555 www.citytaxidebrecen.hu

Parking:

There are free parking area near the venue of the Meeting (some examples of free parkins are labelled on the streetmap)

PROGRAM OUTLINE / OVERVIEW

	January 16, Wednesday
8:30	Registration
8:45	
9:00	
9:15	
9:30	Symposium opening (9:30-9:35) Plenary lecture (9:35-10:05)
9:45	
10:00	Symposium 1 (10:05-11:05) Cognition and bahaviour (1h)
10:15	
10:30	
10:45	
11:00	Coffee break (15 min)
11:15	Symposium 2 (11:20-12:20) Synaptic plasticity and synaptic transmission (1h)
11:30	
11:45	
12:00	
12:15	Lunch (12:20-13:20) Poster session (1h)
12:30	
12:45	
13:00	
13:15	Symposium 3 (13:20-14:20) Investigation within the forebrain (1h)
13:30	
13:45	
14:00	
14:15	Career forum (45 min)
14:30	
14:45	
15:00	Poster session (1h)
15:15	
15:30	
15:45	
16:00	Closing remarks (5min)
16:15	Free program
16:30	
16:45	
17:00	
17:15	
17:30	
17:45	
18:00	
18:15	
18:30	
18:45	
19:00	Dinner and PhD party at VÍZTORONY

PROGRAM

January 16- Wednesday

9:00 - Registration (30 min)

9:30 - Symposium opening and welcome (5 min)

9:35 - **Plenary lecture** (30 min)

The electrical properties of small glutamatergic axons

Brunner, János

Institute of Experimental Medicine – Hungarian Academy of Sciences

10:05 - **Symposium 1 - Cognition and behaviour** (1 h)

The simultaneous study of the cholinergic and dopaminergic systems in associative learning

Király, Bálint[1,2]; Hangya, Balázs[1]

1. Lendület Laboratory of Systems Neuroscience, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary;

2. Department of Biological Physics, Eötvös Loránd University, Budapest, Hungary

Chemogenetically influenced GABAergic neurons in the preoptic area of mice project to pup-activated brain centres and affect maternal behaviours

Dimén, Diána[1]; Puska, Gina [1]; Sipos, Eszter [2]; Zelena, Dóra [2]; Dobolyi, Árpád [1]

1 MTA-ELTE Laboratory of Molecular and System Neurobiology,Insitute of Biology, ELTE, Budapest

2 Department of Behavioral Neuroscience, Institute of Experimental Medicine, Budapest, Hungary

Role of VGluT3 positive cells of the median raphe region in social behaviour

Fazekas, Csilla Lea; Török, Bibiána; Szőllőssy-Csoma, Bálint; Horváth, Hanga Réka; Bellardie, Manon; Sipos, Eszter; Zelena, Dóra

Department of Behavioral Neuroscience, Institute of Experimental Medicine, Budapest, Hungary

Optogenetic inhibition of calretinin positive cells in the dorsomedial thalamus influences sleep behavior

Jász, Anna; Komlósi, Gergely; Acsády, László

MTA Institute of Experimental Medicine, Thalamus Research Group

11:05 - Coffee break (15 min)

11:20 - **Symposium 2 - Synaptic plasticity and synaptic transmittion** (1 h)

Dendritic impulse propagation, neuronal membrane properties and synaptic integration in principal cells of two animal models of Alzheimer's disease

Somogyi, Attila

Department of Anatomy, Histology and Embryology, Medical School. University of Debrecen, Debrecen

The role of substance P pathway in the manifestation of endotoxin-induced fever

Kéringer, Patrik

Institute of Translational Medicine, Medical School, University of Pecs, Pecs

PKD controls endocytic AMPAR trafficking in the synaptic membrane

Ignácz, Attila

Department of Physiology and Neurobiology, ELTE, Budapest

12:20 - **Mini posters during lunch brake** (1h)

13:20 - **Symposium 3 - Investigation within the forebrain** (1 h)

CAMKIIalpha-GFP mouseline providesa new tool for microscopic and electrophysiological analysis of hippocampal neurons

Tagscherer-Micska, Brigitta[1]; Kwakowsky, Andrea[3,4]; Szűcs, Attila[1]; Rátkai, Anikó[1]; Környei, Zsuzsanna[2]; Szabó, Gábor[3]; Schlett, Katalin[1]; Tárnok, Krisztián[1]

1 Department of Physiology and Neurobiology, Eötvös Loránd University, Budapest

2 Momentum Neuroimmunology Research Group, IEM-HAS, Budapest

3 Medical Gene Technology Unit, IEM-HAS, Budapest

4 Centre for Brain Research, Department of Anatomy and Medical Imaging, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

The effect of ultrasound exposition on dendritic growth and branching of the cortical neurons

Ferenczi, Zsuzsanna

Department of Medical Imaging, University of Debrecen, Debrecen

Contrasting the effect of thalamic and extrathalamic inhibition

Salma, András; Faradzs-Zade, Lejla; Acsády, László

Institute of Experimental Medicine, Budapest, Hungary

Frontal hemispheric asymmetry as reflected by sleep EEG spindles: sex and sleep cycle effects

Rottmayer, Dávid; Ali, Dorina; Bódizs, Róbert

Institute of Experimental Medicine, Budapest, Hungary

Semmelweis University, Institute of Behavioural Sciences, Psychophysiology and Chronobiology Research Group

14:20 - **Carrier forum** with young post-docs (45 min)

15:05 - **Mini posters** (55 min)

16:00 - Closing remarks (5 min)

19:00 - Gala dinner and PhD party at **VÍZTORONY**

Abstracts

The numbers of the posters are the same as the page numbers of the abstracts in this booklet

CELL TYPE-SPECIFIC CORTICAL INNERVATION OF THE MESOLIMBIC SYSTEM

Babiczky, Ákos[1,2]

1 Neuronal Networks and Behaviour Research Group, Research Centre for Natural Sciences, Hungarian Academy of Sciences, Budapest, Hungary
2 Doctoral School of Psychology/Cognitive Science, Budapest University of Technology and Economics, Budapest, Hungary

Cortical control over the mesolimbic system is important in reward processes. Prefrontal cortex (PFc) provides a major innervation in the ventral tegmental area (VTA) and the nucleus accumbens (NAc). However, exact details of these pathways are unknown.
Using single retrograde tracings, we found that VTA-projecting cells were located in deep, while NAc-innervating ones in all cortical layers. We also analysed the FoxP2 content of the labelled cells and observed that large proportion of VTA-projecting population originate from deep L6. Then, with double retrograde approach, we investigated the proportion of PFc cells innervating both regions.
To further dissect the layer-specificity of the cortical innervation of the mesolimbic system, we injected adenoassociated viral constructs into the PFc of cortical layer-specific strains of mice. The projection pattern of these cell-types were different in the VTA and the NAc. NTSR1-positive cells did not, while Rbp4- and Thy1-positive neurons intensively innervated both targets. Furthermore, our data showed that the infected neurons in PFc were intermingled with FoxP2 population and each other.
Thus, it suggests that the anatomical layer-specificity of these mouse strains is not entirely valid in the PFc. Our data together opens new opportunities to investigate the cortical control of mesolimbic reward system in a celltype specific manner.

PROBABILISTIC TRACTOGRAPHY SHOW CORRELATION WITH CORTICO-CORTICAL EVOKED POTENTIALS (CCEP) OVER ICTAL AREAS

Barnaföldi, Luca
Semmelweis University, Budapest, National Institute of Clinical Neurosciences, Budapest

For patients suffering from drug-resistant epilepsy, surgery can be the most effective treatment; but it is less successful for extratemporal lesions when seizures are not associated with structural malformations. Our aim was to predict the results of CCEP mapping using probabilistic tractography, in order to better describe fiber-tracks and networks participating in the seizure genesis.

Our four selected epileptic patients were candidates for epilepsy surgery and were implanted with subdural electrodes prior to surgical resection. CCEP mapping was performed using bipolar stimulation on every neighboring electrode pairs while the evoked potentials were recorded on the remaining electrodes. We selected midpoints between stimulation electrode pairs as seed regions, and every recording electrode was marked as a target region for probabilistic tractography. Probabilistic fiber tracking was initiated from each bipolar stimulation zone to the remaining contacts. The z-score of the CCEP amplitudes and mean connectivity values of probabilistic tractography were correlated using bivariate Pearson correlation.

From 126 cortico-cortical stimulations placed over ictal areas, 55.2% correlated significantly with the results of tractography. Two patients showed high correlation (75%) and two patients showed low correlation (35.42%).

Using non-invasive mapping methods, we attempt to substitute invasive surgical investigations to reveal the underlying epileptic network.

THE M-CURRENT IS A POTENTIAL SYNCHRONIZER OF MESENCEPHALIC CHOLINERGIC NEURONS

Bayasgalan Tsogbadrakh; Kovács, Adrienn.*; Szentesi, Péter; Baksa, Brigitta; Csemer, Andrea; Szücs, Péter; Pál, Balázs
Molecular Medicine, Department of Physiology, University of Debrecen

The pedunculopontine nucleus (PPN) is a cholinergic part of the reticular activating system, which provides cholinergic and non-cholinergic fibers to several subcortical areas. Cholinergic PPN neurons also receive cholinergic inputs, which inhibits the M-current, a voltage-gated potassium current. In the present work, we investigated the presence, subunit composition and functional roles of the M-current in cellular, network and behavioral levels.
Cellular electrophysiological experiments were performed on midbrain slices and thalamus-midbrain blocks, as well as activity wheel test was done on KCNQ4 knockout mice and wild type littermates.
M-current was only present on the cholinergic neurons. Inhibition of the M -current decreased spike frequency adaptation, whereas M-current activators increased it. High threshold membrane potential oscillations were almost completely inhibited by blockade of M-current. M-current activators increased its activation threshold and slightly reduced its amplitude. Optogenetic activation of LDT cholinergic neurons led to M-current inhibition of the PPN cholinergic neurons. Paired recordings of uncoupled neighboring PPN cholinergic neurons revealed that the M-current inhibition decreases the level of spontaneous synchronization between them.
The activity cycles of KCNQ4 knockout mice changed in a significantly different way responding to changes of light-darkness cycles compared to wild type littermates.
One can conclude that the M-current is a hallmark of the cholinergic neurons in the PPN. The channel responsible for M-current is partially, but not exclusively, formed by KCNQ4 subunits. The M-current of PPN cholinergic neurons seem to participate in neuronal synchronization and thus in regulation of PPN activity and sleep-wakefulness cycles.

*equal contribution

ANALYSIS OF LEMUR TYROSINE KINASE 2 EXPRESSION IN NEURODEGENERATIVE DEMENTIAS

Bencze, János [1]; Hortobágyi, Tibor[2,3,4]

1 Institute of Pathology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary
2 Institute of Pathology, Faculty of Medicine, University of Szeged, Szeged, Hungary
3 MTA-DE Cerebrovascular and Neurodegenerative Research Group, Debrecen, Hungary
4 Department of Old Age Psychiatry, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

In physiological neurons harmonized axonal transport is essential for normal synaptic function. Changes in Lemur tyrosine kinase 2 (LMTK2) level may contribute to the disruption of molecular transport leading to synaptic loss and neurodegeneration.

Our aim was to characterize the LMTK2 expression in Alzheimer's disease (AD) and Dementia with Lewy bodies (DLB) compared to age-match controls.

Samples were collected from MRC London Brain Bank. The assessed brain region was determined by neuropathologist (TH), then we applied LMTK2 antibody and scanned the slides. Ten images/case were taken and post-processed with ImageJ software. We selected cells based on size, cytoplasmic volume and visibility of nuclei and identified the pyramidal cells as the target subgroup. We measured the mean grey value of these neurons and determined mean, median and mode intensity profiles for each case.

One-way ANOVA showed significant differences in mean and median intensity among the three groups. Comparing two-two groups with T-test there were statistically significant differences in mean and median intensities.

Our results indicate significant changes in LTMK2 expression among age-match control and disease groups, as well as between AD and DLB patients. Further analysis of the protein's role in underlying pathomechanism may provide a promising new therapeutic target in dementias.

Acknowledgement: Supported by the ÚNKP-18-3 New National Excellence Program of the Ministry of Human Capacities; EFOP-3.6.3-VEKOP-16-2017-00009; Hungarian Brain Research Program (2017–1.2.1-NKP-2017-00002); GINOP-2.3.2–15–2016-00043.

DOES LEMUR TYROSINE KINASE 2 EXPRESSION CORRELATE WITH THE SEVERITY OF TAU PATHOLOGY?

Bencs, Viktor
Institute of Pathology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary

Lemur tyrosine kinase 2 (LMTK2) has important role in axonal transport, regulation of apoptosis and phosphorylation of tau. Since, disruption of these mechanisms identified in early Alzheimer's disease (AD), LMTK2 may contribute to AD pathogenesis.
Our aim was to characterize the connection between tau pathology and LMTK2 expression in different stages of AD.
We selected FFPE samples of 5-5 patients with Braak I and Braak VI stage AD. Regions of interest were determined: middle frontal gyrus – spared in early stages of AD, and anterior hippocampus – affected in both stages. Immunohistochemistry was performed. After scanning the slides, we took 5 photos/cases and analysed with ImageJ. We measured mean and median greyscale intensities of pyramidal cells in each region and calculated the percentage of mean grey value of the samples. Moreover, we determined the individual differences between the percentages of mean greyscale intensities of the two regions. Results were compared between the two stages.
We detected significant alteration ($p<0,05$) in the mean greyscale intensities of the two regions, as well as in the differences between percentages of mean intensities ($p<0,01$) in relation with BraakI and BraakVI stages. According to our results LMTK2 might be a promising therapeutic target in the future.

THE ELECTROPHYSIOLOGICAL PROPERTIES OF A NOVEL CORTICO -TRN PATHWAY

Bősz, Emília; Hádinger, Nóra; Acsády, László
Institute of experimental medicine, Laboratory of Thalamus Research

The thalamic reticular nucleus (TRN) of the thalamic nucleus consists of only GABAergic neurons. Different sectors of the TRN form reciprocal connections with a particular thalamic relay nucleus.. Recently, our group discovered a novel corticothalamic pathway from layer 5 (L5) of the frontal cortex to a well-defined sector of TRN. We investigated the electrophysiological properties of L5-TRN pathway in vivo in anesthetized mice via juxtacellular recording of TRN single cell responses following the optogenetic activation of L5. Short latency, reliable TRN responses could be evoked by activating L5 cells. The response probability increased gradually by increasing the laser intensity. It raises the question, whether the increased TRN response is the result of increased L5 response probability or increased recruitement of L5 neurons. Thus, we recorded the responses of L5 neurons at different laser intensities. L5 response probabilities had a sharp threshold with increasing laser power, meaning increased recruitment of activated cells at population levels. Increased recruitment of L5 indicates significant convergence of L5 neurons on one TRN cell. These data show that TRN cells integrate the activity of multiple cortical cells, and level of cortical synchrony can be translated to the strength of thalamic feed forward inhibiton.

OREXINERGIC NEUROMODULATORY ACTIONS MODIFY OCCURRENCE OF SLOW INWARD CURRENTS ON NEURONS IN THE PEDUNCULOPONTINE NUCLEUS

Csemer, Andrea; Kovács, Adrienn; Baksa, Brigitta; Bayasgalan, Tsogbadrakh; Pál, Balázs

University of Debrecen, Faculty of Medicine, Department of Physiology

Orexins are neuromodulatory peptides of the lateral hypothalamus, which regulate important homeostatic mechanisms including sleep-wakefulness cycles. Orexinergic actions stabilize wakefulness by acting on nuclei of the reticular activating system (RAS) including the pedunculopontine nucleus (PPN). Orexinergic actions in the PPN on cellular level comprise of the development of a tonic inward current or depolarization; mediated by calcium- and mixed cationic conductances, as well as occurrence of noisy background currents and an increase of excitatory postsynaptic current frequency and amplitude.

It was previously shown that serotonergic, cholinergic and cannabinoid actions on the PPN can elicit various responses including depolarization and hyperpolarization. Independently from it, astrocyte-dependent and NMDA receptor mediated 'slow inward currents' (SICs) were regulated in a way related to the previous SIC activity.

In the present project, we investigated orexinergic neuromodulatory actions on SICs of PPN neurons and their relationships with tonic currents by using slice electrophysiology on preparations from mice. We demonstrated that - in contrast with several other neuromodulatory actions and in line with literature data- orexin almost always elicited a tonic inward current. Independently from the tonic currents, actions on SICs were also detected which resembled to other neuromodulatory actions: if SICs were almost absent on the neuron, orexin induced an increase of the charge movements by SICs, whereas if SIC activity was abundant on the neurons, orexin exerted inhibitory action on it.

This finding might strengthen the theory that an astrocyte-dependent neuromodulatory action exists in the PPN, which uniformly responds to several different actions and sets a certain low level of 'random' neural activity.

CHEMOGENETICALLY INFLUENCED GABAERGIC NEURONS IN THE PREOPTIC AREA OF MICE PROJECT TO PUP-ACTIVATED BRAIN CENTRES AND AFFECT MATERNAL BEHAVIOURS

Dimén, Diána[1]; Puska, Gina[1]; Sipos, Eszter[2]; Zelena, Dóra[2]; Dobolyi, Árpád[1]

1 MTA-ELTE Laboratory of Molecular and System Neurobiology, Institute of Biology, Hungarian Academy of Science and Eötvös Loránd University, Budapest, Hungary
2 Department of Behavioral Neuroscience, Institute of Experimental Medicine, Budapest, Hungary

The early mother-infant relationships have long-term effects on the offsprings. The expression of the maternal behaviour in mammals is regulated mostly by the medial preoptic area (MPOA). Previous results of our laboratory suggest that the tuberoinfundibular peptide 39 is involved in the control of maternal motivation. In this study, we examined the GABA-ergic neurons of the MPOA regarding their role in maternal behavioural control and their innervation by TIP39-containing terminals as well as their projections from the MPOA. First, we performed immunohistochemistry in mice expressing a fluorescently tagged vesicular GABA transporter and found that many TIP39-containing fibers target the GABAergic neurons in the MPOA. Then, to determine brain-wide outputs from GABAergic neurons of the MPOA, we used adeno-associated virus-MCherry tracing. Most of the brain areas that play role in parenting, receive inputs from the injected cells. Furthermore, to reveal the function of GABA-ergic neurons on the maternal care we measured spontaneous maternal test on the VGAT-Cre virgin female mouse stimulated chemogenetically following AAV-mediated DREADD-infection in the MPOA. The results demonstrate that inhibition of GABA-ergic neurons attenuated, while the excitation of these cells intensified maternal behaviour. The results suggest a critically important role of GABA-ergic neurons in the maternal responsiveness.
Grant support: NKFIH-4300-1/2017-NKP_17 (NAP2)

SPINAL EXPRESSION AND DISTRIBUTION OF P2X4 RECEPTOR IN CHRONIC PAIN.

Ducza, László; Gajtko, Andrea; Bakk, Erzsébet; Holló, Krisztina
Department of Anatomy, Histology and Embriology, University of Debrecen, Debrecen, Hungary

Long-term and intense noxious stimulation related to chronic inflammation lead to central sensitization and plasticity within the superficial spinal dorsal horn. It is widely accepted, that interleukins play a pivotal role in spinal pain processing. By a purinergic receptor mediated action, the activation of nociceptive primary afferents and the consecutive release of ATP induce considerable increase of interleukin-1βeta within the spinal dorsal horn contributing to the hyperexcitability of the neural circuit. Accumulating evidence suggests that the P2X4 receptor may be one of the major key mediators that are involved in the cytokine secretion including IL-1β. Our knowledge is moderately scanty regarding the role and expression of P2X4 in chronic pain conditions. Thus, in the present experiment we investigated the expression and distribution of this receptor in the spinal dorsal horn of adult male Wistar rats suffering in chronic inflammatory pain evoked by unilateral plantar injection of complete Freund adjuvant (CFA). Single immunoperoxidase reactions revealed a substantial P2X4 receptor expression within the lamina I-II of the spinal gray matter following CFA injection which was further validated by Western blot analysis. The cellular distribution of P2X4 was examined by using double- and triple immunofluorescent labelings. Beyond the colocalisation of P2X4 receptor with various interneuronal and primary afferent markers we observed abundant increase of the purinergic expression on excitatory but not inhibitory axon terminals in CFA model compared to control.

ROLE OF VGLUT3 POSITIVE CELLS OF THE MEDIAN RAPHE REGION IN SOCIAL BEHAVIOUR

Fazekas, Csilla Lea; Török, Bibiána; Szőllőssy-Csoma, Bálint; Horváth, Hanga Réka; Bellardie, Manon; Sipos, Eszter; Zelena, Dóra

Department of Behavioral Neuroscience, Institute of Experimental Medicine, Budapest, Hungary

Although median raphe region (MRR) is known to be a serotoninergic nucleus with significant contribution to social interaction, but it also contains glutamatergic neurons, characterised by vesicular glutamate transporter 3 (VGluT3) with unknown role.

We used Cre and pharmacogenetic techniques (synthetic receptor) in mice to assess the function of VGluT3 in locomotion (open field/OF); social behaviour (sociability; social interaction/SI; resident intruder test/RI); anxiety (elevated plus maze/EPM); and memory (Y-maze; social discrimination/SD, 24h after sociability, the later without CNO (the arteficial ligand) injection).

In OF the inhibitory group moved less. During sociability all groups had intact social interest, and the excitatory group spent less time with the objects and conspecifics. In SD the inhibitory group spent more time with conspecifics without discrimination. Inhibition of synthetic receptor increased friendly social contacts in SI with a tendency in RI test. In EPM the excitatory group entered more often to the open arm. Y-maze revealed no differences between the groups.

The activity of MRR VGluT3+ neurons was inversely proportional to friendly social behaviour and decreased anxiety. Pharmacogenetic manipulation has a long lasting effect as seen in SD.

THE EFFECTS OF ULTRASOUND EXPOSITION ON DENDRITIC GROWTH AND BRANCHING OF THE CORTICAL NEURONS

Ferenczi Zsuzsanna
University of Debrecen, Department of Medical Imaging

Ontogeny of the cerebral cortex requires complex spatial and temporal orchestration of postmitotic neurons for populating the highly organized laminated structure of the brain. After migration and lamination appropriate dendritic growth and branching is essential for correct function of neurons. Coordinated dendritic growth is largely determined not only by intrinsic factors but also by environmental effects. Ultrasound (US) examination is one of the most important and commercial examination during pregnancy worldwide. US stimuli can modify the number of proliferation of neurons in vivo, but we do not know exactly how this stimuli effects on dendritic differentiation. Thus, we investigated the effect of US stimuli on dendritic development in the frontal cortex and the hippocampus of prenatal mice.
We labelled cortical plate neurons at E14.5 with GFP by in utero electroporation which was followed by ultrasound exposition for 10 minutes (frequency: 3.0 MHz, mechanical index 0.9, thermal index: 0. 9) at E18 and then at P3 the newborn mice were sacrificed and their brains were processed for immunhistology for the detection of TRPC4. Analysis of hippocampal and cortical pyramidal cells was performed with Imaris and Neurolucida software.
During the examination of pyramidal cells there seemed to be a higher branching frequency and there was an increase in spine density as well compared to the neurons of the nontreated animals. Our data suggest that ultrasound has prolonged effects on the morphology of differentiating cortical neurons.

CYTOKINE EXPRESSION OF REACTIVE ASTROCYTES IN CHRONIC INFLAMMATORY PAIN

Gajtko, Andrea; Bakk, Erzsebet; Hollo, Krisztina

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

Several studies investigated the role of astrocytes in chronic inflammatory pain within the central nervous system. Upon activation spinal glial cells produce inflammatory cytokines, which influence neuronal functions leading to central sensitization and enhanced pain states. The most prominent representative of proinflammatory cytokines is interleukin-1beta (IL-1β). Our earlier data showed that the spinal astrocytes are the main source of IL-1β in the chronic phase of inflammatory pain, in addition astrocytes also express the ligand binding IL-1RI unit of the IL-1 receptor. The IL-1β ligand acts on its neuronal and astrocytic interleukin-1 receptor type 1 (IL-1RI) leading to cell-type specific responses.

In the current study inflammatory pain was induced by intraplantar injection of complete Freund adjuvant (CFA). To selectively investigate the role of astrocytes primary cultures were produced from spinal cords of C57BL6 wild type and IL-1RI deficient mice. For the activation of astrocytes IL-1β stimulation was applied.

In the spinal cord of CFA-injected mice we observed a significant increase of IL-1β level on post injection day 4 which correlates with the nociceptive test results. By using cytokine array method, we demonstrated a significant increase in the expressional level of several proinflammatory cytokines in the supernatant of astrocyte cultures upon IL-1β stimulation. Furthermore, we validated the expressional changes of these cytokines by Western Blot, ELISA and Immunohistochemical experiments.

Our data show that IL-1β triggers a cascade of astrocytic cytokine release, which probably further increase neuron-glia and glia-glia interaction.

THE ROLE OF PARVALBUMIN POSITIVE BASAL FOREBRAIN NEURONS IN CODING SURPRISE AND VALENCE DURING PAVLOVIAN CONDITIONING

Hegedüs, Panna; Heckenast, Julia; Hangya, Balázs
Institute of Experimental Medicine, Hungarian Academy of Sciences

The basal forebrain (BF) has widespread cholinergic, GABAergic and glutamatergic projections which are thought to mediate multiple cognitive functions. The BF may be involved in broadcasting signals related to outcome expectations. To directly test this hypothesis, we trained mice on an auditory pavlovian cued outcome task. Next, we recorded and optogenetically identified parvalbumin (PV)-positive GABAergic neurons from the frontally projecting portion of the BF (horizontal limb of the diagonal band of Broca, HDB) while mice were performing the task.
We found that identified parvalbumin (PV) positive neurons were responding differentially to reinforcement valence by phasic activation to punishment but not to reward. Moreover these neurons respond with stronger activation to surprising punishment. Further supporting this notion, higher frequency of anticipatory licking, which can be considered a proxy for higher reward expectations, predicted stronger responses of PV neurons to punishment.
With anterograde virus injections revealed that HDB PV-neurons may serve as a major input to the limbic navigation system, transmitting negative valence and surprise value to these structures. This pathway may be crucial in context dependent learning of aversive stimuli.

INTERLEUKIN 6 (IL-6) AS A PLEIOTROPIC CYTOKINE AND THE MEMBER OF THE PRO- AND ANTI-INFLAMMATORY PATHWAYS HAS CRITICAL ROLE IN CNS FUNCTION AND MAY CONTRIBUTE IN DEVELOPMENT OF SEVERAL NEUROLOGICAL DISEASES.

Horváth, Krisztina
Institute of Experimental Medicine, Hungarian Academy of Sciences

Aim: To observe behavioral alterations in IL-6 knockout mice.
Method: Wild type FVB/Ant and IL-6 KO on FVB/Ant background were used in sociability and social novelty-, social interaction-, aggression-, elevated plus maze-, Y maze-, shuttle box-, operant conditioning-, startle-, conditional fear- and tail suspension tests. We measured body-, thymus-, spleen- and adrenal weights and determined plasma IL-6 levels by ELISA.
Results: IL-6 deficient mice showed significantly more defensive behavior during aggression test and visited significantly more arms in the Y maze compared to the control group. In the shuttle box test IL-6 KO mice failed to escape or escaped with significantly higher latency from the foot shock than control animals. Their startle responses, freezing frequencies and immobility time were significantly higher in the startle-, conditional fear- and tail suspension tests compared to the control group.
Conclusion: In conclusion, IL-6 deficiency resulted in passive coping and defense. These findings underscore the importance of cytokines in general and IL-6 in particular in the behavioral phenotype.

PKD CONTROLS ENDOCYTIC AMPAR TRAFFICKING IN THE SYNAPTIC MEMBRANE

Ignácz, Attila
Eötvös Loránd University, Department of Physiology and Neurobiology, Budapest, Hungary

Activity of protein kinase D (PKD) family of serine/threonine kinases is required for LTP formation in hippocampal neurons and regulates actin dynamics within the dendritic spines. In this study, we investigated a potential role of PKD in AMPA receptor turnover within the synaptic membrane.

In murine hippocampal neuronal cultures, surface expression of the AMPAR subunit GluA1 was assessed through biotinylation and Western Blot analysis upon agonist-induced receptor internalisation. Short-term inhibition of PKD activity significantly increased surface GluA1 amount indicating that PKD is required for proper GluA1 endocytosis. This was further corroborated by antibody feeding experiments followed by quantitative microscopic evaluation within the PSD of dendritic spines.

To test the dynamics of PKD-mediated AMPA receptor loss, we expressed super-ecliptic pHluorine tagged GluA1 (SEP-GluA1) in the neurons. Photobleaching SEP-GluA1 in the dendritic spines followed by the analysis of fluorescence recovery revealed that inhibition of PKD activity significantly increased the recovery half time of the surface GluA1 signal.

Taken together our results indicate a role for PKD in promoting activity-dependent turnover of AMPA receptors.

Supported by the National Brain Research Program (2017-1.2.1-NKP-2017 -00002), by NRDIO (VEKOP-2.3.3-15-2016-00007), and by the German Research Foundation (DFG HA-.3557/11-2).

OPTOGENETIC INHIBITION OF CALRETININ POSITIVE CELLS IN THE DORSOMEDIAL THALAMUS INFLUENCES SLEEP BEHAVIOR

Jász, Anna; Komlósi, Gergely; Acsády, László
MTA Institute of Experimental Medicine, Thalamus Research Group

The unique anatomical connections and physiological activity of the calretinin positive (CR+) neurons in the dorso-medial thalamus (DMT) suggest that these neurons have role in collecting and transferring the ascending arousal signals to the forebrain.
Previously we have identified, that graded optogenetic stimulation of DMT/CR+ cells can generate biological relevant arousal patterns. However, it is unclear, whether DMT is necessary to maintain wakefulness. Here, using optogenetic manipulations with polysomnographic recordings, we investigated, how the effect of inhibition of DMT/CR+ neurons for wakefulness inmice.
We monitored the behavior in the beginning of the light phase, with and without optogenetic inhibition of DMT/CR+ cells for 36 minutes. We found that during inhibition, the amount of movement and EMG activity was significantly reduced, while EEG delta power significantly increased, compared to the non-inhibited days. These difference persisted even after switching the laser off. The altered activity could largely be attributed to the significantly shorter sleep onset due to the inhibition. The sleep structure of the animals was not different between the inhibited and non-inhibited cases.
Our data show, that inhibition of DMT/CR+ activity decrease arousal, manifested in reduced locomotion and shorter sleep onset. We propose, that DMT/CR+ activity are necessary for proper wakefulness.

CHRONIC STRESS INDUCED METABOLIC CHANGES

Juhász Balázs
Institute of Experimental Medicine, Hungarian Academy of Sciences

Introduction: The nervous, the neuroendocrine and the immune system generate together an adaptive resistance to eliminate the effects of chronic stress. This systemic adaptation requires a huge amount of energy and if the permanent stress did not eliminate, it would cause a numerous psychological and metabolic dysfunction.
Aim: To observe the mechanism of chronic stress induced metabolic dysregulation and how can the fractalkine signaling take part in these mechanism.
Method: The fractalkine receptor deficient transgenic and wild type C57BL6 mice were exposed to chronic variable stress for 4 weeks. After stress, the body weight were calculated, the mass of adrenal gland, the plasma corticosterone and triglicerid concentration were measured. Moreover the gene expression changes were investigated in PVN and liver.
Results: The peripheral measurements imply that the CVS treated animals were in a stress condition. The key enzymes of the catabolic pathway gene expression were elevated, however the Pgc1-α level was not increased in the transgenic mice. In addition, FbP-1 gene expression was decreased in the CVS treated animals.
Conclusion: In conclusion, CVS treated mice increased their catabolic pathway because of the β oxidation and the high acetyl-CoA production, which is a fundamental source of the citric acid cycle.

A THALAMO-HYPOTHALAMIC PROJECTION THAT MAY ACTIVATE OXYTOCIN NEURONS IN RESPONSE TO SOCIAL INTERACTION

Keller, Dávid

Laboratory of Neuromorphology, Department of Anatomy, Histology and Embryology, Semmelweis University, Budapest 1094, Hungary

Oxytocin is released from neurons in the paraventricular hypothalamic nucleus (PVN) in mothers upon suckling and during social interactions. However, neuronal pathways that activate oxytocin neurons in social contexts are not established yet. Neurons in the posterior intralaminar complex of the thalamus (PIL), which contain tuberoinfundibular peptide 39 (TIP39) were addressed as possible inputs. Innervation of oxytocin neurons by TIP39 neurons was examined by double labeling in combination with electron microscopy and retrograde tract-tracing. Potential classical neurotransmitters in TIP39 neurons were investigated by in situ hybridization histochemistry. Neurons activated after encounter with a familiar conspecific female were mapped with c-fos technique. PVN oxytocin neurons were innervated by asymmetric (presumed excitatory) synapses of TIP39 terminals. PIL TIP39 neurons were retrogradely labeled from the PVN. TIP39 neurons expressed VGLUT2 but not GAD67. PIL contained c-Fos-positive neurons in response to social encounter with familiar and also with unfamiliar adult female. Furthermore, PIL neurons received ascending input from the spinal cord and the inferior colliculus. Thus, TIP39 neurons in the PIL may receive sensory input in response to social interactions and project to the PVN to excite oxytocin neurons, suggesting that the PIL-PVN projection contributes to the activation of oxytocin neurons in social contexts.

Acknowledgement: Support was provided by New National Excellence Program of the Ministry of Human Capacities (UNKP), NKFIH-4300-1/2017-NKP_17, and OTKA K116538 research grants.

THE ROLE OF SUBSTANCE P PATHWAY IN THE MANIFESTATION OF ENDOTOXIN-INDUCED FEVER

Kéringer, Patrik
Institute for Translational Medicine, Medical School, University of Pecs, Pecs

Introduction: The neurokinin-1 (NK1) receptor and its ligand (Substance P) were shown to contribute to the development of lipopolysaccharide (LPS)-induced fever, but the exact mechanism is unknown.
Methods: We used adult NK1 receptor knockout (*Tacr1*$^{-/-}$) and wild type (*Tacr1*$^{+/+}$) mice of both sexes. After intraperitoneal administration of LPS (120 µg/kg), thermoregulatory responses and changes in inflammatory biomarkers were studied in the mice.
Results: At 40 minutes after LPS administration, the increase in deep body temperature and oxygen consumption was attenuated in *Tacr1*$^{-/-}$ mice compared to wild type mice (38.1±0.2 vs. 38.5±0.2°C and 173±9 vs. 189±6 ml/kg/min; $p < 0.05$). The fever response to intracerebroventricular administration of PGE_2 was unchanged in *Tacr*$^{-/-}$ mice. After LPS administration, COX-2 mRNS expression increased in the lungs, liver, and brain in both genotypes. The LPS-induced increase in COX-2 protein expression was attenuated in the lungs and it tended to be diminished in the liver of *Tacr1*$^{-/-}$ mice. After injection of LPS, PGE_2 concentration significantly increased in the lungs of *Tacr1*$^{+/+}$ (but not *Tacr1*$^{-/-}$) mice.
Conclusion: Our results suggest that NK1 receptors contributes to the early phase of LPS-induced fever through enhancement of peripheral COX-2 protein expression.
Support: NKFIH FK124483, UNKP-18-4-PTE-109.

A COMPARATIVE STUDY OF TARGETED GERM-LINE GENOME EDITING METHODS BASED ON CRISPR /CAS9 SYSTEM

Kerti, Ádám; Varga, Rita; Balázs, Anita; Szücs, Péter; Mészár, Zoltán

Department of Anatomy, Histology and Embryology, University of Debrecen

Generation of germ-line transgenic animal with targeted mutation requires a series of time consuming and expensive methods by an advanced researcher. Male pronuclear microinjection of foreign DNA is a classical method for generating transgenic animals. Together with other gene delivery methods including viral and embryonic stem cell mediated gene transfer have several limitations, however. For precise, one-step targeted mutation the use of CRISPR / Cas9 gene editing system can overcome most of the time-consuming steps required for the targeted embryonic stem cell line selection. The aim of or study is to simplify and accelerate the generation of targeted mutations to reveal transgenic mice by using a combination of testicular electroporation and CRISPR system. To compare the effectiveness of the CRISPR system we delivered the elements (Cas9 enzyme, crRNA, trRNA and homologue template) in different forms by testicular electroporation. For the mutation we used a homologue template cassette containing a floxed bicistronic open reading frame including a marker GFP that was targeting the ROSA26 allele. The integration of the gene was confirmed by PCR. Our improved methodology for generating targeted mutations is a cost and time efficient and can be easily approved by various biomedical researchers.

THE SIMULTANEOUS STUDY OF THE CHOLINERGIC AND DOPAMINERGIC SYSTEMS IN ASSOCIATIVE LEARNING

Király, Bálint[1,2]; Hangya, Balázs[1]

1 Lendület Laboratory of Systems Neuroscience, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary
2 Department of Biological Physics, Eötvös Loránd University, Budapest, Hungary

Acetylcholine and dopamine are neuromodulatory neurotransmitters that control the behaviour of diverse populations of neurons, influencing neural information processing at a variety of temporal scales. Different neuromodulatory systems participate in overlapping cognitive processes and often code similar behaviourally relevant variables (such as reward prediction error or reinforcement surprise), hence their unique roles in cognitive functions such as learning, memory and attention are not well characterized. To address this, it is crucial to study them under the same experimental conditions. Moreover, to reveal potential redundancies in neuromodulatory codes, it is necessary to investigate these systems simultaneously.

First, we designed a new auditory operant learning paradigm suitable for dual electrophysiological recordings to study the firing activity of cells with the above requirements. Next, we started recording basal forebrain (HDB) and midbrain (VTA) neurons using optogenetical tagging to identify cholinergic and dopaminergic neurons from awake behaving mice, and analysed their behavior while the animal learned new reward or punishment predicting auditory cues.

The overarching goal of the project is to study the simultaneous activity of the cholinergic and the dopaminergic systems during learning and explore the inter-relationships between the two systems using traditional linear and non-linear information theory based correlation measures.

HIGH-RESOLUTION RETINOTOPIC MAPPING USING INTRINSIC SIGNAL OPTICAL IMAGING

Kocsis, Zsolt[1]; Srivastava, Mohit[1]; Julian, Budd[2]; Monier, Cyril[3]; Fregnac, Yves[3]; Kisvárday, Zoltán[1]

1 MTA-DE Neuroscience Research Group, University of Debrecen (Hungary)
2 University of Sussex, Dept. Informatics, School of Engineering and Informatics, Brighton (UK)
3 CNRS-UNIC, Gif-sur-Yvette (France)

Retinotopy is the representation of the visual field, as it is projected through the optics of the eye onto the retina, then via the dLGN into the primary visual cortex. The aim was to obtain high-resolution retinotopic maps in the cat primary visual cortex based on which visual field polar coordinates can be determined for each cortical location.

Anesthetized, paralyzed cats were prepared for in vivo intrinsic signal optical imaging. Monocular visual stimuli were presented on a computer screen 57 cm in front of the animal's eye. The stimulus consisted of a sequence of elongated luminance bars shifted at 1.5 deg steps in vertical (for elevation) or 3.0 deg steps in horizontal (for azimuth) directions. Data acquisition lasted for 4.5 sec for each stimulus condition and was repeated 15 times.

First, the acquired images were subjected to noise reduction. Analysis consisted of the determination of the vertical meridian, calculation of iso-azimuth and iso-elevation lines. High-resolution retinotopic map was generated using interpolation algorithm.

Future applications of the results: retinotopy is an important attribute to explore structurefunction relationship between bouton distribution of single cortical cells and their visual field representation. The present approach, which preseves the structural integrity of the cortical tissue is well suited to be extended with single neuron electrophysiological and labelling approaches.

Supported by NAP2 (2017-1.2.1-NKP-2017-00002 Nemzeti Agykutatási Program 2.0).

PROCESSING AND UTILIZATION OF AUDITORY ACTION EFFECTS DURING SOCIAL INTERACTION

Neszmélyi, Bence[1,2]; Horváth, János[2,3]

1 Budapest University of Technology and Economics,
2 Hungarian Academy of Sciences,
3 Károli Gáspár University of the Reformed Church in Hungary

In many fields, social interactions are gradually replaced by human-machine cooperation. This raises the question whether cognitive processes that enable cooperation (information processing, action control) indeed work identically in these two contexts. In the current study, it was examined if the processing of auditory events and their utilization in motor control processes is affected by the interaction type (social, human-machine) that is responsible for generating the stimuli.

Auditory ERPs and action-effect-related force optimization were compared in two conditions that only differed in the complexity of the causal chain between the motor and sensory event. In the *self-induced condition,* participants generated tones directly by pressing a force-sensitive resistor, while in the *interactive condition,* sounds were generated indirectly relying on the contribution of the partner (paired reaction-time task).

The magnitude of force optimization was similar in both conditions suggesting that effect-based action control processes are not influenced by the nature of the interaction. However, N1 amplitudes elicited by sounds in the interactive condition were reduced when compared to auditory ERPs in the self-induced condition. This might indicate that agency related effects are enhanced for integrated (one's own and coactor's) action representations, although an interpretation based on context-specific attentional processes is also plausible. .

EXAMINATION OF THE PERISOMATIC INHIBITORY INPUT TO PRINCIPAL NEURONS IN DYSGENETIC CORTICIS OF HUMAN EPILEPTIC PATIENTS

Paraczky, Cecília[1]; Szocsics, Péter[1]; Erőss, Lóránd[2]; Barnaföldi, Luca[2]; Havas, Laszló[3]; Maglóczky, Zsófia[1,4]

1 Human Brain Research Laboratory, Institute of Experimental Medicine, HAS, Budapest
2 National Institute of Clinical Neuroscience, Budapest
3 St. Borbála Hospital, Tatabánya
4 Laboratory of Cerebral Cortex, Institute of Experimental Medicine, HAS, Budapest

The previous investigations of our group were performed on hippocampal samples with temporal lobe epilepsy (TLE), and enhanced perisomatic inhibition was found, which may increase the seizure probability. Therefore, changes of perisomatic inhibitory inputs were examined in focal cortical dysplasia (FCD) cases to find whether mechanism of epileptogenesis is similar to TLE.

Surgically removed frontal cortical samples from patients with FCDIIb were compared to post-mortem perfusion fixed cortices of the same cortical regions with short-term interval (4-4 subjects). We used antibodies against NeuN, and SMI32 (labelling pyramidal cells), PV (labelling perisomatic inhibitor elements), GFAP and IBA1 (labelling glial elements). The samples were examined with light, confocal, and electron-microscopy.

In several epileptic samples, there were numerous giant, dysmorphic neurons, appear to have a particularly dense inhibitory input. In some cases, presumably balloon cells were found in the white matter. The quantitative parameters showed a tendency in the elevation of the number of perisomatic terminals in FCD cases. It was most prominent in case of the giant cells.

Our results suggest that perisomatic inhibition is preserved in FCD and cell size correlates with the abnormal perisomatic input, which may have a role in the seizure generation caused by dysgenesis.

support: NKFIH K125436

FITTING HAWKES PROCESSES TO MULTI-UNIT ACTIVITY OF AN EPILEPTIC PATIENT

Perczel, György

Faculty of Information Technology and Bionics, Pázmány Péter Catholic University, Budapest

Department of Functional Neurosurgery and Center of Neuromodulation, National Institute of Clinical Neurosciences, Budapest

Hawkes process is a general framework of self-excitation regarding point processes. In the special case of exponential core function self-excitation is characterized by two parameters, volatility and friction. These control the length and density of trains of events (bursts) to occur, but it can be shown that imbalance of these two parameters may lead to the explosion of the process. We note that an additional parameter – mean firing rate – is used. Our aim was to investigate how processes fitted to human multi-unit activity (MUA) change during epileptic activity.

We recorded MUA from a patient with therapy refractory epilepsy using laminar microelectrodes. After applying a band pass filter (500-3000Hz) the signal was thresholded using a median based filter in order to derive series of events from the continuous signal. Hawkes processes were fitted to distinct epochs of the data using maximum likelihood estimation (MLE). Epochs were represented with their parameters acquired during the MLE. Significance of the results was determined by computing the confidence ellipsoid of a given estimate.

We found clear separation between epochs recorded during interictal periods and seizure in the parameter-space. Also, we observed that processes fitted to seizure-containing epochs drifted towards unstable regimes.

T-TYPE CALCIUM CHANNELS AND HCN CHANNELS REGULATE HOMEOSTATIC PLASTICITY IN HIPPOCAMPAL CELL CULTURES

Rátkai, Anikó
Dept. Physiology and Neurobiology, Eötvös Loránd University, Budapest

Homeostatic plasticity stabilizes the properties of neuronal circuits by adjusting the responsiveness of postsynaptic neurons according to the strength of the trigger inputs. As a model, 48h tetrodotoxin (TTX) treatment was applied in mouse hippocampal cultures and organotypic slice preparations to eliminate spike-evoked synaptic transmission. Neuronal excitability and physiological properties were analyzed by whole-cell current clamp, indicating a characteristic increase of the depolarizing voltage sag and post-inhibitory rebound. These responses were totally abolished upon the application of specific CaV3 and HCN channel inhibitors, NiCl2 and ZD7288, respectively. Our data indicate that the magnitude of the lowthreshold Ca-current associated with the post-inhibitory rebound (PIR) and the h-current mediating the voltage sag increased in a homeostatic manner.
RT-qPCR and western blot analysis indicated upregulation of CaV3.1 and downregulation of HCN1 gene expression. HCN1 protein levels did not change, while CaV3.1 protein levels increased during TTX treatment. Confocal analysis of organotypic hippocampal slice cultures is in progress to reveal positional changes in the dendritic localisation of HCN channels. These results indicate that besides the already known role of AMPA receptors, CaV3 and HCN channels are also specifically regulated during homeostatic plasticity.
Supported by the National Brain Research Program (2017-1.2.1-NKP-2017 -00002) and by NRDIO (VEKOP-2.3.3-15-2016-00007).

FRONTAL HEMISPHERIC ASYMMETRY AS REFLECTED BY SLEEP EEG SPINDLES: SEX AND SLEEP CYCLE EFFECTS

Rottmayer, Dávid; Ali, Dorina; Bódizs, Róbert

Semmelweis University, Institute of Behavioural Sciences, Psychophysiology and Chronobiology Research Group

NREM EEG sleep spindles indicate trait-like and experience-dependent neural plasticity. It would be essential to reveal their functional role in cognitive processing, trait-like differences in frontal brain asymmetry, sex differences in normal and abnormal brain functioning. We analyzed adult sleep spindle data (N = 157, age range: 17−69 years, 71 females), registered from frontal EEG electrode-pairs. Our major purpose was to reveal the sexual dimorphism and sleep cycle-effects in the hemispheric laterality of slow and fast sleep spindles. First we examined separately the male and female participant-group by assuming no laterality in our null hypotheses. Women were characterized by noticeable greater amount of right-dominant sleep spindling, than men. Female vs male group differences in asymmetry indices revealed, that some of the above right laterality measures were higher in women. We observed only one negligible cycle-effect. In conclusion, there is a mild, but significant right frontal hemispheric lateralization of sleep spindles in women, in contrast to men. After all, the aforementioned right-hemispheric lateralization in case of females might indicate the right-lateralization of frontal activity during waking hours (e.g. alpha-asymmetry). These results could help the understanding of right hemisphere related negative affectivity, as well as the higher susceptibility for depression of females.

A NOVEL MEASURE TO ASSESS THE EFFICACY OF THERAPEUTIC WHOLE-BODY HYPOTHERMIA IN SEVERE TRAUMATIC BRAIN INJURY: THE COOLING INDEX

Rumbus, Zoltán
Institute for Translational Medicine, Medical School, University of Pecs, Pecs

We aimed to determine the effectiveness of therapeutic whole-body hypothermia on the mortality of adult patients with severe traumatic brain injury (TBI) by using meta-analysis.
We performed an extensive literature search using PubMed, EMBASE, and Cochrane Library databases from inception to February 2017. The identified human studies were assessed regarding statistical, clinical, and methodological designs to ensure interstudy homogeneity. From the reported cooling parameters, we calculated the cooling index, a measure of therapeutic hypothermia.
We found no difference in the outcome of TBI between cooled and not cooled patients, but interstudy heterogeneity was high. On the contrary, by meta-analysis of randomized clinical trials that were homogenous with regard to statistical, clinical designs, we showed decreased odds ratio for death in therapeutic hypothermia compared with no cooling. As influencing factors, milder and longer cooling, and rewarming at <0.25°C/h were associated with better outcome. The therapeutic whole body hypothermia showed beneficial effect only if the cooling index was sufficiently high.
By analyzing methodologically homogenous studies, we demonstrate that cooling improves the outcome of severe TBI, and this beneficial effect depends on the integrated measure of cooling parameters, namely the cooling index.
Support: NKFIH-FK124483, Janos Bolyai Scholarship of the Hungarian Academy of Sciences

CONTRASTING THE EFFECTS OF THALAMIC AND EXTRATHALAMIC INHIBITION

Salma, András; Faradzs-Zade Lejla; AcsádyLászló
Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary

The thalamus has two distinct inhibitory networks: thalamic inhibition, originating in the nucleus reticularis thalami (nRT) and extrathalamic inhibition (ETI), arising from various extrathalamic sources. TRN projects only to the thalamus whereas ETI nuclei always have collaterals outside the thalamus as well.
In this study we compared the properties of nRT and ETI inhibition in freely moving animals in the thalamic mediodorsal nucleus (MD) which receives both nRT and ETI inputs. The ETI inputs to MD arise from the ventral pallidum (VP). Selective activation of the pathways was achieved by injecting floxed Channelrhodopsin to nRT and VP of vGAT-Cre mice. Fiber optics were implanted to MD and, in case of VP injections, to the ventral tegmental area (VTA) as well, which is also targeted by VP cells.
Activation of nRT terminals in MD with different frequencies had focal synchronizing effect on the cortex, whereas the activation of VP boutons affected the synchrony in most cortical areas. VP stimulations evoked major behavioural changes. Activating VP terminals in VTA largely replicated the effects of MD stimulations.
Our data show that activating GABAergic terminals in the thalamus has significant effects in cortical activity. They also show that ETI has more profound effect on both the cortical activity and on behaviour probably via simultaneously affecting thalamic and extrathalamic targets.

DENDRITIC IMPULSE PROPAGATION, NEURONAL MEMBRANE PROPERTIES AND SYNAPTIC INTEGRATION IN PRINCIPAL CELLS OF TWO ANIMAL MODELS OF ALZHEIMER'S DISEASE

Somogyi, Attila
Department of Anatomy, Histology and Embryology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary
Kenézy Gyula University Hospital, University of Debrecen, Debrecen, Hungary

Two major pathological proteins have been identified in Alzheimer's disease, the beta-amyloid and the hyperphosphorylated tau. We used two animal models to study the effects of these proteins separately in Tg2576 mice overexpressing human amyloid beta precursor protein and in rTg4510 mice expressing high levels of human mutant tau.
We investigated the effects of the pathological proteins on neuronal membrane, subthreshold dendritic impulse propagation and on synaptic integration in principal neurons of the two transgenic mice.
Morphologically faithful passive segmental cable models of mutant and wild type neurons were created by the NEURON simulator. Somatopetal dendritic impulse propagation was studied by analysing current transfers, steady-state and sinusoid voltage transfers, and delays of locally generated dendritic PSPs.
Beta-amyloid leads to changes in both dendritic morphology and neuronal membrane properties, but these effects act parallel and their combined effect makes subthreshold dendritic impulse propagation and synaptic integration unaltered. Mutant tau alters dendritic morphology to variable extent but membrane properties remain virtually unaffected. As a consequence mutant tau affects dendritic signalling differentially in transgenic neurons and in apical and basal dendritic arbours.
All these findings are independent of the somato-dendritic distribution of membrane conductances within physiological ranges.

THE BASAL FOREBRAIN MAY PROVIDE A LINK BETWEEN LOCOMOTION AND LEARNING

Sviatkó, Katalin[1,2]; Széll, András[1,3]; Hegedüs, Panna[1,2]; Bánhidi, Anita [1,4]; Hangya, Balázs[1]

1 Lendület Laboratory of Systems Neuroscience,Department of Cellular and Network Neurobiology, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest,H-1083, Hungary

2 János Szentágothai Doctoral School of Neurosciences, Semmelweis University, Budapest, H-1085, Hungary

3:Department of Measurement and Information Systems, Budapest University of Technology and Economics, Budapest, H-1117, Hungary

4: Eötvös Lorand University, Faculty of Science Institute of Biology, Budapest,H-1117

Brain states are controlled by neuromodulatory centers. Among these the basal forebrain has widespread projections thought to mediate multiple cognitive functions. From these, the GABAergic projection has been implicated in controlling the locomotion-related theta oscillation and the glutamatergic projection can directly control animal speed. At the same time, cholinergic cells respond rapidly and reliably to reinforcement, important for learning. Therefore we hypothesize a relationship between basal forebrain neuronal activity, locomotion and learning.

To test this, head-fixed mice were placed on a wheel and trained on an auditory cued outcome task. This allowed mice to move or stay still voluntarily during the task. We monitored neuronal activity in the medial septum using tetrodes. Thus it was possible to examine whether there were correlated changes in neuronal activity and behavioural performance across the two states.

We found that mice initially trained on a fixed wheel learned faster. When allowed to move freely, mice tended to run after reinforcement delivery, which could reflect approach or escape responses. Neurons displayed a diversity of responses to behaviourally relevant events with dominant subpopulations showing activation or suppression after air puff delivery. These medial septal cell types may convey locomotion dependent learning signals via the septo-hippocampal pathway.

ESSENTIAL ROLE OF THE LATERAL THALAMOAMYGDALAR PATHWAY IN FEAR LEARNING

Szabo, Monika
Hungarian Academy of Sciences Research Centre for Natural Sciences

The basis of associative learning is the association of a neutral stimulus with a valencebaring signal and then, stored them as an emotional memory. At a later time point, the presence of the same neutral stimulus on its own (conditioned stimulus) evokes a behavior linked the valence. This process consists of series of events with distinct time scale, the rapid perception, the temporally longer consolidation, and the eventual retrieval. Here, using loss-of-function approaches, we selected temporally matching, genetic-based silencing methods to investigate how the calretinin-positive (CR+) thalamic population innervating the lateral amygdala, involved in fear associative learning. Timing the chemogenetic inhibition of CR+ TA cells – via hM4Di providing inhibition for several hours – to the conditioning as well as the consolidation phase suppresses fear learning as well as fear expression on the following day. Temporally precise timing of inhibition with optogenetic stimulation of NpHR pumps during perception erased fear behavior in all phases of associative learning. The NpHR animals were indistinguishable from non-shocked animals in many aspects. To investigate, how essential the presence of CR+ TA population in these fear processes, we lesioned them with the cell-type selective difteria toxin (DT)-mediated apoptosis. Our preliminary data show that DT-treated animals expressed elevated rather than suppressed fear in every phases of fear paradigm suggesting a generalized fear behavior. Altogether, these data highlights the pivotal role of CR+ TA cells in forming normal fear behavior.

COMPARATIVE ANALYSIS OF FUSARIUM MYCOTOXINS ON CELL VIABILITY OF PRIMARY NEURONAL AND ASTROGLIAL CELL CULTURES

Szentgyörgyi, Viktória; Tagsherer-Micska, Brigitta; Rátkai, Anikó; SchlettKatalin; Tárnok, Krisztián
Department of Physiology and Neurobiology, Eötvös Loránd University, Budapest

Fumonisin B1, deoxynivalenol and zearalenone mycotoxins are produced by Fusarium mold. They are present in the food chain and represent a risk for health. It is not yet clarified how they influence neural cell functions. We investigated cell viability effects of these toxins on mouse primary neuronal, astroglial and mixed cell cultures after 24 or 48 hours of mycotoxin administration in 1 nM - 50 µM concentration range. MTT-assay revealed that deoxynivalenol decreased cell viability in a dose-dependent manner, independently from the cultures types. Fumonisin B1 increased cell viability significantly on astroglial and mixed cell cultures in lower doses, while in 50 µM, it was highly toxic. Zeralenone had no significant effect on mixed cell cultures, however in 10 nM, it increased the cell viability of neurons and astrocytes. We analyzed the effects of the mycoestrogen zearalenone on the expression of estrogen receptor isotypes ER-alfa and ER-beta with qRT-PCR. In neuronal and mixed cultures, zearalenone decreased ER-alfa expression, while in astroglial cultures, it induced the opposite effect. ER-beta expression was not altered by zearalenone in either culture types. Our results demonstrate that Fusarium mycotoxins are acting on a cell specific manner. Supported by grants from the National Research, Development and Innovation Office (NVKP_16-1-2016-0016 and VEKOP-2.3.3-15-2016-00007).

INVESTIGATION OF PERISOMATIC INPUTS ON GIANT MOTOR NEURONS IN THE HUMAN PRIMARY MOTOR CORTEX

Szocsics, Péter[1]; Papp, Péter[2]; Havas, László[3]; Maglóczky, Zsófia[1,2]

1 Human Brain Research Laboratory, Institute of Experimental Medicine, HAS, Budapest
2 Laboratory of Cerebral Cortex, Institute of Experimental Medicine, HAS, Budapest
3 Szt. Borbála Hospital, Dpt. of Pathology, Tatabánya

One of the most special neuron population of the human central nervous system is the group of giant pyramidal cells in the primary motor cortex (Betz cells). Their axons constitute ca. 10% of the corticospinal tract, and they play an important role in fine motor movements. Our focus was to investigate and characterize their perisomatic input for better understanding their function since the literature is controversial in that field.

We have investigated the primary motor cortices of eight post mortem perfusion-fixed subjects (PMI: 2-5 h) without any known neurological deficits. We used SMI32 and parvalbumin (PV) immunostaining to visualize Betz cells to optical-, fluorescent- and electron microscopic examination. SMI32 labels all of the giant motoneurons, and according to primate data PV is also present in a subpopulation of them. PV-immunostained Betz cells were further investigated in the electron microscope.

In our human samples, various portion of SMI32-labeled Betz cells were PV-immunopositive, too. Betz cells are heavily covered by mostly inhibitory synapses. Asymmetric-like synapses were proved to be vGlut1-negative, originating presumably from subcortical sources. The projecting neurons of the ventral lateral nucleus of the thalamus, which are PV+ in the primata, are the most likely candidates.

Support: 2017-1.2.1-NKP-2017-00002

CAMKIIALPHA-GFP MOUSE LINE PROVIDES A NEW TOOL FOR MICROSCOPIC AND ELECTROPHYSIOLOGICAL ANALYSIS OF HIPPOCAMPAL NEURONS

Tagscherer-Micska, Brigitta[1]; Kwakowsky, Andrea[3,4], Szűcs, Attila[1]; Rátkai, Anikó[1]; Környei, Zsuzsanna[2]; Szabó, Gábor[3] Schlett, Katalin[1];Tárnok, Krisztián[1]

1 Dept. Physiology and Neurobiology, Eötvös Loránd University, Budapest
2 Momentum Neuroimmunology Research Group, IEM-HAS, Budapest
3 Medical Gene Technology Unit, IEM-HAS, Budapest
4 Centre for Brain Research, Department of Anatomy and Medical Imaging, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

CaMKIIalpha-GFP mouse line expresses GFP in a cell-specific manner under the control of CamKIIalpha promoter. In this work, we analyzed the expression of the CaMKIIalpha-GFP transgene in developing mouse brain and checked whether the cellular morphology and electrophysiological properties of neurons were affected by the long-term expression of GFP within hippocampal organotypic slice cultures and dissociated neuronal cultures.

Our results show that GFP expression begins early in brain development and reaches a plateau at the third week after birth. Strong GFP expression is detected in the developing cortex and hippocampal formation, especially in the dentate gyrus and CA1 region. Detailed in vitro analyses showed that GFP expression selectively visualized pyramidal neurons. The lack of glutamate decarboxylase (GAD65/67) immunopositivity indicated that GFP positive cells are not GABAergic neurons. Using pre- and postsynaptic markers, we did not experience any difference in the maturation of these cultures. Analysis of the passive and active membrane properties also confirmed that expression of GFP did not affect the electrophysiological properties of these neurons. Thus CaMKIIalpha-GFP transgenic mice could serve as an ideal tool for further electrophysiological or anatomical studies and labeling of pyramidal neurons.

Supported by the National Brain Research Program (2017-1.2.1-NKP-2017 -00002) and by NRDIO (VEKOP-2.3.3-15-2016-00007).

MODELLING THE PATCH CLAMP PIPETTES AND AMPLIFIER CIRCUITS ENABLES THE REMOVAL OF INSTRUMENTAL DISTORTION

Tarcsay, Gergely; Oláh, Viktor János; Brunner, János
Institute of Experimental Medicine -Hungarian Academy of Sciences, Hungary

Electrophysiological instruments, including pipette and amplifier circuits, inevitably distort patch clamp recorded intracellular signals, especially when the structures are small (such as axons), because their passive parameters are comparable to the instrumental contribution. Consequently, recording instruments not only filter the measured biological signals but also affect the local cellular electrogenesis. To overcome these issues and to retrieve the native signals from small axons we built and tested a model that incorporates not only the biophysical parameters of the recorded and reconstructed structure but the experimental instrumentation as well.
The model implemented (1) pipettes as non-uniform multicompartmental models, which were constrained by the measured original physical parameters, and (2) each element of voltage- and current-clamp circuit, whose contributions were measured by isolating them within the amplifier circuit. Our approach confirmed that instrumentation indeed have significant impacts on recorded signals because the predicted native axonal spikes were (1) considerably larger and faster than the measured signals and (2) similar to the theoretically expected signals. Our observations also suggest that by precisely modelling the recording instruments it is possible to retrieve the native electrical properties of small neuronal structures after their inevitably distorted direct recordings.

ROLE OF DIFFERENT CELL-TYPES OF THE MEDIAN RAPHE REGION IN SOCIAL BEHAVIOR

Török, Bibiána[1,2]; Bellardie, Manon[1,3]; Szőllőssy-Csoma, Bálint[1,4]; Sipos Eszter[1]; Zelena, Dóra[1]

1 Institute of Experimental Medicine, Hungarian Academy of Sciences
2 Semmelweis University János Szentágothai School of Ph.D. Studies, Neurosciences
3 Université François Rabelais in Tours
4 Semmelweis University, Faculty of Medicine

Disfunctions of median raphe region (MRR) are associated with many psychiatric disorders due to its role in anxiety and social behavior. Optogenetic stimulation of MRR acutely decreased aggressive behavior in mice, but the contributing cell-types were unknown. MRR has heterogeneous composition: serotoninergic, GABA-ergic, glutamatergic and yet unknown cell populations have been described.

Our aim was to detect further neuron-types in MRR and reveal their function in social behavior.

Control, stimulatory or inhibitory DREADD sequence was injected into MRR of VGAT-Cre (vesicular GABA transporter), VGluT3-Cre (vesicular glutamate transporter 3), CRH-Cre (corticotropin releasing hormone) and DAT-Cre (dopamine transporter) mice using AAV vectors. Thirty minutes after intraperitoneal injection of clozapine-N-oxide (ligand of DREADD) social interaction (SI) and resident-intruder (RI) tests were conducted.

We confirmed the presence of all studied cell-types in MRR. Inhibition of VGAT-Cre in MRR increased friendly SI and diminished aggression. VGluT3-Cre inhibition increased social contacts without any sign of aggression. In contrast, inhibition of CRH and stimulation of dopaminergic neurons decreased friendly SI and increased aggressive behavior in SI test with similar tendencies in RI.

MRR GABA-ergic, glutamatergic and dopaminergic neurons may contribute to aggression, while CRH-ergic neurons has opposite effect, more resembling the whole MRR stimulation. As SI reflects anxiety as well, it can be assumed that MRR glutamatergic neurons are important in social interaction among anxiogen conditions. Thus, each neuron-type of MRR may contribute to the fine regulation of social behavior.

CELL-TYPE SPECIFIC THALAMIC MODULATION OF THE AMYGDALAR ASCILLATORY AND UNIT ACTIVITY

Váncsodi, Melinda

Faculty of Information Technology and Bionics, Pázmány Péter Catholic University, Budapest

Research Centre for Natural Sciences, Hungarian Academy of Sciences, Budapest; Department of Physiology, University of Szeged, Szeged

The calretinin-positive (CR+) midline thalamic (MT) nuclei convey arousal -related signal, while the posterior intralaminar/suprageniculate cells (PIL/SG) transfer sensory information to the amygdala, which are both necessary in emotional memory formation. Moreover, the amygdalar gamma oscillations are known to play an important role in these processes, which raises the question how these thalamic inputs impact the amygdalar activity and oscillations. Here, we examined the modulation of the local field potential (LFP) and multiunit-activity (MUA) within the amygdala in response to optogenetic activation of these two thalamic inputs. Activation of MT inputs had excitatory effect in the amygdalostriatal transitional area (AStr) and intercalated amygdala cells (ITC), which then induced strong inhibition in the basal amygdala (BA). Similar activation of PIL/SG axonal arbors elicited excitation in the AStr, ITC and basomedial amygdala (BMA), but had an inhibitory effect on the lateral amygdala (LA). The peripheral shock stimuli triggered identical areas and effects as the PIL/SG stimulation. The strength of the amygdalar gamma oscillation increased in response to both thalamic excitation and aversive stimulus but was strongest in case of PIL/SG inputs. Altogether, these data indicate complex but distinct nuclei-specific thalamic effects on segregated amygdalar microcircuits which could drive gamma oscillation-mediated emotional behaviors.

REISISTANCE OF PREVIOULSY ACQUIRED COGNITIVE CAPABILITIES TO IMPAIRMENT INDUCED BY CHRONIC UNPREDICTABLE STRESS IN RATS

Varga, Bence Tamás
Department of Pharmacology and Pharmacotherapy, Semmelweis University, Budapest

We have developed a cognitive test system where rats are simultaneously trained in different cognitive tasks and then subjected to an impairment method with the aim to test cognitive enhancer agents. In our present experiment, we examined the effects of chronic unpredictable stress as impairing agent.
Twenty-one month old male Long-Evans rats were regularly trained in the five-choice serial reaction time test (model of attention and impulsivity), in the Morris water-maze (spatial memory), in a co-operation-test in skinner-box (social cognition), and in a pot-jumping task (motor-learning). The latter two methods were internally developed. During the stress period animals had to learn a new task (T-maze alternation), too. The animals were randomized to stressed (N=24) and non-stressed (N=10) groups based on their test-performances. The unpredictable stress procedure was applied for 4 weeks and consisted of various combinations of restrain, electric foot -shock, exhaust swimming, frequent cage-moving, wet litter, cage tilting, water deprivation, randomly played dog barking, altered light-dark cycle. The cognitive performance was measured both during and after the stress procedure.
Stress caused a significant, 13% decrease in bodyweight and a 250% increase in corticosterone level. However, with the exception of a transient impairment in the five-choice reaction time test on the 10^{th} stress-day, significant changes were not detected in any of the cognitive assays.
Our results show that well-trained tasks are resistant to even massive chronic stress. As in human disorders established knowledge deteriorates this resistance should be taken into account in designing models for testing putative cognitive enhancers.

SEMA3 SIGNALING PLAYS ROLE IN MORPHOLOGICAL FORMATION OF SPINAL DORSAL HORN NEURONS

Varga, Rita; Szücs, Péter; Mészár, Zoltán
Department of Anatomy, Histology and Embryology, University of Debrecen, Hungary

The spinal dorsal horn has a highly organized laminated structure, where different laminae shows large heterogeneity in both morphological and functional way. By contrast, the spinal dorsal horn neuron originated from only a few different types of progenitor cell. Thus, the microenvironmental factors play major part in formation of neuronal morphology. Secreted semaphorins play major role in guidance of axon growth cone and forming the morphology of neurons including spinal cord. Several semaphorin family member molecules are identified involved in the organization of ascending and descending tracts or midline crossing of axons of spinal neurons. The exact morphogenic effect in the spinal dorsal horn hasn't been clarified, however.

Our primary aim in present study was revealing a detailed developmental map from expression pattern of secreted semaphorins during laminarization and differentiation of spinal dorsal horn using immunohistochemistry and in situ hybridization. Secondly, using dominant negative transgenic technology, we examine the putative function of the semaphorin signalization in spinal dorsal horn neuron differentiation. We found, that migrating or just arrived cells were positive for Sema3A and Sema3F, and these neurons were also positive for semaphoring receptors neuropilin 1 and plexinA2. Our data are indicating that both neuropilin 1 and plexinA2 are transmitting the Sema3 in spinal dorsal horn.

CONSERVED SEROTONERGIC BACKGROUND OF EXPERIENCE-DEPENDENT BEHAVIOURAL RESPONSIVENESS

Varga, Zoltán Kristóf
Institute of Experimental Medicine, Hungarian Academy of Sciences

Effectively responding threats requires the emergence of stress-induced internal states. Such ability depends on early experiences and, in connection, the adequate formation of central modulatory systems, particularly the development of serotonergic pathways. In the current study we use zebrafish as a model to unravel the serotonergic background of experience-dependent behavioural responsiveness due to its relatively simple CNS and robust stress responses. We characterised a highly reactive period during development in which we subjected individuals to chronic social isolation. Socially isolated fish showed delayed avoidance and sensory responsiveness during novelty challenges compared to socially reared subjects. In line with such decreased reactivity, isolation exerted lower basal and increased novelty-induced whole-brain serotonin content compared to controls. We detected similar stress-induced differences on the level of forebrain limbic structures. Pharmacological blockade of serotonergic signalling prevented isolation-induced physiological a behavioural effects as well. Interestingly, the isolation-induced decrease in reactivity was specific to noveltyinduced visually-driven challenges. In summary, we found that the absence of adequate stimuli during development impairs responsiveness through the emergence of atypical neuromodulation. Our results support the idea, that serotonergic signalling is one fundamental and ancient channel that transmits early-life information to the adult phenotype, establishing contextually relevant challenge coping.

Gala dinner

Venue: Nagyerdei Víztorony

Address: Debrecen, Pallagi út 7, 4032