Theoretical Medical Sciences

Technical and informatical inventions in the examination of glucose-monitoring neurons in the nucleus accumbens and the orbitofrontal cortex

Ph.D. thesis

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1. Introduction

The homeostasis, the dynamic equilibrium of the body, maintained by complex processes adapting to the continuously changing conditions and challenges of the endogenous and exogenous environments, is essential for a healthy life. This balance of the internal milieu – as the determinant factor – ensures proper food and fluid intake, maintenance of body weight, body temperature control and co-regulation of metabolic rate, in which the plasma level of various metabolites remains permanently in the healthy physiological range. Our organization achieves the smooth functioning of these processes with the help of complex, coordinated control mechanisms, and in this regard the central nervous system plays a fundamental integrating role.

For these reasons, it is essential to define and ascertain as precisely as possible the homeostatic regulatory functions of the central nervous system, and in this regard, the orbitofrontal cortex and the nucleus accumbens are of particular importance as key constituents of the forebrain limbic network.

The soluble chemical substances, responsible for the taste of food, are detected by taste receptors. These receptors, which specifically recognize the five basic taste qualities (sweet, salty, sour, bitter and umami) are located at the beginning of the gastrointestinal tract: on the tongue, on the palate, in the pharynx, in the epiglottis around larynx and in the initial part of the esophagus [7, 73]. According to recent research reports, there are chemoreceptors also in the lower parts of the gastrointestinal tract (stomach, small intestine, colon) which are able to sense, for example, D-glucose (sweet) [50, 61], sodium glutamate (MSG) (umami) [50, 60], and sodium chloride (salt) [50].

The D-glucose molecule plays a key role in carbohydrate metabolism and regulation of food intake. Electrophysiological studies at the beginning of the second half of the 20th century have proven that, like in the periphery, there are neurons also in the central nervous system which alter their firing rate when locally or systemically glucose is administered [4, 45, 46]. These neurons, which are capable to detect changes in glucose concentration in the extracellular space by a change in membrane potential, are called *glucose-monitoring (GM)* neurons. Based on their responsiveness to glucose, two types can be distinguished: nerve cells that increase their firing frequency are the so-called *glucose-receptor (GR)* neurons, and the cells that reduce their firing rate are the so-called *glucose-sensitive (GS)* neurons. Nerve cells,

that use glucose only during their metabolism and do not show responsiveness in its presence, are called *glucose-insensitive (GIS)* neurons [47].

The presence of neurons forming a network of such chemosensory cells, has been proven in several different brain areas: lateral hypothalamic area [5, 17, 19, 22, 47-49], ventromedial nucleus of the hypothalamus [14, 22, 26, 36, 47-49, 59, 63], nucleus tractus solitarius [1, 3, 37], area postrema [2, 9], amygdala [15, 20, 43, 44], globus pallidus [18, 27], nucleus accumbens [52], prefrontal cortex [39-41, 48], orbitofrontal cortex [21, 22, 32-34, 66, 67]. These glucose-monitoring neurons show responsiveness to both exogenous (e.g. taste, odor) and endogenous (e.g. neurotransmitters) chemical and other signals [16, 18, 19, 28], thus, play an important role in the integrative and adaptive processing of feeding-relevant information.

Streptozotocin (STZ) is a molecule similar to D-glucose, which was isolated as an antibiotic substance at the end of the 1950s from the bacterial strain *Streptomyces achromogenes*, but was used as the only indication in the therapy of metastatic tumors originated from pancreatic β-cells. STZ can selectively kill such cells and is, therefore, widely used as an animal model for DM type 1 [10, 11, 30, 68]. STZ enters the cells through the GLUT2 transporter, where it causes oxidative stress and necrosis by free radical formation [13, 30, 56, 68].

This effect of STZ can not only be exerted on the periphery, but can also be absorbed by the central nervous system GM nerve cells containing GLUT2. When STZ administered intracerebrally, these glucose-monitoring neurons are specifically damaged by it, and after definitive cessation of their activity, severe feeding and metabolic disturbances, and characteristic symptoms of DM type 2-like status develop [22-24].

The two sub-divisions of the nucleus accumbens (NAcc) play different roles in the regulation of food intake: damage of the shell region causes hyperphagia, while destruction of the core region decreases the food intake motivation (hunger) [35]. Cortical structures also play a significant role in the central regulation of feeding. Decorticated animals are incapable of self-feeding, but foods placed in their mouth are capable of triggering motorized responses, such as chewing, swallowing, etc. [72]. The orbitofrontal cortex (OFC) is capable of tuning the perception and motor output through its multiple, gustatory and visceral, as well as somatosensory and motor inputs, depending on motivational state of the organism [38].

2. Aims

Numerous studies have been conducted on the central regulation of feeding and metabolism, however, in many aspects our knowledge is incomplete. Our research team has been actively involved in the study of the role of NAcc [52, 70, 71] and OFC [21, 22, 31-34, 65-67] in food and fluid intake and metabolic regulation processes for decades. In our present research, the objectives are:

1. To determine the endogenous and exogenous chemical sensitivity of the nucleus accumbens neurons, extracellular single neuron activity was recorded during microelectrophoretic administrations, intraoral taste stimulations and intragastric infusions.
2. To determine the endogenous and exogenous chemical sensitivity of neurons in the medial and lateral orbitofrontal cortex, extracellular single neuron activity was recorded during microelectrophoretic administrations, intraoral taste stimulations and intragastric infusions.
3. Perfectuating technical and IT inventions by which both data acquisition and experimental devices are computer controlled, and data can be analyzed accurately and quickly.
4. After intracerebral administration of streptozotocin, which selectively damages GLUT2 receptor containing glucose-monitoring neurons, the role of medial orbitofrontal cortical neurons was investigated
    a. in the control functions of blood glucose level during intraperitoneal glucose tolerance test;
    b. on metabolic functions by examining a blood sample taken from the tail vein;
    c. in taste sensation during taste reactivity tests;
    d. in learning processes related to taste sensation in conditioned taste-aversion experiments.

3. Materials and methods

3.1. Subjects

In our experiments, 337 adult male Wistar and Sprague-Dawley rats were used. The body weight of the test animals at the start of the studies was 250-350 g. In the rat room, a constant temperature (21±2 °C) and humidity (55-60%) were provided. Animals were housed in a 12/12 hour light/dark cycle. The rats were kept and cared for in accordance with the institutional (BA02/2000; BA0104L 12; ZOHU0104L 08; BA02/2000-8/2012), national (Act XXVIII of 1998 on the protection and sparing of animals, Decree No. 40 of 2013 of the Hungarian Government, 2013/20) and the international regulations (NIH Guidelines, 1997; 86/609/EEC Council of Europe, 1986, 2006; 2010/63/EU Directives of the European Parliament).

3.2. Electrophysiological experiments

3.2.1. Surgery

For the anesthesia of rats, intraperitoneally administered urethane (0.6 ml/100 μg, 25% fresh solution, Sigma) was used. The head of the animals was fixed in a stereotaxic device, and in order to avoid their choking due to possible aspiration of the taste solutions, the clamping frame was placed at an angle of 15° in the forward tilted position. After cutting the scalp and cleaning the skull, a 4-5 mm diameter hole was drilled on the skull with a dental drill, and after the dura was incised, the microelectrode was positioned with a micromanipulator (MN-33, Narishige, Japan), then we drove it to the target area by means of a hydraulic micromanipulator (Narishige MO-10, Japan). Coordinates of NAcc by the brain atlas of Pellegrino [54]: AP: B+3.2-3.7; ML: 1.2-1.6; V: 5.6-7.6. The coordinates of OFC according to the brain atlas of Paxinos and Watson [53]: medial OFC (mOFC): AP: B+3.8-4.4; ML: 0.8-1.2; V: 3.0-3.5; lateral OFC (lOFC): AP: B+3.8-4.4; ML: 2.5-3.5; V: 2.5-3.5.

3.2.2. Microelectrode

For the extracellular single neuron recordings and for the microelectrophoretic administration of neurochemicals, we used a tungsten wire multibarreled glass microelectrode manufactured and prepared by our research group. Single neuron activity was recorded via the tungsten wire in the central tube, and the solutions used for microiontophoresis were filled into 9 capillary tubes surrounding the central tube. The diameter of the tungsten wire was 10 μm, and it protruded from the tip of the glass electrode by approx. 10 μm. The diameter of the orifice in the surrounding tubes was between 0.1 and 0.3 μm. The impedance of the microelectrodes used for the recording at 50 Hz was 1.5-6 MΩ.

3.2.3. Signal processing

The extracellularly recorded action potentials, through the tungsten wire in the central tube of the electrode, after filtration and amplification (Supertech Kft., Hungary) were transferred to an analog/digital converter (CED Micro 1401 mk II, Cambridge Electronic Design, Cambridge, UK), so we could save and analyze the signals with the aid of computer. Analog signals were continuously monitored on oscilloscope (PeakTech P-1145, Heinz-Günter Lau GmbH, Ahrensburg, Germany). With the help of the Spike2 program (Cambridge Electronic Design, Cambridge, UK), a frequency histogram was created for each nerve cell activity, on-line and off-line analyzes were performed using the scripts I wrote.

3.2.4. Microiontophoresis

Microiontophoretic device (NeuroPhore BH-2, Medical Systems, Great Neck, New York, USA) was used to deliver solutions filled into the barrel micropipettes of the electrode. With this device, an electric potential gradient is created between the surrounding tubes and the extracellular space of the given brain area, so that charged particles can be administered into the immediate environment of the neurons. The most important factors determining the outflow from the electrode’s tip are the ejection current, the material's diffusion constant, the hydrostatic pressure gradient, and the degree of electro-osmosis [6, 25, 55].

3.2.5. Neurochemical examinations

Various neurotransmitters and neuromodulators were loaded into the barrel tubes of the electrode during neurochemical stimulation. Among others, we studied the neuronal firing rate altering effect of the following substances: D-glucose, noradrenaline (NA), dopamine (DA), acetylcholine (Ach) and GABA. The effect of each neurochemical was tested at three different ejection current levels (±15-90 nA, low-medium-high). Administration was performed for 10-15 seconds, and after vaining of the effect had subsided at least one minute elapsed before the next microelectrophoretic solution was administered.

3.2.6. Intraoral taste stimulations

We also examined the taste responsiveness of nerve cells during extracellular single neuron recording. In case of the gustatory studies, a polyethylene tube was placed into the oral cavity of the rats, through which the solutions corresponding to the five basic taste qualities were administered at two different concentrations. We also examined the effect of orange juice as a complex taste solution. The volume of 1-1.5 ml of taste solutions was injected into the oral cavity of the animal in 3-5 seconds. The end of the taste tube is designed to allow the taste solution to reach all parts of the oral cavity. The gustatory stimulus presentation was followed by rinsing with distilled water, followed by air to purify the system from the taste solution. According to our taste stimulation protocol, we waited for at least one minute between two administrations of taste solutions. The stereotaxic device was fixed in a position such that the head of the experimental animal was lower than its body, so that the administered solution spontaneously dripped out from its oral cavity, thus, saving the animal from swallowing or aspirating the solution.

3.2.7. Intragastric infusion

For intragastric infusion, during stable anesthesia, a thin polyethylene tube (Hibiki 3, Japan) was led into the stomach of the experimental animal with the aid of a gastric probe. The effects of the following solutions were examined during the single neuron activity recording: NaCl (60 mM and 150 mM), D-glucose (60 mM) and MSG (60 mM). Solutions were administered using an infusion pump (Cole-Parmer EW-74900 Multichannel Syringe Pumps, Cole-Parmer Instrument Company, Vernon Hills, Illinois, USA) in a volume of

1 ml/100 bwg. Waiting for one minute after filling the intragastric tube, preceded the injection of the solution at a rate of 18 ml/h. The system was then flushed with distilled water and air, and 7 minutes break was held until the next administration.

3.3. Metabolic and behavioral experiments

In order to clarify the metabolic role of the mOFC GM neurons, local STZ microinjection was performed. For this purpose, a guide cannula was fixed to the skull of the experimental animals, through which we were able to place the infusion delivery cannula in the appropriate position in alert rat.

3.3.1. Surgery

For the anesthesia, intraperitoneally injected ketamine (Calypsol, 50 mg/ml; Richter Gedeon Plc., Hungary; 0.3 ml / 100 µg) was used. The head of the animals was fixed in a stereotaxic apparatus, and then a longitudinal incision was cut on the scalp. After cleaning the skull surface, a 4-5 mm diameter hole was drilled in front of the Bregma using a dental drill. Based on the Paxinos and Watson brain atlas (AP: B+4.2 mm; ML: 0.9 mm) [53], the guide cannula was positioned with a micromanipulator (MN-33, Narishige, Japan).

The guide cannula made of stainless steel tube (23 G) was placed on the surface of the dura, and then fixed to the screws and to the skull with dental acrylic. At the end of the operation we used antiseptic talcum powder (Tetran, Gedeon Richter Plc., Hungary) and closed the wound with staples.

In animals that were included in the taste reactivity test, a chronic intraoral taste cannula made of polyethylene tube (Hibiki No. 4, Inter Medical Co., Ltd., Tokyo, Japan; outer diameter: 1.33 mm) was also implanted. The buccal end of the taste cannula has been widened previously by melting it over flame, and thus, to prevent this flaired end from slipping in or out through the taste tubing track. The taste cannula was led from behind the upper first molar tooth to the neck region under the skin, where it was sutured with surgical thread to fix its position. After the operation, the condition of the cannulas was checked continuously (did not slip, do not prevent the animals in feeding, there is no inflammation), and their permeability is sufficient.

Following a one-week recovery period after surgery, bilateral intra-OFC STZ microinjection was performed.

3.3.2. Microinjection

In alert, relaxed and hand-hold rats, bilateral microinjection was performed with solution containing 7.5 µg of STZ (Sigma S-0130 dissolved in 10 µg/µl of physiological saline) (STZ group) or 0.75 µl of physiological saline (control group). The stainless steel infusion delivery cannulas (30 G) directed to the mOFC (according to Paxinos and Watson brain atlas [53]: AP: B+4.2 mm; ML: 0.9 mm; V: 2.3 mm from the dura) were introduced through the previously implanted stainless steel guide cannulas. Infusion cannulas were connected via a polyethylene tube to a 25 µl Hamilton microsyringe, and for administration a micro-infusion pump (Cole-Parmer EW-74900 Multichannel Syringe Pumps, Cole-Parmer Instrument Company, Vernon Hills, Illinois, USA) was used with 0.75 µl/min flow rate. The delivery process ended by a 1 minute additional waiting period to complete the diffusion of the solution into the target area and prevent it from flowing back when removing the cannula.

3.3.3. Metabolic experiments

After bilateral microinjection of STZ or physiological saline in alert animals, an intraperitoneal glucose tolerance test was performed and plasma level of relevant metabolites was measured.

3.3.3.1. Intraperitoneal glucose tolerance test

After 12 hours fasting of the test animals, a glucose tolerance test (GTT) was performed, in accordance with international standards. Sugar loading was done by intraperitoneally administered 20% D-glucose solution (0.2 g/100 bwg/ml) two times, first 20 minutes after intra-OFC microinjection (acute GTT) as well as 4 weeks later (subacute GTT). The blood sample for analysis was obtained from the rat's tail vein, first before the sugar load and then, 9, 18, 30, 60 and 120 minutes after the load. Measurements were performed with a semi-automatic manual glucometer (Glucometer Elite, Bayer, Germany).

3.3.3.2. Measurement of plasma metabolites

Plasma levels of total cholesterol, triglycerides, and uric acid were determined – following international standards – after 12 hours of food withdrawal. A blood sample was obtained from the tail vein 30 minutes after the intracerebral microinjection, and determination of the metabolites was done by using a dry chemistry analyzer (Spotchem EZ SP4430, Arkay, Japan).

3.3.4. Behavioral experiments

After bilateral microinjection of STZ or physiological saline solution in alert animals, conditioned taste aversion and taste reactivity tests were performed.

3.3.4.1. Conditioned taste aversion

Conditioned taste aversion is a learned behavior which is manifested as avoidance of potentially dangerous food items. If gastrointestinal discomfort occurs after eating a given food, we will avoid or refuse that food in the future. Conditioned taste aversion already occurs after even the first association, and it develops even if it takes hours between the conditional (food taste) and the unconditional stimulus (disease).

During the experiment, we first taught the rats to take their daily fluid in a 30 minutes long period between 10:00 am and 10:30 am. After a successful learning period, the guide cannula was implanted, and the animal had a week-long recovery period during *ad libitum* could consume water. On the conditioning day (four days after STZ or physiological NaCl microinjection), the animals were allowed to consume saccharin for 30 minutes, and 30 minutes later gastrointestinal discomfort was induced by intraperitoneal administration of lithium chloride (0.15 M, 20 ml/bwkg). Then, the animals received water again for 30 minutes for 3 days, then on the fourth day (test day), the water was replaced again with saccharin solution during the drinking period. Statistical calculations compared the consumption of saccharin solution in the STZ treated and control groups on the conditioning and test days.

3.3.4.2. Taste reactivity test

Preparation for the taste reactivity test already started in the main operation session when, in addition to positioning the guide cannula on the top of the head, a taste cannula was also implanted into the oral cavity of the animals. After a one-week recovery period, bilateral intra-OFC microinjection of STZ or NaCl took place. In the next 6 days, the rats have got accustomed to staying in the plexiglass cylinder used during the experiment, and their taste cannula was rinsed daily with distilled water. The taste reactivity test was performed 1 week after the intracerebral microinjection.

To observe the behavioral patterns, facial and locomotory reactions, also the mouth movements of the experimental animals, a mirror was fixed at an angle of 45° under the glass cylinder (height and diameter: 30 cm each). The behavior of the rats was recorded with a Full HD camcorder (Panasonic HC-V270) and analyzed frame by frame.

The animals received two different concentrations of solutions corresponding to the five basic taste qualities. With the help of a micro-infusion pump (Cole-Parmer EW-74900 Multichannel Syringe Pumps, Cole-Parmer Instrument Company, Vernon Hills, Illinois, USA), 0.5 ml of a flavor solution was injected at a constant rate (0.5 ml/min) twice in 1-1 minute sessions into the oral cavity of the rats through their taste cannula, keeping a short break between the two injections. The taste cannula was then rinsed with distilled water and blown over with air.

We used the modified, internationally validated protocol of Grill and Norgren [12, 40, 64, 69] to evaluate the species-specific mimic, postural and locomotory responses of the animals. According to the protocol, the ingestive or accepting reactions are the rhythmic mouth movements, the midline and lateral rhythmic tongue protrusion and the paw licking. Aversive or rejecting behavioral patterns are the gaping, chin rubbing, head shaking, forelimb flailing, and rapid locomotion around the cylinder.

In the double blind evaluation process, for each taste solution, based on the occurrence, intensity, and duration of response patterns, both ingestive and aversive behaviors are scored on a 0 to 3 scale by at least three experienced examiners. To calculate the ingestive and aversive taste reactivity indices, the average score given by the examiners was divided by the maximum score, so the taste reactivity index for each taste solution could be between 0 and 1.

3.4. Histology

At the end of all experiments, to determine the relative cannula positions compared to the target brain area, the experimental animals were deeply anesthetized with urethane (20%, 8 ml/bwkg), then were perfused transcardially, first with saline and afterwards with 4% formalin. The samples were fixed in 4% formalin, and then 50 μm sections made and stained with 0.5% cresyl violet.

3.5. Statistics

In our electrophysiological experiments, on-line and off-line analyzes were performed using my own scripts written for the Spike2 v6.16 software. At the time of the evaluation, we considered the changes to inhibition or excitation in which cases the firing rate of neurons under examination changed by at least ±30% (or ±2 SD) compared to the spontaneous firing rate, and when the response was shown to be intensity dependent and repeatable. For statistical evaluation of group effects, we used χ^2 test using the SPSS Statistics 25 (IBM, Armonk, New York, USA) software.

The results of our behavioral and metabolic experiments were evaluated by Student's t-test and multi-factor analysis of variance (ANOVA) using the above-mentioned program package. We used the Tukey's test for post-hoc comparisons.

Differences were considered to be significant at $p < 0.05$.

4. Results

4.1. Results of experiments in the nucleus accumbens

4.1.1. Neurochemical experiments

In the nucleus accumbens, the activity of altogether 161 neurons was examined during microelectrophoretic administration of various drugs. In the core region, compared to the shell, there was a greater proportion of neurons that altered their firing rate in response to the microiontophoretic delivery of D-glucose. In the core, GR cells were the dominant GM units, while in the shell, the GS cells were the main representatives of the GM units.

Although there was no significant difference between the two regions in sensitivity to Ach and DA, the dopamine D1 receptor antagonist SCH 23390 in the core changed the response rate of the cells to a greater extent, while the D2 receptor antagonist sulpiride is typically more effective in the shell subdivision.

4.1.2. Intraoral taste stimulations

In the nucleus accumbens, altogether 141 neurons were tested for intraoral taste stimulation. Neurons responded to intraorally administered salty, sour, umami and bitter taste solutions in the shell region in a higher proportion, while to the sweet taste in the core region. The orange juice used as a complex taste solution, affected the neurons in the same ratio in both areas.

4.1.3. Intragastric infusion

Altogether 64 neurons in the nucleus accumbens were examined for intragastric chemical sensitivity. During intragastric infusions, significant difference in the responsiveness of neurons between the two regions was exclusively verified for 60 mM MSG: neurons were more likely to change in activity in the core compared to the shell subdivision. The other tested solutions (glucose 60 mM, NaCl 60 and 150 mM) had the same effect in both sub-divisions of NAcc.

A few times in case of intraoral sweet and umami taste stimulations, the intragastric infusion changed the responsiveness of the neurons to the repeated intraoral stimulation.

4.2. Results of experiments in the orbitofrontal cortex

4.2.1. Electrophysiological experiments

4.2.1.1. Neurochemical experiments

In the orbitofrontal cortex, the activity of altogether 55 neurons was examined during microelectrophoretic neurochemical stimulations. In the lOFC, the tested neurons showed responsiveness to each microiontophoretically administered drug in the same or higher

percentages as in the mOFC. The most striking difference is the effect of D-glucose, NA and GABA, while the sensitivity of the two regions is similar to Ach and DA.

A specific endogenous chemical response character of the medial orbitofrontal cortical GM neurons has been established, which is typically different from the glucose-insensitive cells here. None of the DA-sensitive cells found here were GM cells, while a quarter of DA-insensitive cells showed a change in response to D-glucose. In case of NA, there was no such difference between the sensitivity of GM and GIS cells. All the Ach-insensitive neurons were GIS cells, while a quarter of Ach-sensitive cells were proved to be glucose-monitoring neurons. The ratio of GM neurons was nearly twice as high among GABA-sensitive cells, as among GABA-insensitive cells.

4.2.1.2. Intraoral taste stimulations

In the orbitofrontal cortex, altogether 41 neurons were tested for intraoral taste stimulation. The sour, umami and bitter taste solutions as well as the orange juice caused a greater change in activity in the mOFC than in the lOFC. There is, practically, no difference between the two regions regarding the salty and sweet tastes.

4.2.1.3. Intragastric infusion

In the medial and lateral orbitofrontal cortex, 37 neurons were tested for intragastric chemical stimulation. During intragastric infusions, activation of nerve cells was found in both regions to 60 mM MSG and 150 mM NaCl, but the 60 mM NaCl solution triggered neuronal responses in the lOFC only; the excitatory and inhibitory activity changes observed in similar proportion. Neither of the examined regions showed a change in activity to the 60 mM glucose solution.

4.2.2. Metabolic changes

4.2.2.1. Changes is blood sugar level

In the acute and subacute intraperitoneal glucose tolerance test, male rats were tested after intracerebral microinjection of streptozotocin or physiological saline into the mOFC. During the acute GTT (20 minutes after the treatment) there was no difference between the

values of the two groups at 9th and 18th minutes, but in the subsequent period the dynamics of changes in blood glucose parameters of the animals treated with streptozotocin was different: the peak was higher in the STZ group compared to the control group (30': $p < 0.01$; 60': $p < 0.005$). In the 120th minute – although the blood glucose levels of STZ microinjection rats were higher than those of the controls – the statistical analysis did not show significant differences between the two groups.

4.2.2.2. Changes in plasma metabolite levels

Plasma metabolite levels were studied in adult male rats. The total serum cholesterol, triglyceride and uric acid were measured in the STZ-treated and control groups 30 minutes after the microinjection into mOFC. Intraorbitofrontal cortical STZ microinjection resulted in significant increase of the plasma triglyceride concentrations ($p < 0.005$), whereas cholesterol and uric acid levels did not differ at all.

4.2.3. Behavioral experiments

4.2.3.1. Conditioned taste aversion

In the conditioned taste aversion tests, the taste associated learning ability of male Wistar rats was studied. Conditioning took place 4 days after the mOFC microinjection was performed: the STZ-treated rats consumed more saccharin than the animals in control group, but this difference was not significant. On the test day, the animals of both groups consumed significantly less saccharin than on the conditioning day, and there was no difference between the two groups.

4.2.3.2. Taste reactivity changes

The behavioral patterns of adult male rats were examined in taste reactivity tests. One week after the bilateral microinjection of STZ or NaCl in mOFC, stimulus solutions corresponding to the 5 basic taste qualities were administered to the oral cavity of the animals through the taste cannula. In case of the pleasant tastes, there was a significant difference between the ingestive and aversive scores in the two groups, while in case of the unpleasant taste solutions, this difference was only observed in the control group. Despite the lack of

major differences in the general taste reactivities, the STZ-treated animals found both pleasant and unpleasant tastes more pleasant than the rats in the control group.

5. General conclusions

Glucose-monitoring neurons – i.e., nerve cells that change their firing rate to increasing of intracerebral extracellular level of D-glucose – have been identified in many brain regions of rats and rhesus monkeys, from brainstem [1], through the higher forebrain areas [19, 22, 23, 52] to the prefrontal-orbitofrontal cortical regions [22, 23, 33, 39, 41]. Not only the responses of these neurons to the endogenous neurotransmitters and neuromodulators differ from those of glucose-insensitive cells [39, 41, 52], but also react different way to exogenous chemical stimuli such as taste stimuli [39]. Our research has shown that similar endogenous and exogenous chemical sensitivity is characteristic for the GM cells in both examined regions of the nucleus accumbens and orbitofrontal cortex, which differs from the GIS units. Previous studies have also shown that the two types of GM neurons (GR and GS) have different dominance in the two NAcc subdivisions [52], as confirmed by our experiments. These chemosensory neurons are present in a relatively high proportion in the regions we investigate, so that their functional attributes can remarkably alter the regulatory processes of this important limbic forebrain sites. Our present data, along with our earlier orbitofrontal cortical findings in rhesus monkeys [22, 23], definitely support our view that these orbitofrontal cortical neurons, as important elements of the glucose-monitoring network in the limbic forebrain, with simultaneous monitoring and integration of humoral signals of the internal and external environment, they are indispensable participants in the sensitive regulatory processes that ensure the proper balance of homeostasis.

An important task of the central nervous system in a healthy organism is to regulate the very fine control of metabolic processes, in which metabolic (degradable nutrients, fatty acids, amino acids, various metabolites, etc.), humoral-hormonal (insulin, leptin, glucagon, GLP-1, etc.) and complex neural factors are involved, including particular information originating from not only the periphery but also from specific chemosensory neurons of different brain regions [22, 29, 51, 57]. Physiologically effective metabolism, which maintains the balance of homeostasis under very extreme environmental conditions, is highly dependent on the retained central perception of various peripheral signals. If there is any disturbance in the

functioning of specific chemosensory neurons that perform this task, severe metabolic-homeostatic disease states may develop, such as, obesity or diabetes mellitus [22, 29].

Literature data are available about differentiated topographical distribution of neurons sensitive to different taste qualities [58, 62]. There was a difference between the sub-regions of both NAcc and OFC examined in their responses to intraorally administered solutions. The presence of chemoreceptors capable of detecting, e.g. D-glucose [50, 61], sodium glutamate [50, 60], and sodium chloride [50] has already been shown in the stomach. During the intragastric stimuli, we proved the presence of umami and sodium chloride sensitive neurons in both examined brain areas, and the neurons of NAcc were also able to detect the administration of sweet solution into the stomach.

In our research group, GM neurons have already been found in NAcc and their role in taste perception have been previously detected [52], but we have not had information so far about the role of these neurons in the detection of gastrointestinal solutions. In our studies we detected first time neurons in this area of the brain that can participate in the regulation of food intake, digestive and absorption processes by their exogenous chemical sensitivity.

Our recent experiments have also provided evidence that chemosensory neurons in the medial orbitofrontal cortex actually play an important role in the central regulation of metabolism. First time in the literature, it has been shown that bilateral microinjection of STZ into this area results in a complex metabolic syndrome: GTT exhibits abnormal glucose tolerance, a specific intolerance, and elevated plasma triglyceride level in metabolite measurements. The combined presence of these lesions confirms the severe judgment of the condition as a complex metabolic disease, which is also supported by the fact that high plasma triglyceride levels, typically among others, may occur in diabetes mellitus and obesity. Disorders of both carbohydrate and fat metabolism in other forebrain structures (ventromedial nucleus of the hypothalamus, mediodorsal prefrontal cortex) were the usual consequence of streptozotocin treatment [22, 42]. On the basis of the above, it is generally also true that the destruction of GM nerve cells by streptozotocin in various brain areas leads to specific nutritional and metabolic disorders [8, 22-24].

The technical and informatical inventions that have taken place during the research have greatly contributed to the accurate execution of the tests and the proper evaluation of the data obtained. With the help of computer-controlled devices, which were designed, programmed and built by me, became not only the endogenous and exogenous stimuli more accurate, but also by analyzing the feedback signals of the infusion devices we can be sure about the time and amount of the administrations. The on-line script, wrote by me, used during the recording

not only controls the tools used in the experiments, but also analyzes the data to enable immediate decision-making on the continuation of the test. With the off-line script, every detail of the examination can be analyzed with a few clicks, the final data and graphics can be exported, so they can be used immediately in statistical programs or presentations and publications.

Based on our results, glucose-monitoring neurons in the nucleus accumbens, medial and lateral OFC by integrating endogenous and exogenous chemical information and by organizing humoral-metabolic processes are likely to play an important role in the processing of taste information and in the adaptive mechanisms of regulation of feeding and metabolism. Following our findings, it is also rightly hoped that a more detailed understanding of the newly recognized structures in homeostasis regulation, including OFC, can contribute to the identification of new drug targets, and the development of effective new therapeutic strategies.

6. Summary

Our studies to examine the involvement of the nucleus accumbens and orbitofrontal cortex in the central regulation of homeostasis provided the following results.

1. In our extracellular single neuron recordings, glucose-monitoring neurons were identified in each of the examined sub-regions of NAcc and OFC. There is a higher proportion of GM cells in the core (mainly GR cells) in the NAcc, while in the OFC it is higher in the lateral region.
2. In the NAcc core region can be found the NA-sensitive cells in significantly higher proportion, mainly NA-stimulated neurons.
3. In both regions of NAcc, the neurons showed the same response rate to the microiontophoretically administered DA, but their response patterns are different in each area: the neurotransmitter-inhibited neurons are presented in the shell region at a higher rate, while in the core the DA-stimulated cells. The D1 receptor antagonist altered the response rate of the neurons to a greater extent in the core, while the D2 receptor antagonist produced the same effect in the shell.
4. In the OFC, the neurons tested in the lOFC showed responsiveness in a higher percentage for each microiontophoretically administered drug than in the mOFC.

5. In the mOFC, the endogenous chemical responsiveness of GM neurons, which is typically different from glucose-insensitive neurons, is confirmed.
6. In NAcc, for intraorally administered salty, sour, umami and bitter taste solutions in the shell region responded the neurons in a higher proportion.
7. The GR neurons in NAcc either did not react to the taste solutions at all, or changed their firing rate to minimum 2 different tastes. These cells showed a higher rate of sensitivity to sour, sweet and bitter flavors.
8. In OFC, intraorally administered taste solutions in mOFC caused a greater or equal change in activity than in lOFC.
9. For intragastrically infused solutions (glucose, MSG, NaCl) in the NAcc, the neurons in the core region showed a higher or equal sensitivity than in the shell region.
10. In OFC, neurons sensitive to intragastrically administered MSG and NaCl solutions were detected in both regions, but no cells found in these regions which changed the activity for D-glucose infusion.
11. In the glucose tolerance test following bilateral microinjection of STZ in mOFC, the blood glucose levels of treated animals at 30 and 60 minutes were significantly higher than in the control group.
12. Following the destruction of mOFC GM nerve cells with STZ, the triglyceride levels of the blood were significantly higher in the STZ treated animals compared to the control group, while no significant differences were found for the other tested metabolites (uric acid, cholesterol).
13. In the mOFC, there was no detectable difference between the STZ-treated and the control group in the development of the conditioned taste aversion.
14. During the taste reactivity tests, the STZ treated animals showed more ingestive and less aversive patterns for both pleasant and unpleasant taste solutions compare to the control group.
15. Discovering the above-mentioned changes and achieving new results to a great extent are due to the technical and IT inventions we have made.

7. References

1. Adachi, A., et al., *Convergence of hepatoportal glucose-sensitive afferent signals to glucose-sensitive units within the nucleus of the solitary tract.* Neurosci Lett, 1984. **46**(2): p. 215-8.
2. Adachi, A., et al., *Chemosensitive neurons in the area postrema of the rat and their possible functions.* Brain Res Bull, 1991. **26**(1): p. 137-40.
3. Adachi, A., M. Kobashi, and M. Funahashi, *Glucose-responsive neurons in the brainstem.* Obes Res, 1995. **3 Suppl 5**: p. 735S-740S.
4. Anand, B.K., et al., *Activity of Single Neurons in the Hypothalamic Feeding Centers: Effect of Glucose.* Am J Physiol, 1964. **207**: p. 1146-54.
5. Aou, S., et al., *Behavioral significance of monkey hypothalamic glucose-sensitive neurons.* Brain Res, 1984. **302**(1): p. 69-74.
6. Bloom, F.E., *To spritz or not to spritz: the doubtful value of aimless iontophoresis.* Life Sci, 1974. **14**(10): p. 1819-34.
7. Chaudhari, N. and S.D. Roper, *Molecular and physiological evidence for glutamate (umami) taste transduction via a G protein-coupled receptor.* Ann N Y Acad Sci, 1998. **855**: p. 398-406.
8. Egyed, R., B. Lukats, and Z. Karadi, *Diabetes mellitus-like metabolic deficits elicited by ventromedial hypothalamic streptozotocin microinjection.* J. Physiol. (Lond.), 2000. **526**: p. 173-174.
9. Funahashi, M. and A. Adachi, *Glucose-responsive neurons exist within the area postrema of the rat: in vitro study on the isolated slice preparation.* Brain Res Bull, 1993. **32**(5): p. 531-5.
10. Ganda, O.P., A.A. Rossini, and A.A. Like, *Studies on streptozotocin diabetes.* Diabetes, 1976. **25**(7): p. 595-603.
11. Garvey, W.T., T.P. Huecksteadt, and M.J. Birnbaum, *Pretranslational suppression of an insulin-responsive glucose transporter in rats with diabetes mellitus.* Science, 1989. **245**(4913): p. 60-3.
12. Grill, H.J. and R. Norgren, *The taste reactivity test. I. Mimetic responses to gustatory stimuli in neurologically normal rats.* Brain Res, 1978. **143**(2): p. 263-79.
13. Kadowaki, T., et al., *Decreased autophosphorylation of the insulin receptor-kinase in streptozotocin-diabetic rats.* J Biol Chem, 1984. **259**(22): p. 14208-16.
14. Kang, L., et al., *Physiological and molecular characteristics of rat hypothalamic ventromedial nucleus glucosensing neurons.* Diabetes, 2004. **53**(3): p. 549-59.
15. Karadi, Z., et al., *Lateral hypothalamic and amygdaloid neuronal responses to chemical stimuli in the rhesus monkey.* In: H. Morita (Ed.), Proceedings 22nd Japanese Symposium on Taste and Smell, Asahi University Press, Gifu, 1988: p. 121-124.
16. Karadi, Z., et al., *Olfactory coding in the monkey lateral hypothalamus: behavioral and neurochemical properties of odor-responding neurons.* Physiol Behav, 1989. **45**(6): p. 1249-57.
17. Karadi, Z., et al., *Responses of lateral hypothalamic glucose-sensitive and glucose-insensitive neurons to chemical stimuli in behaving rhesus monkeys.* J Neurophysiol, 1992. **67**(2): p. 389-400.
18. Karadi, Z., et al., *Glucose-sensitive neurons of the globus pallidus: II. Complex functional attributes.* Brain Res Bull, 1995. **37**(2): p. 157-62.
19. Karadi, Z., et al., *Role of forebrain glucose-monitoring neurons in the central control of feeding: II. Complex functional attributes.* Neurobiology (Bp), 1995. **3**(3-4): p. 241-56.

20. Karadi, Z., et al., *Complex functional attributes of amygdaloid gustatory neurons in the rhesus monkey.* Ann N Y Acad Sci, 1998. **855**: p. 488-92.
21. Karadi, Z., et al., *Integrative processing of endogenous and exogenous chemical signals by glucose-monitoring neurons of the primate orbitofrontal cortex.* Appetite, 1998. **31**(2): p. 263.
22. Karadi, Z., et al., *The central glucose-monitoring neural network: major protector of the adaptive homeostatic balance for well being of the organism.* International Congress Series, 2004. **1269**(0): p. 30-33.
23. Karadi, Z., et al., *Involvement of forebrain glucose-monitoring neurons in taste information processing: electrophysiological and behavioral studies.* Chem Senses, 2005. **30 Suppl 1**: p. i168-9.
24. Keszthelyi, Z., et al., *The central effect of chromium on glucose metabolism.* Pharmacopsychiatry, 2004. **37**(5): p. 242.
25. Kruk, Z.L., M. Armstrong-James, and J. Millar, *Measurement of the concentration of 5-hydroxytryptamine ejected during iontophoresis using multibarrel carbon fibre microelectrodes.* Life Sci, 1980. **27**(22): p. 2093-8.
26. Kuriyama, K., et al., *Actions of interferon alpha and interleukin- 1 beta on the glucose-responsive neurons in the ventromedial hypothalamus.* Brain Res Bull, 1990. **24**(6): p. 803-10.
27. Lenard, L., et al., *Glucose-sensitive neurons of the globus pallidus: I. Neurochemical characteristics.* Brain Res Bull, 1995. **37**(2): p. 149-55.
28. Lenard, L., et al., *Role of forebrain glucose-monitoring neurons in the central control of feeding: I. Behavioral properties and neurotransmitter sensitivities.* Neurobiology (Bp), 1995. **3**(3-4): p. 223-39.
29. Levin, B.E., *Metabolic sensing neurons and the control of energy homeostasis.* Physiol Behav, 2006. **89**(4): p. 486-9.
30. Like, A.A. and A.A. Rossini, *Streptozotocin-induced pancreatic insulitis: new model of diabetes mellitus.* Science, 1976. **193**(4251): p. 415-7.
31. Lukats, B., et al., *Homeostatic alterations induced by interleukin-1beta microinjection into the orbitofrontal cortex in the rat.* Appetite, 2005. **45**(2): p. 137-47.
32. Lukats, B., R. Egyed, and Z. Karadi, *Single neuron activity changes to interleukin-1beta in the orbitofrontal cortex of the rat.* Brain Res, 2005. **1038**(2): p. 243-6.
33. Lukats, B., et al., *Electrophysiological and behavioral evidences of the feeding-related neuronal processes in the orbitofrontal cortex.* International Congress Series, 2007. **1301**(0): p. 230-233.
34. Lukáts, B., et al., *Feeding-related neuronal processes of the orbitorfrontal cortex: electrophysiological and behavioral studies in rats and rhesus monkeys*, in *FENS*. 2006.
35. Maldonado-Irizarry, C.S. and A.E. Kelley, *Excitotoxic lesions of the core and shell subregions of the nucleus accumbens differentially disrupt body weight regulation and motor activity in rat.* Brain Res Bull, 1995. **38**(6): p. 551-9.
36. Minami, T., Y. Oomura, and M. Sugimori, *Electrophysiological properties and glucose responsiveness of guinea-pig ventromedial hypothalamic neurones in vitro.* J Physiol, 1986. **380**: p. 127-43.
37. Mizuno, Y. and Y. Oomura, *Glucose responding neurons in the nucleus tractus solitarius of the rat: in vitro study.* Brain Res, 1984. **307**(1-2): p. 109-16.
38. Mogensen, J. and I. Divac, *Behavioural changes after ablation of subdivisions of the rat prefrontal cortex.* Acta Neurobiol Exp (Wars), 1993. **53**(3): p. 439-49.
39. Nagy, B., et al., *Glucose-monitoring neurons in the mediodorsal prefrontal cortex.* Brain Res, 2012. **1444**: p. 38-44.

40. Nagy, B., et al., *Taste reactivity alterations after streptozotocin microinjection into the mediodorsal prefrontal cortex.* Behav Brain Res, 2012. **234**(2): p. 228-32.
41. Nagy, B., et al., *Noradrenaline and acetylcholine responsiveness of glucose-monitoring and glucose-insensitive neurons in the mediodorsal prefrontal cortex.* Brain Res, 2014. **1543**: p. 159-64.
42. Nagy, B., et al., *Impaired glucose tolerance after streptozotocin microinjection into the mediodorsal prefrontal cortex of the rat.* Acta Physiol Hung, 2016. **103**(4): p. 403-12.
43. Nakano, Y., et al., *Feeding-related activity of glucose- and morphine-sensitive neurons in the monkey amygdala.* Brain Res, 1986. **399**(1): p. 167-72.
44. Nakano, Y., et al., *Functional involvement of catecholamines in reward-related neuronal activity of the monkey amygdala.* J Neurophysiol, 1987. **57**(1): p. 72-91.
45. Oomura, Y., et al., *Reciprocal Activities of the Ventromedial and Lateral Hypothalamic Areas of Cats.* Science, 1964. **143**(3605): p. 484-5.
46. Oomura, Y., et al., *Glucose and osmosensitive neurones of the rat hypothalamus.* Nature, 1969. **222**(5190): p. 282-4.
47. Oomura, Y., *Input-output organization of the hypothalamus relating to food intake behavior*, in *Handbook of the hypothalamus*, P.J. Morgane and P. J., Editors. 1980: Marcel Dekker, New York. p. 557-620.
48. Oomura, Y. and H. Yoshimatsu, *Neural network of glucose monitoring system.* J Auton Nerv Syst, 1984. **10**(3-4): p. 359-72.
49. Oomura, Y., *Chemical and neuronal control of feeding motivation.* Physiol Behav, 1988. **44**(4-5): p. 555-60.
50. Otsubo, H., et al., *Induction of Fos expression in the rat forebrain after intragastric administration of monosodium L-glutamate, glucose and NaCl.* Neuroscience, 2011. **196**: p. 97-103.
51. Pannacciulli, N., et al., *Postprandial glucagon-like peptide-1 (GLP-1) response is positively associated with changes in neuronal activity of brain areas implicated in satiety and food intake regulation in humans.* Neuroimage, 2007. **35**(2): p. 511-7.
52. Papp, S., et al., *Glucose-monitoring neurons in the nucleus accumbens.* Neuroreport, 2007. **18**(15): p. 1561-5.
53. Paxinos, G.W.C., *The Rat Brain in Stereotaxic Coordinates.* Academic Press, Inc., 1997.
54. Pellegrino, L.J., A.S. Pellegrino, and A.J. Cushman, *A Stereotaxic Atlas of the Rat Brain*. 2nd ed. 1979: Plenum Press: New York.
55. Purves, R.D., *Microelectrode methods for intracellular recording and iontophoresis.* London: Academic Press, 1981.
56. Rakieten, N., M.L. Rakieten, and M.R. Nadkarni, *Studies on the diabetogenic action of streptozotocin (NSC-37917).* Cancer Chemother Rep, 1963. **29**: p. 91-8.
57. Rocca, A.S. and P.L. Brubaker, *Role of the vagus nerve in mediating proximal nutrient-induced glucagon-like peptide-1 secretion.* Endocrinology, 1999. **140**(4): p. 1687-94.
58. Rolls, E.T., *Functions of the orbitofrontal and pregenual cingulate cortex in taste, olfaction, appetite and emotion.* Acta Physiol Hung, 2008. **95**(2): p. 131-64.
59. Routh, V.H., *Glucosensing neurons in the ventromedial hypothalamic nucleus (VMN) and hypoglycemia-associated autonomic failure (HAAF).* Diabetes Metab Res Rev, 2003. **19**(5): p. 348-56.
60. San Gabriel, A.M., et al., *mGluR1 in the fundic glands of rat stomach.* FEBS Lett, 2007. **581**(6): p. 1119-23.

61. Sclafani, A., *Sweet taste signaling in the gut.* Proc Natl Acad Sci U S A, 2007. **104**(38): p. 14887-8.
62. Scott, T.R., et al., *Gustatory neural coding in the amygdala of the alert macaque monkey.* J Neurophysiol, 1993. **69**(6): p. 1810-20.
63. Song, Z., et al., *Convergence of pre- and postsynaptic influences on glucosensing neurons in the ventromedial hypothalamic nucleus.* Diabetes, 2001. **50**(12): p. 2673-81.
64. Spector, A.C., P. Breslin, and H.J. Grill, *Taste reactivity as a dependent measure of the rapid formation of conditioned taste aversion: a tool for the neural analysis of taste-visceral associations.* Behav Neurosci, 1988. **102**(6): p. 942-52.
65. Szabo, I., et al. *Complex functional attributes of neurons in the orbitofrontal cortex (in Hungarian).* in *2nd Interdisciplinary Doctoral Conference*. 2013. Pécs, Hungary.
66. Szabo, I., et al., *[Glucose-monitoring neurons of the medial ventrolateral prefrontal (orbitofrontal) cortex are involved in the maintenance of homeostasis].* Orv Hetil, 2017. **158**(18): p. 692-700.
67. Szabo, I., et al., *Multiple functional attributes of glucose-monitoring neurons in the medial orbitofrontal (ventrolateral prefrontal) cortex.* Neurosci Biobehav Rev, 2018. **85**: p. 44-53.
68. Szkudelski, T., *The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas.* Physiol Res, 2001. **50**(6): p. 537-46.
69. Takacs, G., et al., *Taste reactivity alterations after IL-1beta microinjection into the ventromedial hypothalamic nucleus of the rat.* Neurosci Res, 2008. **62**(2): p. 118-22.
70. Takacs, G., et al., *Homeostatic alterations after IL-1beta microinjection into the nucleus accumbens of the rat.* Appetite, 2010. **54**(2): p. 354-62.
71. Takacs, G., et al., *Insulin and leptin plasma levels after the microinjection of interleukin-1beta into the nucleus accumbens of the rat.* Acta Physiol Hung, 2012. **99**(4): p. 472-8.
72. Villablanca, J.R., C.E. Olmstead, and I. de Andres, *Effects of caudate nuclei or frontal cortical ablations in kittens: responsiveness to auditory stimuli and comparisons with adult-operated littermates.* Exp Neurol, 1978. **61**(3): p. 635-49.
73. Watanabe, S. and M.T. Matheus, *[Comparative study of the gustatory sensory receptors of mammals].* Rev Assoc Paul Cir Dent Reg Aracatuba, 1980. **1**(1): p. 39-43.

8. Publications

The complete publication list is available:
https://m2.mtmt.hu/gui2/?type=authors&mode=browse&sel=10016612
Cumulative impact factor: 30,792; number of independent citations: 48 (with self-citations: 74).

8.1. Publications related to the thesis

Szabó I, Nagy B, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Az idegsejtek komplex funkcionális sajátosságai az orbitofrontalis kéregben. IDK2013 konferenciakötet (2014)

Szabó I, Hormay E, Csetényi B, Nagy B, Karádi Z: A medialis ventrolateralis praefrontalis (orbitofrontalis) kéreg glükózmonitorozó idegsejtjei szerepet játszanak a homeosztázis fenntartásában. Orvosi Hetilap 158:(18) pp. 692-700. (2017) [IF: 0.322]

Szabó I, Hormay E, Csetényi B, Nagy B, Lénárd L, Karádi Z: Multiple functional attributes of glucose-monitoring neurons in the medial orbitofrontal (ventrolateral prefrontal) cortex. Neurosci Biobehav Rev. 85: pp. 44-53. (2018) [IF: 8.037]

Nagy B, **Szabo I**, Csetenyi B, Hormay E, Papp S, Keresztes D, Karadi Z: Noradrenaline and acetylcholine responsiveness of glucose-monitoring and glucose-insensitive neurons in the mediodorsal prefrontal cortex. Brain Research 1543: pp. 159-164. (2014) [IF: 3.125]

Nagy B, **Szabó I**, Takács G, Csetényi B, Hormay E, Karádi Z: Impaired glucose tolerance after streptozotocin microinjection into the mediodorsal prefrontal cortex of the rat. Physiology International 103:(4) pp. 403-412. (2016) [IF: 0.571]

8.2. Other publications with impact factor

Vereczkei A, Szalay C, Aradi M, Schwarz A, Orsi G, Perlaki G, Karádi Z, Németh L, Hanna S, Takács G, **Szabó I**, Bajnok L, Mohos E, Lénárd L, Dóczi T, Janszky J, Komoly S, Horváth ÖP: Ízstimulációval kiváltott agyi tevékenység funkcionális MR-vizsgálata elhízásban. Magyar Sebészet: 2011 Dec;64(6):289-93 [IF: 0.12]

Nagy B, **Szabó I**, Papp Sz, Takács G, Szalay Cs, Karádi Z: Glucose-monitoring neurons in the mediodorsal prefrontal cortex. Brain Research 1444: pp. 38-44. (2012) [IF: 3.125]

Szalay Cs, Aradi M, Schwarcz A, Orsi G, Perlaki G, Németh L, Hanna S, Takács G, **Szabó I**, Bajnok L, Vereczkei A, Dóczi T, Janszky J, Komoly S, Horvath ÖP, Lénárd L, Karádi Z: Gustatory perception alterations in obesity: An fMRI study. Brain Research 1473: pp. 131-140. (2012) [IF: 3.125]

Nagy B, Takács G, **Szabó I**, Lénárd L, Karádi Z: Taste reactivity alterations after streptozotocin microinjection into the mediodorsal prefrontal cortex. Behavioural Brain Research 234:(2) pp. 228-232. (2012) [IF: 3.173]

Takács G, Szalay Cs, Nagy B, **Szabó I**, Simon D, Berki T, Karádi Z: Insulin and leptin plasma levels after the microinjection of interleukin-1β into the nucleus accumbens of the rat. Acta Physiologica Hungarica 99:(4) pp. 472-478. (2012) [IF: 0.571]

Petykó Z, Gálosi R, Tóth A, Máté K, Szabó I, **Szabó I**, Karádi Z, Lénárd L: Responses of rat medial prefrontal cortical neurons to Pavlovian conditioned stimuli and to delivery of appetitive reward. Behav Brain Res. 287: pp. 109-119. (2015) [IF: 3.173]

Csetényi B, Hormay E, **Szabó I**, Takács G, Nagy B, László K, Karádi Z: Food and water intake, body temperature and metabolic consequences of interleukin-1β microinjection into the cingulate cortex of the rat. Behav Brain Res. 331: pp. 115-122. (2017) [IF: 3.173]

Hormay E, László B, **Szabó I**, Ollmann T, Nagy B, Péczely L, Mintál K, Karádi Z: The effect of loss of the glucose-monitoring neurons in the anterior cingulate cortex: Physiologic challenges induce complex feeding-metabolic alterations after local streptozotocin microinjection in rats. Neuroscience Research (2019) [IF: 2.277]

8.3. Other publications without impact factor

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Hideg B, Karádi Z: Cinguláris kérgi IL-1β mikroinjekció hatása a táplálkozásra és anyagcserére laboratóriumi patkányban. IDK2014 konferenciakötet (2015)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Hideg B, Bajnok Góré M, Karádi Z: A cinguláris kéreg streptozotocin mikroinjekciójának hatása a glukóz toleranciára laboratóriumi patkányban. IDK2014 konferenciakötet (2015)

Guth K, Budai A, Mikó-Baráth E, **Szabó I**, Jandó G: Innovatív megoldások a látásszűrésben. VI. Interdiszciplináris Doktorandusz Konferencia 2017 – Tanulmánykötet (2017)

Guth K, Budai A, **Szabó I**, Jandó G: Látásszűrés az informatika segítségével. Tavaszi Szél 2017 – Tanulmánykötet (2017)

Szabó I, Hormay E, Csetényi B, Karádi Z: Íz-érzékelés a gasztrointesztinális rendszerben. Tavaszi Szél 2018 – Tanulmánykötet (2018)

Szabó I, Hormay E, Csetényi B, Karádi Z: Endogenous and exogenous chemical responsiveness in nucleus accumbens. VII. Interdiszciplináris Doktorandusz Konferencia – Tanulmánykötet (2018)

8.4. Abstracts published in international journals

Nagy B, **Szabó I**, Papp Sz, Takács G, Szalay Cs, Faragó B, Keresztes D, Fotakos D, Karádi Z: The effect of intragastric and intraoral chemical stimulation on glucose monitoring neurons in the mediodorsal prefrontal cortex. Acta Physiologica Hungarica 97:(4) p. 463. (2010)

Takács G, Szalay Cs, Nagy B, **Szabó I**, Fotakos D, Csulak T, Németh L, Keresztes D, Hanna S, Hideg B, Faragó B, Csulak E, Karádi Z: Taste perception alterations in the background of interleukin-1β mediated anorexia in the limbic forebrain. Acta Physiologica Hungarica 97:(4) p. 480. (2010)

Karádi Z, Nagy B, **Szabó I**, Fotakos D, Keresztes D, Hideg B, Faragó B: Responsiveness of forebrain glucose-monitoring neurons to intraorally and intragastrically delivered monosodium glutamate. Chemical Senses 36:(1) p. E10. (2011)

Karádi Z, Nagy B, **Szabó I**, Szalay Cs, Takács G, Keresztes D, Hideg B, Faragó B, Góré MB, Lénárd L: Complex functional attributes of forebrain glucose-monitoring neurons in the maintenance of homeostasis. Acta Physiologica 202:(Suppl684) p. 49-50. (2011)

Nagy B, **Szabó I**, Papp Sz, Takács G, Szalay Cs, Keresztes D, Faragó B, Hideg B, Góré MB, Karádi Z: Characteristic dopamine sensitivity pattern and chemical information precessing of glucose-monitoring neurons in the mediodorsal prefrontal cortex. Acta Physiologica 202:(Suppl684) p. 85. (2011)

Szabó I, Nagy B, Takács G, Szalay Cs, Papp Sz, Hideg B, Faragó B, Góré MB, Keresztes D, Karádi Z: Glucose monitoring neurons: Endogenous and exogenous chemical sensitivity in the nucleus accumbens. Acta Physiologica 202:(Suppl684) p. 112. (2011)

Nagy B, **Szabó I**, Keresztes D, Faragó B, Hideg B, Góré MB, Karádi Z: Electrophysiological characteristics of feeding associated mdPFC neurons. Ideggyógyászati Szemle/Clinical Neuroscience 65:(Suppl1) p. 47. (2012)

Szabó I, Nagy B, Hideg B, Faragó B, Góré MB, Karádi Z: Endogenous and exogenous chemical responsiveness of umami sensitive neurons in the nucleus accumbens. Ideggyógyászati Szemle/Clinical Neuroscience 65:(Suppl1) p. 62. (2012)

Szabo I, Hormay E, Csetenyi B, Nagy B, Gore MB, Karadi Z: Complex functional attributes of glucose-monitoring neurons in medial orbitofrontal cortex and their homeostatic significance. Acta Physiologica 211:(697) p. 150. (2014)

Csetenyi B, Hormay E, Nagy B, **Szabo I**, Gore MB, Karadi Z: IL-1 beta modifies the taste reactivity in the cingulate cortex of the rat. Acta Physiologica 211:(697) pp. 143-144. (2014)

Hormay E, Csetenyi B, **Szabo I**, Nagy B, Hideg B, Gore MB, Karadi Z: Complex functional attributes of cingulate cortex glucose-monitoring neurons and their metabolic significance. Acta Physiologica 211:(697) p. 144. (2014)

Petyko Z, Toth A, Galosi R, **Szabo I**, Mate K, Szabo I, Karadi Z, Lenard L: Neuronal responses of the rat medial prefrontal cortex during appetitive classical conditioning. Acta Physiologica 211:(697) p. 160. (2014)

Szabó I, Hormay E, Csetényi B, Torda V, Tóth M, Karádi Z: Complex functional attributes of orbitofrontal cortical glucose-monitoring neurons. Obesitologia Hungarica 14:(Suppl2) p. 58. (2015)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Tóth M, Torda V, Karádi Z: Cingulate cortex IL-1β mediated mechanisms in the regulation of feeding and metabolism in the rat. Obesitologia Hungarica 14:(Suppl2) pp. 57-58. (2015)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Torda V, Tóth M, Karádi Z: Glucose-monitoring neurons of the rat cingulate cortex: feeding and metabolic significance. Obesitologia Hungarica 14:(Suppl2) pp. 57-58. (2015)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Torda V, Tóth M, Karádi Z: A cinguláris kérgi glukóz monitorozó neuronok szerepe a táplálkozás és anyagcsere szabályozásban. Obesitologia Hungarica 16:(Suppl1) p. 14. (2017)

8.5. Conference abstracts

Nagy B, Takács G, Szalay Cs, **Szabó I**, Keresztes D, Hideg B, Fotakos D. és Karádi Z: A mediodorzális prefrontalis kéreg idegsejtjeinek endogén és exogén kémiai érzékenysége. Biológus doktoranduszok konferenciája 2009, Pécs (presentation)

Nagy B, **Szabó I**, Takács G, Szalay Cs, Keresztes D, Hideg B, Fotakos D, Faragó B, Karádi Z: Neurochemical attributes and taste responsiveness of neurons in the mediodorsal prefrontal cortex. IBRO International Workshop 2010, Pécs (poster)

Fotakos D, Hideg B, **Szabó I**, Takács G, Szalay Cs, Nagy B, Karádi Z: The effect of intraoral and intragastric administrations of chemicals on glucose monitoring neurons in the cingulate cortex of the rat. IBRO International Workshop 2010, Pécs (poster)

Takács G, Szalay Cs, Nagy B, Fotakos D, **Szabó I**, Keresztes D, Németh L, Hanna S, Csulak T, Hideg B, Faragó B, Karádi Z: Feeding and taste perception alterations after IL-1 beta microinjection into the nucleus accumbens. IBRO International Workshop 2010, Pécs (poster)

Nagy B, **Szabó I**, Takács G, Szalay Cs, Faragó B, Keresztes D, Fotakos D, Karádi Z: Intragastrikus és intraorális kémiai stimuláció hatása a mediodorsalis prefrontalis kéreg neuronjaira. A Magyar Élettani Társaság (MÉT) LXXIV. Vándorgyűlése és a Magyar Kísérletes és Klinikai Farmakológia Társaság (MFT) II. közös tudományos konferenciája, Szeged, 2010 (poster)

Takács G, Szalay Cs, Nagy B, **Szabó I**, Fotakos D, Csulak T, Németh L, Keresztes D, Hanna S, Hideg B, Faragó B, Csulak E, Karádi Z: Íz-percepciós változások a limbikus előagyi interleukin-1β mediálta anorexia hátterében. A Magyar Élettani Társaság (MÉT) LXXIV. Vándorgyűlése és a Magyar Kísérletes és Klinikai Farmakológia Társaság (MFT) II. közös tudományos konferenciája, Szeged, 2010 (poster)

Fotakos D, Hideg B, **Szabo I**, Szalay C, Takacs G, Nagy B, Karadi Z: The effect of gustatory and intragastric chemical stimulation on glucose-monitoring neurons in the cingulate cortex of the rat. 7th FENS Forum of European Neuroscience, Amsterdam, The Netherlands, 2010 (poster)

Nagy B, **Szabo I**, Takacs G, Szalay C, Keresztes D, Hideg B, Fotakos D, Farago B, Karadi Z: Mediodorsal prefrontal cortex glucose-monitoring neurons change in activity in response to intraorally and intragastrically delivered chemical stimuli. 7th FENS Forum of European Neuroscience, Amsterdam, The Netherlands, 2010 (poster)

Takács G, Szalay C, Nagy B, Fotakos D, **Szabó I**, Keresztes D, Németh L, Hanna S, Csulak T, Hideg B, Faragó B, Karádi Z: Involvement of interleukin-1beta in the control of feeding and taste perception in the nucleus accumbens. 7th FENS Forum of European Neuroscience, Amsterdam, The Netherlands, 2010 (poster)

Karádi Z, Nagy B, **Szabó I**, Fotakos D, Keresztes D, Hideg B, Faragó B: Responsiveness of Forebrain Glucose-Monitoring Neurons to Intraorally and Intragastrically Delivered Monosodium Glutamate. ECRO, European Chemoreception Research Organization, XXth Congress, Avignon, France, 2010 (poster)

Szabó I, Nagy B, Takács G, Szalay C, Papp S, Hideg B, Faragó B, Bajnok Góré M, Keresztes D, Karádi Z: Endogenous and Exogenous Chemical Sensitivity of Glucose Monitoring Neurons in the Nucleus Accumbens. 13th Conference of the Hungarian Neuroscience Society (MITT), Budapest, Hungary, 2011 (poster)

Nagy B, **Szabó I**, Papp S, Takács G, Szalay C, Keresztes D, Faragó B, Hideg B, Bajnok Góré M, Karádi Z: Glucose-monitoring neurons in the mediodorsal prefrontal cortex: responsiveness to dopamine and exogenous chemical stimuli. 13th Conference of the Hungarian Neuroscience Society (MITT), Budapest, Hungary, 2011 (poster)

Karádi Z, Nagy B, **Szabó I**, Szalay Cs, Takács G, Keresztes D, Hideg B, Faragó B, Bajnok Góré M, Lénárd L: Complex functional attributes of forebrain glucose-monitoring neurons in the maintenance of homeostasis. A Magyar Farmakológiai, Anatómus, Mikrocirkulációs, Élettani Társaságok közös tudományos konferenciája (FAMÉ), Pécs, 2011 (presentation)

Szabó I, Nagy B, Takács G, Szalay Cs, Papp Sz, Hideg B, Faragó B, Bajnok Góré M, Keresztes D, Karádi Z: Glukóz-monitorozó idegsejtek: endogén és exogén kémiai érzékenység a nucleus accumbens-ben. A Magyar Farmakológiai, Anatómus, Mikrocirkulációs, Élettani Társaságok közös tudományos konferenciája (FAMÉ), Pécs, 2011

Nagy B, **Szabó I**, Papp Sz, Takács G, Szalay Cs, Keresztes D, Faragó B, Hideg B, Bajnok Góré M, Karádi Z: A mediodorzális prefrontális kéreg glukóz-monitorozó idegsejtjeinek sajátos dopamin érzékenységi mintázata és kémiai információ feldolgozása. A Magyar Farmakológiai, Anatómus, Mikrocirkulációs, Élettani Társaságok közös tudományos konferenciája (FAMÉ), Pécs, 2011 (poster)

Szabó I, Nagy B, Hideg B, Faragó B, Bajnok Góré M, Karádi Z: Endogenous and exogenous chemical responsiveness of umami sensitive neurons in the nucleus accumbens. IBRO International Workshop 2012, Szeged, Hungary (poster)

Nagy B, **Szabó I**, Keresztes D, Faragó B, Hideg B, Bajnok Góré M, Karádi Z: Electrophysiological characteristics of feeding associated mdPFC neurons. IBRO International Workshop 2012, Szeged, Hungary (poster)

Szabó I, Nagy B, Ábrahám I, Lénárd L, Karádi Z: Ösztrogén hatása a nucleus basalis magnocellularis idegsejtjeinek neurokémiai excitabilitására egérben in vivo. A Magyar Élettani Társaság, a Magyar Anatómusok Társasága, a Magyar Biofizikai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság Kongresszusa, Debrecen, 2012 (poster)

Csetényi B, Hormay E, **Szabó I**, Nagy B, Hideg B, Faragó B, Bajnok Góré M, Karádi Z: Endogén és exogén kémiai ingerek hatása az umami-érzékeny idegsejtekre patkány cinguláris kérgében. A Magyar Élettani Társaság, a Magyar Anatómusok Társasága, a Magyar Biofizikai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság Kongresszusa, Debrecen, 2012 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Faragó B, Hideg B, Bajnok Góré M, Karádi Z: Patkány cinguláris kéreg glukóz-monitorozó idegsejtjeinek exogén és endogén kémiai érzékenysége. A Magyar Élettani Társaság, a Magyar Anatómusok Társasága, a Magyar Biofizikai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság Kongresszusa, Debrecen, 2012 (poster)

Nagy B, **Szabó I**, Takács G, Faragó B, Hideg B, Bajnok Góré M, Karádi Z: A prefrontális kéreg glukóz-monitorozó idegsejtjeinek szerepe az íz-reaktivitási mintázatok kialakulásában. A Magyar Élettani Társaság, a Magyar Anatómusok Társasága, a Magyar Biofizikai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság Kongresszusa, Debrecen, 2012 (poster)

Szabó I, Nagy B, Takács G, Papp S, Hideg B, Faragó B, Bajnok Góré M, Karádi Z: Endogenous and exogenous chemical sensitivity of glucose-monitoring and glutamate sensitive neurons in the nucleus accumbens. 8th FENS Forum of Neuroscience, Barcelona, Spain, 2012 (poster)

Nagy B, Takács G, **Szabó I**, Szalay C, Keresztes D, Faragó B, Hideg B, Bajnok Góré M, Karádi Z: Taste reactivity deficit after streptozotocin microinjection into the mediodorsal prefrontal cortex. 8th FENS Forum of Neuroscience, Barcelona, Spain, 2012 (poster)

Szabó I, Nagy B, Csetényi B, Hormay E, Bajnok Góré M, Zoltán Karádi: Endogenous and exogenous chemical responsiveness in the medial orbitofrontal cortex. A Magyar Idegtudományi Társaság XIV. Konferenciája, Budapest, 2013 (poster)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Hideg B, Karádi Z: Homeostatic alterations after IL-1β microinjection into the cingulate cortex of the rat. A Magyar Idegtudományi Társaság XIV. Konferenciája, Budapest, 2013 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Hideg B, Bajnok Góré M, Karádi Z: Catecholamine responsiveness of glucose-monitoring neurons in the cingulate cortex of the rat. A Magyar Idegtudományi Társaság XIV. Konferenciája, Budapest, 2013 (poster)

Szabó I, Nagy B, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Az idegsejtek komplex funkcionális sajátosságai az orbitofrontalis kéregben. II. Interdiszciplináris Doktorandusz Konferencia, Pécs, 2013 (presentation)

Szabó I, Nagy B, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Medialis és lateralis orbitofrontalis kérgi idegsejtek komplex funkcionális sajátosságai. A Magyar Élettani, Farmakológiai és Mikrocirkulációs Társaságok 2013. évi közös Tudományos Kongresszusa, Budapest, 2013 (poster)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Hideg B, Karádi Z: A cinguláris kéregbe adott IL-1β mikroinjekció homeosztatikus hatásai patkányban. A Magyar Élettani, Farmakológiai és Mikrocirkulációs Társaságok 2013. évi közös Tudományos Kongresszusa, Budapest, 2013 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Hideg B, Bajnok Góré M, Karádi Z: A glukóz-monitorozó idegsejtek katekolamin érzékenysége és intraorális íz-ingerlésre adott válaszai patkány cinguláris kérgében. A Magyar Élettani, Farmakológiai és Mikrocirkulációs Társaságok 2013. évi közös Tudományos Kongresszusa, Budapest, 2013 (poster)

Nagy B, **Szabó I**, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Kóros glukóz tolerancia a mediodorzális prefrontális kéreg streptozotocin mikroinjekcióját követően patkányban. A Magyar Élettani, Farmakológiai és Mikrocirkulációs Társaságok 2013. évi közös Tudományos Kongresszusa, Budapest, 2013 (poster)

Szabó I, Nagy B, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Neurochemical responsiveness and taste sensitivity of neurons in the medial and lateral orbitofrontal cortex of the rat. 2nd International Doctoral Workshop on Natural Sciences 2013, Pécs, 2013 (poster)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Hideg B, and Karádi Z: Interleukin-1β microinjection into the cingulate cortex induces homeostatic changes in the rat. 2nd International Doctoral Workshop on Natural Sciences 2013, Pécs, 2013 (presentation)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Bajnok Góré M, Karádi Z: Complex functional attributes of neurons in the cingulate cortex of the rat. 2nd International Doctoral Workshop on Natural Sciences 2013, Pécs, 2013 (presentation)0

Nagy B, **Szabó I**, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Metabolic alterations after streptozotocin microinjection into the mediodorsal prefrontal cortex. 2nd International Doctoral Workshop on Natural Sciences 2013, Pécs, 2013

Szabó I: The central regulation of feeding and metabolism: The glucose-monitoring system. Encontro com Pesquisadores de Universidade de Pécs (Hungria): reforcando a internacionalização da USP, Universidade de São Paulo (USP), Brazília, 2013 (presentation)

Szabó I: The central regulation of feeding and metabolism: The glucose-monitoring system. Programa de Pós-graduação em Fisiopatologia Clínica e Experimental, Centro Biomédico, Faculdade de Ciências Médicas, Universidade do Estado do Rio de Janeiro (UERJ), Brazília, 2013 (presentation)

Szabó I, Nagy B, Hormay E, Csetényi B, Bajnok Góré M, Karádi Z: Nucleus Accumbens and Orbitofrontal Cortex: Endogenous and Exogenous Chemical Responsiveness of Neurons in the Rat. IBRO Workshop 2014, Debrecen, 2014 (poster)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Hideg B, Karádi Z: Feeding and metabolic consequences of IL-1β microinjection into the cingulate cortex in the rat. IBRO Workshop 2014, Debrecen, 2014 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Hideg B, Bajnok Góré M, Karádi Z: Streptozotocin microinjection into the cingulate cortex alters glucose tolerance in the rat. IBRO Workshop 2014, Debrecen, 2014 (poster)

Nagy B, **Szabó I**, Csetényi B, Hormay E, Bajnok Góré M, Karádi Z: Metabolic Effects of Local Microinjection of Streptozotocin into the Mediodorsal Prefrontal Cortex. IBRO Workshop 2014, Debrecen, 2014 (poster)

Hartung K, Kósa B, Füge K, **Szabó I**, Koller Á: The Role of Women in PhD Education at the University of Pécs and Changing Tendencies over Time. 9th ORPHEUS Conference, Lausanne, Svájc, 2014 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Hideg B, Bajnok Góré M, Karádi Z: A cinguláris kéreg streptozotocin mikroinjekciójának hatása a glukóz toleranciára laboratóriumi patkányban. III. Interdiszciplináris Doktorandusz Konferencia 2014, Pécs, 2014 (poster)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Hideg B, Karádi Z: Cinguláris kérgi IL-1β mikroinjekció hatásai a táplálkozásra és anyagcserére laboratóriumi patkányban. III. Interdiszciplináris Doktorandusz Konferencia 2014, Pécs, 2014 (poster)

Szabó I, Hormay E, Csetényi B, Nagy B, Bajnok Góré M, Karádi Z: Complex functional attributes of glucose-monitoring neurons in medial orbitofrontal cortex and their homeostatic significance. FEPS2014 (Joint Meeting of the Federation of European Physiological Societies (FEPS) and the Hungarian Physiology Society), Budapest, 2014 (poster)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Bajnok Góré M, Karádi Z: IL-1ß modifies the taste reactivity in the cingulate cortex of the rat. FEPS2014 (Joint Meeting of the Federation of European Physiological Societies (FEPS) and the Hungarian Physiology Society), Budapest, 2014 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Hideg B, Bajnok Góré M, Karádi Z: Complex functional attributes of cingulate cortex glucose-monitoring neurons and their metabolic significance. FEPS2014 (Joint Meeting of the Federation of European Physiological Societies (FEPS) and the Hungarian Physiology Society), Budapest, 2014 (poster)

Petykó Z, Tóth A, Gálosi R, **Szabó I**, Máté K, Szabó I, Karádi Z, Lénárd L: Neuronal responses of the rat medial prefrontal cortex during appetitive classical conditioning. FEPS2014 (Joint Meeting of the Federation of European Physiological Societies (FEPS) and the Hungarian Physiology Society), Budapest, 2014 (poster)

Szabó I: Az idegsejtek komplex funkcionális sajátosságai a medialis orbitofrontalis kéregben. Pécsi Tudományegyetem Idegtudományi Centrum és Szentágothai János Kutatóközpont PhD és TDK konferencia, Pécs, 2014 (presentation)

Szabó I, Hormay E, Csetényi B, Nagy B, Bajnok Góré M, Karádi Z: Medial Orbitofrontal Cortex: Complex Functional Attributes of Glucose-Monitoring Neurons and Their Metabolic Significance. 15th Biannual Conference of the Hungarian Neuroscience Society (MITT2015), Budapest, 2015 (poster)

Petykó Z, Tóth A, Gálosi R, **Szabó I**, Máté K, Szabó I, Karádi Z, Lénárd L: Responses of rat medial prefrontal cortical neurons to Pavlovian conditioned stimuli and to delivery of appetitive reward. 15th Biannual Conference of the Hungarian Neuroscience Society (MITT2015), Budapest, 2015 (poster)

Szabó I, Hormay E, Csetényi B, Nagy B, Karádi Z: A medialis orbitofrontalis kérgi glukóz-monitorozó idegsejtek komplex funkcionális sajátosságai. Tavaszi Szél Konferencia, Eger, 2015 (presentation)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Karádi Z: Patkány cinguláris kérgébe adott IL-1β mikroinjekció homeosztatikus hatásainak vizsgálata. Tavaszi Szél Konferencia, Eger, 2015 (presentation)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Karádi Z: Glukóz tolerancia változások laboratóriumi patkányban cinguláris kérgi streptozotocin mikroinjekciót követően. Tavaszi Szél Konferencia, Eger, 2015 (presentation)

Szabó I, Hormay E, Csetényi B, Nagy B, Karádi Z: A medialis orbitofrontalis kéregbe adott streptozotocin mikroinjekció metabolikus és magatartási hatásai patkányban. A Magyar Élettani Társaság 79. Vándorgyűlése és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság 2015. évi konferenciája, Szeged, 2015 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Karádi Z: A cinguláris kéreg streptozotocin mikroinjekciójának metabolikus hatása laboratóriumi patkányban. A Magyar Élettani Társaság 79. Vándorgyűlése és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság 2015. évi konferenciája, Szeged, 2015 (poster)

Nagy B, **Szabó I**, Csetényi B, Hormay E, Karádi Z: Effect of stress associated neurotransmitters on the mediodorsal prefrontal cortex. 5th International Regional (North America) ISBS Neuroscience and Biological Psychiatry „Stress and Behavior" Conference, Miami, FL, USA, 2015 (presentation)

Szabó I: The central regulation of feeding and metabolism: The glucose-monitoring system. Division of Behavioral Physiology, Department of Behavioral Sciences, Graduate School of Human Sciences, Osaka University, Osaka, Japán, 2015 (presentation)

Szabó I, Hormay E, Csetényi B, Torda V, Tóth M, Karádi Z: Complex functional attributes of orbitofrontal cortical glucose-monitoring neurons. 5th Central European Congress on Obesity (CECON), Budapest, 2015 (presentation)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Tóth M, Torda V, Karádi Z: Cingulate cortex IL-1β mediated mechanisms in the regulation of feeding and metabolism in the rat. 5th Central European Congress on Obesity (CECON), Budapest, 2015 (poster)

Hormay E, Csetényi B, **Szabó I**, Nagy B, Torda V, Tóth M, Karádi Z: Glucose-monitoring neurons of the rat cingulate cortex: feeding and metabolic significance. 5th Central European Congress on Obesity (CECON), Budapest, 2015 (poster)

Szabó I, Hormay E, Csetényi B, Torda V, Tóth M, Karádi Z: A medialis orbitofrontalis kérgi glukóz-monitorozó idegsejtek metabolikus és magatartási funkcióinak vizsgálata patkányban. Doctoral Workshop 2015, Pécs, 2015 (presentation)

Csetényi B, Hormay E, Nagy B, **Szabó I**, Tóth M, Torda V, Karádi Z: Cinguláris kérgi IL-1β mikroinjekció homeosztatikus hatásainak vizsgálata patkányban. Doctoral Workshop 2015, Pécs, 2015 (presentation)

Hormay E, Csetényi B, Nagy B, **Szabó I**, Torda V, Tóth M, Karádi Z: Patkány cinguláris kérgi glukóz-monitorozó neuronok táplálkozási és metabolikus szerepe. Doctoral Workshop 2015, Pécs, 2015 (presentation)

Szabó I, Hormay E, Csetényi B, Nagy B, Karádi Z: A glukóz-monitorozó neuronok komplex funkcionális sajátosságai a medialis orbitofrontalis kéregben. Magyar Farmakológiai, Anatómus, Mikrocirkulációs és Élettani Társaságok Közös Tudományos Konferenciája (FAMÉ 2016), Pécs, 2016 (poster)

Csetényi B, Hormay E, **Szabó I**, Nagy B, Karádi Z: Cinguláris kérgi interleukin-1ß mikroinjekció íz-percepciót módosító hatásának vizsgálata patkányban. Magyar Farmakológiai, Anatómus, Mikrocirkulációs és Élettani Társaságok Közös Tudományos Konferenciája (FAMÉ 2016), Pécs, 2016 (poster)

Hormay E, Csetényi B, **Szabó I**, Karádi Z: Patkány cinguláris kérgi glukóz-monitorozó neuronok elektrofiziológiai sajátosságai és metabolikus jelentősége. Magyar Farmakológiai, Anatómus, Mikrocirkulációs és Élettani Társaságok Közös Tudományos Konferenciája (FAMÉ 2016), Pécs, 2016 (poster)

Szabo I, Hormay E, Csetenyi B, Karadi Z: Glucose-monitoring neurons in the medial orbitofrontal cortex of rat. IBNS 2016 Annual Meeting, Budapest, 2016 (presentation)

Szabó I, Hormay E, Csetényi B, Karádi Z: A mediális orbitofrontális kérgi glukóz-monitorozó idegsejtek metabolikus szerepe a homeosztázis szabályozásában. Tavaszi Szél Konferencia, Miskolc, 2017 (presentation)

Guth K, Budai A, **Szabó I**, Jandó G: Modernkori informatika a látásszűrés szolgálatában. Tavaszi Szél Konferencia, Miskolc, 2017 (presentation)

Guth K, Budai A, Mikó-Baráth E, **Szabó I**, Jandó G: Óvodáskorú gyermekek látásszűrésének új lehetőségei. III. Cholnoky László Nemzetközi Szakkollégiumi Szimpózium, Pécs, 2017 (presentation)

Guth K, Budai A, Mikó-Baráth E, **Szabó I**, Jandó G: Modern information technology in vision screening. VI. Interdiszciplináris Doktorandusz Konferencia, Pécs, 2017 (presentation)

Szabó I, Hormay E, Csetényi B, Karádi Z: A medialis orbitofrontalis kérgi glukóz-monitorozó neuronok szerepe a homeosztázis fenntartásában. A Magyar Élettani Társaság, a Magyar Kísérletes és Klinikai Farmakológiai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság közös Vándorgyűlése (ÉFM), Debrecen, 2017 (poster)

Csetényi B, Hormay E, **Szabó I**, Karádi Z: Cinguláris kérgi interleukin-1β mikroinjekció metabolikus hatásai patkányban A Magyar Élettani Társaság, a Magyar Kísérletes és Klinikai Farmakológiai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság közös Vándorgyűlése (ÉFM), Debrecen, 2017

Guth K, Budai A, Mikó-Baráth E, **Szabó I**, Jandó G: Modernkori informatika a látásszűrés szolgálatában. A Magyar Élettani Társaság, a Magyar Kísérletes és Klinikai Farmakológiai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság közös Vándorgyűlése (ÉFM), Debrecen, 2017 (poster)

Szabo I, Hormay E, Csetenyi B, Karadi Z: Multiple functional significance of the glucose-monitoring neuronal network in the medial orbitofrontal cortex. 26th Annual Meeting of the International Behavioral Neuroscience Society (IBNS), Hiroshima, Japán, 2017 (poster)

Szabó I, Hormay E, Csetényi B, Karádi Z: The role of medial orbitofrontal cortical glucose-monitoring neurons in the maintenance of homeostasis. FENS Regional Meeting, Pécs, 2017 (poster)

Csetényi B, Hormay E, **Szabó I**, Karádi Z: Metabolic effects of interleukin-1β microinjection into the cingulate cortex of the rat. FENS Regional Meeting, Pécs, 2017 (poster)

Hormay E, Csetényi B, **Szabó I**, Karádi Z: Feeding and metabolic attributes of the glucose monitoring-neurons in the cingulate cortex. FENS Regional Meeting, Pécs, 2017 (poster)

Mikó-Baráth E, Budai A, Fülöp D, Nemes V, Kerekes J, Juszt J, Guth K, Horváth G, **Szabó I**, Buzás P, Jandó G: Increasing the sensitivity of a new, web-based amblyopia screening application. FENS Regional Meeting, Pécs, 2017 (poster)

Guth K, Mikó-Baráth E, **Szabó I**, Jandó G: A térlátás szűrésének innovációs lehetőségei. Doktoranduszok a Klinikai Kutatásokban (DKK17), Pécs, 2017 (presentation)

Csetényi B, Hormay E, **Szabó I**, Karádi Z: Metabolic alterations after interleukin-1β microinjection into the cingulate cortex of the rat. 6th Central European Congress on Obesity (CECON) & 15th Slovak Congress on Obesity, Pozsony, Szlovákia, 2017 (poster)

Hormay E, Csetényi B, **Szabó I**, Karádi Z: Feeding and metabolism altering attributes of the glucose-monitoring neurons in the cingulate cortex of the rat. 6th Central European Congress on Obesity (CECON) & 15th Slovak Congress on Obesity, Pozsony, Szlovákia, 2017 (poster)

Hormay E, Csetényi B, **Szabó I**, Karádi Z: A cinguláris kérgi glukóz monitorozó neuronok szerepe a táplálkozás és anyagcsere szabályozásban. A Magyar Elhízástudományi Társaság 25. éves Jubileumi Kongresszusa - 69. tudományos rendezvénye "Az elhízás elmélete, klinikai gyakorlata és a megelőzés lehetőségei", Budapest, 2017 (presentation)

Szabó I: Endogén és exogén kémiai érzékenység a nucleus accumbens-ben. XI. Nemzetközi és XVIII. Országos Interdiszciplináris Grastyán Konferencia, Pécs, 2018 (presentation)

Szabó I, Hormay E, Csetényi B, Karádi Z: Ízérzékelés a gasztrointesztinális rendszerben? Tavaszi Szél Konferencia 2018, Győr, 2018 (presentation)

Csetényi B, Hormay E, **Szabó I**, Mintál K, Karádi Z: Az interleukin-1β íz-percepciót módosító hatása patkány cinguláris kérgében. Tavaszi Szél Konferencia 2018, Győr, 2018 (presentation)

Guth K, **Szabó I**, Mikó-Baráth E, Jandó G: A térlátás vizsgálatának új távlatai. Tavaszi Szél Konferencia 2018, Győr, 2018 (presentation)

Szabó I, Hormay E, Csetényi B, Karádi Z: Taste responsiveness of neurons in nucleus accumbens. VII. Interdiszciplináris Doktorandusz Konferencia, Pécs, 2018 (presentation)

Szabó I, Hormay E, Csetényi B, Karádi Z: Endogenous and exogenous chemical responsiveness in nucleus accumbens. VII. Interdiszciplináris Doktorandusz Konferencia, Pécs, 2018 (poster)

Guth K, Szabó I, Mikó-Baráth E, Jandó G: A térlátás szűrése digitális platformokon. VII. Interdiszciplináris Doktorandusz Konferencia, Pécs, 2018 (presentation)

Szabó I: A homeosztázis szabályozásában alapvető előagyi glukóz-monitorozó neuronok működési sajátságainak vizsgálata. Új Nemzeti Kiválósági Program (ÚNKP) Konferencia, Pécs, 2018 (presentation)

Szabó I, Hormay E, Csetényi B, Karádi Z: Az idegsejtek komplex funkcionális sajátosságai a nucleus accumbens-ben. Magyar Élettani Társaság Vándorgyűlése, Szeged, 2018 (poster)

Csetényi B, Hormay E, **Szabó I**, Mintál K, Karádi Z: Íz-reaktivitás változások patkány cinguláris kérgébe adott interleukin-1β hatására. Magyar Élettani Társaság Vándorgyűlése, Szeged, 2018 (poster)

Szabó I, Hormay E, László B, Karádi Z: New methodological approach for the examination of taste and texture detection of neurons. Medical Conference for PhD Students and Experts of Clinical Sciences 2018 (MEDPécs), Pécs, 2018 (poster)

Szabo I, Hormay E, Laszlo B, Karadi Z:Electrophysiological examination of underlying neuronal mechanisms of taste reactivity in the nucleus accumbens of behaving rats. 16th Annual Conference of the Hungarian Neuroscience Society, Debrecen, 2019 (poster)

László BR, Hormay E, **Szabó I**, Mintál K, Karádi Z: Taste reactivity alterations after interleukin-1β microinjection into the cingulate cortex of the rat. 16th Annual Conference of the Hungarian Neuroscience Society, Debrecen, 2019 (poster)

Hormay E, László B, **Szabó I**, Mintál K, Karádi Z: Glucose-monitoring neurons in the cingulate cortex of the rat. – Microelectrophysiological study. 16th Annual Conference of the Hungarian Neuroscience Society, Debrecen, 2019 (poster)

Szabo I, Hormay E, Laszlo B, Karadi Z: Electrophysiological examination of neurons during taste reactivity test in the nucleus accumbens and medial orbitofrontal cortex of the rat. 13th Göttingen Meeting of the German Neuroscience Society, Göttingen, Németország, 2019 (poster)

Szabó I: Új módszertani megközelítés az idegsejtek íz- és textúraérzékelésének vizsgálatára. XII. Nemzetközi és XIX. Országos Interdiszciplináris Grastyán Konferencia, Pécs, 2019 (presentation)

Szabó I: A nucleus accumbens idegsejtjeinek vizsgálata íz-reaktivitási tesztekben. Új Nemzeti Kiválósági Program (ÚNKP) Konferencia, Pécs, 2019 (presentation)

Szabó I, Hormay E, László B, Karádi Z: Examination of the role of neurons in taste reactivity. Interdisciplinary Doctoral Conference 2019, Pécs, 2019 (poster)

Szabó I, Hormay E, László B, Lénárd L, Karádi Z: Limbikus előagyi neuronok szerepe a táplálkozás és az anyagcsere szabályozásában. Magyar Kísérletes és Klinikai Farmakológiai Társaság, Magyar Anatómus Társaság, Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság, Magyar Élettani Társaság közös Vándorgyűlése (FAMÉ 2019), Budapest, 2019 (presentation)