УЧЕНЫЕ ЗАПИСКИ КАЗАНСКОГО УНИВЕРСИТЕТА.
СЕРИЯ ЕСТЕСТВЕННЫЕ НАУКИ

2018, Т. 160, кн. 4
С. 621–629

ISSN 2542-064X (Print)
ISSN 2500-218X (Online)

UDC 612.8

DEVELOPMENT OF NEUROPEPTIDE Y-ERGIC INNERVATION OF THE SMALL INTESTINE IN RATS

P.M. Masliukov [a], *J.P. Timmermans* [b], *A.A. Zverev* [c], *T.L. Zefirov* [c]

[a] *Yaroslavl State Medical University*, *Yaroslavl*, *150000 Russia*
[b] *University of Antwerp*, *Antwerp*, *2000 Belgium*
[c] *Kazan Federal University*, *Kazan*, *420008 Russia*

Abstract

Neuropeptide Y (NPY) acts as a neurotransmitter in the autonomic nervous system, including in the metasympathetic intramural ganglia of the intestine. In this study, NPY-positive neurons were detected using immunohistochemical methods in intramural ganglia of the duodenum in the following age groups of rats: newborn pups; 10-, 20-, 30-, and 60-day-old; 1- and 2-year-old rats.

As a result of the immunohistochemical analysis, the NPY-containing neurons were found in small number in the intramural ganglia of the myenteric plexus from the moment of birth and during other periods of life. In ganglia of the submucosal plexus, NPY-immunoreactive neurons were detected in large numbers only starting from day 10 of life. Their proportion did not change until the age of one year and then decreased in the two-year-old rats. The density of Y1R and Y2R receptors increased, while the proportion of Y5R receptors decreased. These changes can be associated with the trophic action of the NPY.

It was concluded that neuropeptide Y is a fairly common neuropeptide in various parts of the autonomic nervous system, including sympathetic, parasympathetic, and metasympathetic, and plays an important role in the processes of age-related neuronal development.

Keywords: neuropeptide Y, receptors, autonomic nervous system, rats, ontogenesis

Introduction

Neuropeptide Y (NPY) and its receptors are present in all major tissues of the body and implicated in numerous internal processes: NPY is widely distributed in the central and peripheral nervous systems; it has been functionally related to feeding behavior, anxiety, memory processing, and cognition in the central nervous system, as well as to vasoconstriction and gastrointestinal tract motility in the peripheral nervous system [1]. NPY also acts an important developmental factor by promoting proliferation and differentiation of a variety of cells. During embryogenesis, NPY expression results from a complex combination of regulatory cues [2].

The biological effects of NPY and its homologs are mediated by the activation of at least five receptors, known as the Y1R, Y2R, Y4R, Y5R and Y6R. Y1R, Y2R, and Y5R are the three major subtypes of NPY receptors that mediate the biological functions of NPY in humans and rats. All known NPY receptors belong to the large superfamily of G-protein-coupled heptahelical receptors. NPY affects peripheral target organs mostly through postsynaptic Y1R, Y5R, and presynaptic Y2R [3, 4].

As already mentioned, NPY plays an important developmental role by promoting growth and/or differentiation of a variety of cells in a receptor-specific manner. Via its Y1R, Y2R, and Y5R, NPY promotes angiogenesis and preadipocyte differentiation [5–7]. NPY has been shown to be a potent, multifunctional angiogenic factor, which stimulates proliferation, migration, and capillary tube formation in endothelial cells. NPY is angiogenic at concentrations below those required for vasoconstriction [8].

The neurochemical specificity of autonomic ganglionic neurons is changed during pre- and postnatal development [9–11]. In sympathetic ganglia, NPY is identifiable from birth. In ontogenesis, the percentage of NPY-positive sympathetic neurons increases during the first month of life [12, 13]. In the rat heart, Y1R and Y2R expression is upregulated, whereas Y5R expression is downregulated during the development [14].

The chemical coding of neurons in the mouse and guinea-pig small intestine has been already investigated in detail [15, 16]. Most literature sources are more focused on the distal parts of the small intestine [17]. However, the age-related aspects of synaptic transmission in the enteric intramural ganglia involving neuropeptide Y remain unclear. The aim of this work was to investigate the developmental changes of NPY-immunoreactive (IR) intramural ganglionic neurons, Y1R, Y2R, and Y5R, in the small intestine of rats of different ages (from the newborn period up to and through senescence) using immunohistochemistry.

Materials and Methods

All animal procedures were approved by the Institutional Animal Care and Use Committee of the Yaroslavl State Medical University and were conducted in accordance with the relevant Guidelines of the Russian Ministry of Health for scientific experimentation on animals. Wistar rats (2 × 7 groups, each containing 5 animals) – newborn, 10-day-old, 20-day-old, 30-day-old, 2-month-old, 1-year-old, and 2-year-old – were used to label NPY and Y1R, Y2R, Y5R in the small intestine by immunohistochemistry. All rats were kept in acrylic cages with wood shavings in an acclimatized room (12/12h light/dark cycle; 22 ± 3 °C) and were provided with water and pellets ad libitum.

The rats were sacrificed with a lethal dose of sodium pentobarbital (Nembutal®, 300 mg/kg, i.p.). Then they were perfused transcardially with 20 mL (newborn and 10-day-old), 100 mL (20- and 30-day-old), or 500 mL (2-month-old and older) of physiological saline and 1 mL heparin followed by a similar volume of the fixative composed of 4% paraformaldehyde (PF) in 0.1 M phosphate buffer. After the perfusion, the duodenum was dissected out, rinsed in physiological solution, and immersed in 4% PF for 1–2 h at room temperature. Following the fixation, it was washed in three 30-min changes of phosphate-buffered saline (PBS; 0.01 M; pH 7.4), cryoprotected by overnight immersion in 20% buffered (pH 7.4) sucrose solution at 4 °C, mounted in TissueTek (Sakura Finetek Europe, Zoeterwoude, Netherlands) on a cryostat chuck, and frozen. Twelve-μm-thick cross sections were cut with a cryostat, mounted on poly-L-lysine-coated slides, and air-dried for 1 h.

Table 1

a) Primary antisera used for immunohistochemistry

Primary antisera	Host species	Dilution	Source
NPY	Sheep	1:500	Abcam, ab6173
PGP9.5	Rabbit	1:200	Abcam, ab10404
Y1R	Rabbit	1:500	Abcam, ab73897
Y2R	Rabbit	1:500	Santa Cruz, H-147
Y5R	Rabbit	1:500	Abcam, ab133757

b) Secondary antisera used for immunohistochemistry

Secondary antisera	Dilution	Source
Donkey anti-rabbit IgG FITC	1:200	Jackson Immunoresearch
Donkey anti-rabbit IgG CY3	1:200	Jackson Immunoresearch
Donkey anti- sheep IgG FITC	1:200	Jackson Immunoresearch
Donkey anti-sheep IgG CY3	1:200	Jackson Immunoresearch

CY3 – cyanine 3, FITC – fluorescein isothiocyanate.

The obtained serial sections were processed for immunohistochemistry. The sections were preincubated for 30 min at room temperature with the blocking buffer containing 5% normal donkey serum (Jackson ImmunoResearch Laboratories, USA) and 0.3% Triton X-100 (Sigma, USA) in PBS to prevent non-specific binding of secondary antibodies. In order to visualize NPY, Y1R, Y2R, Y5R, single or double immunostaining with antibodies (raised in different host species; see Table 1, *a*) was performed. The antibodies to PGP9.5 were used to label the neuronal cell bodies in the intramural ganglia.

Subsequently, the sections were incubated in the primary antisera for 24 h at room temperature, rinsed in PBS, and further incubated in the corresponding secondary antisera for 2 h at room temperature (see Table 1, *b*). The sections were then rinsed three final times in PBS, mounted on glass slides, allowed to dry overnight, and coverslipped using VectaShield (Vector Bioproducts, USA). The control experiments were carried out with the primary antibody replaced with NDS.

The specimens were examined under the Olympus BX43 fluorescence microscope (Tokyo, Japan) fitted with filter sets that allowed separate visualization of FITC or CY3. The images from the fluorescence microscope were recorded using a TCH 5.0 cooled CCD digital camera and ISCapture version 3.6 for Windows imaging software (Tucsen, China). Each image was processed using a sharpen filter and contrast and brightness adjustment only. All photomicrographic plates were made using Adobe Photoshop 6.0 software (Adobe Systems, USA).

To determine the percentage of NPY-IR profiles, we counted the total number of PGP-IR neurons in the measured area and took them as 100%. The NPY-IR neuronal profiles were counted in randomly selected measured areas (1 microscopic field was 0.12 mm^2) at 200-fold magnification. To avoid duplicate counts of neurons in the serial sections of the ganglia, only those nerve cell bodies containing a clearly identified nucleus were counted in any given section. Data from 10 measured areas per ganglion per age group, per animal, were included in this study. Data from individual ganglia in each age group were meaned yielding group sizes of $n = 5$.

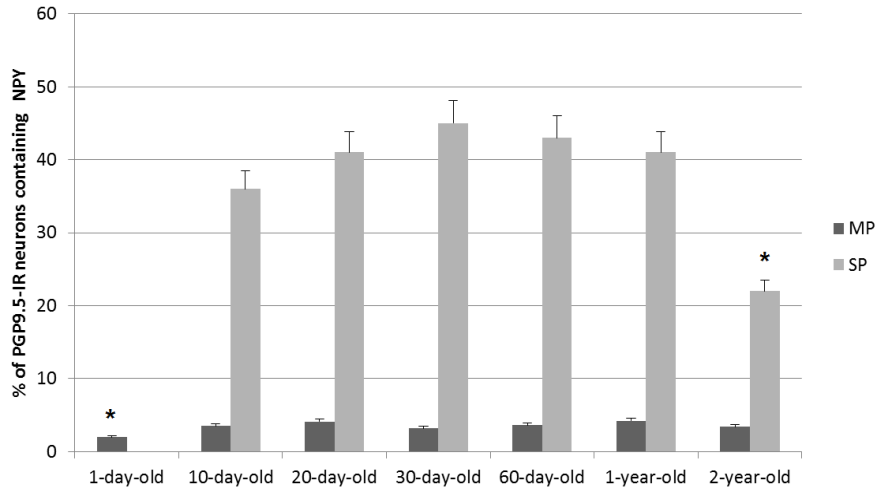

Fig. 1. Percentages of PGP-IR neurons containing NPY in the myenteric (MP) and submucous (SP) plexus of the duodenum in rats of different ages. The error bars represent the standard error of the mean. (*$p < 0.05$, when compared to 10-day-old)

The applied statistical methods include calculation of the mean and standard error of the mean value. Differences in the mean values were subjected to one-way ANOVA followed by Tukey's post-test of multiple comparisons. Differences were considered statistically significant at $p < 0.05$.

Results

NPY immunoreactivity was observed in the myenteric plexus of all studied animals from birth onwards.

The results of the immunohistochemistry showed that the NPY-containing neurons were found in the small intestine in the myenteric plexus from the moment of birth. Their percentage slightly but significantly increased from 2.1 ± 0.12% in the newborn rats to 3.5 ± 0.36% in the 10-day-old rats ($p < 0.05$) and did not change significantly in the further development through the senescence (Fig. 1).

In the submucosal plexus, NPY immunoreactive neurons were detected in large numbers only from the 10th day of life (36.7 ± 4.09%, Fig. 1). Their proportion did not change until the age of one year (41.7 ± 4.18%, $p < 0.05$), but substantially decreased in the two-year-old rats (22.6 ± 2.16%, $p < 0.001$).

Y1R-immunoreactivity was most distinct on the membrane of smooth muscles, with additional granular intracellular labeling. The density of Y1R significantly increased between days 10 and 20 of life. A faint Y2R-immunoreactivity was only observed after 20 days of life. Y2R granules were located in smooth muscles. The density of Y2R-IR granules increased in the 30-day-old rats as compared with the 20-day-old rats and did not change during subsequent development. In contrast, the highest level of Y5R expression was registered in the newborn pups as compared with the older rats. In the newborn rats, the receptors were observed in the vessels, villi, and NPY-IR nerve fibers.

All neurons in the intramural ganglia also exhibited Y1R and Y5R immunoreactivity. No Y2R-IR profiles were observed in the ganglia during the development.

Discussion

The present study shows changes in the expression of NPY, Y1R, Y2R, and Y5R in the small intestine of rats during their postnatal development. We did not observe NPY-IR neurons in the submucous plexus of the newborn rats. The literature data suggest that the submucosal plexus is not yet formed at the time of birth [18, 19]. The percentage of NPY-IR neurons in the intramural ganglia of the myenteric plexus slightly increased in the first 10 days of life. In ganglia of the submucosal plexus, NPY-immunoreactive neurons were detected in large numbers only on day 10 of life. Their proportion significantly increased in the rats aged from 10 to 20 days, and then decreased in the two-year-old rats. In the majority of the mammalian autonomic ganglia, an increase in the proportion of NPY-containing neurons occurs in the development [10–12, 20]. This process varies in different ganglia. The greatest increase is found in the heart intramural ganglia, the lowest one is observed in the enteric ganglia [14, 19]. In contrast to the sympathetic and heart intramural ganglia, the percentage of NPY-IR neurons decreased in the older rats.

Unfortunately, there are no data available on embryonic changes of NPY in the enteric neurons in rats. The entire length of the gut is colonized by neural crest cells on embryonic day 14 in mice [21] and 16.5 in rats [22]. We suggest that the development of enteric neurons in rats is similar to that one in mice with a short delay.

In our previous work, we found the same pattern of the development of NPY receptors in the rat heart. Y5R expression was the largest in the newborn pups and significantly decreased the first 10 days, without subsequent changes. In contrast, the density of Y1R and Y2R increased in ontogenesis. Y1R were detected in a small number in the newborn rats and their number increased significantly in the first 20 days of life; Y2R were detected only in the 20-day-old rats, without changes in the degree of expression [14]. The developmental changes of Y5R were also found in the central nervous system, where Y5R inhibited synaptic excitation in the hippocampal slice only in young rats and their contribution declined with age [23].

NPY acts as a trophic factor by promoting growth and/or differentiation of a variety of cells in a receptor-specific manner. The hypertrophic effect of NPY is accompanied by an increased activity of cytosolic creatine kinase, protein kinase C, and protein kinase C-dependent activation of mitogen activated protein kinase in adult and neonatal myocytes and activation of phosphoinositol 3-kinase in adults [24].

Via its Y1R, Y2R, and Y5R, NPY promotes angiogenesis [5–7], where Y5R acts as an enhancer [25]. According to our data, the highest level of expression is observed in Y5R in the first 10 days of life. We suggest that Y5R has the most important role in stimulating blood vessels growth during the early development. The growth-stimulating effect of the Y5R activation leads to increased protein kinase C-activity, cAMP inhibition, and to mitogen activated protein kinase phosphorylation and activity [26, 27].

Thus, in the heart of a newborn rat, NPY may play a trophic function via Y5R promoting growth of smooth muscle cells and capillaries. This type of receptors may be very important during the period of rapid increasing of the intestine weight and establishing of autonomic innervation.

Conclusions

Thus, in rats, NPY-ergic innervation of the gut is present from the moment of birth. In early postnatal ontogenesis, there are small differences in the number of NPY-containing neurons between newborn and older rats. The density of Y1R and Y2R increases, while the proportion of Y5 receptors decreases. Probably, these changes are associated with the trophic action of NPY. Further physiological and pharmacological studies using selective agonists and antagonists of NPY receptors are required to better understand the function of NPY during the development. The obtained results can be a basis for future studies on the mechanisms of development of autonomic regulation.

References

1. Nozdrachev A.D., Masliukov P.M. Neuropeptide Y and autonomic nervous system. *J. Evol. Biochem. Physiol.*, 2011, vol. 47, no. 2, pp. 121–130. doi: 10.1134/S0022093011020010.
2. Hansel D.E., Eipper B.A., Ronnett G.V. Neuropeptide Y functions as a neuroproliferative factor. *Nature*, 2001, vol. 410, pp. 940–944. doi: 10.1038/35073601.
3. Balasubramaniam A.A. Neuropeptide Y family of hormones: Receptor subtypes and antagonists. *Peptides*, 1997, vol. 18, no. 3, pp. 445–457. doi: 10.1016/S0196-9781(96)00347-6.
4. Michel M.C., Beck-Sickinger A., Cox H., Doods H.N., Herzog H., Larhammar D., Quirion R., Schwartz T., Westfall T. XVI. International Union of Pharmacology recommendations for the nomenclature of neuropeptide Y, peptide YY, and pancreatic polypeptide receptors. *Pharmacol. Rev.*, 1998, vol. 50, no. 1, pp. 143–150.
5. Kuo L.E., Kitlinska J.B., Tilan J.U., Li L., Baker S.B., Johnson M.D., Lee E.W., Burnett M.S., Fricke S.T., Kvetnansky R., Herzog H., Zukowska Z. Neuropeptide Y acts directly in the periphery on fat tissue and mediates stress-induced obesity and metabolic syndrome. *Nat. Med.*, 2007, vol. 13, pp. 803–811. doi: 10.1038/nm1611.
6. Parker S.L., Balasubramaniam A. Neuropeptide Y Y2 receptor in health and disease. *Br. J. Pharmacol.*, 2008, vol. 153, no. 3, pp. 420–431. doi: 10.1038/sj.bjp.0707445.
7. Zhang P., Qi Y.X., Yao Q.P., Chen X.H., Wang G.L., Shen B.R., Han Y., Gao L.Z., Jiang Z.L. Neuropeptide Y stimulates proliferation and migration of vascular smooth muscle cells from pregnancy hypertensive rats via Y1 and Y5 receptors. *PLoS One*, 2015, vol. 10, no. 7, art. e0131124, pp. 1–13. doi: 10.1371/journal.pone.0131124.
8. Zukowska-Grojec Z., Karwatowska-Prokopczuk E., Rose W., Rone J., Movafagh S., Ji H., Yeh Y., Chen W.T., Kleinman H.K., Grouzmann E., Grant D.S. Neuropeptide Y: A novel angiogenic factor from the sympathetic nerves and endothelium. *Circ. Res.*, 1998, vol. 83, no. 2, pp. 187–195. doi: 10.1161/01.res.83.2.187.
9. Masliukov P.M., Shilkin V.V., Nozdrachev A.D., Timmermans J.-P. Histochemical features of neurons in the cat stellate ganglion during postnatal ontogenesis. *Auton. Neurosci.*, 2003, vol. 106, no 2, pp. 84–90. doi: 10.1016/S1566-0702(03)00051-1.
10. Masliukov P.M., Shilkin V.V., Timmermans J.-P. Immunocytochemical characteristic of neurons of the mouse truncus sympaticus stellate ganglion in postnatal ontogenesis. *Morfologiya*, 2005, vol. 128, no 5, pp. 41–44. (In Russian)
11. Maslyukov P.M., Korzina M.B., Emanuilov A.I., Shilkin V.V. Neurotransmitter composition of neurons in the cranial cervical and celiac sympathetic ganglia in postnatal ontogenesis. *Neurosci. Behav. Physiol.*, 2010, vol. 40, no. 2, pp. 143–147. doi: 10.1007/s11055-009-9247-y.

12. Masliukov P.M., Konovalov V.V., Emanuilov A.I., Nozdrachev A.D. Development of neuropeptide Y-containing neurons in sympathetic ganglia of rats. *Neuropeptides*, 2012, vol. 46, no. 6, pp. 345–352. doi: 10.1016/j.npep.2012.08.003.
13. Masliukov P.M., Emanuilov A.I., Moiseev K., Nozdrachev A.D., Dobrotvorskaya S., Timmermans J.P. Development of non-catecholaminergic sympathetic neurons in para- and prevertebral ganglia of cats. *Int. J. Dev. Neurosci.*, 2015, vol. 40, pp. 76–84. doi: 10.1016/j.ijdevneu.2014.12.004.
14. Masliukov P.M., Moiseev K., Emanuilov A.I., Anikina T.A., Zverev A.A., Nozdrachev A.D. Development of neuropeptide Y-mediated heart innervation in rats. *Neuropeptides*, 2016, vol. 55, pp. 47–54. doi: 10.1016/j.npep.2015.10.007.
15. Sang Q., Young H.M. Chemical coding of neurons in the myenteric plexus and external muscle of the small and large intestine of the mouse. *Cell Tissue Res.*, 1996, vol. 284, no. 1, pp. 39–53. doi: 10.1007/s004410050565.
16. Furness J.B. Types of neurons in the enteric nervous system. *J. Auton. Nerv. Syst.*, 2000, vol. 81, nos. 1–2, pp. 87–96. doi: 10.1016/S0165-1838(00)00127-2.
17. Mann P.T., Furness J.B., Southwell B.R. Choline acetyltransferase immunoreactivity of putative intrinsic primary afferent neurons in the rat ileum. *Cell Tissue Res.*, 1999, vol. 297, no. 2, pp. 241–248. doi: 10.1007/s004410051352.
18. Kapur R., Yost C., Palmiter R. A transgenic model for studying development of the enteric nervous system in normal and aganglionic mice. *Development*, 1992, vol. 116, no. 1, pp. 167–175.
19. Masliukov P.M., Budnik A.F., Nozdrachev A.D. Neurochemical features of metasympathetic system ganglia in the course of ontogenesis. *Adv. Gerontol.*, 2017, vol. 7, no. 4, pp. 281–289. doi: 10.1134/S2079057017040087.
20. Masliukov P.M., Emanuilov A.I., Nozdrachev A.D. Developmental changes of neurotransmitter properties in sympathetic neurons. *Adv. Gerontol.*, 2016, vol. 29, no 3, pp. 442–453.
21. Newgreen D.F., Hartley L. Extracellular matrix and adhesive molecules in the early development of the gut and its innervation in normal and spotting lethal rat embryos. *Acta Anat.* (Basel), 1995, vol. 154, no. 4, pp. 243–260. doi: 10.1159/000147776.
22. Young H.M. Functional development of the enteric nervous system-from migration to motility. *Neurogastroenterol. Motil.*, 2008, vol. 20, suppl. 1, pp. 20–31. doi: 10.1111/j.1365-2982.2008.01098.x.
23. Ho M.W.Y., Beck-Sickinger A.G., Colmers W.F. Neuropeptide Y_5 receptors reduce synaptic excitation in proximal subiculum, but not epileptiform activity in rat hippocampal slices. *J. Neurophysiol.*, 2000, vol. 83, no. 2, pp. 723–734. doi: 10.1152/jn.2000.83.2.723.
24. Protas L., Qu J., Robinson R.B. Neuropeptide Y: Neurotransmitter or trophic factor in the heart? *News Physiol. Sci.*, 2003, vol. 18, no. 5, pp. 181–185. doi: 10.1152/nips.01437.2003.
25. Movafagh S., Hobson J.P., Spiegel S., Kleinman H.K., Zukowska Z., Neuropeptide Y induces migration, proliferation, and tube formation of endothelial cells bimodally via Y1, Y2, and Y5 receptors. *FASEB J.*, 2006, vol. 20, no. 11, pp. 1924–1926. doi: 10.1096/fj.05-4770fje.
26. Pellieux C., Sauthier T., Domenighetti A., Marsh D.J., Palmiter R.D., Brunner H.R., Pedrazzini, T. Neuropeptide Y (NPY) potentiates phenylephrine-induced mitogen-activated protein kinase activation in primary cardiomyocytes via NPY Y5 receptors. *Proc. Natl. Acad. Sci. USA*, 2000, vol. 97, no. 4, pp. 1595–1600. doi: 10.1073/pnas.030533197.

27. Sheriff S., Ali M., Yahya A., Haider K.H., Balasubramaniam A., Amlal H., Neuropeptide Y Y5 receptor promotes cell growth through extracellular signal-regulated kinase signaling and cyclic AMP inhibition in a human breast cancer cell line. *Mol. Cancer Res.*, 2010, vol. 8, no. 4, pp. 604–614. doi: 10.1158/1541-7786.MCR-09-0301.

Recieved
July 11, 2018

Masliukov Petr Mikhailovich, Doctor of Medical Sciences, Professor, Department of Normal Physiology with Biophysics

Yaroslavl State Medical University
ul. Revolyutsionnaya, 5, Yaroslavl, 150000 Russia
E-mail: *mpm@ysmu.ru*

Timmermans Jean Pierre, PhD, Professor, Department of Veterinary Sciences

University of Antwerp
St-Jacobsmarkt 9-13, Antwerp, 2000, Belgium

Zverev Aleksei Anatol'evich, Candidate of Biological Sciences, Associate Professor, Department of Human Health Protection

Kazan Federal University
ul. Kremlevskaya, 18, Kazan, 420008 Russia
E-mail: *Alekcei5@rambler.ru*

Zefirov Timur L'vovich, Doctor of Medical Sciences, Professor, Department of Human Health Protection

Kazan Federal University
ul. Kremlevskaya, 18, Kazan, 420008 Russia
E-mail: *zefirovtl@mail.ru*

УДК 612

Нейропептид Y-ергическая иннервация тонкого кишечника у крыс в онтогенезе

П.М. Маслюков[1], *Ж.П. Тиммерманс*[2], *А.А. Зверев*[3], *Т.Л. Зефиров*[3]

[1]*Ярославский государственный медицинский университет*, *г. Ярославль*, *150000*, *Россия*
[2]*Антверпенский университет*, *г. Антверп*, *2000*, *Бельгия*
[3]*Казанский* (*Приволжский*) *федеральный университет*, *г. Казань*, *420008*, *Россия*

Аннотация

Нейропептид Y (НПУ) выполняет нейромедиаторные функции в автономной нервной системе, в том числе в метасимпатических интрамуральных узлах кишки. В ходе исследования мы регистрировали иммуногистохимическими методами НПУ-позитивные нейроны в интрамуральных узлах двенадцатиперстной кишки крыс следующих возрастных групп: новорожденных; 10-, 20-, 30-, 60-суточных;1-, 2-летних.

Результаты иммуногистохимического анализа показали, что НПУ-содержащие нейроны присутствуют в интрамуральных узлах межмышечного сплетения у крыс с рождения (в незначительном количестве) и далее на протяжении всех возрастных периодов. В узлах подслизистого сплетения НПУ-иммунореактивные нейроны были выявлены в большом количестве только начиная с 10-го дня жизни. Их число не менялось на протяжении первого года жизни, а затем уменьшалась у крыс, достигших возраста двух лет. Плотность рецепторов Y1R и Y2R увеличилась, а доля рецепторов Y5R уменьшилась. Эти изменения могут быть связаны с трофическим действием НПУ.

Сделан вывод о том, что нейропептид Y достаточно распространен в различных отделах автономной нервной системы, включая симпатический, парасимпатический и метасимпатический, и играет важную роль в процессах возрастного развития нейронов.

Ключевые слова: нейропептид Y, рецепторы, автономная нервная система, крысы, онтогенез

Поступила в редакцию
11.07.18

Маслюков Петр Михайлович, доктор медицинских наук, профессор кафедры нормальной физиологии с биофизикой

Ярославский государственный медицинский университет
ул. Революционная, д. 5, г. Ярославль, 150000, Россия
E-mail: *mpm@ysmu.ru*

Тиммерманс Жан Пьер, доктор наук, профессор кафедры ветеринарии

Антверпенский университет
Ст-Якобсмаркт 9-13, г. Антверп, 2000, Бельгия

Зверев Алексей Анатольевич, кандидат биологических наук, доцент кафедра охраны здоровья человека

Казанский (Приволжский) федеральный университет
ул. Кремлевская, д. 18, г. Казань, 420008, Россия
E-mail: *Alekcei5@rambler.ru*

Зефиров Тимур Львович, доктор медицинских наук, профессор кафедра охраны здоровья человека

Казанский (Приволжский) федеральный университет
ул. Кремлевская, д. 18, г. Казань, 420008, Россия
E-mail: *zefirovtl@mail.ru*

***For citation*:** Masliukov P.M., Timmermans J.P., Zverev A.A., Zefirov T.L. Development of neuropeptide Y-ergic innervation of the small intestine in rats. *Uchenye Zapiski Kazanskogo Universiteta. Seriya Estestvennye Nauki*, 2018, vol. 160, no. 4, pp. 621–629.

***Для цитирования*:** *Masliukov P.M., Timmermans J.P., Zverev A.A., Zefirov T.L.* Development of neuropeptide Y-ergic innervation of the small intestine in rats // Учен. зап. Казан. ун-та. Сер. Естеств. науки. – 2018. – Т. 160, кн. 4. – С. 621–629.