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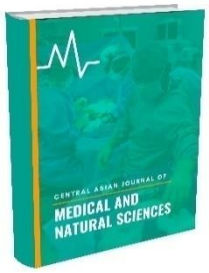

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Hypothalamic-Pituitary Neurosecretory System in Fetuses and Offspring of Animals Poisoned with Chlorpyrifos During Pregnancy

1. **Djumaniyazov Shavkat Atanazarovich**
2. **Karabaev Aminjon Gadaevich**

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[1]Assistant of the Department of Physiology of the Samarkand State Medical University, Samarkand, Uzbekistan
jradi63@mail.ru

[2]Associate Professor. Head of the Department of Physiology of Samarkand State Medical University, Samarkand, Uzbekistan
karabaev.aminion@bk.ru

Abstract: The article investigates the hypothalamic-pituitary neurosecretory system of laboratory rats in ontogenesis under antenatal exposure to organophosphate pesticide chlorpyrifos. The study was carried out at the level of large-cell nuclei of the anterior hypothalamus (supraoptic and paraventricular nuclei), median eminence and posterior pituitary gland. The lesions observed in the HPNS are characterized by disorganization and inhibition of neurosecretory processes, circulatory disorders and increased death of neurons in the hypothalamus. In all age groups, there remains a marked lag in the growth and development of neurons in the large-cell nuclei of the hypothalamus compared with intact rats of the same age. In 2-week-old rat pups and older animals, signs of strained functioning of the HPNS are observed, which, apparently, is associated with the need to maintain disturbed homeostasis. At the same time, such increased activity is accompanied by a high content of neurons in the large-cell nuclei of the hypothalamus in the stages of "deposition" and dystrophy. At the same time, the volumes of neuronal nuclei do not reach the indicators characteristic of intact baby rats.

Key words: Hypothalamo-pituitary neurosecretory system, paraventricular nucleus, supraoptic nucleus, neurohypophysis, neurosecretion, ontogeneziz, organophosphate pesticides.

The relevance of the problem.

The widespread use of pesticides contributes to the expansion of human and animal contact with toxic substances, the occurrence of poisoning cases and the increase in morbidity of the population in areas of intensive use of pesticides and can provide a fatal outcome [4,5,7,15,18,13,14,21,28]. In the pathogenesis of intoxication of the body under the influence of various factors, an important role is played by the functional state of the regulatory systems of the body and, especially, the

neuroendocrine system, the autonomic nervous system, which largely determines the development of reactions to harmful effects and, at the same time, is the most vulnerable [3, 19, 20, 23,25, 30]. The perinatal (intrauterine) period of development is the most vulnerable, since the environment affects the formation and physiology of the fetus through epigenetic mechanisms [17]. Factors acting during critical periods of fetal development can trigger a number of maladaptive mechanisms, which has a great impact on the structure and function of tissues, while the predominance of catabolic processes at the cellular level ensures the development of dystrophic changes at the cellular level and the productive state remains at a disadvantage [8,9 Bobokandova].Accordingly, the effects of toxic substances acting during pregnancy can be transmitted from generation to generation [1, 2, 6, 12, 26, 10, 11, 26]. It should be noted that the morphofunctional state of the neuroendocrine system in the ontogenetic aspect in the conditions of an unfavorable course of pregnancy has not been sufficiently studied [29, 32].

The aim of the study was to study the development and formation of the neurosecretory function of HPNS in fetuses and offspring of animals poisoned with various doses of chlorpyrifos FOP during the entire period of pregnancy.

Materials and methods of research This study was conducted on mongrel white rats weighing 180-200 g. and their offspring of various periods of postnatal development. The animals were divided into 2 groups. The first group consisted of intact animals. In group 2, rats were poisoned with chlorpyrifos during the entire period of pregnancy at a dose of 1/50 LD50.The slaughter of animals was carried out on the I, 7, 14, 21, 30 days after birth by simultaneous decapitation. Pieces of the brain, including the hypothalamus with the pituitary gland, were fixed in Buena's fluid (for staining by the Gomori method) or Carnois (for staining by Nissl). After the alcohol wiring, the pieces were poured into paraffin, then sections 5-7 microns thick, oriented frontally or sagittal, were prepared from them. The sections were stained with one of the following methods: I) cresilviolet according to Nissl; 2) paraldehyde-fuchsin (PAF) according to Gomori-Gabe; 3) chromhematoxylin according to Gomori with nucleolar staining according to Heidenhain.

The study of the hypothalamic-pituitary neurosecretory system was carried out at the level of the nuclei of the hypothalamus (SON and PVN), the median elevation and the posterior lobe of the pituitary gland. The change in the morphofunctional state of the neurosecretory cells (NSC) of the supraoptic and paraventricular nuclei was determined by calculating the percentage ratio of individual types of neurosecretory cells [3, 4, 31]. Along with this, the content of nerve secretion in the hypothalamic-pituitary tract and in the posterior part of the neurohypophysis (PPN) was taken into account.

The volume of neuronal nuclei was measured in hypothalamic nuclei (SON and PVN) to assess the state of functional activity of the NSC. When describing the morphological state of the neurosecretory nuclei, attention was also paid to structural changes in cells, to the state of blood vessels and glia.

In addition to these indicators, we took into account data on the general condition of animals, indicators of the onset and preservation of pregnancy, the number of pre- and postnatal death of offspring.

RESEARCH RESULTS AND THEIR DISCUSSION

I. Development of HPNS in intact animals

A study of the HPNS in intact rats showed that the large-cell nuclei of the hypothalamus of newborn baby rats are isolated into well-distinguishable formations. But, at the same time, morphological analysis of the HPNS shows that this system is far from the degree of development characteristic of adult animals, this is manifested not only by the small size of the nuclei and nucleoli of neurons, but

also by the absence of a well-defined cytoplasm. The relative looseness of the distribution of neurons in the nuclei, the presence of mitotically dividing cells and a small amount of Nissl substance in the cytoplasm of neurons also testify to the incompleteness of the maturation process of HPNS. In the process of postnatal ontogenesis of baby rats, there is an increase in the size of hypothalamus neurons.

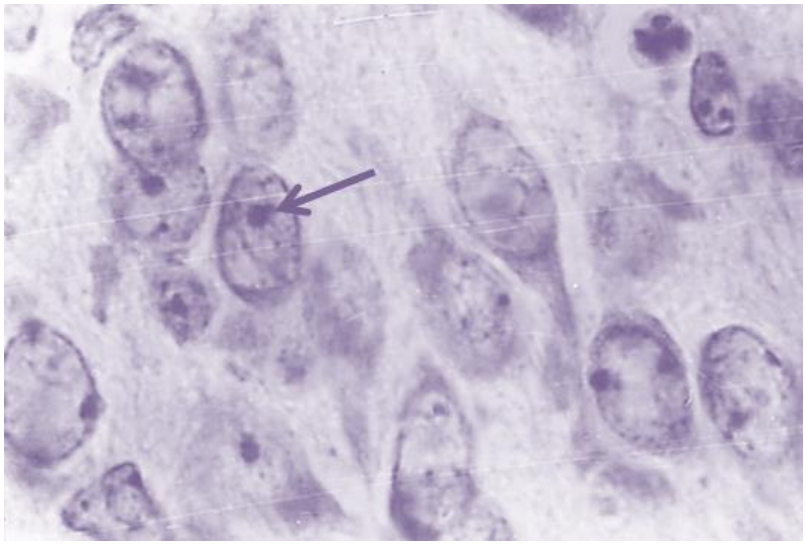

Fig.1 Large nucleoli of neurons of the paraventricular nucleus in intact newborn rats. Chrome hematoxylin. Magnification 10x90

At the same time, the content of the neural secret in various departments of the GGNS is increasing. By the end of the 3rd week of the rat's life, the morphological picture of the neuroendocrine system approaches that which is characteristic of adult animals. Starting from the 21st day of postnatal development, neurons in various phases of the secretory cycle can be seen in large-cell nuclei. By the 30th day of life, the neurosecretory system of baby rats becomes almost identical to that of adults [32].

2. HPNS in case of chlorpyrifos poisoning at a dose of 1/50 LD_{50} throughout the entire period of pregnancy.

In this experimental group, the most significant destructive changes were observed in the HPNS and the general condition of the offspring of poisoned rats compared with intact animals.

The changes observed in the HPNS of newborn rats were characterized by disorganization and inhibition of neurosecretory processes, circulatory disorders and increased death of neurons in the large-cell part of the hypothalamus. Destructive processes were more pronounced in SON than in PVN.

In subsequent age groups, a significant lag in the growth and development of neurons in the large-cell nuclei of the hypothalamus remains noticeable compared with intact rats of the same age. In 2-week-old and older rat pups, signs of intense functioning of the HPNS are observed, which is apparently associated with the need to maintain disturbed homeostasis. At the same time, such increased activity of the system is accompanied by a high content of neurons in the large-cell nuclei of the hypothalamus in the stages of "deposition" and dystrophy. At the same time, the volumes of neuronal nuclei do not reach the indicators characteristic of intact baby rats. (Table I)

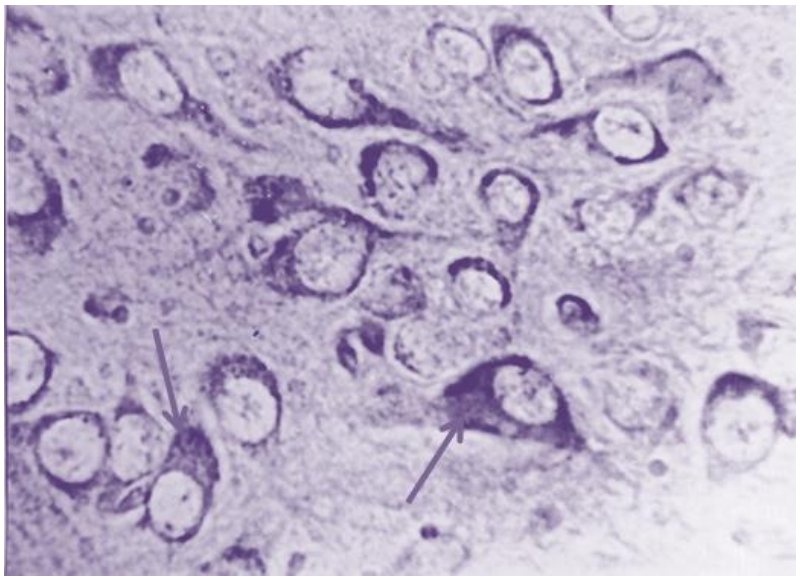

Fig.2 Perinuclear arrangement of the neurosecretory substance in the PVN of a 14-day-old baby rat. Poisoning with chlorpyrifos at a dose of 1/50 LD_{50} . Paraldehyde-fuchsin. Magnification :10x 40

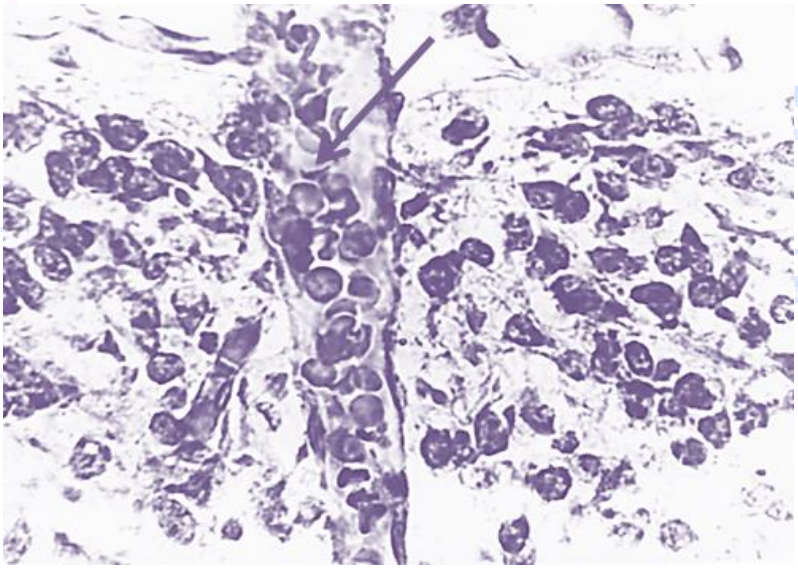

Fig. 3 Vascular hyperemia, loose arrangement of neurons. SON of a newborn baby rat. Poisoning with chlorpyrifos at a dose of 1/50 LD_{50}. Chrome hematoxylin. Ok. x 10, vol. x 20.

Table I The volumes of nuclei (in mm^3) of SON and PVN neurons in the offspring of rats poisoned with chlorpyrifos at a dose of 1/50 LD_{50} during the entire period of pregnancy.

Nuclei	Age of baby rats / days/				
	1	7	14	21	30
SON	196,6** ± 6,03	289,3*** ± 8,46	425,6** ±10,04	430,3* ± 12,2	416,4** ± 9,16
PVN	182,1** ± 5,15	280,7** ± 8,22	443,6* ± 7,82	421,2* ± 10,17	425,3** ± 8,27

Notes: * - P<0.05; ** - P <0.01; ***- P < 0.001 relative to intact rats of the appropriate age. At least 150 measurements were carried out in each case.

Conclusions

Analyzing the morphofunctional state of the HPNS of fetuses and rats of the first month of life in this series of experiments, it should be noted that

1. Antenatal poisoning of antio at a dose of 1/50 LD_{50} causes a violation of the formation and development of the neuroendocrine system at all stages of early ontogenesis. If destructive processes in the HPNS prevail in newborn baby rats, then in older animals there is a strained functioning of the system and its depletion.

2. The reaction of immature rat pups to poisoning is completely different from the reaction of an adult organism, which has a clear phase character (A.G. Karabaev, 2013-2022). We explain this situation by the fact that the tissues of young animals, and especially fetuses, are very sensitive to toxic effects, and the neuroendocrine system does not have a complete structure [16, 22, 27].

3. In addition to disorders in the HPNS in rats in this experimental group, we noted high pre- and postnatal mortality, the phenomena of general hypotrophy and later periods of the animals' epiphany. It is very likely that in these phenomena, the destruction and disintegration of the offspring in the HPNS played an important role.

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