POST-NATAL DEVELOPMENT OF THE HYPOTHALAMIC NEUROSECRETION IN THE DOG

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Works of a number of recent investigators are substantial to the concept that the supraoptic together with the paraventricular nuclei secrete physiologically active principles which represent the vasopressor and the oxytocic effects of the so-called posterior lobe hormones (Bargmann, 1954; Scharrer and Scharrer, 1954).

Concerning the mode of elaboration of the neurosecretory material, which has been stated as representing a carrier or vehicle of the hormonic principles mentioned, majority of authors in this field of research agree in that the cytoplasmic activity is mainly responsible for observed secretory behaviours in neuron somata of the hypothalamic nuclei, though there are several indications pointing to the possibility of elaboration of neurosecretory material through the agency of the cell nucleus (Scharrer, 1934; Mazzi, 1941; Palay, 1943; Hild, 1949; Enami, 1951, 1955).

Present report deals with the occurrence of cytologic signs of nuclear secretion and also with some consecutive changes of secretory behaviour in the neurosecretory cells of the hypothalamus in the course of post-natal development of the dog.

MATERIAL AND METHOD

Observations were based on histological sections of the brains of juvenile dogs killed by decapitation one day, 3 weeks and 3 months respectively after birth. After having been fixed in Helly's fluid, brains were cut in 6μ thicknesses in sagittal planes after the routine paraffin technique, and the sections were stained after Gomori's chrome alaum hematoxylin and phloxine method. Results obtained with the juvenile dogs were brought into comparison with those with adult animals.

OBSERVATIONS

Principal results of the present observations are described as follows:

Histological pictures in the dogs one day after birth

In histologic preparations stained after Gomori's chrome-aluam hematoxylin (CH) and phloxine method, a number of neuron somata distributed around the infundibular recess in the median eminence showed occurrence of CH-positive granules or droplets within the nuclei. As illustrated by Figs. 1 and 2, the material in question made apperition either in the close proximity to the nucleolus (Fig. 1, B,

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D and F; Fig. 2, A, B and E) or as scattered dots within karyoplasm, being associated or unassociated with the nucleus (Fig. 1, C, D, G, H, I and K; Fig. 2, A, B, C, D and F). In parallel with the occurrence of such intra-nuclear granules, seeming decrease of chromatin took place. There were pictures indicating release of the CH-positive material through the nuclear membrane to the surrounding cytoplasm to attain eventually to either the extra-cellular space (Fig. 1, G, H and I; Fig. 2, C and D) or the axoplasm (Fig. 1, K; Fig. 2, E).

All of such pictures appeared much indicative of elaboration of a kind of CH-positive material through the agency of nuclear activity though no definitive findings resulted as regards the details of secretory behaviour. The product mentioned was occasionally found on the way of isolation from the cell body to be

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**Fig. 1.** Different views of nuclear secretion. NN, N, X and Y designate nucleolus, nucleus, axon and cytoplasm respectively. CH-positive material is figured by black spot.
conveyed in all possibility along the paralymphatic system. Nevertheless, not a few observations were concerned with the apparition of the CH-positive material in the axons suggesting possible axonal transport of it.

Similar signs of nuclear secretion was observed in the area of the supraoptic nucleus too, though most of the component cells showed apparent pictures of cytoplasmic secretion viz., apparition of CH-positive fine granules at the area of the Nissl substance or in the basophilic cytoplasm directly surrounding the nucleus.

It was of much interest to observe that the cells in the median eminence as

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**Fig. 2.** Histological pictures showing production of CH-positive material within nucleus, Arrow indicates CH-positive material.
well as in the supraoptic nucleus showing the picture of nuclear secretion were provided with the voluminous nuclei, suggesting that the secretory activity in question would be characteristic to the cells with comparatively large measure of nucleus/cytoplasm ratio. Counts of secretory active cells in the supraoptic nucleus showed that nearly 90% represented cytoplasmic secretion, while the cells showing nuclear secretion were at the order of 10% or so.

Concerning the cells in the paraventricular nucleus, secretory behaviour was tacitly observed in only small fractions of the component cells, which were characterized by signs of nuclear secretion exclusively.

Within the neurohypophysis CH-positive granules were diffusely present, which, because of the observed predominance in secretory activity of neuron somata, was deduced to have been sent from the cells of the supraoptic nucleus, though at least certain fractions of accumulated secretory colloid might be originated in the cells showing pictures of nuclear secretion.

It is added that any significant local accumulation of CH-positive material that deserved the nomination of the Herring body was not observed along the whole hypothalamo-neurohypophyseal tract in animals under consideration.

*Histological pictures in dogs 3 weeks after birth*

Marked decrease of the cells showing nuclear secretion was noticed in the region of the median eminence, though the activity was maintained in certain number of the cells.

Cells in the supraoptic nucleus showed marked signs of promotion of cytoplasmic activity, though overall pictures of the area were by no means comparable to the average picture of significant activity in adult animals. It seems noteworthy that the area of the supraoptic nucleus in animals killed 3 weeks after birth did not show signs of nuclear secretion any more, and that the nuclei in some of the cells underwent characteristic red pyknosis, which is of occasional occurrence in the cells of the same nucleus in adult dogs.
Except a few cells which showed the nuclear secretion, cells of paraventricular nucleus were found almost at rest (Fig. 4, D), which stood out in marked contrast against increased secretory activity in the cells of the suprapoptic nucleus.

Neurohypophysis was found filled with considerable amount of CH-positive colloid, and large and small CH-positive formations simulating the so-called Herring body in the adult were located along the nerve fiber tracts in the stalk as well as at the proximal aspect of the neurohypophysis.

Fig. 4. Various aspects of development of secretory activity in the supraoptic and paraventricular nuclei. A, C, and E show cells of supraoptic nucleus, and B, D and F show of paraventricular nucleus, in dogs killed one day, 3 weeks and 3 months after birth respectively.
Histological pictures in dogs 3 months after birth

No apparent sign of nuclear secretion was observable in the whole area covering the anterior hypothalamus and the median eminence.

In the supraoptic nucleus, the constituent cells showed pronounced cytoplasmic secretion, which was comparable to the average status in adult animals. Red pyknosis of the nucleus was met with in certain number of the cells in line with observations with adult animals as well as with animals killed 3 weeks after birth.

In the paraventricular nucleus, perikarya of the neurons were filled with varying amounts of CH-positive granules, showing initiation of cytoplasmic secretory activity (Fig. 4, F). Among the secretory active cells, some were found in the stage of formation of red pyknosis, which, together with the observation on the cells of the supraoptic nucleus, suggests that such a peculiar pyknotic change might be elicited by certain unknown physiological demand raised in parallel with the initiation of cytoplasmic secretory activity.

In parallel with highly elevated secretory activity in both the supraoptic and the paraventricular nucleus, accumulation of CH-positive material within the neurohypophysis became far more pronounced as compared with the cases in animals killed one day and three weeks after birth respectively.

Herring bodies with characteristic features in adult animals were observed along the hypothalamo-neurohypophyseal tract in various amounts, though they were not so significant as those in the adults in both number and size.

CONSIDERATION

It is generally accepted that, while the activity of some of the endocrine glands is initiated during fetal life (Jost, 1953; Wingstrand, 1953), sufficient coordination for adaptive display of the glands is not established until post-natal life begins. In connection with such a view, informations such as (a) new-born animals are unable to concentrate their urine to the same degree as the adults under restricted water intake (McCance and Young, 1941; Heller, 1949), (b) neurohypophysis of new-born animals contains considerably less antidiuretic hormone than that of the adults (Heller, 1947; Heller and Zaimis, 1949) and (c) effect of stress for ACTH discharge from the anterior lobe of the pituitary is not observable in new-born animals (Jailer, 1950) are worthy of citation.

In accordance with such lines of informations, the neurohypophysis, as stated already by Dawson (1953) and Diepen (1954), provided with only a few amounts of stainable material, and no remarkable Herring body was observable along the hypothalamo-neurohypophyseal system in the present dogs examined one day after birth.

It appears of interest that, in parallel with the occurrence of significant cytoplasmic secretion in nearly 90% of the component cells of the supraoptic nucleus, the neurohypophysis became filled with CH-positive material, though some of the material should have been originated in the paraventricular neurons as well as in the cells located proximal to the hypophyseal stalk.

Difference in secretory behaviour between the supraoptic and the paraventricular nuclei was most marked in the early post-natal period, which suggests
dissociative maturity of neuron somata in the two nuclei. There is clearly possibilities, but the most likely seems to be that the nuclei have a different kind of function each other and so the nuclei represent themselves as the different histological pictures of secretory activity in quality and quantity.

As regards the process of formation of secretory materials in neurosecretory cells in general, it has been considered that cytoplasmic as well as intra-nuclear basophils are representing sites of initial occurrence of submicroscopic secretory granules. The Nissl substance, the perinuclar basophil cytoplasm and the nuclear chromatin are ascribed with such responsibility (Scharrer, 1936). In this connection the behaviour of ribonucleic acid attracts special attention, and it does not seem surprising that the hypothalamic neurosecretion is initiated by a kind of nuclear secretion in the course of the development of the juvenile dogs.

At present it is impossible to answer a question how the nucleolus is related with the formation of intra-nuclear secretory material, though some informations are available concerning the relationship in question (Duryee, 1947).

Concerning the occurrence of pyknotic change of the nucleus in the hypothalamic neurosecretory cells, no definitive saying of its physiological significance would be premature. However, the authors are inclined to assume the phenomenon might represent a phase of normal secretory behaviour rather than some feature of degenerative process of the cells concerned.

**SUMMARY**

Hypothalamic neurosecretion in the dog was observed in the early period of post-natal development with the following results.

The earliest sign of production of secretory material was observed as a kind of nuclear secretion, and the widely known cytoplasmic secretory activity was found to follow the initial activity of the nucleus.

Nuclear secretion was learned to be characteristic to juvenile cells with enlarged nuclei.

Occurrence of nuclear secretion, initiation and development of cytoplasmic neurosecretion showed marked disagreement in the cellular activity between the supraoptic and the paraventricular nuclei in the course of post-natal growth of the dog, which suggests possible functional discrepancy of the nuclei from each other.

**REFERENCES**