Concentration of Vasopressin in the Cerebrospinal Fluid and Some Structural Features of the Hypothalamo-Neurohypophyseal System in Stress and Aging

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One of the main components of neuroendocrine regulation underpinning stress reactions is the hypothalamo-neurohypophyseal system and its product, vasopressin (VP), with its multiple biological activities and effects on the processes of aging. During aging the role of VP increases in the regulation of the cardiovascular system in health and in pathology [4]. In addition, there is a wealth of published data on pronounced changes at different levels of the VP regulatory system in stress and aging. Attention has been focused on the age-dependent variations in the blood content of this hormone [1,7]. On the other hand, the level of VP in the cerebrospinal fluid (CSF) under stress and aging has hardly been studied, mostly due to technical problems with regard to obtaining a sufficient amount. Yet it is precisely this index which is essential, because VP is directly transported to the fluid by the neurosecretory fibers that form the axoventricular contacts. Such contacts are particularly numerous in early ontogenesis [3,5]. VP can also diffuse into the CSF from the brain intracellular fluid. Only to a small extent can VP enter the fluid from the systemic circulation due to the low permeability of the blood-brain barrier for this hormone. Thus, the VP content in the CSF quite accurately reflects the level of its production and release both in the hypothalamic and in the extrahypothalamic regions of the brain. In addition, an accepted and objective criterion of the functional activity of the hypothalamo-neurohypophyseal system is the size of the nuclei of neurosecretory cells.

The aim of the present investigation was to compare the VP concentration in the CSF and the morphological indexes of the hypothalamo-neurohypophyseal system (the areas and structural organization of the neuronal nuclei in the macrocellular hypothalamic nuclei) in normal physiological aging and under stress.

MATERIALS AND METHODS

Experiments were carried out on male Wistar rats of two age groups: adult (6-8 months old) and old (26-28 months old). Water deprivation was used as the stress factor and performed by depriving the animals of water and of moist food during 2, 3, and 4 days. The CSF was taken with Pasteur pipets from the cisterna occipitalis major of the intact and deprived (for 4 days) animals under sodium thiopental anesthesia (100 mg/kg, i.p.). The concentration of arginine-vasopressin (AVP) in the fluid was assessed by the radioimmune method using commercial kits (Buhlmann Lab. Ltd., Switzerland). For a histological examination a portion of the hypothalamus with the supraoptic nucleus (SON) was fixed in 2.5% glutaraldehyde solution on a phosphate buffer (pH=7.4), postfixed with 1% osmium tetroxide solution, dehydrated, and embedded in Epon-812. The semithin sections were pre-

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pared with an LKB-III ultramicrotome, stained with hematoxylin, and examined under a light microscope. Karyometry of the SON secretory neurons was performed using a semiautomatic system of image analysis (Leitz -A.S.M., Germany).

RESULTS

A significant increase of the AVP concentration in CSF is noted in aging (Fig.1). Its blood concentration in rats of the same ages is also elevated in aging, as it was shown previously [1]. The stepped-up VP level may be related both to the structural changes in the secretory neurons, such as increased number of VP-containing fibers, directly connected with the CSF, that results in enhanced release of this hormone into the fluid, and to a boosted synthesis of the hormone in aging. Indeed, our immunohistochemical assay did reveal a pronounced increase of VP-containing fibers , which run through the third ventricle wall, in the subependymal region, and, probably, form axoventricular contacts [2]. Moreover, karyometry findings attested to an enlargement of the SON neurosecretory nuclei in aging, and therefore to an enhancement of their specific activity (Fig. 2).

Our findings are in good agreement with the results of the morphometric studies which revealed a 11-16% increase of the volume of these neuronal nuclei in aging [6], as well as an activation of the hypothalamo-hypophyseal system in old age [8].

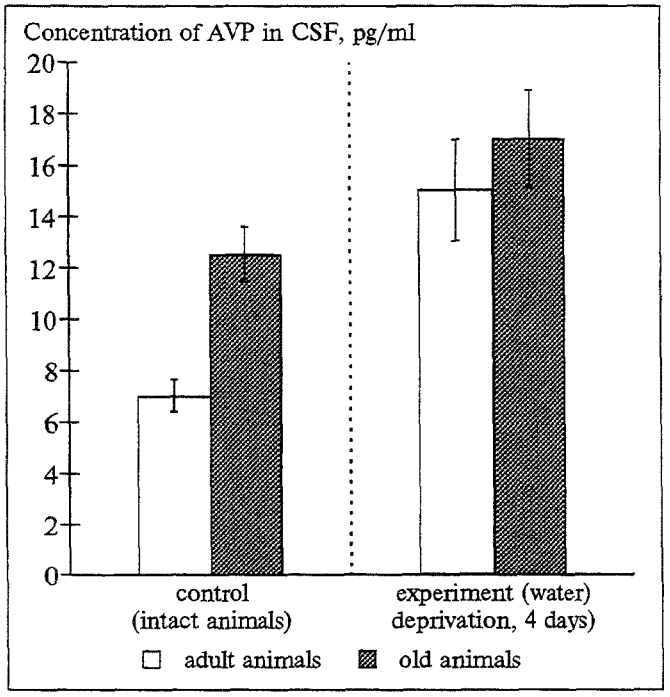

Fig. 1. AVP concentration in rat CSF in aging and under water deprivation.

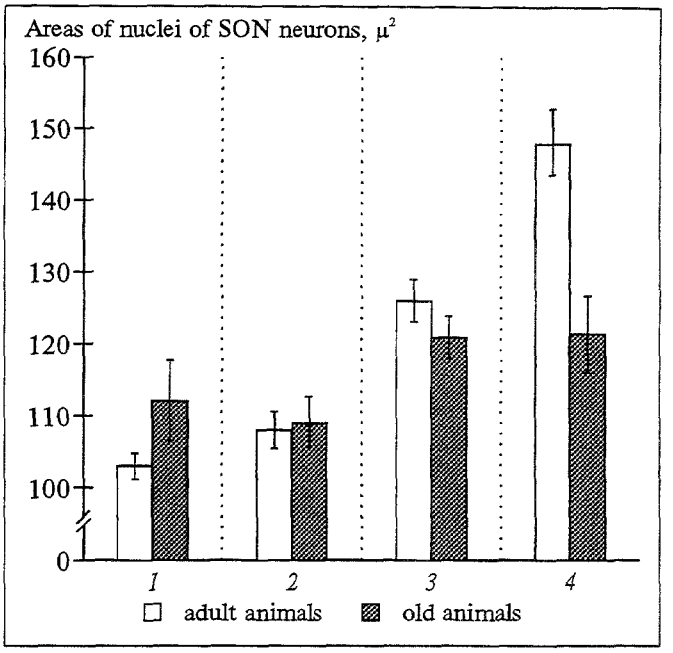

Fig. 2. Areas of nuclei of secretory neurons in SON of rat hypothalamus in aging and under water deprivation. *1*) control (intact animals), *2*) water deprivation, 2 days; *3*) water deprivation, 3 days; *4*) water deprivation, 4 days.

The deprived animals of both age groups demonstrated an elevated AVP content in the cisternal fluid (Fig. 1) and enlarged areas of the secretory neuron nuclei (Fig. 2). The adult animals showed a more pronounced increase of these parameters than did the old animals: whereas the AVP concentration in CSF in the former rose 2.2 times, the same index in the latter rose only 1.4 times. Moreover, the reaction of the hypothalamic nuclei to stress was delayed in the old animals. Whereas the increase in the size of the SON nuclei in adults was observed 2 days after the beginning of the experiment, the same index at the same time in the old animals was not affected and began to rise only after 3 days of deprivation (Fig.2).

A study of the structural features of SON also testified that adult animals exhibit a more active process of VP synthesis and discharge, than old ones. Adult rats demonstrated in the experiment a prevalence of giant, light-colored cells with a loose cytoplasm which contained fine neurosecretory granules in the perinuclear region, and large swollen nuclei with several hypertrophic nucleoli. The findings are in agreement with our previous results indicating that the VP blood content under stress increases much faster in adult animals than in old rats [1].

All these considerations attested to a limited reserves of the hypothalamo-neurohypophyseal system in aging and to age-related decline of its reaction to stress. The elevation of the VP concentration in stress has an adaptive value, which prob-

ably declines in old age. But, in spite of the diminished release of the hormone in the old animals, its effects may be involved in the development of harmful mechanisms which stem from the hypersensitivity of the vascular wall to VP in aging [1]. Thus, pronounced changes in VP regulation occur in aging, especially under stress, that may be of key importance the development of senile disorders and pathological processes. The role CSF plays in the VP regulation of brain functions is probably intensified in aging.

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Catecholamines in the Salivary Glands, Oral Mucosa, and Saliva of Rats with Acute Inflammation of Oral Soft Tissues

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Disordered secretory function of the salivary glands in sialadenitis frequently goes hand in hand with dystrophic changes in the oral mucosa. In aphthous stomatitis, on the other hand, not only is the secretory activity of these glands grossly impaired, but strongly marked changes occur in the excretion of catecholamines with the saliva [4]. Catecholamines are known to exert trophic influences on the mucosa [3]. The purpose of this study was to examine to what extent catecholamine levels are altered in the salivary glands, saliva, and oral mucosa of animals with inflammation of the oral soft tissues.

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MATERIALS AND METHODS

For the experiments, 69 random-bred rats of both sexes weighing 157.3±13.3 g were used. They were divided into six groups: *1*) intact rats with background (basal) saliva secretion; *2*) intact rats with saliva secretion stimulated by pilocarpine injected subcutaneously at 1 mg/kg body weight; *3* and *4*) rats with background saliva secretion at an early (2 h) and a late (24 h) stage, respectively, of acute inflammation of the oral soft tissues produced by injection, under sterile conditions, of a staphylo-

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