ALDEHYDE DEHYDROGENASE ACTIVITY IN BARRIER STRUCTURES OF THE BRAIN

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UDC 611.81:577.152.12

KEY WORDS: aldehyde dehydrogenase, rat brain, capillaries, glial cells.

Aldehydes are substances with high biological activity which, even in minimal concentrations, can modify the metabolism and functions of brain neurons [4, 6], whereas in high concentrations they may have a neurotoxic action [10]. Many of the central effects of exogenous ethanol may be brought about by its primary oxidation product, namely acetaldehyde [5], which is formed chiefly in the liver, from which some of it enters the blood stream. The acetaldehyde concentration in the rat CSF in such cases amounts to 60-80% of its blood level [9], and its concentration in the interstitial fluid of the brain may be 5-20 μM compared with 15-40 μM in the blood stream [14]. Acetaldehyde is detected in brain homogenates only if its blood level exceeds 70 μM [12], or even 200 μM [11]. This suggested that a metabolic barrier for aldehydes exists between the blood and brain tissues, and its function is performed by aldehyde dehydrogenase (AlDH) of the capillary endothelium and glial cells [11, 12]. It has been shown by biochemical methods that the aldehyde-oxidizing capacity of the brain fraction of capillaries and glial cells is 5-6 times higher than that of the neurons [13]; AlDH activity in the fraction of microvessels is 1.5 times higher than in the gray matter of the brain [8]. However, investigations such as these do not exclude the possibility that the fraction of microvessels and gliocytes may be contaminated by neuronal structures, thus concealing regional differences. It was accordingly decided to undertake a histochemical study of AlDH activity in the capillaries and glial structures of different parts of the rat CNS.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino rats weighing 200-220 g. The animals were kept under standard animal house conditions and killed by decapitation at 10 a.m. Blocks of tissue from the forebrain, mid- and hindbrain, and the spinal cord (C_3-C_5) were frozen in liquid nitrogen. Serial frozen sections 25 μ thick were stained for AlDH activity by a method devised by the writers [1]. An incubation medium with acetaldehyde in a final concentration 30 mM was used as the substrate. The relative activity of the enzyme in the structures tested was determined by means of the MTsFU-2MP microscope-photometer (Leningrad Medical Optical Combine) at a wavelength of 580 nm, the diameter of the part of the preparation subjected to photometry being 1.75 μ, and the result was expressed in optical density units $\times 10^3$ (U). Brain structures were identified by reference to the atlas [7]. No fewer than 20 measurements were made in each structure tested; mean values were obtained from five animals and analyzed statistically. AlDH activity was studiedin capillaries of 52 microdivisions of the CNS and also in different types of brain glial structures.

EXPERIMENTAL RESULTS

The writers previously demonstrated considerable heterogeneity of AlDH activity in different types of neuronal structures of the rat CNS: from 16 to 1140 U [2, 3]. Relative AlDH activity in the capillary endothelium was about 200 U, with only small variations in different microdivisions of the brain (Fig. 1a). It was minimal in capillaries of the anterior olfactory nucleus, corpus callosum, and inferior colliculi (140 U), maximal in capillaries of the molecular layer of the olfactory bulbs and the spinal tract of the trigeminal nerve (250-270 U). The distribution of AlDH activity in the capillaries of different microdivisions of the CNS correlated with total activity of the enzyme in these micro-

Institute of Biochemistry, Academy of Sciences of the Belorussian SSR, Grodno. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 106, No. 9, pp. 283-284, September, 1988. Original article submitted April 29, 1987.

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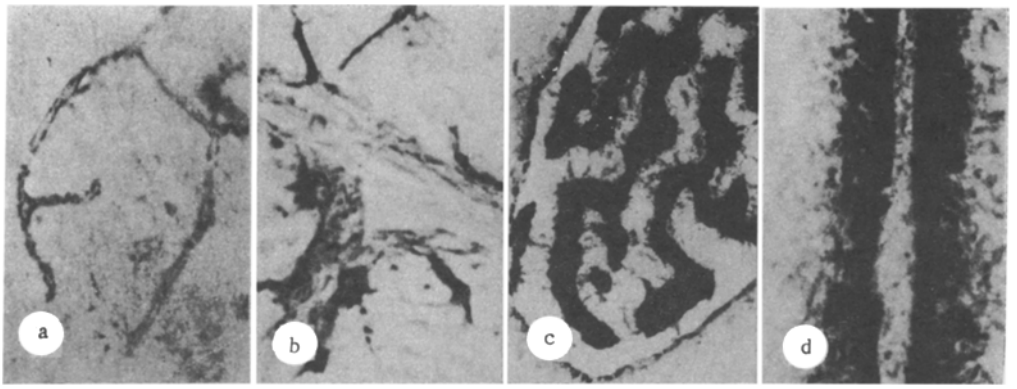

Fig. 1. AlDH activity in barrier structures of the rat brain. Stained by the method in [1]. a) Capillaries of parietal cortex. 530 ×; b) astrocytes of lateral lemniscus of spinal cord. 530 ×; c) vascular and ciliated ependymocytes of lateral ventricle. 240 ×; d) ependymocytes of third ventricle. 530 ×.

divisions ($r = 0.568$; $p < 0.001$), but not in the perikarya of the neurons in these same divisions ($r = 0.103$). AlDH activity in astrocytes of the CNS varied much more; it was maximal in astrocytes of the spinal cord (Fig. 1b). AlDH activity in the glial structures of the brain was respectively (in $U \cdot 10^3$; M ± m): 550 ± 32 in ciliated ependymocytes of the central canal of the spinal cord, 614 ± 25 in the lateral ventricle, 756 ± 71 in the fourth ventricle, 1035 ± 80 in the third ventricle, 756 ± 61 in the tanycytes of the third ventricle, 1258 ± 82 in the ependymocytes of the choroid plexus of the lateral ventricle, 1312 ± 63 in the fourth ventricle, 193 ± 32 in astrocytes of the corpus callosum, 180 ± 5.8 in the internal capsule, 273 ± 26 in the white matter of cerebellum, 404 ± 37 in the lateral lemniscus of the spinal cord, 572 ± 64 in the pia mater; 307 ± 38 in the duramater; 417 ± 53 in the oligodendrocytes of the motor nuclei of the spinal cord, and 582 ± 38 in the facial nerve nuclei. Thus in both structural components of the blood-brain barrier AlDH activity was higher than in the white matter of the brain and in most interneurons, but lower than in the effector and receptor neurons of the CNS [2, 3].

The relative activity of the enzyme in ependymocytes of the vascular plexuses producing CSF was higher than in other brain structures. In the ependymocytes lining the ventricles and canals of the CNS AlDH activity also was quite high; it was maximal in the ciliated ependymocytes of the third ventricle and minimal in ependymocytes of the central canal of the spinal cord (Fig. 1c, d). It was high also in the satellite oligodendrocytes of the motor nuclei of the brain stem and spinal cord and also in the astrocytes of the pia mater.

The data described above demonstrate the existence of at least three metabolic barriers for aldehydes in the rat CNS at the systemic level: between blood and nerve tissue (represented by AlDH of the capillary endothelium and surrounding astrocytes), between the blood and CSF (AlDH of the ependymocytes of the vascular plexuses), and between the CSF and nerve tissue (AlDH of the ependymocytes lining the cavity in which the CSF circulates), and at the level of individual microdivisions, between the interstitial fluid and neurons (AlDH of the satellite oligodendrocytes). The functioning of these barriers can be judged by the concentration gradient of aldehydes in the order: blood—CSF—tissue fluid—nerve tissue. If AlDH in the brain is inhibited, the effectiveness of functioning of these barriers is sharply reduced [9, 14], leading to injury to the nerve tissue under conditions of hyperaldehydemia [10]. Under physiological conditions the AlDH of the barrier structures of the rat brain can be regarded as a mechanism ensuring preservation of the aldehyde pools of the brain and peripheral tissues, and also the utilization of aldehydes formed during natural metabolism actually in the capillaries and glial cells.

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