REGIONAL DISTRIBUTION OF LACTATE DEHYDROGENASE ISOENZYMES IN HUMAN BRAIN

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ABSTRACT

The regional distribution of LDH isoenzymes was studied in human brain tissues. In all the regions the anodic fractions were predominantly noted. There were wide variations in the distribution of LDH_5 fraction, with the highest activity noted in the optic nerve, caudate nucleus and putamen.

INTRODUCTION

VARIATIONS in oxidative enzymes mediating in several metabolic pathways in brain have been noted at various stages of development and also in different regions of brain. Among the various enzymes, extensive studies have been carried out on lactic dehydrogenase (LDH) and its isoenzymes (IE). Mammalian brains show a predominance of fast moving isoenzymes and the proportion of these fractions increases with the level of phylogenetic development[1].

Normal human brain shows predominantly the fast moving isoenzymes LDH_1, LDH_2 and LDH_3 with very little LDH_4 and LDH_5. As it is difficult to obtain fresh tissues from different regions of the human brain, these studies have been carried out on the laboratory animals. However, the limited number of reports available on human material has been confined only to a few areas of the brain. The distribution of LDH IE in different topographic locations of human brain is studied with a view to determine the possible variations of LDH isoenzymes in cerebrospinal fluid (CSF) and serum following pathological involvement of different parts of brain. This study reports the regional distribution of LDH IE in normal human brain.

MATERIALS AND METHODS

Human brain tissues were obtained at autopsy (after obtaining consent from the near relatives) 4–6 hr after postmortem from patients who succumbed to cervical cord injury or sudden death due to non-neurological causes. The ages of the diseased were 5, 15, 30, 50, 55 and 58 years. Samples from various parts of the cerebral isocortex and other areas were collected, washed in saline and then stored at $-20°C$. Subsequent analysis was, however, completed within 48 hr.

A 5% homogenate in cold distilled water was spun at low speed using a refrigerated centrifuge. The supernatant was processed to determine the total LDH activity by the method of Wroblewsky and La Due[2]. The LDH isoenzymes were separated by cellulose acetate electrophoresis at pH 7.4 and visualized by PMS-NBT method of Rosalki[3]. Quantification was done by using a densitometer and the results expressed as percentage of the total activity. The total LDH activity is expressed as units per litre of the homogenate. The unit is defined as the amount of enzyme that catalyzes the conversion of 1 μmol of substrate per minute at 30°C.

RESULTS

The total LDH activity was slightly higher in the parietal lobe (motor cortex), the occipital lobe, the midbrain, and the medulla, when compared with the rest of the cerebral cortex. The levels were somewhat low in thalamus and pineal gland (however, the values were from one sample only) (table 1).

In all the areas LDH_1, LDH_2 and LDH_3 were the predominant fractions. However, LDH_5 showed a differential pattern. The various areas of the cerebral cortex, thalamus and different regions of brain stem had low levels of LDH_5. The putamen and caudate nuclei, though anatomically contiguous to thalamus, showed higher LDH_5 indicating the capacity to gain energy via the anaerobic glycolysis. The low LDH_5 seen in dentate nucleus (located in cerebellum) is in keeping with the high neuronal density. The optic nerve was distinct in having very high level of LDH_5.

Table 1 *Regional distribution of LDH isoenzyme(*) in normal human brain**

Region	No.	Total LDH (U/L)	LDH_1 (%)	LDH_2 (%)	LDH_3 (%)	LDH_4 (%)	LDH_5 (%)
Frontal	6	245 ± 48	21.6 ± 3.0	26.9 ± 3.0	24.8 ± 2.2	20.9 ± 2.2	5.8 ± 1.0
Temporal	6	242 ± 32	21.6 ± 2.9	25.9 ± 3.4	26.2 ± 3.2	20.8 ± 3.2	5.5 ± 1.0
Parietal	6	260 ± 38	22.5 ± 3.0	25.5 ± 2.0	26.5 ± 3.0	20.0 ± 3.8	5.5 ± 2.4
Occipital	6	254 ± 32	22.4 ± 3.2	26.8 ± 5.2	25.6 ± 4.8	19.8 ± 2.8	5.4 ± 1.8
Hippocampus	1	225	22.7	28.1	30.6	11.0	7.6
Cerebellum	6	224 ± 38	24.8 ± 2.4	24.4 ± 5.0	24.5 ± 4.0	20.5 ± 1.8	5.8 ± 1.8
Dentate Nucleus	1	210	23.1	29.0	30.0	13.3	4.6
Thalamus	1	156	24.0	25.4	26.0	19.3	5.3
Caudate Nucleus	1	208	20.0	26.0	32.0	13.1	8.9
Putamen	1	240	20.3	22.2	26.2	21.4	10.4
Midbrain	5	280 ± 40	20.4 ± 4.2	26.4 ± 2.8	26.1 ± 3.2	21.6 ± 3.2	5.5 ± 2.2
Pons	6	240 ± 52	22.5 ± 2.9	26.3 ± 3.2	26.8 ± 3.8	18.8 ± 2.8	5.6 ± 2.0
Medulla	6	260 ± 44	22.6 ± 4.2	28.2 ± 4.4	26.9 ± 4.2	16.2 ± 2.2	6.1 ± 2.0
Spinalcord	6	200 ± 50	24.0 ± 4.0	30.0 ± 4.4	26.0 ± 2.4	12.4 ± 2.2	7.6 ± 2.0
Optic Nerve	1	220	15.6	19.8	25.3	21.8	17.5
Pineal Gland	1	148	16.5	30.9	28.8	18.6	5.2

*5, 13, 30, 50, 55 and 58 years age; (*) Values are mean and S.D.

DISCUSSION

Many workers have shown the predominance of anodic pattern of LDH isoenzymes in human brain[4-6]. Studies using rabbit brain have shown marked anodal pattern in the brain stem, while the cerebral hemisphere and the basal ganglia showed an even distribution of the isoenzyme fractions[7,8]. Van der Helm *et al*[9] reported that isoenzyme pattern was the same in different regions of the human brain, but subsequently using microtechniques he reported slightly different distribution. Some of these variations could be due to differences in the technique employed for estimation.

The present study showed that the isoenzyme pattern of various areas of cerebral cortex and cerebellum was essentially similar and showed predominance of anodic pattern. Our findings on caudate nucleus and putamen agree with those on autopsy material[10]. The caudate nucleus and putamen are among the regions showing highest oxidative enzyme activity in the brain[11]. The high levels of LDH_5 noted in these areas have probably a protective action against anoxic damage.

A predominance of LDH_5 in retina, lamina quadrigemina anterior, optic chiasma and optic tract has been noted in contrast to other areas in the rat. It is suggested that the higher LDH_5 content of the visual pathway is favourable to neuronal differentiation[12]. High levels of LDH_5 (17.5%) noted in our study on the human optic nerve also have similar implications.

The differences in the profile of isoenzymes in regions of close proximity in contrast to similarity in the pattern of isoenzymes in regions of functional integration, though anatomically apart, e.g. 1) retina, optic nerve, quadrigeminal body, 2) cerebral cortex and thalamus, 3) caudate nucleus and putamen suggest that the varying patterns reflect functional rather than morphological differences.

From the present observations it is obvious that studies on human material are essential for meaningful inferences on clinical material, rather than extrapolation of the data from lower animals. Additional work in this line, using larger sample size, is needed.

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