THE QUANTITATIVE HISTOCHEMISTRY OF BRAIN

IV. LACTIC, MALIC, AND GLUTAMIC DEHYDROGENASES*

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The brain is an exceedingly complex histological structure, and, while some information is available concerning the metabolism of brain as a whole, very little is known concerning the metabolism of its component parts. In view of morphological and functional differences within the nervous system, it seems likely that the axons, dendrites, and cell bodies, as well as glial elements and even homologous parts of different neurons, may differ in their metabolic capacity. Previous reports indicate marked differences in the quantitative distribution of a number of enzymes, as well as of lipide and phosphorus fractions (1–6).

This is a report of the histochemical distribution in a few regions of the brain of lactic, malic, and glutamic dehydrogenases (LDH, MDH, and GDH). For this purpose sensitive and simple micromethods (requiring 0.2 to 3 γ of dried brain) for assaying these enzymes were developed.

Materials and Methods

Quantitative measurements of the activity of each enzyme have been made on relatively minute pieces of young adult rabbit brain or cord. These pieces were cut out from frozen-dried histological sections under a dissecting microscope to provide histologically distinct samples which had been neither fixed nor embedded (1). Samples were obtained from Ammon's horn, cerebellar vermis, striate cortex, hypothalamus, retina, medulla, and cervical spinal cord. The dissected fragments (0.2 to 5 γ) were weighed (1) and transferred directly to assay tubes. Some samples were also extracted with alcohol and hexane to obtain the fat-free weights (1).

Enzyme Measurements—The enzyme methods that were used are based on the rate of reduction of diphosphopyridine nucleotide (DPN^+) measured at 340 mμ (7) in a Beckman spectrophotometer. Special microchemical techniques and tools have been described previously (2). The flat bottomed assay tubes were made from 7 mm. Pyrex tubing selected to fit snugly in a special black plastic holder (2). Selection for uniform inner

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diameter (0.474 cm. ± 1 per cent) was based on readings with a colored solution.

The tube containing the tissue fragment is placed in ice water and the complete substrate reagent (70 to 250 μl.) is added. After 1 minute the tube is tapped or gently vibrated (2) and placed in a rack in a water bath at 32° ± 0.2°. Each tube is wiped and read after 1 minute for temperature equilibration and again after appropriate intervals. With a light path of 0.474 cm. and 100 μl. of substrate a change in optical density of 0.2 per hour corresponds to $(0.2 \times 10^{-4})/(6280 \times 0.474) = 6.73 \times 10^{-9}$ mole of DPN^+ reduced per hour ($\epsilon = 6280$ (8)).

The substrate reagents are prepared in quantity without the DPN^+ and are stored frozen. The DPN^+ is added just before use as a dry powder as follows: 0.7, 1.3, and 3.5 mg. per ml. (calculated as pure DPN^+) for LDH, MDH, and GDH, respectively. In this study the substrates consisted of (*a*) 85 per cent racemic sodium lactate (Mallinckrodt Chemical Works, St. Louis), (*b*) potassium L-malate prepared from L-malic acid (Nutritional Biochemicals Corporation, Cleveland), which had been recrystallized (from warm ethyl acetate by the addition of petroleum ether) to remove an inhibitor present in some samples, and (*c*) monosodium L-glutamate (Nutritional Biochemicals Corporation). The DPN^+ was either 65 or 90 per cent (Sigma Chemical Company, St. Louis).

The composition of the buffer-substrate mixture for each enzyme measurement is given in Table I, with the amounts of tissue convenient to use in each assay. At the high dilutions of rabbit brain employed neither reduction of DPN^+ by endogenous substrates nor reoxidation of reduced DPN^+ was observed. Keto acid formation has been shown to equal exactly DPN^+ reduction under the assay conditions.[1]

The recommended assay conditions are based on studies of the properties of rabbit brain LDH, MDH, and GDH (Table I, Fig. 1). All of these enzymes are measured in the less favorable direction as far as equilibrium is concerned. However, in the case of LDH and MDH, both the high substrate levels and the high pH result in initial velocities of the same order of magnitude as those in the reverse direction.[2]

[1] Robins, E., Roberts, N. R., Eydt, K. M., and Lowry, O. H., to be published.

[2] The maximal initial velocities depend on both the equilibrium constants and the respective K_m values (10). A high pH optimum and differences in K_m have a considerable effect on the ratio of maximal initial velocities. For example, in the case of LDH, at pH 7, with equal DPN^+ and reduced DPN^+, the equilibrium ratio of lactate to pyruvate is about 30,000:1 (11). However, at the pH optimum of 9.2 this equilibrium ratio is much more favorable, about 200:1. In addition, the K_m for lactate is about 500 times larger than the K_m for pyruvate. As a result, at pH 9.2, the initial velocities should be approximately equal. A similar result is obtained for MDH with a recent value for the MDH equilibrium constant (12).

TABLE I

Constants and Assay Conditions for Three Dehydrogenases of Rabbit Brain

	LDH	MDH	GDH
Constants of enzymes			
K_m for substrate, mM	5.0*	1.3	0.85
" " DPN+, mM	0.056	0.3	1
Optimal pH	9.2	10.2	8.1
Q_{10}	2.2	2.3	
Assay conditions			
Buffer (at pH optimum of enzymes), M	0.1 glycine	0.1 glycine	0.05 Veronal
Substrate concentration, M	0.2 (D, L)	0.2 (L)	0.03 (L)
DPN+ concentration, mM	1	2	5
Activity of whole rabbit brain, *moles per kilo dry weight per hr.*†	7	32	0.8
Weight of dry brain for convenient rate in 100 μl., γ	1.5	0.3	10

* Calculated for concentration of L-lactate.

† Rabbit brain contains 22 per cent dry weight.

Under the conditions chosen all three reactions are linear until the optical density increase exceeds 0.200. The assays are proportional to time up to 2 hours and to the amount of rabbit brain homogenate added, provided that the optical density increase does not exceed 0.200 (Fig. 2). The sensitivity of the methods is indicated by the high dilutions employed.

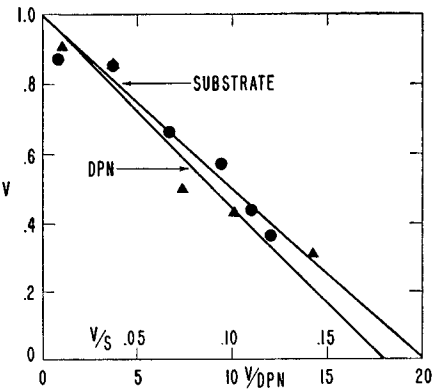

FIG. 1. Substrate-velocity and DPN-velocity relationships for LDH. The plot is made according to Eadie (9). V is expressed as a fraction of $V_{max.}$. S and DPN+ are expressed in millimoles per liter. The intercepts on the abscissa are the reciprocals of the respective K_m values in the same terms.

The sensitivity could be increased by reducing the volume and by increasing the incubation temperature to 38° and the incubation time. In the case of MDH, such modifications should permit analysis of 0.0015 γ of brain (dry weight); this is the weight of a single moderate sized cell. GDH is much less active than the other two enzymes in brain. Nevertheless, by using an incubation time of 1 hour and a 70 μl. volume about 3 γ of brain (dry weight) are conveniently analyzed.

Carbonyl-trapping reagents such as cyanide, hydrazine, and hydroxylamine have been found by previous workers employing other assays to accelerate reaction rates of these enzymes by removing the keto acids formed. Under the conditions proposed, however, all of these substances

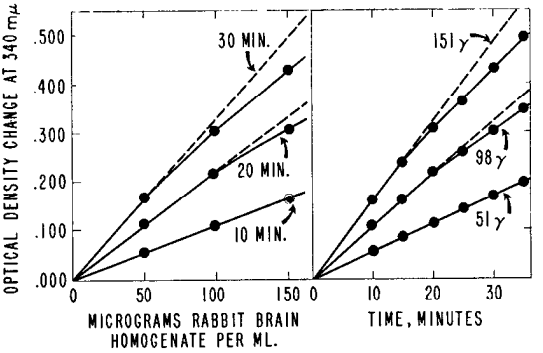

FIG. 2. Linearity of assay for LDH activity with respect to quantity of rabbit brain and time. These assays were carried out in a 1 ml. volume. The concentration of wet brain during assay is indicated.

were inhibitory. In 0.5 M cyanide (at pH 9.2) which has been used previously in an assay for lactic dehydrogenase in which oxygen consumption was measured (13), no lactic dehydrogenase activity could be demonstrated spectrophotometrically. With 1.1, 2.5, and 4.5 mmoles per ml. of cyanide the velocity was 43, 21, and 8 per cent, respectively, of the rate without cyanide. (A small increment in optical density owing to complex formation between DPN^+ and cyanide (14) was observed. Lactate and brain homogenate were not added until the optical density became constant.) Nicotinamide had no effect on the reaction rates.

Purification of Enzymes and Addition of Purified Enzymes to Assay System with Homogenate—The estimation of enzyme concentration based on measurement of a catalytic property of the enzyme would be subject to serious errors if accelerators or inhibitors of reaction rate were present in the tissue being analyzed. The three enzymes from rabbit brain homogenate have, therefore, been partially purified, and assays have been carried out to see

whether the activities of the purified enzymes and homogenates are strictly additive when combined.

LDH and MDH were purified together, each 10- to 15-fold (based on protein), by reprecipitation with $(NH_4)_2SO_4$ between 2.1 and 2.9 M at pH 7.5. GDH precipitated between 1.25 and 1.70 M. Several fractionations between these limits yielded a preparation 100-fold purified in 90 per cent yield. For all three enzymes the sum of the rates obtained for purified enzyme alone or for homogenate alone was equal (within analytical error) to the rate obtained when the assay was performed with purified enzyme plus homogenate.

Effects of Freezing, Drying, and Storage on Apparent Enzyme Concentration—MDH and LDH in homogenates showed no loss of activity on freezing and drying. In fact, in some homogenate samples activity increased 5 or 10 per cent on freezing and another 5 or 10 per cent on freeze-drying. Since the initial values were low in these samples, these increases can probably be attributed to incomplete homogenization and better disruption of the tissue by freeze-drying.

These two enzymes also survived storage quite well in the frozen-dried state. Loss of activity on standing at room temperature (25°) for 2 days was 6 to 8 per cent both in homogenates and in samples from sections, and homogenates lost about 40 per cent during 2 weeks at room temperature. No significant decrease was observed on storage at −20° for 13 days. Samples of zona radiata of Ammon's horn which had been stored at −20° for about a year had 92 per cent of the LDH and 90 per cent of the MDH activity of newly prepared samples (from another rabbit).

The stability of GDH was not tested so extensively. However, 1 year-old samples of sections from radiata of Ammon's horn contained 125 per cent of the activity of a 1 week-old sample from another rabbit.

The analyses reported in this paper were carried out on samples from sections stored in the deep freeze for a maximum of 2 weeks and exposed to room temperature for a maximum of 8 hours.

Results

Ammon's Horn—This is a part of the hippocampus (allocortex) which is divided sharply into six layers of the following thickness and composition: (1) alveus, 200 μ, myelinated fibers, (2) oriens, 250 μ, non-myelinated axons and dendrites, (3) pyramidalis, 50 μ, densely packed cell bodies of small pyramidal cells, (4) radiata, 400 μ, closely packed dendrites, (5) lacunosum, 150 μ, dendrites plus myelinated fibers, (6) molecularis, 200 μ, neuropile, *i.e.* terminal arborizations of dendrites and axons.

The dendrite and non-myelinated fiber areas are richest in both LDH and MDH (Table II), especially on a fat-free basis (Fig. 3). It is to be noted

TABLE II

Dehydrogenases of Ammon's Horn

The enzyme activities are expressed as moles per kilo dry weight per hour. The values are the averages of five to eight analyses each (standard errors indicated). Fat-free weight is per cent of total dry weight.

	LDH	MDH	GDH	Fat-free weight	$\frac{MDH}{LDH}$	$\frac{LDH}{GDH}$
Alveus (myelinated fibers)	6.94 ±0.37	24.8 ±2.2	0.662 ±0.055	38	3.6	10
Oriens (axons and dendrites)	18.2 ±0.8	63.0 ±3.2	0.638 ±0.061	59	3.5	28
Pyramidalis (cell bodies)	21.8 ±0.6	54.8 ±1.9	0.363 ±0.016	78	2.5	60
Radiata (dendrites)	19.8 ±0.7	57.1 ±0.9	0.477 ±0.055	62	2.9	41
Lacunosum (dendrites and myelinated fibers)	14.5 ±0.4	50.4 ±1.8	0.443 ±0.053	49	3.5	33
Molecularis (neuropile)	15.3 ±0.4	61.0 ±1.2	0.962 ±0.080	61	4.0	16

that on a fat-free basis the cell body layer is not conspicuously rich in either enzyme. In fact the myelinated fiber layer, which is quite low in both activities on a total dry weight basis, is almost as rich on a fat-free basis as the cell body layer (Fig. 3). The distribution of these two enzymes in Ammon's horn resembles that previously reported for aldolase, acid phosphatase, and adenosinetriphosphatase (4).

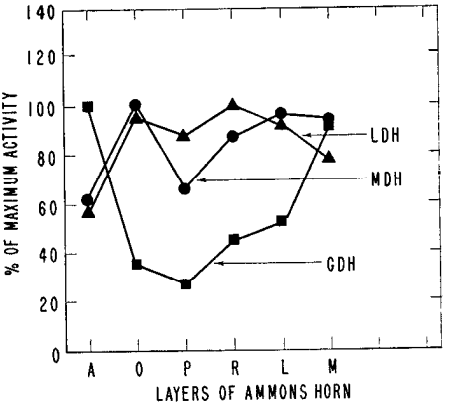

FIG. 3. Distribution of enzymes in layers of Ammon's horn, expressed in terms of activity per fat-free dry weight and plotted in per cent of maximal activity for each enzyme. *A* = alveus, *O* = oriens, *P* = pyramidalis, *R* = radiata, *L* = lacunosum, *M* = molecularis (see the text for description of the layers).

GDH has an entirely different distribution. The myelinated fibers and neuropile are relatively very rich in GDH. The cell body layer, the lowest area, had only one-fourth the activity of the myelinated fibers on a fat-free basis (Fig. 3).

Cerebellum, Striate Cortex, Supraoptic Nucleus, and Hypothalamus (Table III)—The cell body (granular) and molecular layers of cerebellum and striate cortex are very similar to corresponding areas in Ammon's horn in regard to the activities of LDH and MDH. The supraoptic nucleus and the hypothalamic area immediately adjacent to it were analytically almost indistinguishable and contain lower activities of both LDH and MDH than the other cell body and non-myelinated fiber-dendrite areas. The relative proportions of activities are also slightly different, the MDH:LDH ratios being 4.4 and 4.7, compared to values of 2.5 to 4.0 in Ammon's horn, cerebellum, and striate cortex. Abood *et al.* have reported (15) that respiratory and glycolytic activity in supraoptic nucleus is the same as that found in other hypothalamic areas.

Optic Nerve and Retina—Optic nerve and optic tract (obtained from the hypothalamic sections) contain unusually high LDH activity (Table III). These fiber tracts are as rich in this enzyme on a dry weight basis as cell body and molecular layers elsewhere and contain about twice as much activity as these areas on a fat-free dry weight basis. The LDH values are 2 to 6 times higher than those of other myelinated fiber tracts analyzed (Table III). Malic dehydrogenase is very low in optic nerve and tract, perhaps one-fourth of the level in alveus. The MDH:LDH ratio of 0.4 is extraordinarily different from all other regions of the nervous system examined. Consequently, some relatively crude data were obtained for the layers of rabbit retina. Only a partial separation of layers was attempted. Nevertheless, most of the data were surprisingly consistent and striking. The retinal fibers (Layer 9) and the adjacent Layers 6, 7, and 8 (composed of the ganglion cells, whose axons form the retinal fiber tract and optic tract, the inner reticular (synaptic) layer, and the inner nuclear layer of bipolar cells) have a composition in keeping with the unusual composition of the optic tract. Layers 6 to 8 have the highest LDH activity found in this study and have an MDH:LDH ratio of about 0.4.

The next two layers, the outer reticular and outer nuclear layer, have a much lower LDH activity and an extremely high MDH activity which gives a ratio of 4.9. The samples of the rod layer appeared to fall into two groups, one with low MDH activity and the other with extraordinarily high amounts of this enzyme and an MDH:LDH ratio of at least 14. From data on monkey retina[3] it is clear that the high and low MDH

[3] Lowry, O. H., and Roberts, N. R., to be published.

activities correspond to the inner and outer rod segments. The chorioid is low in both enzymes.

Myelinated Fibers—The other myelinated fiber tracts analyzed are not similar to optic nerve and tract (Table III). They seem to group two

TABLE III

Dehydrogenases in Various Regions of Rabbit Brain

The values are averages of usually six analyses each and are expressed as moles per kilo dry weight per hour (standard errors indicated).

	LDH	MDH	$\frac{MDH}{LDH}$		LDH	MDH	$\frac{MDH}{LDH}$
Cerebellum				Retina			
Molecularis	16.5 ±0.6	60.2 ±4.2	3.7	Fibers	28.6 ±0.6	11.2 ±0.5	0.39
Purkinje cell layer	17.2 ±1.0	60.2 ±4.8	3.5	Ganglion + inner reticular + inner nuclear	51.5 ±3.5	27.2 ±1.1	0.53
Granular layer	14.7 ±0.5	58.5 ±4.2	4.0	Outer reticular + outer nuclear	19.5 ±0.6	95.2 ±5.4	4.9
Medulla (myelinated fibers)	6.94 ±0.24	19.9 ±1.3	2.9	Rods* (*a*)	11.2	157	14
Striate cortex				" (*b*)	4.3	11	2.5
Molecularis (I)	16.0 ±0.3	55.3 ±1.3	3.5	Chorioid	5.33 ±0.21	9.67 ±0.43	1.8
Layer II	15.8 ±0.4	50.7 ±0.7	3.2	Pyramidal tract (medulla)	4.89 ±0.18	13.1 ±0.18	2.7
" V	15.7 ±0.3	51.2 ±1.7	3.3	Spinal cord			
" VIII (myelinated fibers)	4.37 ±0.15	11.0 ±1.0	2.5	Posterior columns	3.87 ±0.12	8.08 ±0.69	2.1
Hypothalamic area				Ventral root	2.59 ±0.14	8.13 ±0.42	3.1
Hypothalamus	9.25 ±0.27	43.7 ±1.7	4.7	Dorsal "	2.66 ±0.28	7.11 ±0.53	2.7
Supraoptic nucleus	10.55 ±0.34	46.8 ±0.9	4.4	" " ganglion	9.81 ±0.34	36.1 ±1.1	3.7
Optic tract	15.8 ±0.22	4.93 ±0.33	0.31				
" nerve	16.4 ±0.4	7.66 ±0.28	0.47				

* The values for the rod layer fell in two groups which have been arbitrarily averaged separately (see the text).

ways: (1) those which are relatively low in both MDH and LDH (Layer VII of striate cortex, ventral and dorsal root, pyramids, posterior column) and (2) those which are relatively high in both MDH and LDH (myelinated layer of cerebellum, alveus of Ammon's horn). There did not seem to be any simple relationship to the content of total lipide. In sections of a dor-

sal root ganglion in which no nerve fibers could be seen the activity of both LDH and MDH was considerably higher than in the dorsal root, but was substantially lower than in other cell body areas.

Aldolase and Fumarase in Myelinated Fibers—Some of the myelinated fibers were analyzed for another glycolytic enzyme, aldolase, and another enzyme of the Krebs cycle, fumarase. In general LDH activity was paralleled by aldolase activity (LDH-aldolase ratio relatively constant) and

TABLE IV

Aldolase, Fumarase, and Relationships with LDH and MDH of Five Fiber Tracts

Data for aldolase and fumarase expressed as moles per kilo fat-free weight per hour. They are the average of about six analyses each (standard errors indicated). Fat-free weight is per cent of total dry weight.

	Fat-free weight	Aldolase* (A)	Fumarase* (F)	$\frac{MDH}{LDH}$	$\frac{F}{A}$	$\frac{LDH}{A}$	$\frac{MDH}{F}$	$\frac{LDH}{A}$ adjusted†
Retinal fiber layer	39.2	12.0 ± 0.3	10.6 ±0.2	0.39	0.88	6.1	2.5	6.5
Optic tract	28.7	7.8 ± 0.1	7.0 ±0.2	0.31	0.90	7.1	2.5	7.4
Cerebellar myelinated fibers	32.3	5.0 ± 0.4	20.4 ±2.7	2.9	4.1	4.3	3.0	6.2
Posterior columns	24.0	3.24 ± 0.12	10.0 ±0.3	2.1	3.1	5.0	3.4	6.7
Alveus of Ammon's horn	38.3	4.3‡	16.6‡	3.6	3.9	4.2	3.9	6.9

* These determinations were kindly carried out on our material by Dr. Mei-Ling Wu using methods previously described (3).

† Calculated by subtracting 2.5 per cent of the malic dehydrogenase values from the aldolase values before calculating the ratios (see the text).

‡ Data from Lowry *et al.* (4).

MDH activity was paralleled by fumarase activity (MDH-fumarase ratio relatively constant) (Table IV).

DISCUSSION

It will be noted that very high activities are obtained for both LDH and MDH with the assay systems employed. The MDH activity calculated at 38° would be 60 moles of DPN^+ reduced (or malate oxidized) per kilo dry weight per hour. This may be compared to earlier values for MDH based on oxygen consumption, *e.g.* 3 moles per kilo dry weight per hour for rabbit brain (16) or mouse brain (17), and to the maximal rate of glycoly-

sis or respiration in intact brain, neither of which is more than 0.5 mole per kilo dry weight per hour. Even at pH 7 both LDH and MDH activity are quite high compared to the over-all metabolism. The earlier measurements of these dehydrogenases were undoubtedly limited by the accessory enzymes required in more complex systems, inability to work at an optimal pH, and some accumulation of keto acids in spite of precautions to remove them. However, a recent determination of GDH in rat brain (18), 0.4 mole per kilo dry weight per hour, also based on oxygen consumption, is in fair agreement with our value.

In regard to the histochemical data, the surprisingly high activity of several enzymes in the myelinated layer of Ammon's horn (4), and the high respiratory and glycolytic activity of white matter in general (19), have been previously noted. This study shows that LDH and MDH may also be rather active in fiber tracts, particularly when calculated on a fat-free basis. The large differences found among different myelinated tracts indicate that different types of fibers may vary widely in their metabolism. Clearly the histological composition of each tract in regard to both fibers and glia will need to be evaluated before enzymes can be safely assigned to particular structures in these tracts.

There is some suggestion from the data presented that metabolic activities in nerve fibers may mirror in part the activities in the cell bodies from which the fibers originate. For example, the low MDH and LDH activity in dorsal root fibers is paralleled by relatively low activity in dorsal root ganglion cell bodies, and the high LDH and MDH activity of optic nerve and tract is reflected in similar findings in the retinal ganglion cell layer. Nevertheless, it also seems probable that fibers have a special metabolism, not related to the metabolism of the cell bodies. The very high GDH activity in the myelinated layer contrasted with very low activity in the cell body layer of Ammon's horn may be such an example.

Warburg, Posener, and Negelein (20) first reported that both glycolysis and respiration in intact retina were unusually high. They stated (1924), "If we consider how different the formed elements of the retina are, then we can hardly assume that all elements contribute in the same measure to the special metabolism of the organ. But if we compute the glycolytic action of the organ on its individual parts—perhaps on the sensory epithelium—then we arrive at values which are incommensurable with the metabolism of other body cells." The present data for LDH and MDH seem to confirm at least the first part of this speculation. High LDH activity was found only in ganglion (and inner nuclear) cells and their axons. Since these cells and axons also have a very low MDH activity, they presumably have a predominantly glycolytic metabolism. Deeper in the retina are structures (outer nuclear cells, rods, pigment epithelium) with

an unusually high MDH activity and a low LDH activity. Presumably their metabolism is predominantly oxidative. It seems probable, therefore, that the high glycolytic and respiratory activities of intact retina are manifestations of metabolic processes occurring in different cells, and the high DPN^+ content of all retinal layers (21)[4] may be related to different dehydrogenases in different cells. This unusual chemical organization and the fact that the retina is a particularly accessible portion of the central nervous system having a highly organized structure suggest that valuable information about the chemical relations of a special multineuron chain might be learned here and invite further quantitative histochemical study.

It would be a great simplification in studies of this kind if it were possible to use the measurement of a single enzyme in a metabolic pathway as a measure of the extent to which that metabolic pathway is functionally active. This not only requires the reasonable but unproved assumption that enzyme activity *in vitro* is directly related to functional activity *in vivo*, but also requires that the enzymes along a given pathway be present in a nearly constant ratio unless there is an intervening fork in the metabolic path. Some support for this idea is provided in the approximate parallelism noted between LDH and aldolase and also between MDH and fumarase in fiber tracts of widely different absolute enzyme activities (Table IV). Since aldolase is on the pathway leading to pyruvate for both oxidation and lactic acid formation, strict parallelism between aldolase and LDH might not be expected. Instead, aldolase activity should be a function of both LDH and of the citric acid cycle enzymes. The data are actually in good agreement with the empirical equation, aldolase = LDH/7 × MDH/40 (Table IV).

SUMMARY

1. Micromethods for determination of LDH, MDH, and GDH in 3 γ of brain (dry weight) or less have been developed. The assays are based on measurement of DPN^+ reduction in the presence of appropriate substrate. Optimal assay conditions were established through kinetic studies of these enzymes in rabbit brain.

2. Quantitative data have been obtained for LDH and MDH in six layers of Ammon's horn, four layers of cerebellum, four layers of striate cortex, supraoptic nucleus, hypothalamus, optic nerve and tract, four layers of retina, four additional myelinated fiber tracts and dorsal root ganglion cells. GDH has been determined only in the layers of Ammon's horn.

3. The distribution of LDH and MDH in Ammon's horn parallels the

[4] The assumption that the DPN^+ content of the retinal fibers is comparable to that of other nerve fibers and therefore low (21) may not be valid, in view of the very high lactic dehydrogenase in these fibers.

distribution of aldolase. The non-myelinated fiber and dendrite layers are particularly rich in these activities. GDH, in sharp contrast, occurs principally in the myelinated fibers and molecular layer of Ammon's horn.

4. Three types of fiber tracts have been distinguished on the basis of LDH and MDH activity.

5. Retinal ganglion cells and their axons (optic nerve) are very rich in LDH and very poor in MDH. Some structures deeper in the retina have a high MDH activity and a low LDH activity. The high glycolytic and respiratory rates in intact retina are, therefore, probably manifestations of different metabolic processes in different cells.

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