Changes of Hexokinase in the Enzyme Activity Pattern of Muscle in Human Myotonia Congenita and in Experimental Myotonia of the Rat*

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Summary. Enzyme activity patterns of selected key enzymes in energy-supplying metabolism were determined in muscle biopsy specimens of patients with myotonia congenita (autosomal recessive inherited) and in skeletal muscle of rats with 20,25-diazacholesterol-induced myotonia. A close correlation exists in muscles of normal humans between the activity levels of hexokinase and citrate synthase. This correlation is disturbed both in human and experimental myotonia and consists in an increase of the relative hexokinase activity in the human and a decrease in the rat.

Key-words: Myotonia congenita, experimental myotonia, 20,25-diazacholesterol, enzyme activity pattern, constant enzyme proportions, hexokinase, citrate synthase, energy-supplying metabolism.

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Enzymological studies on muscle disorders have provided etiologic explanations of some myopathies which are the expression of enzyme defects. However, the majority of myopathies cannot yet be ascribed to such defects. Nevertheless, it may not be excluded that metabolic disorders are concomitant in other myopathies and may be reflected at the level of enzymatic organization of energy-supplying metabolism in the muscle. This organization was established by comparative analysis of enzyme activity patterns of energy-supplying metabolism in different vertebrate muscle types [1-6], and was defined by distinct characteristics: Thus, activity ratios of certain enzymes in energy-supplying metabolism have been found to be relatively constant despite marked variations of their absolute levels. Constant enzyme activity ratios represent therefore common characteristics of the enzyme activity pattern. These findings may be regarded as a methodological basis for the study of enzyme activity patterns in myopathies.

The present study was undertaken under this aspect. Enzyme activity patterns were investigated in human myotonia congenita and in 20,25-diazaehol-esterol-induced myotonia of the rat. The study of the enzyme activity patterns comprised the main enzymes of glycogenolysis [glycogen phosphorylase (EC 2.4.1.1)], phosphoglucomutase [EC 2.7.5.1], glycolysis (hexokinase [EC 2.7.1.1], glucosephosphate isomerase [EC 5.3.1.9], phosphofructokinase [EC 2.7.1.11], fructose-1,6-diphosphat aldolase [EC 4.1.2.13]), triosephosphate isomerase [EC 5.3.1.1], triosephosphate dehydrogenase [EC 1.2.1.12], phosphoglycerate kinase [EC 2.7.2.3], glyceraldehyde phosphate mutase [EC 2.7.5.3], phosphopyruvate hydratase [EC 4.2.1.11], pyruvate kinase [EC 2.7.1.40], lactate dehydrogenase [EC 1.1.1.27], glucose oxidation (glucose-6-phosphate dehydrogenase [EC 1.1.1.49]), glycero-phosphate cycle (extramitochondrial glycerol-3-phosphate dehydrogenase [EC 1.1.1.8], intramitochondrial glyceraldehyde phosphate dehydrogenase [EC 1.1.1.95]), citric acid cycle (citrate synthase [EC 4.1.3.7], NADP-isocitrate dehydrogenase [EC 1.1.1.42], succinate dehydrogenase [EC 1.3.99.1], fumarate hydratase [EC 4.2.1.2]), malate dehydrogenase [EC 1.1.1.37], amino-metabolism (glutamate dehydrogenase [EC 1.4.1.3], alanine aminotransferase [EC 2.6.2.12], aspartate aminotransferase [EC 2.6.1.1]), fatty acid oxidation (3-hydroxyacyl-CoA dehydrogenase [EC 1.1.1.35]), 3-ketoacyl-CoA thiolase [EC 2.3.1.16]) and energy-rich phosphate transfer [adenylate kinase [EC 2.7.3.4], creatine kinase [EC 2.7.3.2]].

**Methods**

Small pieces of muscle (200-500 mg) were obtained in local anesthesia from m. vastus lateralis of patients with clinically manifest myotonia congenita. Enzymes were plotted with their activities relative to the activity of triosephosphate dehydrogenase (TPDH). The values of absolute TPDH activity are given in the bottom line.

**Results**

**Myotonia Congenita (Autosomal Recessive Inherited)**

Fig. 1 summarizes activity patterns of selected enzymes in biopsy samples of eight different patients. With a single exception, the evaluation of the complete enzyme activity patterns of myotonic muscle revealed no significant difference from the normal. In order to emphasize this deviation, only activities of certain key enzymes are demonstrated in Fig. 1. The activities of these enzymes were plotted, in their abbreviated form in a logarithmic scale.

It may be noted that in each pattern enzyme activities have been referred to that of triosephosphate dehydrogenase. The absolute levels of triosephosphate dehydrogenase are given at the bottom of Fig. 1. They vary by a factor of 2.4. In order to exclude these variations of absolute activities, Fig. 1 presents relative enzyme activity ratios. This comparison of enzyme activity ratios refers to key enzymes representing the following metabolic systems: triosephosphate dehydrogenase (glycolysis), phosphorylase (glycogenolysis), hexokinase (glucose phosphorylation), citrate synthase and malate dehydrogenase (citric acid cycle), 3-hydroxyacyl-CoA dehydrogenase (fatty acid oxidation). With the only exception of hexokinase, the activity ratios of the enzymes listed in Fig. 1 correspond to their normal range in normal human muscle. The listed hexokinase activities refer to the total activity, i.e., the sum of the soluble and particle-bound activities.

As may be seen, differences are observed in absolute activities of individual enzymes. These variations may be due to constitutional factors (e.g., differences in training) or to the expression of varied fibre composition. Likewise, can not be excluded that variations in