EFFECT OF SHORT-TERM EXERCISE ON GLUCONEOGENESIS BY RAT KIDNEY CORTEX

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1. Introduction

The effect of physical training on renal gluconeogenesis has been described by Krebs et al. [1], who showed enhanced rates of gluconeogenesis from lactate, pyruvate and fumarate. We have found an increase in the activity of phosphoenolpyruvate carboxykinase (PEPCK) in rat kidney after 2 hr of swimming [2] which is probably related to the accompanying metabolic acidosis. The latter is known to accelerate renal gluconeogenesis by increasing PEPCK activity [3–7].

In this paper, we report the effect of short-term exercise on gluconeogenesis from several substrates in slices from rat kidney cortex. To evaluate further the role of acidosis in exercise-induced renal gluconeogenesis, kidney slices from animals given bicarbonate were also studied.

2. Experimental

Female Wistar rats weighing 150–200 g were used. The animals were forced to swim in a water bath (22°) for 2 hr. In some experiments acidosis was prevented by tubefeeding the rats with 10 ml of a 200 mM $NaHCO_3$ solution prior to the exercise, the control animals being fed 10 ml of a 200 mM NaCl solution.

The rats were sacrificed by cervical dislocation. The measurement of gluconeogenesis was carried out according to Krebs [8], by incubating washed cortex slices in a saline medium to which substrates had been added in a 10 mM concentration, at 40° for 1 hr, with $O_2 + CO_2$ (95:5) as the gas phase. Tissue (3–10 mg dry wt) was suspended in 4 ml of the medium and shaken in 25 ml conical flasks. After incubation, the slices were removed and weighed after drying at 110°. Glucose was determined by the glucose-oxidase method [8, 9].

The PEPCK activity was assayed spectrophotometrically in the direction of oxalacetate synthesis as previously described [2].

3. Results and discussion

The results given in the table show that the production of glucose was significantly greater with slices from exercised animals when L-lactate, pyruvate, L-glutamine and L-glutamate were used as gluconeogenic substrates than with slices from control animals. When dihydroxyacetone and fructose were used, the increases of glucose production were lower.

These findings indicate that, as expected, glucose production is considerably enhanced only from substrates that enter the gluconeogenic pathway before the step catalysed by PEPCK. They are in agreement with the results obtained by Goodman et al. [10], who demonstrated an acceleration of gluconeogenesis from glutamine, glutamate, α-ketoglutarate and oxalacetate but not from fructose or glycerol in kidney slices from rats made acidotic by ammoniun chloride administration. The similarity between the metabolic behaviour of rat kidney cortex in experimental metabolic acidosis and after muscular exercise is evident as far as gluconeogenesis is concerned. It suggests that the stimulatory effect of exercise on renal PEPCK activity and gluconeogenesis is produced by the increase in lactic acid production leading to metabolic acidosis.

Table 1
Effect of muscular exercise on gluconeogenesis from various substrates and on the PEPCK activity in rat kidney cortex slices.

Substrate added (10 mM)	Glucose production* Control	Exercise (2 hr)	Control + $NaHCO_3$	Exercise (2 hr) + $NaHCO_3$
L-Lactate	110.0 ± 2.3(10)	155.4 ± 1.3(10)	94.7 ± 4.3(4)	94.2 ± 4.1(7)
Pyruvate	194.5 ± 3.9(6)	305.4 ± 8.3(6)	176.6 ± 6.2(4)	178.3 ± 5.2(3)
L-Glutamine	117.3 ± 3.6(6)	164.0 ± 4.2(6)	104.7 ± 2.3(6)	84.8 ± 9.5(6)
L-Glutamate	150.1 ± 1.7(7)	246.0 ± 8.0(6)	139.7 ± 10.6(3)	118.0 ± 11.1(4)
Fructose	547.1 ± 9.4(4)	643.3 ± 15.9(5)	648.9 ± 8.2(3)	666.6 ± 12.4(3)
Dihydroxyacetone	207.9 ± 3.7(4)	221.1 ± 7.7(5)	210.0 ± 6.3(3)	208.4 ± 6.6(4)
PEPCK activity**	25.0 ± 1.3(7)	52.6 ± 1.9(8)	21.5 ± 1.4(4)	36.4 ± 1.1(4)

* The glucose formed is expressed in μmoles/g dry wt/hr.
** PEPCK activity is expressed in nmoles of oxalacetate formed at 30° per mg of protein.
The results are given as means ± S.E.M. with the number of observations in parentheses. Experimental details are given in the text.

Further evidence supporting this assumption is provided by results obtained with exercised rats in which acidosis was prevented by giving sodium bicarbonate. This treatment completely counteracted the stimulatory effect of exercise on gluconeogenesis from lactate, pyruvate, glutamine and glutamate (see table). With glutamine and glutamate the values decreased below those of the respective controls indicating that the enzymatic steps between glutamine and α-ketoglutarate are specially sensitive to acid-base changes. This favors the hypothesis of Preuss who proposed that "the controlling factor for ammonia formation from glutamine and glutamate may be the availability of oxidized coenzyme, NAD, to the glutamate dehydrogenase pathway" [11, 12].

The PEPCK activity was decreased in exercised rats given by $NaHCO_3$ but the values were above the controls. Nevertheless, when $NaHCO_3$ was given half an hour before swimming, values similar to the controls were obtained (26.1 ± 1.8, average of five experiences), confirming a close relation between acidosis and renal PEPCK activity.

The early increase of renal gluconeogenic capacity after muscular exercise is important from a physiological standpoint. The enhanced capacity of kidney cortex to produce glucose after muscular exercise would contribute to the restoration of the acid-base balance altered by accumulation of plasma lactate. Also, the carbon skeleton of lactate would be reconverted to glucose and used again by the peripheral tissues as a metabolic fuel.

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