Mammalian metabolite flux rates in a teleost: lactate and glucose turnover in tuna

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WEBER, JEAN-MICHEL, RICHARD W. BRILL, AND PETER W. HOCHACHKA. *Mammalian metabolite flux rates in a teleost: lactate and glucose turnover in tuna.* Am. J. Physiol. 250 (Regulatory Integrative Comp. Physiol. 19): R452–R458, 1986.— Lactate and glucose turnover rates were measured by bolus injection of [U-^{14}C]lactate and [6-^{3}H]glucose in cannulated lightly anesthetized skipjack tuna, *Katsuwonus pelamis*. Our goals were *1*) to find out whether the high rates of lactate clearance reported during recovery from burst swimming in tuna could be accounted for by high blood lactate fluxes; *2*) to extend the observed correlation between lactate turnover and lactate concentration in mammals to a nonmammalian system, and *3*) to assess the importance of lactate and glucose as metabolic fuels in tuna and to compare their flux rates with values reported for mammals. Measured lactate turnover rates ranged from 112 to 431 μmol·min^{-1}·kg^{-1} and were correlated with blood lactate concentration. Glucose turnover rate averaged 15.3 μmol·min^{-1}·kg^{-1}. When correcting for body mass and temperature, skipjack tuna has at least as high or even higher lactate turnover rates than those recorded for mammals. Tuna glucose turnover rate is similar to that of mammals but much higher than levels found in other teleosts. Even the highest lactate turnover rate measured in tuna cannot fully account for the rate of blood lactate clearance observed during recovery, suggesting that some of the lactate produced in skeletal muscle must be metabolized in situ. After injection of [U-^{14}C]lactate, <5% of the total blood activity was recovered in glucose, suggesting that the Cori cycle is not an important pathway of lactate metabolism in tuna.

replacement rate; carbohydrate metabolism; fish; *Katsuwonus pelamis*; scaling

OVER THE PAST FEW YEARS, exercise physiologists and biochemists have shown renewed interest in the study of lactate with the realization that this metabolite plays a double role in muscle metabolism. It is not simply an end product of anaerobic glycolysis but also an important fuel for aerobic work (18). In mammals, muscle lactate production starts long before O_2 becomes limiting (11), and lactate turnover rate increases with blood lactate concentration (10, 12, 13, 20, 23).

As elite swimmers, tuna are characterized by a combination of endurance and sprint capabilities. Not only can they sustain moderate swimming speeds over very long distances, but they can reach top velocities of >20 body lengths/s (33). The metabolic machinery supporting tuna locomotion must meet the challenges imposed by this lifestyle, and it should include *1*) fast fluxes of fuels to the working muscles during aerobic endurance swimming and *2*) fast fluxes of anaerobic end products to their sites of catabolism during recovery from burst exercise.

While swimming at high speed, skipjack tuna can generate lactate very rapidly, up to record concentrations of 90 μmol/g in white muscle (16). During recovery, blood lactate clearance occurs much faster in tuna than in other teleosts. Minimum blood lactate concentrations are reached after <2 h of recovery in exhausted skipjacks (3). Even with a much smaller lactate load, clearance takes 12 h in rainbow trout (6).

Present views of exercise and recovery in fish rely mainly on the interpretation of metabolite concentration measurements. Estimates of metabolic fluxes would provide a new dimension to the understanding of fuel metabolism as a dynamic process. However, glucose turnover rate has only been measured in kelp bass and coho salmon (5, 26), and lactate fluxes have not been investigated in fish.

The goal of this study, therefore, was to measure lactate and glucose turnover rates in skipjack tuna to *1*) find out whether the high rate of lactate clearance reported in tuna during recovery could be accounted for by high blood lactate fluxes, *2*) extend the observed correlation between lactate turnover rate and lactate concentration in mammals to a nonmammalian species, *3*) assess the importance of lactate and glucose as metabolic fuels in a fast pelagic fish and compare their flux rates with values measured in mammals, and *4*) obtain some insight into the possible operation of the Cori cycle in tuna.

MATERIALS AND METHODS

Experimental animals. Skipjack tuna, *Katsuwonus pelamis*, were caught with barbless hooks off the coast of Oahu, HI, from May to August 1984. They were brought back to the Kewalo Research Facility (National Marine Fisheries Service, Honolulu laboratory) in the bait wells of commercial fishing vessels and transferred to 75,000-liter circular holding tanks supplied with well-aerated 25°C seawater. The fish were not fed in captivity and were used in the first 4 days after capture. The status of their carbohydrate stores was determined in a control group of five fish to assess whether capture and captivity

caused glycogen or glucose depletion. The control animals were kept for 4 days in captivity under the same conditions as the fish used in turnover experiments. They were caught with a net and killed with a sharp blow on the head. A blood sample was immediately taken by cardiac puncture. Approximately 1 g of white muscle, red muscle, and liver were freeze clamped in liquid N_2 and extracted in perchloric acid by use of previously described procedures (16). Glucose, glucose 6-phosphate, and glycogen concentrations were determined in these tissues.

Fish to be used in turnover experiments swam vigorously around their holding tanks from 1 to 10 min and then were directed to a large funnel leading to a 10-liter plastic bag containing O_2-supersaturated water with MS-222 (tricaine methanesulfonate, 1:2,000, wt/vol) an effective fish anesthetic.

Catheterization. As soon as the fish stopped moving, it was brought into the laboratory and placed ventral side up on an operating table. The gills were irrigated with aerated 24°C recirculating seawater containing MS-222 (1:15,000). A catheter (Surflo I.V. Catheter 20 g × 2 in., ID 0.80 × 51 mm, Terumo, Japan) was inserted at a 45° angle ~2 cm in front of the pelvic fins, directed toward the head for the percutaneous cannulation of the ventral aorta just anterior to the heart. The catheter was connected to a pressure transducer for pressure verification of catheter position. A 40-cm piece of PE-160 was attached to the catheter and sutured to the underside of the animal. Double cannulation (ventral and dorsal aorta) was attempted on a few individuals. The dorsal aorta cannulation was done through the mouth by use of a technique described in Jones et al. (21).

Catheters, PE tubing, and syringes were always rinsed with heparinized saline (10 U/ml) before use. Total cannulation time never exceeded 20 and 35 min for single and double cannulations, respectively. Once the catheter(s) was in place, heart rate and blood pressure were monitored via the transducer. The tuna was uprighted, strapped to a Plexiglas holder, and submerged. The anesthetic concentration was then reduced to ~1:30,000 and was adjusted individually for each fish throughout the turnover experiments. The animals were slowly moving their tail without thrashing.

Preinjection measurements of heart rate and blood pressure together with blood glucose concentration were valuable indicators of the state of the animal after surgery. Animals showing a blood glucose concentration of <1 mM were not used for turnover experiments. In some cases, blood glucose concentration started to decrease after several hours. Whenever this occurred the tail ends of decay curves were not included in the analysis. After this operation, sampling times for all turnover experiments ranged from 2 to 6 h, and the assumptions of steady-state kinetics required by the bolus injection technique were met.

Injection of labeled metabolites and blood sampling. A bolus of 25–35 μCi [U-^{14}C]lactate (sp act >100 mCi/mmol), 10 μCi [U-^{14}C]glucose (4 mCi/mmol) or 25–30 μCi [6-^{3}H]glucose (300 mCi/mmol) was injected via the catheter at *time 0*. In two specimens [U-^{14}C]glucose and [6-^{3}H]glucose were injected simultaneously to estimate glucose carbon recycling. The line was flushed with 3 ml heparinized saline immediately after injection. Blood samples (0.5 ml) were drawn starting 1 min after injection to allow the bolus to equilibrate in the rapidly mixing pool. Samples were drawn about every 40 s during the first 5 min and then at appropriate intervals. The catheter was flushed with 0.5 ml saline between samples. The amount of blood drawn throughout an experiment never exceeded 10% of total blood volume. Radiochemicals were purchased from New England Nuclear (Boston, MA) and Amersham (Oakville, Ontario).

Metabolite assays and counting. Blood samples were deproteinized immediately in 1–2 parts cold perchloric acid (8%) and spun down. The supernatant was stored at −4°C. Lactate and glucose concentrations were determined enzymatically at 340 nm following the procedure of Bergmeyer (4). Tissue glycogen of the control fish was determined by the amyloglucosidase hydrolysis technique (4). All metabolite assays were performed in duplicate, at the latest 7 days after sampling.

Blood glucose was separated to determine its activity. Blood perchloric acid extract (200 μl) was incubated with 4 ml 1 M glucose and 0.6 g Amberlite MB-3 resin (Sigma, St. Louis, MO). The mixture was shaken for 2 h at 25°C, allowing all the charged compounds to bind to the resin. The resin was then spun down, and 1 ml of the supernatant was counted. After separation 90.1% of the total glucose was recovered as determined with [6-^{3}H]glucose standards.

Lactate activity was measured by counting 40 μl perchloric acid extract and correcting for the activity found in glucose. Scintillation counting was performed on a Beckman LS-9000 by use of an external standard quench correction system. All samples were mixed with 10 ml aqueous counting scintillant II (Amersham) and left in the dark for at least 12 h before counting. Single-label counting showed an efficiency of 94% for ^{14}C and 42% for ^{3}H (dual label: 73 and 35%, respectively).

Calculations and statistics. Under steady-state conditions the rate of appearance equals the rate of utilization and is called turnover rate. Measurements of turnover rate by the bolus injection technique requires steady-state metabolite concentration because the rate of appearance and the rate of utilization cannot be estimated separately. In this study, turnover rate was calculated as the dose injected (in dpm) divided by the surface area under the specific activity decay curve [in dpm·μmol^{-1}·min^{-1}, see Katz et al.(23)]. To calculate this surface area the decay curve was first fitted with a multiexponential function by use of the nonlinear regression program P3R from BioMedical Data Processing (BMDP) (35), which determines the least-squares estimates of the function parameters by a modified Gauss-Newton algorithm. The fitted function was then integrated between *time 0* and the time when 5% of the maximum possible specific activity was reached. The maximum possible activity was calculated as the dose injected divided by the volume of the rapidly mixing pool estimated to be 8% of the body volume. Metabolic clearance rate (MCR) was calculated as turnover rate divided by the steady-state metabolite concentration (23).

RESULTS

Glucose, glucose 6-phosphate, and glycogen concentrations in tissues of animals from the control group are given in Table 1. Skipjack tuna blood glucose concentration appeared to be regulated because it was relatively constant throughout the turnover experiments (Tables 2 and 3, Fig. 3*B*). However, the set point was different between individuals, and the mean blood glucose concentration ranged from 1.2 to 6.8 mM. In each turnover experiment a blood sample was drawn before injection of the radioactive bolus. Lactate and glucose concentrations of the preinjection sample were always within 2% of the means given in Tables 2 and 3.

Lactate turnover. After injection of [U-^{14}C]lactate the activity recovered in glucose never exceeded 5% of total blood activity, even after 6 h. The lactate specific activity decay curves were best fitted with three exponential functions (Fig. 1A). In all cases the calculated functions fitted the observed values extremely well. *Fish 4* had a relatively low blood lactate concentration and the lowest turnover rate. Specific activity decreased sharply over the first 10 min after injection and then more gradually (Fig. 1*A*). Blood lactate concentration was relatively stable throughout the experiment (Fig. 1B).

Turnover rates and MCR are given for seven individuals in Table 2. These animals were selected because the coefficient of variation of their mean blood lactate concentration was <15%. These seven individuals had stable enough lactate concentrations to justify the use of steady-state kinetics in our calculations. Mean blood lactate concentrations in individual fish ranged from 10.2 to 27.6 mM. Turnover rate was positively correlated with lactate concentration (Fig. 2), and the slope was highly significantly different from zero ($F = 40$, $P < 0.001$, 1 df/7 df, ANOVA).

MCR was not affected by blood lactate concentration. A linear regression for blood lactate concentration vs. MCR (graph not shown) had a slope of 0.044 ($r^2 = 0.0134$), which is not significantly different from zero ($F = 0$, $P > 0.5$, 1 df/7 df, ANOVA). Mean MCR was 14.0 ± 0.9 (SE) ml·min^{-1}·kg^{-1} ($n = 9$).

Simultaneous sampling from the dorsal aorta and the ventral aorta was performed on *fish 6* and 7. Turnover rates determined from both sampling sites were similar (Table 2, Fig. 2), indicating that these two sites could be used interchangeably. Differences between the dorsal aorta and ventral aorta lactate specific activity decay curves did not allow us to quantify lactate utilization by the gills.

Glucose turnover. As in mammalian species, the turnover rate for glucose was much lower than for lactate. A typical specific activity decay curve is given for *fish 9* (Fig. 3*A*), which exhibited an average turnover rate. The decay curves for glucose were best fitted with the sum of two exponential functions. Turnover rate and MCR for

TABLE 1. *Tissue metabolite concentrations in control group of skipjack tuna*

Tissue	Glucose	Glucose 6-Phosphate	Glycogen, Glucosyl Units
White muscle, μmol/g wet wt	0.68±0.12	4.16±0.97	92.54±9.17
Red muscle, μmol/g wet wt	0.84±0.17	1.30±0.34	24.22±5.20
Liver, μmol/g wet wt	3.54±0.34		4.06±0.87
Blood, μmol/ml	3.04±0.39		

Values are means ± SE for 5 fish. Animals were handled and kept in captivity under same conditions as tuna used in turnover experiments.

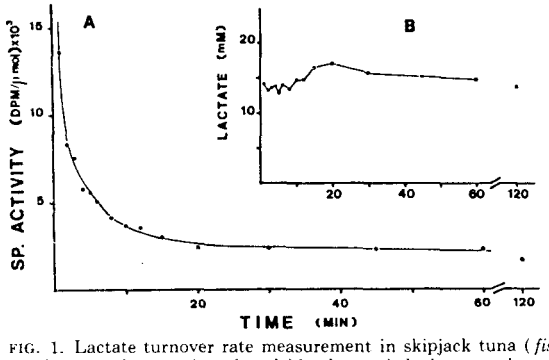

FIG. 1. Lactate turnover rate measurement in skipjack tuna (*fish 4*). Radioactive bolus injected and blood sampled via ventral aorta catheter. *A*: blood lactate specific activity decay curve after injection of 25 μCi [U-^{14}C]lactate at *time 0*. Curve fitted with sum of 3 exponential functions. *B*: blood lactate concentration during sampling period.

TABLE 2. *Blood metabolite concentrations and rate of lactate turnover in skipjack tuna*

Fish No.	Sampling Site	Wt, g	Glucose, mM	Lactate, mM	*n*	Lactate Turnover Rate, μmol·min^{-1}·kg^{-1}	Metabolic Clearance Rate, ml·min^{-1}·kg^{-1}
1	VA	1,065	4.35±0.08	27.5±1.0	11	380.9	13.9
2	VA	1,298	4.26±0.12	25.0±0.4	13	296.0	11.8
3	VA	1,440	2.30±0.07	19.1±0.5	12	299.8	15.7
4	VA	1,436	6.31±0.14	14.6±0.3	15	112.6	7.7
5	VA	1,880	1.85±0.03	12.0±0.5	13	199.9	16.7
6	VA	1,405	4.10±0.11	11.6±0.3	11	180.8	15.6
	DA		4.12±0.09	10.2±0.4	11	131.8	12.9
7	VA	1,412	1.23±0.02	26.5±0.3	10	415.2	15.7
	DA		1.22±0.02	27.6±0.5	11	431.4	15.6

Values are means ± SE. *n*, number of blood samples; VA, ventral aorta; DA, dorsal aorta. *Fish 6* and *7* were sampled simultaneously from VA and DA. Turnover rate was determined by bolus injection of [U-^{14}C]lactate.

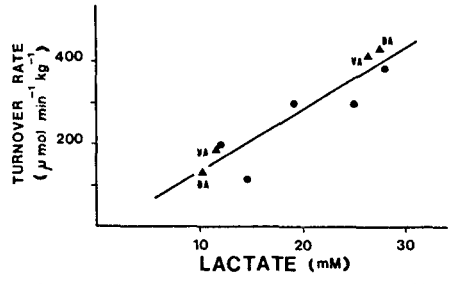

FIG. 2. Relationship between lactate turnover rate and blood lactate concentration in skipjack tuna. *Circles*, animals with single ventral aorta catheter; *triangles*, 2 animals (*fish 6* and 7) sampled simultaneously from ventral aorta (VA) and dorsal aorta (DA). Line was fitted by linear regression (slope = 15.1, $r^2 = 0.85$).

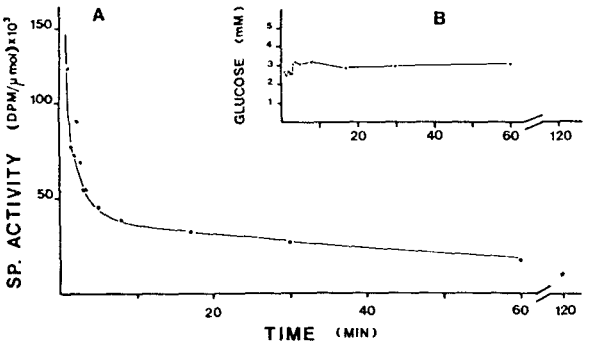

FIG. 3. Glucose turnover rate measurement in skipjack tuna (*fish 9*). Injection and blood sampling are same as Fig. 1. *A*: blood glucose specific activity after injection of 28.2 μCi [6-^{3}H]glucose at *time 0*. Curve fitted with sum of 2 exponential functions. *B*: blood glucose concentration during sampling period.

TABLE 3. *Blood glucose concentration and turnover rate in skipjack tuna*

Fish No.	Wt, g	Label	Glucose, mM	*n*	Glucose Turnover Rate, μmol·min^{-1}·kg^{-1}	Metabolic Clearance Rate, ml·min^{-1}·kg^{-1}
8	1,680	^{3}H	2.52±0.08	11	14.8	5.9
9	1,497	^{3}H	2.83±0.09	13	15.2	5.4
10	1,320	^{3}H	6.77±0.17	13	11.0	1.6
11	1,671	^{3}H	2.46±0.03	11	17.3	7.0
		^{14}C			12.5	5.1
12	1,597	^{3}H	5.19±0.10	13	18.1	3.5
		^{14}C			15.2	2.9

Values are means ± SE. *n*, number of blood samples. Turnover rates were determined by bolus injection of [6-^{3}H]glucose or [U-^{14}C]glucose. *Fish 11* and *12* were injected with both isotopes. Injection of radioactive bolus and blood sampling were done via ventral aorta catheters.

glucose are given in Table 3. Turnover rate was independent of glucose concentration ($F = 1$, $P > 0.25$, 1 df/3 df, ANOVA) and averaged 15.3 ± 1.2 (SE) μmol·min^{-1}·kg^{-1} as determined with [6-^{3}H]glucose ($n = 5$). MCR was 4.7 ± 1.0 (SE) ml·min^{-1}·kg^{-1} ($n = 5$). *Fish 10* and *12* showed a high blood glucose concentration, but their turnover rate was not elevated. Consequently, glucose MCR was lower than average for these two fish.

[6-^{3}H]glucose is considered an irreversible tracer because its predominant end product is tritiated H_2O. The reincorporation of labeled water into glucose is insignificant because rapid equilibration occurs within the large amount of body H_2O. [U-^{14}C]glucose is a reversible tracer because ^{14}C incorporated into other metabolic intermediates can be recycled back to glucose. This recycling slows down the decay of the specific activity curve, causing an underestimation of the true rate of glucose turnover. In this study, turnover rate determined with [6-^{3}H]glucose was much higher than with [U-^{14}C]glucose (Table 3), indicating that glucose carbon recycling is relatively high in tuna (28 and 16% for *fish 11* and *12*, respectively).

DISCUSSION

The lactate turnover rates reported here for skipjack tuna range from 112 to 431 μmol·min^{-1}·kg^{-1}. These values are higher than the rates reported by Okajima et al. (28) for resting rats (70 μmol·min^{-1}·kg^{-1}) and are comparable to values obtained at rest (200 μmol·min^{-1}·kg^{-1}) and different levels of exercise (up to 500 μmol·min^{-1}·kg^{-1}) by Donovan and Brooks (12), also in rats.

The animals used in this study were not overly stressed by capture, transportation, and short-term captivity without food. They were not exhausted because their carbohydrate stores were far from being depleted. Red muscle glycogen concentration was only 30% lower than in the group of resting skipjack tuna reported by Guppy et al. (16); white muscle concentration was 90% higher. Glucose and glucose 6-phosphate levels in the two muscle types were similar to the resting fish of Guppy et al. (16). Surprisingly, liver glycogen concentrations were low compared with other teleosts, but no other values are available for tuna liver. There is no doubt that the experimental situation used in our measurements was very artificial because the animals were restrained and lightly anesthetized. However, fish treated with MS-222 do not show any changes in blood glucose and lactate concentrations compared with untreated individuals (34). The same anesthetic causes a reduction in the levels of circulating catecholamines (27), suggesting a possible depression of carbohydrate metabolism. Until now, all attempts to carry out this type of experiment on unanesthetized free-swimming tuna have been unsuccessful.

It is important to realize that metabolite turnover rates generally depend on several critical factors that should be taken into account if meaningful comparisons are to be made, particularly with mammalian values. To begin with, the effects of exercise, body mass, and temperature will be considered in some detail. Then the possible mechanisms allowing tuna to support such high turnover rates will be discussed.

Lactate turnover rate has been shown to be positively correlated with blood lactate concentration in resting rats (28) and in resting dogs infused with different lactate concentrations (13). Turnover rate also increases with exercise intensity (10, 12, 20), but this effect is twofold because both perfusion and blood lactate concentration increase as work rate goes up. This paper shows that lactate turnover rate is also correlated with blood lactate concentration in tuna (Fig. 2), and this is the first time such a demonstration is made for a nonmammalian species. Measurements of heart rate and blood pressure (results not shown) made before the bolus injections indicate that perfusion was probably similar between individuals showing different steady-state blood lactate concentrations. Unfortunately, these measurements were not made throughout the turnover experiments, and cardiac output may have differed between individuals. However, MCR was not correlated with lactate concentration. When studying exercising animals a positive correlation between MCR and work rate would indicate different perfusion rates between different levels of exercise. Therefore, the constancy of MCR over our observed range of lactate concentrations also suggests that the relationship shown in Fig. 2 probably represents the true effect of lactate concentration independent of perfusion rate. The respective contributions of lactate

concentration and perfusion rate on turnover increase should be investigated separately.

The relationship between body mass and whole-body lactate turnover (R_t, in $\mu mol \cdot min^{-1}$) is presented for a few mammalian species in Fig. 4. A linear regression across the turnover rates of resting mammals (circles) has been drawn (slope = 0.64, $r^2 = 0.85$). The correlation is not better because it is difficult to standardize resting conditions for a wide range of body shapes and sizes, knowing that lactate production and removal rates are influenced by activity. Furthermore, lactate R_t measurements are not available for many species. The effect of exercise on turnover rate is also illustrated for rat, dog, and humans (triangles in Fig. 4). The range of values obtained for skipjack tuna in 25°C water is also plotted. These values fall well within mammalian rates even without considering the effect of temperature.

Ocean-caught skipjack tuna can have a core temperature 10°C higher than ambient, but such a high difference is only observed after feeding frenzies at sea. Captive animals subjected to violent exercise do not show more than a 5°C excess core temperature (31). It is very unlikely that the body temperature of the fish used in this study exceeded water temperature by >2–3°C. If we assume a Q_{10} of 2, the lactate turnover rates measured at 25°C should approximately double at 37°C.

It is interesting to notice that, even with a high lactate turnover rate of 400 $\mu mol \cdot min^{-1} \cdot kg^{-1}$, an exhausted tuna with 1 kg of white muscle at a lactate concentration of 90 μmol/g (16) would take >3 h to metabolize its lactate load of 90 mmol. However, complete recovery appears to be achieved in <2 h (3). Also, one of our cannulated animals showed a drop in blood lactate concentration from 32 to 12 mM in <2 h. These observations suggest that not all lactate passes via the blood compartment during recovery but that a significant portion is metabolized directly in white muscle.

How can a tuna turn over lactate at the same rate or faster than a 37°C mammal? Perfusion is lower in a 2-kg tuna [cardiac output of ~90 ml/min (7)] than in a mammal of similar size. Blood lactate concentration is higher in tuna, allowing faster diffusion between blood- and lactate-utilizing tissues. However, this diffusional advantage cannot fully compensate for the effect of a 10°C difference in body temperature. Therefore, tuna must have other adaptations allowing them to cycle lactate as fast as they do. The very high aerobic potential of lactate-utilizing tissues, such as red muscle (16), could allow fast lactate diffusion by maintaining a steep concentration gradient between the blood and this "lactate sink." A second possibility involves use of the central vascular countercurrent heat exchanger to accelerate movements between lactate-producing white muscle and lactate-oxidizing red muscle (P. W. Hochachka, R. W. Brill, J.-M. Weber, B. Emmett, C. Daxboeck, S. Perry, and T. W. Moon, unpublished observations).

Tuna appear to regulate their blood glucose concentration much more tightly than other teleosts (Tables 2 and 3, Fig. 3). Cannulated kelp bass (5) and rainbow trout (Weber, unpublished observations) show wide fluctuations in blood glucose levels. Tuna and mammalian insulins demonstrate similar properties (25), which may allow these fish to achieve glucose homeostasis. Even though each tuna maintained a steady blood glucose concentration, the set points ranged from 1.2 to 6.8 mM in different individuals. The significance of these observed differences is not clear but may represent different nutritional states.

Glucose turnover rate has only been measured in two other fish species. Bever et al. (5) showed that kelp bass, *Paralabrax* sp., has a rate of ~2 $\mu mol \cdot min^{-1} \cdot kg^{-1}$. A similar value was found for coho salmon, *Oncorhynchus kisutch* (26). The rates measured in fish species other than tuna are ~1/30 those found in resting rats (22).

Although the data base is very restricted for fish, mammalian values are available for a wide range of body sizes. The relationship between body mass and whole-body glucose turnover at rest (R_t, in $\mu mol \cdot min^{-1}$) is

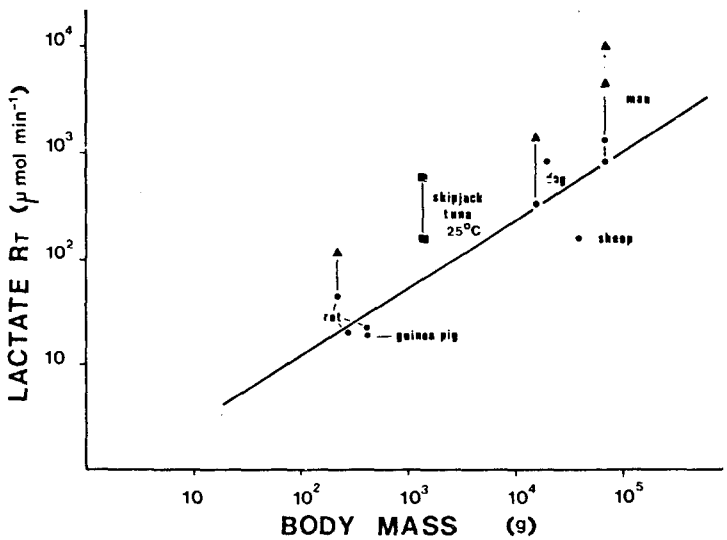

FIG. 4. Relationship between body mass and whole-body lactate turnover rate (R_t) on log-log plot for mammals and skipjack tuna. Mammals are at rest (*circles*) and exercising (*triangles*). Line fitted by linear regression using resting values for mammals only. Turnover rates measured with [^{14}C]lactate in all cases. References: rat (12, 15, 28), guinea pig (15), dog (13, 20), sheep (29) and humans (10, 30).

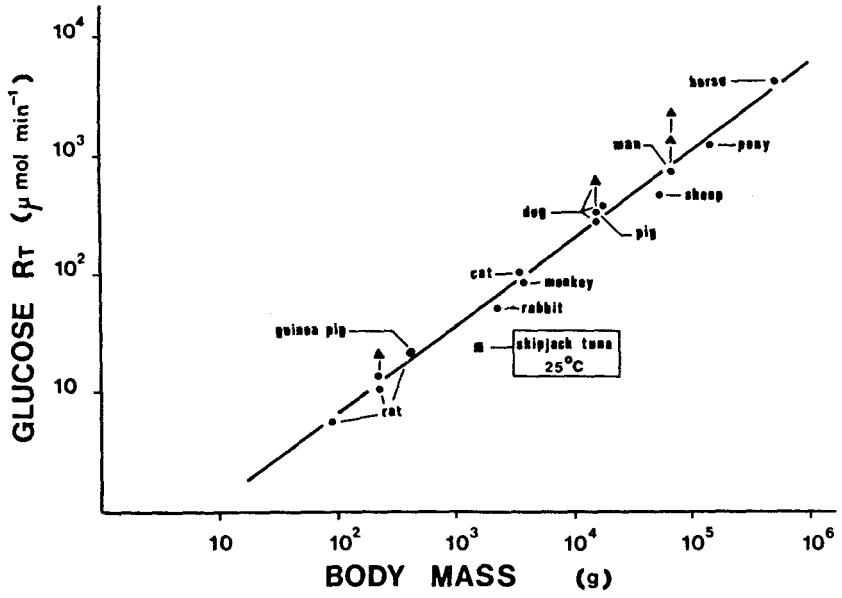

FIG. 5. Relationship between body mass and whole-body glucose turnover rate (R_t) on log-log plot for mammals and skipjack tuna. Same symbols as in Fig. 4. Linear regression fitted for resting mammals only. Turnover rates determined with [^{3}H]glucose in all cases except for horse (^{14}C). References: rat (9, 15, 22, 24), guinea pig (15), rabbit (22), cat (24), monkey (2), dog (19, 20), pig (32), sheep (8), humans (17), pony (1), horse (14).

presented in Fig. 5 on a double logarithmic scale (slope = 0.72, r^2 = 0.99, linear regression). Interestingly, this slope is not significantly different from the slope found for the classic body mass vs. metabolic rate relationship. The same analogy can be drawn for body mass vs. mass-specific glucose turnover rate (in μmol·min^{-1}·kg^{-1}, graph not shown, slope = −0.27, r^2 = 0.94). The close correlations obtained suggest that it is of minimal importance to directly measure resting glucose turnover rate in mammals unless there are good reasons to predict that the species under study will depart from this line (extremely sluggish organism or elite animal athlete) When corrected for temperature the mean glucose R_t found for tuna falls on the mammalian line. The effect of exercise on glucose R_t in mammals (triangles in Fig. 5) is much less pronounced than on lactate R_t (Fig. 4).

Under our experimental conditions very little labeled lactate was converted to blood glucose, indicating that the role played by the Cori cycle in tuna lactate metabolism is not important. It is not clear why glucose recycling was so high nor with what other compounds glucose may have been exchanging.

In conclusion, this study shows that skipjack tuna can support lactate and glucose turnover rates at least as high as those reported for mammalian species. Glucose is turned over much faster in tuna than in other teleosts, probably as a consequence of their high metabolic rate. Tuna lactate turnover rates are higher than values measured in mammals, and they are correlated with lactate concentration. These fish may be able to achieve such high turnover rates because they evolved particular anatomic and enzymatic adaptations for high-performance swimming. These high values, however, cannot fully account for the reported rates of lactate clearance during recovery, suggesting that part of the lactate produced in white muscle is metabolized in situ. The Cori cycle is probably not an important pathway for lactate clearance in tuna.

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