

RAT SPLANCHNIC NET OXYGEN CONSUMPTION, ENERGY IMPLICATIONS

By J. CASADO, J. A. FERNÁNDEZ-LÓPEZ, M. ESTEVE, I. RAFECAS,
J. M. ARGILÉS AND M. ALEMANY

*From the Department de Bioquímica i Fisiologia, Universitat de Barcelona,
08028 Barcelona, Spain*

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SUMMARY

1. The blood flow, P_{O_2} , pH and P_{CO_2} have been estimated in portal and suprahepatic veins as well as in hepatic artery of fed and overnight starved rats given an oral glucose load. From these data the net intestinal, hepatic and splanchnic balances for oxygen and bicarbonate were calculated. The oxygen consumption of the intact animal has also been measured under comparable conditions.

2. The direct utilization of oxygen balances as energy equivalents when establishing the contribution of energy metabolism of liver and intestine to the overall energy expenses of the rat, has been found to be incorrect, since it incorporates the intrinsic error of interorgan proton transfer through bicarbonate. Liver and intestine produced high net bicarbonate balances in all situations tested, implying the elimination (by means of oxidative pathways, i.e. consuming additional oxygen) of high amounts of H^+ generated with bicarbonate. The equivalence in energy output of the oxygen balances was then corrected for bicarbonate production to 11–54% lower values.

3. Intestine and liver consume a high proportion of available oxygen, about one-half in basal (fed or starved) conditions and about one-third after gavage, the intestine consumption being about 15% in all situations tested and the liver decreasing its oxygen consumption with gavage.

INTRODUCTION

In the prandial state, the fate of the foodstuffs taken up by the intestine and brought to the liver via the portal vein, has been the subject of extensive discussion (McGarry, Kuwajima, Newgard, Foster & Katz, 1987). The peripheral tissues (muscle and adipose masses, essentially) seem to play a significant role in the immediate uptake of most of the substrates released by the intestine (Katz, Glickman, Rapaport, Ferrannini & DeFronzo, 1983; Ferrannini, Björkman, Reichard, Pilo, Olsson, Wahren & DeFronzo, 1985). Traditionally, the liver has been considered to play a filter or buffer role in the disposal of the materials provided through the intestine (Madison, 1969); however, this primary role in glucose and energy homeostasis has been challenged (McGarry *et al.* 1987) as more information has been

produced concerning the role of peripheral metabolism (Katz *et al.* 1983; Ferrannini *et al.* 1985).

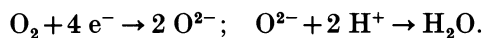
It is rather difficult to establish the individualized metabolic relevance of a given organ in a living context, especially in undisturbed conditions. The effects of anaesthesia are known to alter both glucose and energy homeostasis deeply (Pénicaud, Ferré, Kande, Leturque, Issad & Girard, 1987), affecting the production of heat (Lang, Bagby, Hargrove, Hyde & Spitzer, 1987) and circulatory parameters (Katz & Bergman, 1969; Buelke-Sam, Holson, Bazare & Young, 1978). We have attempted here to determine, with as little disturbance as possible, the overall metabolic activity of both liver and intestine in a prandial context. This is part of quantitative study of the fate of glucose (Casado, 1989; Fernández-López, 1989) and was developed to determine the relative importance of oxidative metabolism of both splanchnic organs under changing dietary situations. It was assumed that the net oxygen balance across a given organ would give a direct quantitative indication of the substrate oxidation.

When measuring arterio-venous oxygen differences, a common source of error is often overlooked: the relative oxygen debt or excess consumption of a given organ that exports or imports protons. The circulating buffers, especially bicarbonate, can absorb these small variations, carrying the excess of protons to other organs. The receiving tissues would then present apparently higher oxygen uptakes because this excess oxygen would be used to restore the buffer to its initial pH and bicarbonate concentration. At the level of the whole animal, this source of error is minimal, since only a minimal part of excess acidity is lost through the urine in situations of acidosis.

The tissue-evolved CO₂ is taken out of the tissues by the bloodstream in at least five different compartments: plasma and red cell dissolved CO₂ and bicarbonate, as well as carbamino-haemoglobin. Of these, the largest proportion is found in both bicarbonate compartments (Severinghaus, Stupfel & Bradley, 1956; Helbacka, Casterline, Smith & Shaffer, 1964), a situation in which its formation represents the release into the tissue of a proton, according to the equation:



The formation of carbamino-haemoglobin also requires the release of a proton from the reduced haemoglobin molecule. The H⁺ are currently used by the tissue (with a concomitant consumption of oxygen), since the pH is seldom deeply altered. However, the release of bicarbonate will eventually result in a net negative balance of protons elsewhere for the reconstitution of carbonic acid and the release of CO₂ in the lungs. There is a correspondence between excess protons and oxygen, as eventually most protons will find a way into water:



The net release of bicarbonate by a given tissue implies that there has been a net utilization of protons by the tissue, thus the oxygen consumption figures must be corrected by the equivalence in oxygen of the protons consumed (4 H⁺ for each molecule of O₂). Besides, the release of bicarbonate implies the utilization of protons in other organs for the reconstitution of CO₂, thus their oxidative metabolism would be underestimated from the oxygen consumption figures. In order to evaluate the

possible importance of the oxygen debt or excess consumption incurred by single organs we measured the pH, bicarbonate and carbon dioxide differences across the vessels irrigating the liver and the intestine.

We also measured the overall oxygen consumption of the animals studied so as to establish the proportion of the oxygen intake used by the splanchnic organs and thus determine their share in overall energy expenditure under the situations tested.

METHODS

Animals and experimental set-up

Wistar albino male rats, weighing 190–210 g were used. The rats were kept in an animal room with uniform temperature (21–22 °C), humidity (70–75%) and light cycle (on from 08.00 to 20.00 h). They were maintained in collective (four rats per cage) polypropylene-bottomed cages with wood shavings as bedding material. The animals were fed a standard pellet diet (type A04 from Panlab, Barcelona) and had free access to tap water. A group of animals was maintained under the stated conditions (fed group) and another was fasted overnight (starved group).

At the beginning of the experiment, the rats were given an oral load of 5.4 ml per kg of body weight as 3 M-glucose in water. The rats were anaesthetized with i.p. sodium pentobarbitone (60 mg/kg body weight) 4–5 min before blood sampling. Then a laparotomy was performed exposing the abdominal cavity; suprahepatic vein, portal vein and arterial blood (from the lower aorta) were sampled with dry heparinized short cannulas connected to glass capillary tubes. The sampling took place at 0, 10, 15, 30 or 60 min after gavage.

The capillary tubes were immediately used for the estimation of blood pH, P_{O_2} and P_{CO_2} with a BMS-3 MM2 Radiometer (Copenhagen) blood gas analyser. Blood packed cell volume was estimated by centrifugation. The concentrations of oxygen (Bork, Vaupel & Thews, 1975; Boutiller, Gibson, Toews & Anderson, 1977), blood cell and plasma bicarbonate (Severinghaus *et al.* 1956) were calculated from the data obtained and the mean haemoglobin content (154 g l⁻¹) of the blood from the Wistar strain used (Riera, Sánchez, Rama & Palacios, 1990).

Oxygen and bicarbonate balances

The portal and suprahepatic blood flows were estimated at the stated time intervals with separate groups of rats by using the *p*-amino-hippuric acid dilution method (Casado, Pastor-Anglada & Remesar, 1987). The mean hepatic artery flow for each group of rats was then calculated. The hepatic oxygen balance (HOB) was estimated from the concentration of suprahepatic (HV), portal (PV) vein and hepatic artery (A) and their flows (Φ_{HV} , Φ_{PV} and Φ_A respectively) from the equation:

$$\text{HOB} = (\text{HV} - \text{A}) \Phi_A + (\text{HV} - \text{PV}) \Phi_{PV}.$$

The intestinal (IB) and splanchnic (SB) balances were calculated from the corresponding means:

$$\text{IB} = (\text{PV} - \text{A}) \Phi_{PV}; \quad \text{SB} = (\text{HV} - \text{A}) \Phi_{HV}.$$

Bicarbonate balances were established from the total bicarbonate content of the blood which was calculated from the packed cell volume and the concentrations in plasma and cells. A negative oxygen or bicarbonate balance represents a net uptake, and positive balances imply a net release. The combined oxygen equivalent balances (OEB) were calculated from the net oxygen and bicarbonate balances using the equation:

$$\text{OEB} = \text{OB} + (\text{BB}/4),$$

where OB is the oxygen balance and BB the blood bicarbonate balance, all expressed in comparable units (micromoles); they represent the combined computed oxygen uptake and oxygen debt incurred per minute for the given organ.

Another set of rats were used for the measurement of overall oxygen consumption. The rats were placed in a thermostatically controlled (25 °C) glass chamber with a constant inflow (350 ml min⁻¹) of dry synthetic air (21% O₂, 79% N₂ by volume). The efflux air was dried with a water- and CO₂-absorbing mixture, measured, and then analysed on line, in an open circuit, for oxygen with a paramagnetic oxygen analyser. The \dot{V}_{O_2} was calculated from the equation:

$$\dot{V}_{O_2} = (\dot{V}_I \times 0.21) - (\dot{V}_O \times \text{OX}),$$

where \dot{V}_i and \dot{V}_o were the nitrogen/oxygen mixture volumes (at 25 °C) passed through the chamber inflow and outflow rotameters and OX the percentage oxygen content in the outflowing gas mixture. The net oxygen consumption by the rat was measured both before and after the glucose gavage and after the same anaesthesia and sampling procedure outlined above. The net overall oxygen consumption of the rats was calculated for each point studied, having taken into account the effect of anaesthesia and its duration.

Energy equivalences of oxygen consumption have been used for comparison with other published data. A 448 kJ (mol O₂)⁻¹ (Passmore & Eastwood, 1986) value was used to convert the oxygen values into energy equivalents. All data have been converted into power units (W) so as to standardize their meaning under different time spans.

Statistical comparisons between means were done using the Student's *t* test.

RESULTS

In Table 1 the partial pressures of oxygen and carbon dioxide in the splanchnic blood samples studied are presented together with blood pH. The concentrations of free protons were extremely low, with very small changes in pH. The partial pressures of oxygen were much higher in the arterial blood, the lowest values being found in the suprahepatic vein blood. The reverse can be said for partial CO₂ pressures, lowest in arterial blood. The effect of starvation resulted in slightly lower arterial blood pH values, with higher oxygen partial pressures in portal blood where arterial levels did not change. Conversely, the CO₂ pressures were somewhat lower than in the fed state for portal and suprahepatic vein blood.

In Table 2 the blood flow values for the intestine and liver vessels are presented. These data have been used for the calculation of balances of materials across the liver and intestine. The actual blood flows were similar for both dietary states studied except for the initial (time 0) values, which were higher in the fed state.

Table 3 presents the oxygen and bicarbonate concentrations derived from the data in Table 1. Blood bicarbonate concentrations are presented in two compartments: plasmatic and intracellular, together with the statistical analysis of the changes observed. The pattern presented was comparable to that already described for Table 1; however, the degree of intergroup variation of these new data was somewhat higher.

The balances of oxygen uptake and bicarbonate release by liver and intestine, as well as the combined oxygen and bicarbonate balances are presented in Table 4. The pattern of liver and intestine combined oxygen balances were complementary in the 10–15 min zone, in which there was a higher energy consumption by the intestine with minimum function in the liver. This pattern was very much alike in both dietary situations studied, with lower overall levels of energy consumption in the starved when compared with the fed situation.

In Fig. 1, the oxygen consumption of the animals subjected to gavage and anaesthesia are presented. Fed animals had a higher overall oxygen consumption rate, anaesthesia considerably lowering the use of oxygen despite the timing of anaesthesia after gavage. Starved rats showed a similar pattern, with lower anaesthesia effects because of the initially lower post-gavage oxygen consumption observed.

In Table 5 the time-adjusted derived oxygen consumption for the intact rats at the points after gavage are presented. These values were calculated by means of an

TABLE 1. P_{O_2} , P_{CO_2} , and pH in the portal, suprahepatic and arterial blood of rats given a glucose gavage

time (min)	pH (HV)	pH (PV)	pH (A)	P_{O_2} (HV)	P_{O_2} (PV)	P_{O_2} (A)	P_{CO_2} (HV)	P_{CO_2} (PV)	P_{CO_2} (A)	
0	7.34 ± 0.00	7.35 ± 0.01	7.44 ± 0.01	37.8 ± 2.8	55.7 ± 0.6	90.0 ± 2.5	43.0 ± 0.0	46.4 ± 2.5	34.4 ± 2.4	
10	7.36 ± 0.00	7.30 ± 0.02	7.46 ± 0.01	38.3 ± 2.4	48.0 ± 2.3†	84.9 ± 5.6	40.1 ± 2.0	38.8 ± 2.3	26.0 ± 1.7†	
15	7.34 ± 0.01	7.37 ± 0.04	7.46 ± 0.01	40.5 ± 5.5	42.5 ± 8.5	84.3 ± 2.3	49.8 ± 5.8	46.5 ± 1.0	28.3 ± 1.8	
30	7.36 ± 0.02	7.34 ± 0.02	7.40 ± 0.02	37.8 ± 5.1	44.5 ± 0.9†	84.5 ± 6.6	40.7 ± 1.2	40.2 ± 2.4	30.5 ± 1.6	
60	7.38 ± 0.02	7.35 ± 0.02	7.41 ± 0.02	38.2 ± 2.6	43.5 ± 2.5†	86.7 ± 5.8	43.2 ± 2.6	42.0 ± 2.4	32.5 ± 2.0	
24 h starved										
0	7.37 ± 0.02	7.33 ± 0.01	7.33 ± 0.03*	42.1 ± 2.3	54.1 ± 3.5	86.1 ± 1.4	33.3 ± 2.7*	39.0 ± 1.3*	29.5 ± 0.9	
10	7.33 ± 0.02	7.34 ± 0.02	7.35 ± 0.02*	47.2 ± 0.4*	56.5 ± 1.3*	88.0 ± 1.5	34.5 ± 2.0	35.6 ± 1.1	31.9 ± 1.6	
15	7.39 ± 0.01*	7.30 ± 0.02	7.36 ± 0.03*	41.8 ± 0.4	47.2 ± 0.4	91.5 ± 1.8	38.5 ± 2.8	42.3 ± 0.9*	30.6 ± 0.4	
20	7.39 ± 0.00	7.36 ± 0.01	7.36 ± 0.01	42.1 ± 1.2	49.1 ± 2.5	82.9 ± 5.6	37.0 ± 2.2	36.8 ± 0.4	28.6 ± 1.0	
60	7.37 ± 0.01	7.36 ± 0.01	7.38 ± 0.02	42.6 ± 2.6	54.8 ± 0.7*	88.8 ± 2.3	34.8 ± 0.2*	368 ± 0.4	32.9 ± 2.1	

The figures are the mean ± s.e.m. of four to eight different animals. Gas partial pressures are expressed in mmHg. PV, portal vein; HV, suprahepatic vein; A, arterial blood; and in all following tables.

Differences between fed and starved groups: * $P < 0.05$.

Differences versus time 0: † $P < 0.05$.

extrapolation of the graphs in Fig. 1 taking into account the effect of anaesthesia, adjusted to the same times in which blood was sampled in the first series of rats. Oxygen consumption was slightly higher for fed rats than for starved ones except 1 h after gavage, when both groups showed the same oxygen consumption. The computed 1 h oxygen consumption was very similar for both groups of rats.

TABLE 2. Blood flow across the liver and intestine of rats given a glucose gavage
Blood flow (ml min⁻¹)

Time (min)	Suprahepatic vein	Portal vein	Hepatic artery
Fed			
0	28.4 ± 3.6	17.8 ± 1.0	10.6
10	35.0 ± 2.8	31.1 ± 3.2	3.9
15	31.6 ± 3.1	26.2 ± 3.2	5.4
30	41.7 ± 2.6	23.9 ± 1.3	17.8
60	33.1 ± 3.2	18.8 ± 2.0	14.3
24 h starved			
0	17.2 ± 0.8	11.0 ± 1.9	6.2
10	33.4 ± 2.9	28.3 ± 3.0	5.1
15	35.5 ± 2.4	27.0 ± 4.5	8.3
30	36.2 ± 1.0	23.4 ± 1.4	12.8
60	30.0 ± 5.6	19.0 ± 0.5	11.0

The figures are the means ± S.E.M. of four different animals.

The computation of the oxygen equivalent balances for the 1 h period studied gave the results presented in Table 6. The oxygen equivalent consumption in the fed state was fractionally higher than in starved rats. Liver and intestine consumption contributed roughly the same amount of combined oxygen and oxygen debt in both cases. The basal data, however, showed a much higher importance of splanchnic bed oxygen consumption prior to the glucose gavage and anaesthesia. Liver oxygen consumption and debt was then much higher than that of intestine.

DISCUSSION

The measurement of substrate balances across an organ *in vivo* present severe constraints that should not be ignored, but simply minimized; in our experiments, the period of anaesthesia has been reduced to the minimum, and three sets of rats have been used, one for measuring the blood flows, the other for actual blood oxygen measurements and the third for overall oxygen consumption estimation. The use of anaesthesia in this type of experiment is widespread (Fafournoux, Rémesy & Demigné, 1983; Niewoehmer & Nuttall, 1988). The use of different sets of animals for the calculation of metabolite balances in the rat is the only reliable technique available at present (Smadja, Morin, Ferré & Girard, 1988; Niewoehmer & Nuttall, 1989), since no hepatic vein chronic catheterization technique has been developed. This methodology can be applied in a non-steady-state situation, since little variation in concentrations or blood flows was observed, and all extractions were carried out in 40–45 s. It assumed that the balance obtained was fully reliable.

TABLE 3. Oxygen and bicarbonate concentrations in hepatic and portal vein and arterial blood of both fed and starved rats

Time (min)	PV [O ₂]		HV [O ₂]		A [O ₂]		Plasma PV [HCO ₃ ⁻]		Plasma HV [HCO ₃ ⁻]		Plasma A [HCO ₃ ⁻]		Red cell PV [HCO ₃ ⁻]		Red cell HV [HCO ₃ ⁻]		Red cell A [HCO ₃ ⁻]	
Fed																		
0	4.24 ± 0.56 † §	7.21 ± 0.16 †	9.00 ± 0.02	22.5 ± 0.4 §	25.8 ± 0.7	22.5 ± 1.3	16.3 ± 0.2 §	18.5 ± 0.4 †	15.5 ± 0.9									
10	4.64 ± 0.61 †	5.58 ± 0.39 † †	8.49 ± 0.13	21.7 ± 0.3 †	18.6 ± 1.3 †	18.1 ± 1.6	15.6 ± 0.3 †	13.7 ± 0.9 †	12.3 ± 1.0									
15	5.27 ± 1.87	6.41 ± 1.17	9.06 ± 0.01	28.8 ± 2.1 † †	30.5 ± 0.7 † †	22.5 ± 0.4	20.3 ± 0.7 † †	21.0 ± 0.5 † †	14.8 ± 0.1									
30	4.91 ± 0.83 †	5.97 ± 0.41 † †	8.75 ± 0.21	24.2 ± 1.0 †	22.7 ± 1.7 †	17.0 ± 1.4 †	17.0 ± 0.5 †	16.1 ± 1.0 †	12.0 ± 0.8 †									
60	5.39 ± 0.69 †	5.49 ± 0.48 † †	8.88 ± 0.11	27.2 ± 2.5	22.3 ± 1.5	20.4 ± 0.8	18.9 ± 1.7	16.0 ± 0.9	14.1 ± 0.6									
24 h starved																		
0	5.17 ± 0.69 †	6.79 ± 0.40 †	8.66 ± 0.77	17.1 ± 0.8 *	19.8 ± 0.7 * † †	15.1 ± 1.3 *	12.8 ± 0.2 *	14.3 ± 0.5 * †	10.9 ± 0.7 *									
10	5.97 ± 0.23 † §	7.36 ± 0.80	8.74 ± 0.58	17.5 ± 0.9 *	18.7 ± 0.7	17.3 ± 1.5	12.7 ± 0.6 *	13.5 ± 0.4	12.3 ± 1.0									
15	5.71 ± 0.04 †	5.72 ± 0.16 † †	8.80 ± 0.06	20.4 ± 0.7 * † †	20.3 ± 1.0 * †	16.3 ± 1.2 *	14.6 ± 0.5 *	14.9 ± 0.6 * †	11.7 ± 0.8									
30	5.47 ± 0.03 † §	6.00 ± 0.18 †	8.76 ± 0.13	21.0 ± 1.6 †	18.7 ± 1.0	15.7 ± 0.8	14.8 ± 1.1 †	13.5 ± 0.6 †	11.2 ± 0.6									
60	5.72 ± 0.42 † §	7.03 ± 0.19 * †	8.83 ± 0.09	21.0 ± 1.1	19.0 ± 0.9	19.0 ± 1.3	14.8 ± 0.8	13.6 ± 0.6	12.6 ± 1.3									

All concentrations are expressed in $\mu\text{mol l}^{-1}$. These data have been calculated from those of Table 1.

Differences between fed and starved groups: * $P < 0.05$.

Differences *versus* time 0: † $P < 0.05$.

Differences *versus* the arterial value: † † $P < 0.05$.

Differences *versus* the suprahepatic vein value: § $P < 0.05$.

TABLE 4. Oxygen and bicarbonate balances across the entero-hepatic units of rats fed or starved

Time (min)	Oxygen balances			Bicarbonate balances			Corrected oxygen balances		
	Hepatic	Intestinal	Splanchnic	Hepatic	Intestinal	Splanchnic	Hepatic	Intestinal	Splanchnic
				Fed					
0	-103.3	-30.6	-136.8	-46.7	55.2	8.5	-115.0	-16.8	-134.7
10	-54.7	-103.5	-158.2	94.5	28.0	122.5	-31.1	-96.5	-127.6
15	-47.5	-72.2	-119.7	-2.2	188.6	186.4	-48.1	-25.1	-73.1
30	-93.5	-66.3	-151.8	143.2	119.5	262.7	-57.1	-36.4	-86.1
60	-51.7	-63.7	-115.5	159.6	35.7	195.3	-11.8	-54.8	-66.7
				24 h starved					
0	-65.8	33.3	-99.1	49.1	73.0	122.1	-53.5	-15.1	-68.6
10	-52.6	-38.7	-91.3	-26.8	36.8	10.0	-59.3	-29.5	-88.8
15	-28.3	-82.9	-107.8	27.2	99.9	127.1	-21.5	-57.9	-76.0
30	-65.7	-53.3	-119.0	103.3	63.2	166.5	-39.9	-37.5	-77.4
60	-47.3	-34.2	-81.3	44.5	9.5	54.0	-36.2	-31.8	-67.8

The data are expressed in μmol released in 1 min.

The oxygen consumption of liver and intestine is not a direct correlate of their actual oxidative metabolism activity, because of a high proton deficit elimination in these tissues. The corrected oxygen consumption values were thus lower than the corresponding direct data of oxygen uptake: 4.28 and 3.19 mmol h⁻¹ for liver in the

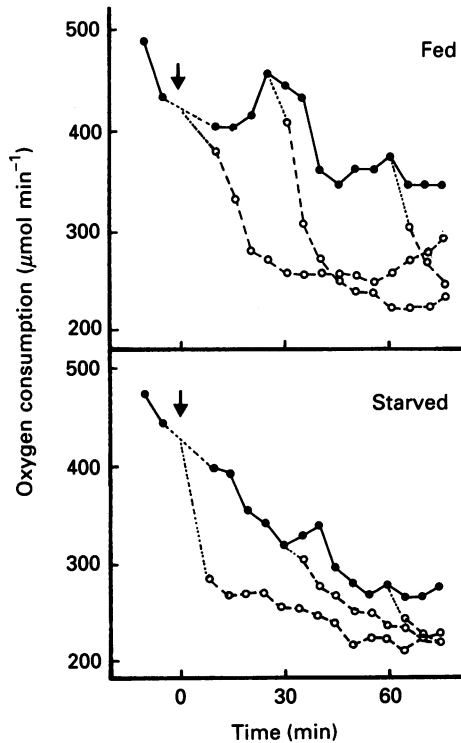


Fig. 1. Oxygen consumption (in $\mu\text{mol min}^{-1}$) of rats given a glucose gavage on min 0 (arrow), and anaesthesia at 0, 30 or 60 min. All results are the means of four different animals. Unanaesthetized rats, ●; anaesthetized rats, ○. The dotted lines represent the estimated course of both unanaesthetized (continuous line) and anaesthetized (dashed line) rats in the minutes taken for gavage, anaesthesia and gas chamber equilibration.

fed and starved conditions respectively; 4.10 and 2.44 for intestine and 8.38 and 5.64 mmol h⁻¹ for the whole splanchnic bed. The remarkable uniformity of the corrected figures irrespective of dietary status contrasts with the higher fed-state combined (uncorrected) balances, suggesting a significant role of proton removal for liver and intestine oxygen (energy) balances.

The overall energy meaning of the oxygen consumption or debt derived for tissue proton balancing is obscure, as there is no direct relationship between the oxygen consumed for this purpose and an energy expression, similar to that found in the complete oxidation of metabolites. The utilization of oxygen as final proton acceptor is just another mechanism that prevents acidification of the blood and tissues and helps the blood to carry larger proportions of CO₂ with smaller variations in pH. However, this process results in higher uptakes of oxygen. The correlation of this crude oxygen uptake with actual energy derived from direct substrate oxidation can

result in exaggerated claims of heat generation, since a correlate between oxygen consumption and net heat production cannot be directly established because of the postulated neutralizing proton role. The oxygen consumption figures decreased for liver and intestine by 11–35% in the starved situation or 52–55% in the fed state when this correction for proton balance was taken into account.

TABLE 5. Oxygen consumption by fed or starved rats receiving a glucose gavage

Time (min)	Oxygen consumption (mmol min ⁻¹)	Power equivalence (W)
Fed		
0	0.283 ± 0.007	2.11
10	0.267 ± 0.014	1.99
15	0.270 ± 0.010	2.02
30	0.278 ± 0.037	2.07
60	0.226 ± 0.041	1.69
Σ 1 h	15.76	1.96
24 h starved		
0	0.245 ± 0.015	1.83
10	0.223 ± 0.022	1.67
15	0.245 ± 0.014	1.83
30	0.246 ± 0.022	1.84
60	0.226 ± 0.007	1.69
Σ 1 h	14.27	1.77

These figures have been extrapolated from the data presented in Fig. 1 and are the means ± s.e.m. of four to five different animals. The oxygen consumption values are given in mmoles consumed per minute (the Σ values are given in mmoles in 1 h), and correspond to rats otherwise untouched. The power equivalence of these figures is expressed in watts.

The proportion of overall rat oxygen consumption actually used by the liver and the intestine in both basal dietary situations studied was considerable, suggesting a significant share in basal or non-adaptive thermogenesis for these organs. This is in agreement with some suggestions actively implying the liver in diet-induced thermogenesis (Ma, Naddeau & Foster, 1987). The importance of the intestine as oxygen consumer stems from its function; despite its relatively small size with respect to body weight (Remesar, Arola, Palou & Alemany, 1981) has a very active metabolism, especially in its outermost epithelial strata, since these are cells with a short life and extremely active metabolism (Dickens & Weil-Malherbe, 1941). The intestine plays a significant role in the control of glucose and gluconeogenic precursor output (Remesy, Demigné & Aufrère, 1978; Nicholls, Leese & Bronk, 1983), as well as in amino acid metabolism (Rémesy *et al.* 1978; Aikawa, Matsutaka, Yamamoto, Okuda, Ishikawa, Kawano & Masumura, 1973) and fat resynthesis (Bisgaier & Glickman, 1983). Thus it can be expected that its residual energy output would be considerable and its oxygen consumption very high.

The intestine and the liver do not act as complementary elements in the generation of bicarbonate, but they actually show an additive pattern; both generate a net higher oxygen consumption in all situations tested. This is apparently in disagreement with the purported generation of lactate by the intestine from glucose

(Rémesy *et al.* 1978; Nicholls *et al.* 1983; Coppen & Davies, 1988), a process that would imply the export of an oxygen debt (because of the anaerobic glycolysis pathway the generation of lactate implies); the liver would use this lactate for gluconeogenesis (Madison, 1969; Exton, 1972) thus covering this exported intestinal oxygen debt. The fact is that the differences between level of lactate efflux (Casado, 1989) and bicarbonate production are far apart, by more than an order of magnitude. Thus the lactate–oxygen debt could be considered negligible compared to massive bicarbonate production by both intestine and liver.

When the basal (time 0) data are computed and compared with those obtained after gavage, it can be seen that the administration of glucose resulted in a significant transient (at 30 min, as compared with the whole 1 h period) increase of hepatic oxygen consumption. The effects upon the intestine were less marked in the fed state, decreasing the oxygen consumption in starved rats. Probably this effect was not apparent in fed animals because their intestine already contained food. This same higher oxygen consumption could be traced to the whole animal. The relatively lower oxygen consumption after gavage can be a consequence of the gavage itself, since the serrated pattern observed in fed animals agrees with that observed when measuring heat production under comparable conditions (Rafecas, Domènech, Esteve, Remesar, Argilés & Alemany, 1989). The lowering of hepatic oxygen consumption observed when anaesthesia and gavage were combined (since we could not discern between their relative independent effects) suggests that liver oxidative (energy metabolism) activity decreases considerably – by about one-half – regardless of feeding status. This can be in line both with the intestinal control of hepatic function (Smadja *et al.* 1988) and the hypothermic effect of anaesthesia (Lang *et al.* 1987) which could, then, be partially traced to this organ as a main site of operation.

The ratios of the available energy being used by the rat splanchnic organs, presented in Table 6, show that both liver and intestine consume a very considerable share of all available oxygen, and an important proportion too of all energy metabolism in the rat. Their combined contribution resulted from *circa* one-half in basal conditions to about one-third of the energy output of the rat after gavage–anaesthesia in the dietary situations tested. The whole-rat data (Fig. 1) were remarkably uniform for both fed and 24 h food deprived rats, the differences being slightly more marked when gavage–anaesthesia were taken into account, especially affecting the intestine. The quantitative importance of the splanchnic bed organs for total energy output of the rat, and the fact that major changes occurred during the period studied confirm that these organs play a significant role in heat production. However, the relative uniformity of the power output share of the splanchnic bed suggests that its contribution to diet-induced thermogenesis (Trayhurn & James, 1981) could be very high but very probably with little thermogenic adaptive capacity, in line with the current hypotheses on thermogenic control (Trayhurn & James, 1981; Yen, McKee & Stamm, 1984).

In conclusion, we can confirm the substantial quantitative importance of intestine and liver in the prandial state both as net heat producers and substrate oxidizing organs. There is a relative uniformity of energy liberation from liver oxidative metabolism and oxygen consumption despite changing dietary availability of energy substrates, which is deeply affected by gavage and/or anaesthesia. The quantitative

importance of organ bicarbonate balances (proton debt/excess consumption) evidences the need to take them into account in the evaluation of actual oxygen (and energy) balances across tissues, since the utilization of oxygen for neutralizing purposes could deeply alter the net oxygen balance.

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TABLE 6. Computed oxygen consumption for 1 h interval of splanchnic organs of fed and starved rats given an oral glucose gavage and of whole rats under the same conditions

Status	Units	Liver	Intestinal	Splanchnic bed	Whole rat
Fed basal*	mmol h ⁻¹	5.32	2.66	8.34	16.96
	W	0.662	0.331	1.042	2.11
	%	31.4	15.7	49.2	100.00
Fed gavage	mmol h ⁻¹	2.76	2.70	5.48	15.76
	W	0.343	0.336	0.682	1.96
	%	17.5	17.1	34.8	100.00
Starved basal*	mmol h ⁻¹	4.68	3.09	7.78	14.72
	W	0.582	0.385	0.968	1.83
	%	31.8	21.0	52.9	100.00
Starved gavage	mmol h ⁻¹	2.37	2.20	4.53	14.27
	W	0.295	0.274	0.564	1.77
	%	16.7	15.5	31.9	100.00

The basal (*) figures correspond to time 0. The % data are the mean % of total corrected oxygen consumption (as power output) expended by these organs with respect to the overall rat oxygen consumption.

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