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Oxygen Consumption of Regenerating Skeletal Muscle.

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In the process of neuromuscular regeneration, the onset of functional reinnervation initiates a rapid and complete restoration of glycogen concentration and a simultaneous but slower recovery of muscle mass and creatine concentration.¹ Because of these findings and the fact that many growing tissues exhibit high metabolic rates, it has seemed of interest to study the rate of oxygen consumption of regenerating muscle. For comparative purposes, the oxygen consumption *in vitro* of totally denervated muscle has also been reinvestigated.

Methods. The experiments were carried out on the soleus muscles of rats matched as to age, weight and stock. Complete denervation was accomplished by section of the tibial nerve. In a number of 110-day-old animals this nerve was crushed with a heavy ligature in order to permit reinnervation and subsequent muscle regeneration. Contralateral normal or denervated solei served as controls.

The determinations were made at 37.5°C in Barcroft-Warburg manometers, using a phosphate-saline medium² and a 100% O₂ gas phase. Muscles from one experimental group were removed under light ether anesthesia while the remaining experiments were carried out on muscles from rats which had been killed by a blow on the head. To facilitate oxygen diffusion the muscles were split lengthwise into strips *in situ*. An average time interval of 35 minutes was consumed in preparation of the muscles, adjusting the apparatus and equilibrating for 15 minutes. The oxygen uptake for the next hour was then measured. The dry weights of the muscles, which ranged from 9 to 28 mg, served both for calculation of the O₂ consumption and estimating the degree of atrophy.

Results. Preliminary determinations on unoperated animals selected at random were made to ascertain the variances in O₂ con-

TABLE I.

Rate of Oxygen Consumption Together with Standard Errors for Normal, Totally Denervated, and Regenerating Soleus Muscles.

Experimental condition		No. of animals	Days after lesion		% muscle weight loss		Q _{O₂}		Q _{O₂} [†]
			L	R	L	R	L	R	
I	Unoperated	9	0	0	0	0	2.21 ± .13	2.30 ± .11	96.8 ± 5.9
II	Left tibial nerve cut	19	14	0	31.8	0	2.66 ± .14	2.40 ± .10	112.2 ± 4.98
III A	Left tibial nerve crushed	14	15-35	0	32.1 (20-50)	0	2.85	2.37 ± .11	122.3
B	Left tibial nerve crushed	13	18-42	0	8.5 (0-20)	0	2.49	2.76 ± .10	91.2
IV A	Left tibial nerve crushed; right tibial nerve cut	10	19	19	34.4*	45.0*	2.78 ± .19	2.82 ± .18	98.8 ± 1.9
B	Left tibial nerve crushed; right tibial nerve cut	6	20	13	25.1*	39.1*	2.65 ± .24	2.95 ± .12	90.6 ± 9.5

* Calculated on basis of normal dry muscle weight to body weight ratio of .0891%.

† Q_{O₂} of left muscle expressed as % of Q_{O₂} of right muscle.

¹ Lazere, B., Thomson, J. D., and Hines, H. M., *Am. J. Physiol.*, 1943, **138**, 357.

² Hastings, A. B., Muus, J., and Bessey, O. A., *J. Biol. Chem.*, 1939, **129**, 295.

sumption between solei from different animals and also between the two solei of single animals (Table I, I).

The tibial nerves of 19 animals were cut and the oxygen consumption measured 14 days later. It was found that the O_2 consumption of denervated muscles was on the average slightly higher than that of their unoperated controls (Table I, II), the statistical probability of the observed increase being significant lying between 95% and 98%. The oxygen consumption following a unilateral nerve crush was measured at time intervals ranging from 15 to 42 days after denervation. When the results were arrayed according to the degree of atrophy it was noticed that the muscles exhibiting greater weight loss tended to possess slightly higher metabolic rates than their unoperated controls (Table I, III A and B). Calculation of the correlation coefficient between the percentage of weight loss and the gain in QO_2 showed that only a fair correlation existed ($r = .52 \pm .14$). To compare the oxygen

uptake of totally denervated muscle with that of regenerating muscle, the left tibial nerve was crushed and the right tibial cut in another series of 110-days-old rats (Table I, IV A and B). When the weight losses of the contralateral muscles were of the same order, no significant difference in O_2 consumption between the regenerating and the completely denervated muscles was detectable.

Conclusions. Although in some instances statistical interpretation of the data was limited by the smallness of the sample size in relation to size of the mean differences and standard deviations, it may be concluded with reasonable certainty that regenerating muscle exhibits a slightly increased rate of oxygen consumption *in vitro* per gram of tissue, but that the rate of oxygen consumption of regenerating muscle does not differ significantly from that of completely denervated muscle which has undergone a similar degree of weight loss.

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Histamine Ineffective in the Rat as a Gastric Secretory Stimulant.

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In the course of a comparative study of gastric secretion it was observed that the rat did not respond to histamine when given in doses found effective in other mammals. This seemed of sufficient interest to warrant special study since in our experience the only animals found refractory to histamine are the elasmobranch fishes¹ and the lower amphibia.²

Young albino rats, from 180 to 240 g body weight, kept on a diet of Purina dog chow, were used. Because of the well known habit

of coprophagy, the stomach ordinarily is found to be filled with ingestia even after withholding food for 48 hours. By enclosing the rat in a specially constructed jacket, Roe and Dyer³ were able to obtain animals with empty stomachs. We used this method but later abandoned it in favor of a simpler one. Keeping the animals without food in specially constructed wide-mesh, false-bottom cages proved satisfactory. Water was allowed *ad lib*. Only 5 to 12% of more than 1000 rats were found to have stomachs containing ingested matter after 24 to 36 hours' fast.

The animal was anesthetized with nem-

¹ Babkin, B. P., Chaisson, A. F., and Friedman, M. H. F., *J. Biol. Board Canada*, 1934, **1**, 251.

² Friedman, M. H. F., *J. Cell. Comp. Physiol.*, 1942, **20**, 379.

³ Roe, J. H., and Dyer, H. M., *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 603.