

Lack of correlation between strength of contractions and oxygen consumption of drug-treated, directly-stimulated rat diaphragm

ROSEMARY A. BERESFORD
(introduced by E. G. McQUEEN)

*Department of Pharmacology, Otago University,
Dunedin, New Zealand*

A correlation has been shown to exist between the oxygen consumption of smooth muscle and its mechanical activity (Weston, 1972). A similar correlation might be expected with skeletal muscle but the following experiments indicate that this is not always so.

All experiments were performed on rat quarter-diaphragms removed from female Wistar rats (180–210 g). The diaphragms (6–10 for each drug) were mounted with a resting tension of approximately 2 g in Krebs Henseleit solution which contained tubocurarine (13 μ M) and which had been aerated with a mixture of oxygen and carbon dioxide (95:5) for not less than 2 h before experimentation. The chamber into which the tissue was inserted was that devised by Fastier & Sullivan (1977) for the simultaneous measurement of oxygen consumption and muscle contractions evoked directly by supramaximal electrical shocks. The oxygen consumption and contractions obtained during a 10 min exposure to a buffered drug solution were compared with those obtained while the muscle was immersed in plain Krebs Henseleit solution.

Drugs such as ouabain (0.01 mM) and phenformin (0.1 mM), which did not affect strength of contraction, did not alter oxygen consumption; furthermore, concentrations of amylobarbitone (5 mM) and pentobarbitone (5 mM) which greatly depressed muscle contractions also reduced the rate of oxygen uptake

significantly. However, a lower concentration (1 mM) of amylobarbitone or pentobarbitone increased muscle contractions significantly, yet decreased oxygen uptake. Phenobarbitone (5 mM) increased muscle contractions significantly without altering oxygen uptake, as did 4-aminopyridine (0.1 mM; 0.5 mM). On the other hand, both 2,4-dinitrophenol (0.05 mM) and *S*-*n*-decylthiuronium (1 mM) decreased the amplitude of the evoked contractions while increasing the oxygen consumption of the tissue.

The response to 2,4-dinitrophenol is that which may be expected of an uncoupling agent (Weeks & Chenoweth, 1951). That to *S*-*n*-decylthiuronium might be due to a disruptive effect on cellular membranes; in the concentrations used, it has been shown to lyse erythrocyte membranes (Beresford, 1976). The increase in muscular activity accompanied by either a reduction in oxygen consumption or an unchanged consumption is more difficult to explain. The more efficient contractile response indicated by the result may be related to an increased release of calcium ions, possibly associated with a reduced consumption of adenosine triphosphate.

References

- BERESFORD, R.A. (1976). The influence of *S*-decylthiuronium on erythrocyte membranes. *Proc. Aust. Physiol. Pharmac. Soc.*, **7**, 114P.
- FASTIER, F.N. & SULLIVAN, P.A. (1977). An improved technique for simultaneously recording the contractility and oxygen consumption of an isolated muscle. *Proc. Univ. Otago med. Sch.*, **55**, 4–5.
- WEEKS, J.R. & CHENOWETH, M.B. (1952). A stationary manometric respirometer for isolated rat diaphragm allowing simultaneous direct registration of mechanical activity. Observations with sodium azide and dinitrophenol. *J. Pharmac. exp. Ther.*, **104**, 187–201.
- WESTON, A.H. (1972). The effects of isoprenaline and phenylephrine on oxygen consumption in isolated smooth muscle. *Br. J. Pharmac.*, **45**, 95–103.