Effects of chronic inactivity on physiological and biochemical characteristics of rat skeletal muscle

H. Xu,[1] G.D. Lamb[2] and R.M. Murphy,[1] [1]La Trobe Institute for Molecular Science, La Trobe University, Melbourne, NSW 3086, Australia and [2]School of Life Sciences, La Trobe University, Melbourne, VIC 3086, Australia.

Chronic inactivity is detrimental to human health. It can lead to changes in skeletal muscle structure and function and metabolic processes (Saltin *et al.*, 1977). The laboratory rat is commonly used for studying muscle physiology, however it must be considered a sedentary animal if housed in conditions where its activity is abnormally reduced (Sherwin, 1988). It is currently unclear what physiological and biochemical changes occur in muscle with such chronic inactivity.

To investigate the effect of sedentary behaviour in rat skeletal muscle, 12 to 18 wk male Sprague-Dawley rats were individually housed either in normal cages (SED, n=9) or in cages with free access to a running wheel (RUN, n=10), which resulted in rats voluntarily running 1-4 km per day. Following 6 or 12 wk intervention, SED and RUN rats were sacrificed with overdose of isoflurane with approval of the La Trobe University Ethics Committee. The *extensor digitorum longus* (EDL) muscle (type II fibres) and *soleus* (SOL) muscle (predominantly type I fibres) were excised for either biochemical measurements in whole muscle homogenates, or for physiological measurements in mechanically-skinned fibres, including calcium sensitivity of the contractile apparatus and the maximum force production.

Calcium sensitivity of contractile apparatus was increased by ~0.04 pCa units in type II muscle fibres from RUN compared with SED animals, which was reversed by dithiothreitol (DTT) treatment (n=27 fibres, $P<0.05$), indicative of oxidative regulation of the contractile apparatus. When fibres were collected from rats that had ceased running for 24 hours prior to experiments, there was no change in calcium sensitivity. Maximum force production was increased in RUN compared with SED animals in both type II (↑ 5%) and type I (↑ 25%) fibres. There was a change in the fibre-type composition in EDL but not SOL muscles from RUN compared with SED animals, with ~8% more MHCIIa fibres. There were no changes in the calcium handling proteins calsequestrin and sarcoplasmic reticulum calcium ATPase (SERCA). In muscle from RUN compared with SED animals, there was a decrease in glycogen synthase (~40%) in SOL muscle and a decrease of glycogenin (~35%) in EDL muscle, with no changes for glycogen phosphorylase, glycogen branching enzyme, glycogen debranching enzyme and GLUT4 in either muscle. Despite no fibre type change, the glycolytic enzyme, GAPDH was ~30% lower in SOL muscle, with no change in EDL muscle, while the other oxidative enzyme COXIV remained unchanged in both muscles. The regulatory Na+-K+-ATPase α1 protein increased in both muscles (~25% EDL, 20% SOL) in RUN compared with SED animals.

These experiments showed that activity induced a reversible short-term, oxidant-dependent increase in Ca^{2+}-sensitivity of the contractile apparatus in type II fibres. Furthermore, the findings suggest that experimental data obtained from sedentary animal models should be viewed with caution, because the sedentary behaviour can alter many of the muscle parameters both physiologically and biochemically.

Saltin B, Henriksson J, Nygaard E, Andersen P, Jansson E. (1977) Fiber types and metabolic potentials of skeletal muscles in sedentary man and endurance runners. *Ann N Y Acad Sci* **301**, 3-29.

Sherwin CM. (1988) Voluntary wheel running: a review and novel interpretation. *Anim Behav* **56**, 11-27