Autoperfused hindlimb as a physiologically relevant model to study skeletal muscle function and metabolism

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The aim of this project, was to establish a small animal model that could provide adequate oxygen delivery at physiological vascular resistance to support studies of metabolism and blood flow in both resting and contracting muscle.

Male Hooded Wistar rats were anaesthetised with sodium pentobarbital (6mg/100g body weight i.p.). Polyethylene tubing filled with 0.9% heparinised saline containing 6% w/v dissolved dextran 70 was used as cannulae at all times. The left carotid artery was cannulated to record mean systemic blood pressure. The right femoral artery (non-perfused) was cannulated to supply arterial blood to the left hindlimb femoral artery (perfused) and allow arterial sampling. This loop was passed through a pump for constant flow with perfused hindlimb pressure recorded via a side arm pressure transducer distal to the pump. Passive venous return occurred via a cannula from the left femoral vein to the right external jugular vein, allowing for venous sampling. The left sciatic nerve was stimulated via a bipolar electrode with force produced recorded. Blood was sampled from the venous and arterial loops and oxygen uptake ($\dot{V}O_2$) determined using the Fick equation. Rats were kept normothermic and were ventilated during experiments to control arterial O_2 content. Extracorporeal blood volume was ≤ 2ml.

At 1 $ml \cdot min^{-1}$ mean systemic pressure was 99.32 ± 4.06 mmHg (n = 44, mean ± SEM), mean hindlimb perfusion pressure was 92.31 ± 3.08 mmHg. $\dot{V}O_2$ was 0.328 ± 0.022 $\mu mol^{-1} \cdot min^{-1} \cdot gww^{-1}$ and $(a\text{-}\bar{v})O_2$diff of 5.03 ± 0.35 $ml \cdot 100ml^{-1}$. At 2 $ml \cdot min^{-1}$ with muscle stimulation mean hindlimb pressure was 166.41 ± 5.16 mmHg (n = 8) with a $\dot{V}O_2$ of 0.570 ± 0.084 $\mu mol^{-1} \cdot min^{-1} \cdot gww^{-1}$ and $(a\text{-}\bar{v})O_2$diff of 4.44 ± 0.69 $ml \cdot 100ml^{-1}$. $\dot{V}O_2$ is decreased at higher flow rates without stimulation (0.190 ± 0.02 $\mu mol^{-1} \cdot min^{-1} \cdot gww^{-1}$) but with muscle contraction was increased. The Table summarises the blood profile during both flow rates.

Arterial		**Venous**	1ml/min	2ml/min + stim
pH	7.37 ± 0.01	pH	7.27 ± 0.01	7.29 ± 0.01
pCO_2(mmHg)	34.77 ± 0.72	pCO_2(mmHg)	51.44 ± 1.11	50.60 ± 1.45
pO_2 (mmHg)	101.47 ± 1.31	pO_2 (mmHg)	46.33 ± 1.49	45.40 ± 2.52
Hct (%)	45.41 ± 0.42	Hct (%)	47.11 ± 0.42	49.75 ± 0.92
K^+ (mmol/l)	3.65 ± 0.04	K^+ (mmol/l)	3.33 ± 0.05	3.70 ± 0.05
Hb (g/dL)	14.80 ± 0.14	Hb (g/dL)	15.37 ± 0.14	16.26 ± 0.31
SO_2 (%)	97.57 ± 0.10	SO_2 (%)	71.22 ± 1.77	71.69 ± 3.71

The development of an autoperfused rat hindlimb by this laboratory gives rise to a physiologically relevant model to study skeletal muscle function and metabolism.