Microvascular PO$_2$ kinetics in hindlimb skeletal muscle of obese diabetic Zucker rats

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Microvascular PO$_2$ (PO$_2$mv) in skeletal muscle reflects the dynamic balance between oxygen delivery and oxygen uptake. PO$_2$mv on-kinetics in the rat spinotrapezius muscle during the rest-contraction transition are faster in both streptozotocin (STZ) and Goto-Kazazaki (GK) diabetic rats. Reduced nitric oxide (NO) availability has been implicated in these diabetic sequelae.

**AIM:** The purpose of this study was to determine the impact of insulin-resistant diabetes on PO$_2$mv kinetics in a hindlimb locomotory muscle, and to assess the role of NO.

**METHODS:** PO$_2$mv (phosphorescence quenching) was measured in the extensor digitorum longus muscle (EDL) of female lean control (LC, n=10, 194 ± 3 g) and obese diabetic (OD, n=9, 356 ± 11 g) Zucker rats. PO$_2$mv was monitored at rest and through the rest-contraction transition. PO$_2$mv on-kinetics were determined using a monoexponential plus time delay model. EDL muscle blood flow (radiolabeled microspheres) was measured at the end of the 150 s contraction period. The experimental protocol involved; 1) pre-stimulation, 2) control stimulation, 3) administration of L-NAME (30 mg/kg), followed by 4) post-L-NAME stimulation.

**RESULTS:** OD rats had elevated blood glucose levels (LC, 5.9 ± 0.4; OD, 25.4 ± 1.8 mmol/L; P<0.05). Resting PO$_2$mv was not different in LC and OD rats (LC, 29 ± 2; OD, 23 ± 3 mmHg; P>0.05). During contractions, PO$_2$mv fell to the same level in both groups (LC, 16 ± 2; OD, 17 ± 2 mmHg). OD rats had both a shorter time delay (LC, 9 ± 2; OD, 7 ± 1 s; P<0.05) and shorter mean response time (LC, 24 ± 2; OD, 17 ± 1 s; P<0.05). EDL blood flow during contractions was not different (LC, 70 ± 15; OD, 67 ± 17 ml/min/100 g). PO$_2$mv was lower after L-NAME in both LC and OD rats. Both time delay and mean response time were shorter in LC and OD rats, but the PO$_2$mv time constant was shorter only in LC rats. Blood flow during contractions was not reduced by L-NAME, but the vascular conductance was reduced. **CONCLUSIONS:** The faster PO$_2$mv on-kinetics observed in the EDL muscle of OD rats is consistent with previous reports in STZ and GK rats, and may be due to a slower rise in blood flow and oxygen delivery at the onset of contractions. These data also suggest that impaired NO production in OD rats may contribute to the more rapid fall in PO$_2$mv at the onset of muscle contractions. (Supported by the AHA, Heartland Affiliate and the KCOM Graduate Program.)

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