Cardiac glucose uptake is linked to the eNOS-dependent mitochondrial biogenesis in adaptation to endurance exercise in mice

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Endurance exercise training increases the cardiac energy metabolism and glucose uptake through poorly understood mechanisms. Nitric oxide (NO), tonically synthesized in cardiomyocytes by endothelial NO synthase (eNOS), plays important roles in cardiac adaptations. Here we demonstrate that NO donors up-regulate peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α), nuclear respiratory factor 1 (NRF-1), and mitochondrial transcription factor A (Tfam) expression, mitochondrial biogenesis, and both basal and insulin-stimulated glucose uptake in HL-1 cardiomyocytes. These effects of the NO donors are suppressed in cells transfected with either PGC-1α or Tfam small interference RNA. Moreover eNOS expression is increased, with a concomitant raise of mitochondrial biogenesis and both basal and insulin-stimulated glucose uptake, in cardiac muscle of swim-trained mice. On the contrary the genetic deletion of eNOS prevents these adaptive phenomena. Our findings demonstrate that endurance exercise training increases cardiac glucose uptake by up-regulating eNOS expression, and that the eNOS-dependent mitochondrial biogenesis is an essential step in this process.