Acute high-intensity exercise-induced redox signalling is associated with enhanced insulin sensitivity in obese middle-aged men

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Background: Reactive oxygen species and their subsequent activation of stress and mitogen activated protein kinases (SAPK) are involved in contraction and insulin stimulated glucose uptake. However, their role in the enhancement of insulin sensitivity in the hours after exercise are not clear.

Methods: We investigated the effect of an acute bout of high-intensity interval exercise (HIIE) on redox homeostasis, SAPK signalling and insulin sensitivity in eleven middle-aged (58.1±2.1 years mean±SEM), obese (33.1±1.4 $kg \cdot m^2$) men. Participants completed a 2 hour hyperinsulinaemic-euglycaemic clamp at rest and another insulin clamp 1-3 weeks later after a single bout of HIIE (4x4 minutes at 95% HR_{peak}, 2 minute recovery periods at 50% HR_{peak}). Data were checked for normality and statistical analysis were conducted at the 95% level of significance ($p \leq 0.05$). Unless otherwise noted, all comparisons are $P<0.05$.

Results: Exercise increased insulin sensitivity (glucose infusion rate and m-value) by ~34-40%. One hour after HIIE (prior to insulin stimulation) plasma catalase activity increased (~40%) and plasma hydrogen peroxide and thiobarbituric acid reactive substances (TBARS) decreased (~16% and ~21%, respectively). Insulin stimulation at rest and after HIIE similarly increased plasma superoxide dismutase activity (~44% and ~43%, respectively), catalase activity (~36% and ~34%), skeletal muscle 4-HNE protein modification (~43% and ~29%) and IRS-1^{ser307} phosphorylation (~35% and ~33%); and decreased TBARS (~20% and ~30%) and hydrogen peroxide (~29% and ~29%). Compared to the rest trial, HIIE increased to a greater extent insulin stimulated phosphorylation of $JNK^{Thr183/Tyr185}$ (~141% *versus* ~321%), p38 $MAPK^{Thr180/Tyr182}$ (~81% *versus* ~471%) and $AS160^{(ser588)}$ (~83% *versus* ~139%). Furthermore, only after HIIE was insulin stimulated phosphorylation of NF-κB p65 increased (~127%) and $PKC\delta/\theta^{Ser643/676}$ decreased (~30%). Insulin sensitivity after exercise was associated with higher insulin stimulated SOD activity and greater phosphorylation of JNK, p38 MAPK and NFκB p65 ($r=0.634$, $r=0.709$, $r=0.724$, $r=0.708$; $P<0.05$, respectively). In contrast, insulin sensitivity tended to correlate with lower phosphorylation of $PKC\delta/\theta^{Ser643/676}$ ($r=-0.571$, $P=0.066$).

Conclusion: This study provides evidence that a single bout of HIIE can transiently improve systemic redox homeostasis by increasing plasma antioxidant capacity and reducing oxidative stress in obese middle-aged men. Furthermore, our findings suggest that redox homeostasis and SAPK signalling are important regulators of insulin stimulated glucose uptake and may play a role, at least in part, in the post-exercise enhancement of insulin sensitivity. As such HIIE may be an attractive option for improving redox homeostasis and insulin sensitivity in obese middle-aged men.