Molecular mechanisms underpinning enhanced insulin action by prior exercise

J.F.P. Wojtaszewski, Copenhagen Muscle Research Centre, Institute of Exercise and Sport Sciences, University of Copenhagen, 13 Universitetsparken, DK 2100, Copenhagen, Denmark. (Introduced by M. Febbraio)

Type 2 diabetes mellitus (T2DM) has become one of the most prevailing diseases world-wide. A hall mark of T2DM is skeletal muscle insulin resistance to increase glucose uptake. Skeletal muscle is responsible for clearing most of the available glucose and increasing insulin sensitivity within this tissue is thought to be a beneficial treatment/prevention strategy. Interestingly, like physical activity, some of the anti-diabetic drugs used today are now known to activate 5′AMP activated protein kinase (AMPK). It is the working hypothesis that AMPK may promote insulin sensitivity not only in response to exercise but also to anti-diabetic drugs targeting skeletal muscle.

Following an acute bout of exercise, glucose transport decreases gradually whereas the sensitivity of muscle to insulin increases. This effect of exercise can persist for several days, even after full glycogen repletion. The mechanism(s) for this increased insulin sensitivity is at present not known, but apparently it is not linked to changes in activity of the proteins involved in the proximal part of the classical phosphatidylinositol 3 kinase insulin signalling cascade.

It is possible that the increase in post-exercise induced insulin sensitivity in skeletal muscle may come about through modulation of further down-stream elements in the insulin signalling pathway. Interestingly, one such element may be the recently discovered Akt substrate of 160 kDa (AS160). AS160 is involved in the insulin regulated glucose transport in skeletal muscle, and AS160 was recently shown to be regulated by various other kinases, including AMPK. The interplay between stimuli such as exercise (AMPK) and insulin (Akt) on the regulation of AS160 suggests that AS160 may be a point of signal convergence leading to enhanced insulin sensitivity post exercise.