54 CELLULAR REGULATION OF EXERCISE-INDUCED INSULIN RESISTANCE

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While the effects of exercise on insulin sensitivity are generally positive, eccentric exercise presents a paradox because

it induces a transient state of insulin resistance that persists for up to 48 h after the exercise bout. Excessive eccentric contractions, such as prolonged downhill running or marathon running, cause muscle damage and disruption of the integrity of the cell. Downregulation of insulin receptor tyrosine phosphorylation and subsequent steps in the insulin signalling pathway, including insulin receptor substrate-1 (IRS-1)-associated phosphotidylinositol (PI) 3-kinase, Akt-kinase serine phosphorylation and activity, and glucose transporter (GLUT-4) protein content are evident in skeletal muscle after eccentric exercise. Furthermore, increased TNF-α secretion from monocytes is associated with the decrease in PI 3-kinase activity after this type of exercise. Recent studies have shown that TNF-α can increase IRS-1 serine/threonine phosphorylation, which impairs IRS-1 docking to the insulin receptor, and this inhibits insulin signalling. Thus, a unifying hypothesis to explain insulin resistance after eccentric exercise may include inflammation arising from disruption of muscle cell integrity, leading to an acute-phase response that includes TNF-α, with the latter inhibiting insulin signalling and subsequent metabolic events. In contrast, exercise training increases insulin signalling and GLUT-4 expression, decreases TNF-α expression in skeletal muscle, and is associated with enhanced insulin sensitivity. These observations highlight the complexity of the cellular and molecular adaptations to exercise. Understanding these adaptations is essential in order to establish a sound theoretical basis for developing optimal training programmes for athletes and for recommending exercise as a therapeutic intervention for enhancing health.