Exercise, GLUT4 and insulin action

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The facilitative glucose transporter GLUT4 has a critical role for skeletal muscle glucose uptake in response to insulin stimulation and muscle contraction during exercise. We have previously demonstrated that both a single bout of exercise and regular exercise training increase skeletal muscle GLUT4 expression and that this is mediated via the HDAC5-MEF2 axis, with upstream involvement of a number of kinases notably the AMP-activated protein kinase (see Richter & Hargreaves, 2013 for review). Recently, our attention has turned to the potential of exercise to alter adipose tissue GLUT4 expression, with implications for whole body insulin sensitivity. The significance of this stems from reports that adipose tissue GLUT4 expression is reduced in patients with type 2 diabetes and that adipose tissue-specific deletion of GLUT4 in mice is associated with impaired whole body insulin action, due partly to a circulating adipokine inhibiting insulin action in skeletal muscle and liver (see Graham & Kahn, 2007 for review). Previous studies have demonstrated that exercise training increases insulin-stimulated glucose uptake in adipose tissue and GLUT4 expression in rodents; however to date, no studies have been undertaken in humans.

A single bout of endurance-type exercise, did not alter GLUT4 gene expression in human, subcutaneous (para-umbilical) adipose tissue, although somewhat surprisingly, GLUT4 protein expression was reduced ~10% 3 h after exercise (Boland *et al.*, unpublished data). Four weeks of exercise training increased both adipose tissue and skeletal muscle GLUT4 expression in patients with type 2 diabetes (Hussey *et al.*, 2011). These latter results support the notion that the beneficial effects of exercise on glucose metabolism and insulin action arise from adaptations in multiple organs (notably skeletal muscle, but also adipose tissue, and indeed, liver and pancreas). A key research challenge is to understand the mechanisms by which exercise increases adipose tissue GLUT4 expression and this is the focus of our current activities.

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