Does Exercise Without Weight Loss Improve Insulin Sensitivity?

It has long been established that a single exercise session can increase insulin-stimulated glucose uptake in previously sedentary adults (1). A single bout of moderate intensity exercise can increase glucose uptake by at least 40% (2). The benefits of exercise diminish rather quickly, however, as the effects generally dissipate within 48 to 72 h of the last exercise session (3). This observation is reinforced by investigations demonstrating that cessation of exercise in trained persons is associated with a marked and rapid decrease in insulin sensitivity (4). A detailed review of the putative mechanisms by which exercise enhances insulin action is the subject of several excellent reviews (5,6).

Although a single bout of exercise improves glucose metabolism acutely, the impact of exercise training (e.g., the summation of acute bouts of exercise) on glucose metabolism is unclear. The issue is not whether exercise training is associated with improvement in glucose tolerance and insulin action. Recognition that exercise training enhances the ability of skeletal muscle to glucose uptake was reported over 30 years ago when Bjorntorp et al. (7) observed that insulin action is greater in physically active than sedentary individuals. Rather, the issue is whether the impact of exercise training on glucose metabolism is a direct effect or an indirect effect that depends on concomitant reduction in body fat and/or the residual effects of the last exercise session. Indeed, several of the early studies that observed significant improvements in glucose tolerance (8) and insulin sensitivity (9) in response to exercise training obtained post-training measurements within 12 to 48 h of the last exercise session, and corresponding reductions in body fat were neither rigorously controlled nor measured. In contrast, Segal et al. (10) report that 12 weeks of exercise in lean, obese, and type 2 diabetic men, during which body weight was held constant by refeeding and then insulin sensitivity measures were obtained 4 days postexercise, did not significantly alter insulin sensitivity. More recently, the findings from a controlled trial have shown that after control for the residual effects of the last exercise session, daily exercise performed for 60 min at 70% of maximal heart rate is not associated with significant improvement in insulin sensitivity in the absence of weight loss in obese men (11). These observations appear to suggest that the impact of exercise training on insulin sensitivity is mediated by diminished body weight and/or adiposity. In other words, exercise training without weight loss is not associated with improvements in insulin action when assessments are made 96 h postexercise.

In this context, the article by Duncan et al. (12) in this issue of *Diabetes Care* describes the effects of 6 months of exercise without weight loss on insulin sensitivity and several markers of lipid metabolism in a group of 18 sedentary men and woman. All participants were asked to refrain from weight loss and insulin sensitivity measures (frequently sampled intravenous glucose tolerance test) were obtained 24–48 h after the last exercise session. The principal finding was that insulin sensitivity and plasma lipase activity increased without a corresponding change in BMI, waist circumference, or cardiorespitarory fitness. From this observation the authors conclude that modest amounts of exercise without weight loss positively affect markers of glucose and lipid metabolism in previously sedentary adults. Although this is surely a positive result with important clinical implications, the authors fail to provide a compelling argument to support the assertion that exercise per se, and not weight loss, was responsible for the improvement in insulin sensitivity. The fact that insulin sensitivity increased despite no change in the mean value for BMI or waist circumference does not necessarily imply that changes in these variables are not associated with the improvement in glucose metabolism. Reliance on the mean change in the primary outcome variables to determine treatment effects may mask the substantial interindividual differences that often characterize the response to treatment. For example, the standard deviation for the change in insulin sensitivity was 75% greater than the mean change. Thus, some individuals' insulin sensitivity increased considerably in response to the training program, whereas others had no increase in insulin action. Thus, it is difficult to resolve whether the changes in insulin sensitivity are associated with changes in body weight (BMI) based on the mean changes alone because of the heterogeneity in response. To consider individual variability across the entire range of responses, it is often desirable to use correlation and regression analyses on the individual scores in addition to examining the mean change in variables. This notion is reinforced by the authors' finding that changes in BMI alone were significantly correlated to corresponding changes in insulin sensitivity and that several lipid and lipase variables were related to corresponding changes in both BMI and waist circumference. Combined with the observation that cardiorespiratory fitness did not change ($V_{O_{2max}}$), one might argue that the effects of 6 months of exercise training on insulin sensitivity and lipid metabolism are attributable to corresponding change in body composition and not exercise training. These observations do not detract from the importance of this study, but rather suggest that the positive outcome may be due to exercise-induced weight loss rather than exercise per se. Either way the conclusion remains the same, that modest exercise is associated with significant improvements in glucose and lipid metabolism.

The findings reported by Duncan et al. (12) add to a growing body of literature indicating that exercise with or without weight loss improves insulin sensitivity. As already noted, it is well established that acute exercise is associated with substantial improvement in insulin sensitivity independent of any change in

cardiorespiratory fitness or body composition. The fact that the beneficial effects of acute exercise diminish quickly simply implies that exercise should be performed on a regular basis, a notion entirely consistent with the recommendation from the U.S. Centers for Disease Control and Prevention that regular physical activity, such as brisk walking for 30–60 min, be performed on most days of the week (13). Furthermore, given that weight loss reverses the insulin resistance that is characteristic of obesity (14), it is reasonable to suggest that the beneficial impact of daily exercise on insulin resistance would be magnified if associated with diminished body weight and/or body fat. Indeed, combined with the fact that modest exercise reduces the morbidity and mortality associated with cardiovascular disease and diabetes (15), it is difficult to imagine a more effective therapeutic strategy for reducing insulin resistance and, more importantly, improving overall health and wellbeing.

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