HIGHLIGHTED TOPIC  | Role of Exercise in Reducing the Risk of Diabetes and Obesity

Fat as an endocrine organ: influence of exercise

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Berggren, Jason R., Matthew W. Hulver, and Joseph A. Houmard. Fat as an endocrine organ: influence of exercise. J Appl Physiol 99: 757–764, 2005; doi: 10.1152/japplphysiol.00134.2005.—The prevalence of diabetes and obesity continues to increase. It is therefore important to identify the pathophysiology underlying these disorders. An inability of insulin to stimulate glucose uptake, i.e., insulin resistance, appears to be a common link between diabetes and obesity. The identification of various adipocyte-secreted cytokines (adipocytokines) that influence satiety, energy balance, and insulin sensitivity provide a novel target for the treatment of these disorders. Adipocytokines are differentially expressed with obesity and diabetes, making them a strong candidate for linking insulin resistance to these pathological conditions. This review explores the role of adipocytokines in insulin action and examines the effect of exercise training on adipocytokine content.

adipocytokines; insulin sensitivity; metabolism

ALTHOUGH ONCE THOUGHT TO BE a mere storage depot of excess energy, it is now apparent that adipose tissue is an endocrine organ and plays a prominent role in energy metabolism. The discovery of leptin, a satiety hormone secreted by adipose tissue, led us to change the way we view the role of adipose tissue in nutrient metabolism. In addition to leptin, other cytokines including tumor necrosis factor (TNF)-α, interleukin-6 (IL-6), resistin, visfatin, acylation stimulation protein, and adiponectin have been identified as adipose-secreted proteins that are collectively referred to as adipocytokines. Adipocytokines have numerous functions that include regulation of satiety, carbohydrate and lipid metabolism, and insulin sensitivity. They are differentially expressed with obesity and diabetes. Metabolic syndrome is characterized as a cluster of metabolic conditions including excess abdominal fat, hyperglycemia, hyperlipidemia, and hyperinsulinemia (75). Peripheral insulin resistance appears to be the common mediator of altered nutrient metabolism observed in these disorders. Because adipocytokines have been shown to influence insulin signaling, regulation of these cytokines may play a role in the etiology of insulin resistance, obesity, and diabetes by altering or influencing carbohydrate and/or lipid metabolism. The study of these novel proteins is important as the prevalence of metabolic syndrome, diabetes, and obesity are increasing at epidemic rates and represent a large portion of health care costs. Weight reduction and exercise are common nonpharmacological interventions for the treatment of insulin resistance.

Exercise may improve insulin sensitivity by modulating the plasma content and/or function of adipocytokines. Therefore, this review will focus on the following topics: 1) what are the roles of adipocytokines in skeletal muscle substrate metabolism and 2) what effect does exercise have on circulating levels of adipocytokines?

ADIPOCYTKINES, INSULIN RESISTANCE, DIABETES, AND OBESITY

Adiponectin. Adiponectin, also referred to as AdipoQ (47) and Acrp 30, is a 30-kDa protein that is encoded by apM-1 (69) and expressed and secreted only by adipose tissue. Adiponectin, which contains an NH₂-terminal collagennous domain and COOH-terminal globular domain, circulates as either low molecular weight trimer-dimer (180 kDa) or high molecular weight complex (>400 kDa) (83, 84). Pajvani et al. (83, 84) recently reported that the higher molecular weight complex is the more biologically active form of the protein. However, most human clinical intervention studies measure total adiponectin, which is proportional to the higher molecular weight complex, via commercially available kits (103).

Adiponectin increases skeletal muscle fatty acid oxidation and reduces plasma glucose concentrations through activation of adenosine monophosphate-activated protein kinase (AMPK) (Table 1) (113). Both the globular domain and full-length adiponectin activated AMPK in skeletal muscle (113). Activation of AMPK leads to phosphorylation, and thus inhibition, of acetyl coenzyme A carboxylase. Acetyl coenzyme A carboxylase is the regulated step in malonyl-CoA production and subsequent fatty acid biosynthesis. Malonyl-CoA is also a potent inhibitor of carnitine palmitoyl transferase-I, the rate-
Table 1. Role of adipocytokines on skeletal muscle substrate utilization in humans

<table>
<thead>
<tr>
<th>Adipocytokine</th>
<th>Mechanism of Action</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin</td>
<td>AMPK activation (113)</td>
<td>Increase substrate utilization (113)</td>
</tr>
<tr>
<td>Leptin</td>
<td>AMPK activation (72, 73)</td>
<td>Increase substrate utilization (72, 73)</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Serine phosphorylation of IRS-1* (43)</td>
<td>Inhibit glucose uptake* (43)</td>
</tr>
<tr>
<td>Resistin</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>IL-6</td>
<td>unknown</td>
<td>Stimulate FAO and lipolysis† (105)</td>
</tr>
</tbody>
</table>

Mechanism and function of the adipocytokines on human skeletal muscle carbohydrate and lipid metabolism. Reference numbers are given in parentheses. *Results from animal models that have not been confirmed in humans. †In adipose tissue.

limiting enzyme of fatty acid uptake into the mitochondria. Therefore, a reduction in malonyl-CoA removes inhibition of mitochondrial fatty acid uptake and stimulates fatty acid oxidation, as well as reduces lipid biosynthesis. Because lipid accumulation is associated with peripheral insulin resistance, increased circulating adiponectin would be favorable.

Adiponectin mRNA expression in adipose tissue (47) and plasma protein content (4) are reduced with obesity and diabetes. Additionally, diabetes, obesity, and metabolic syndrome susceptibility locus has been mapped to chromosome 3q27, which encodes adiponectin (14, 106). Single nucleotide polymorphisms of the adiponectin gene have also been associated with the onset of diabetes (119). The relationship between plasma adiponectin and insulin action appears independent of body mass index (BMI) or body fat (56). When subjects are matched for BMI and stratified according to insulin sensitivity, differences in plasma adiponectin were related to differences in insulin action (56). Furthermore, insulin-resistant lean individuals have reduced plasma content of adiponectin compared with insulin-sensitive subjects (1).

It has been reported that lean and obese African Americans (AAs) have reduced skeletal muscle fatty acid oxidation and increased lipid accumulation compared with lean Caucasians (88), which is consistent with decreased AMPK activation and decreased adiponectin. Interestingly, both lean and obese AAs have reduced fasting plasma adiponectin levels compared with their Caucasian counterparts (49). Thus reduced plasma adiponectin levels, specifically in obese and AA populations, may contribute to a predisposition to weight gain and insulin resistance.

Plasma adiponectin is positively associated with enhanced insulin signal transduction in skeletal muscle (99) and a reduced risk of developing diabetes (97). Administration of adiponectin reverses insulin resistance in mice and reduced intramuscular triglycerides (114) and adiponectin knockout mice have impaired insulin sensitivity. Moreover, plasma adiponectin is increased by surgically induced (gastric bypass) and diet-induced weight loss, both of which are associated with improved insulin action (50).

Because exercise training has a profound effect on the prevention and treatment of obesity and diabetes, it is logical to hypothesize that these effects may be mediated through adiponectin regulation. However, because exercise training is associated with weight loss, it is important to discern the independent effects of exercise without the confounding influence of reductions in fat mass.

Plasma adiponectin has been measured in response to acute exercise bouts as well as moderate to long-term training programs in a variety of populations (Table 2). Neither an acute bout of stationary cycling [60 min at 65% maximal \( \dot{V}O_2 \) max] nor an acute bout (30 min) of higher intensity (79%) running altered plasma adiponectin concentration in healthy men and women (62). Six weeks of cycle training (60 min/day, 5 days/wk), which increased insulin sensitivity, did not increase plasma adiponectin concentration in healthy men. Moreover, a 3-wk exercise intervention in patients with Type 2 diabetes did not alter adiponectin despite improvements in insulin action (117). Finally, a body weight-controlled (no reduction in body mass or fat mass) 6-mo exercise intervention (4 days/wk for ~45 min at 65–80% peak \( \dot{V}O_2 \) consumption) increased insulin sensitivity (98%) despite no change in plasma adiponectin (50). Although weight loss is associated with increased adiponectin levels (115), chronic exercise without reductions in body weight does not affect plasma adiponectin levels in insulin-resistant populations (50). Thus the exercise-mediated enhancement of insulin action appears to be independent of changes in plasma adiponectin (116). However, the level of weight loss may be an important determinant of changes in plasma adiponectin levels. A 6-mo dietary intervention in conjunction with an exercise program that resulted in a 3% decrease in body fat (13% decrease in total fat mass) did not have an effect on plasma adiponectin levels (92). However, other lifestyle modification programs that resulted in greater weight loss increased plasma adiponectin and insulin sensitivity (23). The current evidence would suggest that exercise-induced improvements in insulin action occur independently of changes in plasma adiponectin. Additionally, the observation that the effects of exercise and weight loss on insulin action are additive may indicate that each modality mediates its effects through distinct pathways (17).

Leptin. In the early 1990s it was discovered that defects in the \( ob \) gene lead to obesity in the \( ob/ob \) mouse (120). Leptin is a product of the \( ob \) gene and circulates as a 16-kDa protein (120). Expression and secretion of leptin occurs primarily in white adipose tissue (13, 31, 33, 59); however, additional physiological sites of production have been established such as the stomach (6), brain (22, 111), placenta (67), skeletal muscle (109), bone (91), and arterial endothelium (85). Plasma leptin
exhibits a circadian rhythm with the highest concentrations occurring near midnight and lowest concentrations near mid-morning (8, 31, 34, 52). The diurnal rhythm of leptin secretion is hormonally (growth hormone, insulin, cortisol) influenced (2, 108), is dependent on gender (3, 93) and energy availability (3, 16, 41, 108), and may be altered by meal timing (95) and composition (9, 38).

Similar to adiponectin, leptin directly, or indirectly through hypothalamic-mediated responses, activates AMPK in skeletal muscle, thus increasing fatty acid oxidation and glucose uptake (72, 73). Administration of recombinant leptin to the ob/ob mouse resulted in reductions in food intake and weight loss (31, 34). Leptin has thus been implicated in the control of energy intake and expenditure as well as reproductive function (34). Hyperleptinemia is commonly observed with insulin resistance and Type 2 diabetes mellitus (71), and circulating leptin concentrations correlate with measures of adiposity, such as BMI, body fat percent, and total fat mass in humans and animals (71).

Plasma leptin decreases acutely during fasting or energy restriction and increases with refeeding and overfeeding. Thus it is logical that exercise, a modality that alters systemic energy flux and balance, would change plasma leptin concentration. Many studies have examined the effects of exercise on circulating levels of leptin with the thought that leptin sensitivity would be improved and plasma leptin concentrations reduced. Circulating leptin has been measured in response to short- (45) and long-term exercise training (11, 39, 51, 60, 80, 86, 87, 90, 101) and after single bouts of exercise (maximal, submaximal, short duration, and long duration) (20, 21, 24, 30, 39, 53, 61, 63–65, 77, 81, 87, 89, 96, 102, 110, 118). Short-term training does not influence fasting plasma leptin levels (45). Long-term exercise training decreases circulating leptin, but generally not independent of changes in fat mass (11, 60, 80, 87, 90, 101). Several long-term training investigations have demonstrated reductions in plasma leptin independent of weight reduction (40, 51, 86), but it is unclear whether these changes were due to long-term exercise training or were a result of the last exercise bout. Studies examining the leptin response to single bouts of exercise have produced equivocal results, but it appears that circulating leptin levels are only decreased by exercise bouts of considerably high intensity (21) and long duration (20, 61, 64, 65, 81, 118).

In a report from Hilton and Louches (41), energy intake and exercise-associated energy expenditure were controlled to distinguish the independent effects of energy availability and exercise stress on the diurnal leptin rhythm in healthy young women. When dietary energy intake was sufficient to compensate for the energy cost of exercise, the suppressive effects of exercise on 24-h leptin levels were prevented. Thus the only influence of exercise on the 24-h mean and amplitude of leptin was due to an induction of a negative energy balance caused by the energy cost of exercise. Furthermore, they concluded that the diurnal rhythm of leptin depends on energy and/or carbohydrate availability, which are variables directly influenced by exercise.

On the basis of the current evidence, reductions in circulating leptin in response to short-term exercise and/or single bouts of exercise do not appear to be due to exercise stress but are more likely the result of an induction of a negative energy balance. A change in leptin after long-term exercise training is primarily due to reduced fat mass and/or a result of the negative energy balance induced by the previous exercise bout.

**TNF-α.** TNF-α is a proinflammatory cytokine secreted from a variety of cells including macrophages, muscle (94), and adipose tissue (44). Recent evidence indicates that most of the TNF-α secreted by adipose tissue is derived from macrophage infiltration or other nonfat cell sources (25–27). TNF-α is a 26-kDa protein that undergoes posttranslational modification to form its active 17-kDa structure (74). TNF-α signaling is mediated by the transmembrane receptors TNF-α receptor 1 (p55) and TNF-α receptor 2 (p75). Although extensively studied in cachexia, autoimmune disease, rheumatoid arthritis, sepsis, and other inflammatory disorders, the role of TNF-α and its association with obesity and diabetes is less understood. Infusion of TNF-α in rats impaired insulin-stimulated whole body glucose disposal (43). TNF-α mediates insulin resistance via serine phosphorylation of insulin receptor substrate (IRS-1) in skeletal muscle, which inhibits the ability of insulin to stimulate GLUT-4 translocation to the cell membrane and therefore reduces glucose uptake (43). Conversely, inhibition of TNF-α results in increased insulin-stimulated IRS-1 tyrosine phosphorylation (10, 43). The ability of TNF-α to serine phosphorylate IRS-1 may be mediated via diacylglycerol (DAG). Incubating intact rat skeletal muscle strips with TNF-α significantly increased palmitate incorporation into DAG (7). This is important because DAGs are known activators of conventional and novel protein kinase C isoforms that serine phosphorylate, and thus inhibit, IRS-1. Therefore, as indicated by animal models, conditions associated with elevated TNF-α would be accompanied by insulin resistance.

Although not without conflicting results, it appears that obesity is associated with elevated adipose tissue mRNA expression of TNF-α, which is also positively associated with hyperinsulinemia (42, 44, 57, 112). Paradoxically, inhibition of TNF-α in obese diabetic patients had no effect on insulin sensitivity (79). Although coculture of human skeletal muscle with adipocytes impaired insulin signaling, the effect was independent of TNF-α (18). Additionally, incubating human skeletal muscle with TNF-α did not impair insulin-mediated glucose uptake (78), and some reports indicate an actual increase in glucose uptake (12). Thus human skeletal muscle glucose disposal is not hindered by TNF-α. Because only limited information is available regarding TNF-α and human skeletal muscle carbohydrate and lipid metabolism, it is difficult to provide a rationale for the conflicting results observed with these studies and previously reported results from animal studies.

Because TNF-α is an inflammatory cytokine produced by a variety of cells, distinguishing the effects of exercise on TNF-α content is difficult. TNF-α receptor (p55 and p75) knockout mice have elevated TNF-α mRNA expression in soleus muscle, whereas no difference was observed in gastrocnemius muscle (54). In this model, acute exercise (1 h swimming) reduced skeletal muscle TNF-α mRNA expression to control values. In a human study examining diabetes patients and weight-matched controls, an acute bout of exercise (25 min at 60% VO2 peak) had no effect on plasma TNF-α levels (94). Plasma concentration of TNF-α is unchanged after prolonged endurance exercise (6 h) in trained men (19). Conversely, a combination of aerobic (aqua exercise 60% VO2 peak for 60 min) and resistance training (1 set/wk, 1 set = 8–12 repeti-
tions) for 10 wk tended to increase plasma TNF-α in female participants, which was significantly related to a decrease in visceral fat mass (36). A 6-mo diet and physical activity (3/wk, 30 min 60 – 80% \( \dot{V}_O_2 \) peak) intervention resulted in a decrease in serum TNF-α in subjects with impaired glucose tolerance and tended to decrease serum TNF-α in diabetic subjects (76). However, because there was weight loss, it is difficult to determine the individual effect of exercise alone in these studies (29, 68). Thus TNF-α, as with adiponectin, does not appear to be influenced by exercise independent of weight loss.

Resistin. The recent discovery of resistin, a hormone expressed and secreted by adipocytes, provided promise for determining the link between obesity and diabetes (100). Resistin gene expression is induced during adipocyte differentiation (89). Although the exact mechanism of resistin function has yet to be identified, Steppan et al. (100) observed increased circulating resistin levels in diet-induced and genetic models of obesity. Inhibition of resistin in these models restored insulin action, whereas administration of resistin inhibited insulin action in control animals.

Surprisingly, the evidence linking resistin to diabetes and obesity in humans is less clear. Serum content of resistin is unaffected by obesity and insulin resistance in humans (37). Lee et al. (66) compared BMI, fat mass, and insulin action to resistin levels in 243 subjects (male and female) and observed no relationship. There was also no difference in resistin between lean and obese insulin-resistant subjects. Serum resistin can be elevated in Type 2 diabetes patients, but there was no relationship between adiposity and insulin (70), whereas others have reported no difference in obese, obese diabetic, and nonobese subjects (37). Although there are conflicting reports as to the relationship of resistin to adiposity (5), most investigations agree that resistin is not related to insulin resistance (107).

To date, there is no information on the interaction between exercise and resistin. Because the role of resistin in regulating insulin action is unclear at this time, there appears to be little rationale to investigate the influence of exercise on this particular adipocytokine.

Interleukin (IL-6). IL-6 is a multifunctional cytokine secreted by numerous cell types including immune cells, skeletal muscle, and adipose tissue. In an effort to determine function, Kim et al. (58) pretreated mice with IL-6 before a hyperinsulinemic-euglycemic clamp. IL-6 blunted skeletal muscle glucose disposal as well as IRS-1-associated phosphatidylinositol 3-kinase activity (58). Moreover, IL-6 treatment increased levels of intramuscular fatty acyl CoA (58). Intramuscular long-chain fatty acyl CoAs are increased with obesity (48), are negatively related to insulin sensitivity (15), and decrease with weight loss (46). The effect of IL-6 on insulin action and lipid accumulation was similar to that of lipid infusion alone, indicating that IL-6 effects on muscle metabolism may be mediated through increased lipid availability. Decreases in fatty acid oxidation and increased fatty acid uptake have been proposed as possible mechanisms of increased lipid accumulation, which causes insulin resistance, with obesity (48) and diabetes. Thus elevated fasting plasma IL-6 concentrations would be detrimental to insulin action.

Serum IL-6 levels are elevated with obesity (57) and diabetes (28) and are negatively related with insulin-stimulated glucose disposal during a euglycemic-hyperinsulinemic clamp (57). When subjects were matched for BMI, plasma IL-6 was independently related to level of insulin resistance (57). Systemic release of IL-6 from subcutaneous adipose tissue was also positively correlated with BMI and percent body fat (57). Contradictory to this evidence linking elevated plasma IL-6 to insulin resistance, recent investigations have failed to show a relationship between IL-6 and insulin resistance (98). Inhibition of IL-6 in humans did not impair muscle glucose uptake or whole body glucose disposal, nor did it affect endogenous glucose production (98). Additionally, recent human in vivo studies demonstrate that IL-6 infusion stimulates lipolysis and fat oxidation (105). Weight loss, which decreases long-chain fatty acyl CoA, is associated with decreased IL-6 (76). Reconciliation of these conflicting results is not currently possible considering the relatively small amount of information available on IL-6. It is apparent that more research is needed to determine the role of IL-6 in insulin action and its contribution to obesity and diabetes. Elevated levels of IL-6 often observed with obesity and diabetes may be associative and not a direct cause of insulin resistance.

It has been well documented that acute exercise increases plasma levels of IL-6 (19, 82, 104); however, the influence of exercise on the release of IL-6 from adipose tissue has only recently been investigated. After 1 h of cycling at 60% \( \dot{V}_O_2 \) max, subcutaneous abdominal adipose tissue increased IL-6 production starting at 30 min of recovery and continued for a least 3 h postexercise (68). This temporal release of IL-6 precedes the increase in fatty acid mobilization from adipose tissue stores after exercise. Combined with the observation that IL-6 infusion stimulates lipolysis, this data provides rationale for the hypothesis that IL-6 has a role in regulating lipid metabolism after acute exercise. Additionally, 3 h of cycling at 60% \( \dot{V}_O_2 \) max increased IL-6 mRNA expression in subcutaneous adipose tissue and plasma content (55). This effect was blunted by carbohydrate ingestion (55), suggesting that nutrient availability may affect IL-6 production. However, more research is needed to clarify the role of nutrient availability on IL-6 production.

At rest, skeletal muscle does not appear to contribute to fasting levels of plasma IL-6 (28). However, skeletal muscle contraction increases IL-6 mRNA expression and IL-6 protein release from muscle. An acute bout of cycling (25 min at 60% \( \dot{V}_O_2 \) peak) increased IL-6 release from skeletal muscle. In support of the notion that nutrient availability affects IL-6 production, Steensberg et al. (98) determined that contraction-induced IL-6 release is highest when muscle glycogen content is low. The current evidence does suggest that exercise alters circulating IL-6 concentrations, but more work is needed to discern the metabolic implications of these changes.

CONCLUSIONS

Adipocytokines signal a variety of metabolic functions including satiety, lipid mobilization, and utilization, and modulate insulin-mediated glucose disposal. Their secretion is modulated by energy flux, i.e., carbohydrate and lipid availability (35). Obesity, which is a condition of excess adipose tissue, is associated with insulin resistance and diabetes. A strong link between these disorders is altered secretion of adipocytokines. Of the various adipocytokines, decreased adiponectin appears to show the strongest relationship with insulin resistance and
obesity in humans. Reduced adiponectin results in decreased AMPK activation and subsequently decreased skeletal muscle fatty acid oxidation contributing to increased lipid accumulation and insulin resistance. Although exercise is a common modality for the management of insulin resistance, when body weight is maintained there appears to be little effect on the secretion of adiponectin and leptin. Adiponectin and leptin act via AMPK activation in skeletal muscle to increase fatty acid oxidation and glucose disposal. Considering that exercise (muscle contraction) stimulates the same pathway, modulating adipokynes levels may not be necessary for exercise induced improvements in insulin sensitivity. The effect of resis-
tin and TNF-α on human insulin resistance appears minimal and associations may be indirect. Acute exercise increases IL-6 secretion from adipose tissue, which increases fatty acid availability. Despite the evidence linking increased fatty acid availability to insulin resistance, exercise-trained muscle may be protected from fat-induced insulin resistance. It should be noted that the addition of an exercise regimen to a weight loss program results in an additive effect on insulin action that may be mediated by the more consistent effect of fat mass loss on adipokynes regulation. In conclusion, it appears that exercise may not directly influence adipokynes regulation. Weight loss, however, does appear to regulate adipokynes in a manner that may enhance insulin action. These observations imply that these common interventions for obesity and insulin resistance function through divergent cellular pathways.

FUTURE RESEARCH DIRECTIONS

Although recent investigations have studied the role of adipokynes in obesity, diabetes, and insulin resistance, more research is needed on the tissue-specific secretion and response of these cytokines. For example, a recent study from Gallagher et al. (32) demonstrated that with obesity there is not only an increase in intramuscular fat storage but also an increase in fat deposition between muscle fibers. Interestingly, the amount of deposition is different depending on ethnicity. In light of these findings, future work will need to characterize these lipid pools with regard to adipokynes secretion relative to other lipid pools (i.e., subcutaneous and visceral) because these intermuscular lipid pools may serve as a very important local modulator of skeletal muscle metabolism. Moreover, are these pools more affected by exercise than other lipid pools?

Only when we can fully elucidate the cross-talk mechanisms between various tissues including muscle, adipose tissue, and the liver will we fully understand the complex nature of insulin resistance. Future research should discern the mechanisms by which increased physical activity promotes insulin sensitivity and its relation to adipokynes. Although the concentrations of adipokynes are only marginally influenced by exercise, it is possible that the signaling effects of these cytokines are modulated after training.

REFERENCES

5. Azuma K, Katsukawa F, Oguchi S, Murata M, Yamazaki H, Shima-
toluzzi MN, Moizo L, Lehy T, Guerre-Millo M, Le Marchand-
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Invited Review

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