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Exercise-Induced Regulation in Adipose Tissue Metabolism

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Abstract

Adipose tissue is loose connective tissue composed of adipocytes and originally derived from lipoblasts. Recently its critical role in the human body as a form of energy storage and endocrinological signaling has been recognized. Various physiological, psychosocial and clinical factors influence the amount and distribution of the adipose tissue throughout the human body. Lifestyle change in terms of increased physical activity and exercise is the best nonpharmacological treatment for obesity since these can reduce insulin resistance, counteract the inflammatory state, and improve the lipid profile. Physical activity and exercise are key components of energy expenditure and therefore of energy balance. Changes in energy balance alter fat mass. Physical activity influences adipose tissue both acutely and in the longer term. A single bout of exercise stimulates adipose tissue blood flow and fat mobilization, resulting in delivery of fatty acids to skeletal muscles at a rate well matched to metabolic requirements, except perhaps in vigorous intensity exercise. There is a period following an exercise bout when fatty acids are directed away from adipose tissue to other tissues such as skeletal muscle, reducing dietary fat storage in adipose. With chronic exercise (training), there are changes in adipose tissue physiology, particularly an enhanced fat mobilization during acute exercise. Epidemiological observations support the idea that physically active people have relatively low-fat mass, and intervention studies tend to show that exercise training reduces fat mass. A much-discussed effect of exercise versus calorie restriction in preferentially reducing visceral fat is not borne out by meta-analyses. We conclude that, in addition to the regulation of fat mass, physical activity may contribute to metabolic health through beneficial dynamic changes within adipose tissue in response to each activity bout.

1. Introduction

Adipose tissue is specialized for storage of energy in the form of triacylglycerols. It is also an endocrine organ, releasing a number of peptides and other factors that can act in an endocrine or paracrine fashion. Adipose tissue typically makes up ~20% of body weight in men and 28% in women (1) but in obese people can expand many fold to >80% of body weight.

2. Adipose tissue structure and function

Adipose tissue contains many cell types including endothelial cells and fibroblast-like adipocyte precursors and, particularly in obese people, there may also be macrophages and other leukocytes. Adipocytes typically constitute 80–90% of adipose tissue volume, but only 60–70% of cell number (2). Adipose tissue triacylglycerol content reflects energy balance. Because the body's capacity to store glycogen is finite and relatively small, long-term imbalances between energy intake and energy expenditure are reflected in a change in the amount of triacylglycerol stored in adipocytes. Adipocyte triacylglycerol content in turn reflects the balance between the processes of fat deposition and fat mobilization. It follows that these processes must be regulated in relation to whole-body energy balance. Fat mobilization is readily stimulated by β-adrenergic activation (3). However, the diurnal fluctuation in fat mobilization, which is high after an overnight fast but suppressed after meals, seems to depend more on changing insulin concentrations. Local infusion of propranolol (β-adrenergic blocker) in the post-absorptive state does not change lipolysis (4), although phentolamine (α-adrenergic blocker) causes a large increase, suggesting α -adrenergic inhibition of lipolysis. However, the effect of α-adrenergic blockade may be secondary to changes in blood flow (5). Adipose tissue is arranged in discrete depots, and these depots have different relationships to health. In general, accumulation of adipose tissue in the upper part of the body (abdominal obesity) is associated with detrimental effects on metabolic health and mortality (6), whereas lower-body fat accumulation (gluteofemoral obesity) is associated with protective effects especially after adjustment for upper-body fat and other risk factors for cardiovascular disease (7). Under normal conditions, the adipose tissue is able to finetune a series of neuroendocrine signals to precisely adapt the balance between TAG synthesis (lipogenesis) and breakdown (lipolysis) to meet physiological needs. Lipolysis constitutes the catabolic process leading to the breakdown of TAG into glycerol and NEFA in the adipose tissue (8). Basal lipolytic activity of adipocytes is conditioned by sex, age, physical activity, fat depot location, species and genetic variance, whereas stimulated adipocyte lipolysis is regulated by multiple factors, which are depicted in Fig 1.

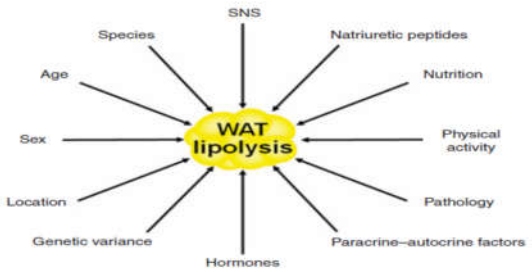

Fig 1. **Main factors influencing adipocyte lipolysis.** SNS, sympathetic nervous system; WAT, white adipose tissue.

In humans the main elements controlling lipolysis are the activity of the autonomic nervous system and the endocrine influence derived from the release of insulin (8). Adipose tissue is richly innervated by both the sympathetic and parasympathetic nervous systems. Thus, electrical

stimulation of sympathetic nervous system nerve endings results in an increase in lipolytic activity, while surgical sympathectomy reportedly reduces lipolysis in the denervated adipose depot (9).

3. Physical activity and adiposity

There appears to be the anticipated inverse relationship between measures of physical activity and measures of fat mass and distribution (10, 11). However, in spite of some large studies, the results are not entirely consistent, and the reported relationships tend to be only modest (10, 11). In one study of over 15,000 men and women across Europe, there was the expected inverse relationship between self-reported leisure-time physical activity and BMI (12). Some studies have reported that self-reported physical activity at baseline modestly predicts future weight gain. Some longitudinal studies found no relationship between baseline physical activity and weight gain. For example, in a study of more than 8,000 young women, there was no relationship between self-reported physical activity at baseline and the change in BMI 4 yrs. later (13). Studies typically measure only one dimension of physical activity (e.g., leisure-time physical activity), usually by self-report. Since such behaviors are imperfect surrogate measures of overall physical activity energy expenditure, this almost certainly weakens the association between physical activity and the outcome measure (e.g., waist circumference). It has been argued that because the measurement of physical activity in observational studies is so much poorer than the measurement of obesity, this may not only attenuate the strength of the relationship but also lead to erroneous conclusions about the direction of causality (11). Given the complexity of physical activity behavior and the limitations of self-report, it has been proposed that observational studies need to include more objective measures to better capture the relationship between physical activity and a given outcome measure (11, 14).

4. Effect of exercise on fat mass and distribution

A meaningful energy deficit created by increased physical activity generally leads to a loss of fat mass from the quantitatively significant depots (15). Although most of the change in total mass in response to exercise interventions is accounted for by changes in fat mass, using total fat mass alone may overlook potentially important and selective regional effects in functionally different adipose tissue depots. Indeed, it has been argued that too much emphasis has been put on weight and/or total fat loss as outcome measures in the past (16). With this in mind, it is noteworthy that a relatively large exercise-induced change in some of the key depots may take place in the context of only a small change in total fat mass (17).

5. Exercise-induced changes in adipocyte size and number

A physical activity-induced reduction in fat mass could, in theory, be explained by either a

reduction in adipocyte size and/or adipocyte number. Trained women have smaller adipocytes in both the abdominal and femoral region than age-matched sedentary controls (18). In support of these cross-sectional comparisons, the direct evidence showing that physical activity interventions reduce adipocyte cell size in humans is limited but generally consistent (19). For example, Despres et al. 1984, conducted a 20-wk exercise training intervention and found that young men lost~3 kg body mass and showed a reduction in abdominal SCAT cell weight, whereas young women did not lose weight (or fat mass) and there was no change in abdominal SCAT cell weight (19). Exercise energy expenditure plus caloric restriction over a 6-mo period in obese postmenopausal women produced similar changes in abdominal and gluteal SCAT adipocyte diameter compared with isoenergetic caloric restriction alone (20, 21).

6. Acute exercise and adipose tissue metabolism and function

Acute changes with exercise could play a role in broader aspects of adipose tissue function, and this could potentially explain some of the beneficial metabolic consequences of regular exercise over and above an energy deficit from caloric restriction alone.

7. During exercise: fatty acid mobilization

The reductions in fat mass ultimately rely on the breakdown of stored triacylglycerol (lipolysis) exceeding that of storage. Fat is an important metabolic substrate during prolonged exercise (22). Measurements at the whole body level show that fat oxidation increases profoundly in response to low-intensity exercise, with further modest increases up to intensities of ~60–65% VO2max (23). The rate of appearance of non-esterified fatty acids (Ra NEFA) during exercise is typically two to three times that observed at rest and, with the exception of high-intensity exercise, there is a remarkably good coupling between the delivery of NEFA from adipose and oxidation by working skeletal muscle (24). A schematic view of this relationship is shown in Fig 4. It has been estimated that subcutaneous adipose tissue contributes the greatest proportion of fatty acids that are ultimately oxidized during moderate intensity exercise, with only a small contribution coming from intra-abdominal (visceral) fat (23). This may reflect the relatively small size of the visceral depot, but it should be noted that these estimates were mostly derived from studies in lean young men, and it is less clear if this is the case when the visceral depot is enlarged. There is also a contribution from intramuscular triacylglycerol, particularly during exercise of a moderate intensity (25). It is appropriate to highlight at this stage that circulating NEFA concentrations represent the balance between release and uptake of NEFA and therefore will only provide a limited picture of fatty acid mobilization. The release of fatty acids from adipose tissue during exercise is potentially influenced by adipose tissue lipolysis, the rate of fatty acid re-esterification, and adipose

tissue blood flow (ATBF). Measurements in vivo in a range of different subjects and exercise protocols using microdialysis (8, 26) and arteriovenous (a–v) difference (27, 28) provide direct evidence that fatty acids are mobilized from SCAT during exercise. At least part of the increase during exercise appears to be due to decreased rates of fatty acid re-esterification (25). According to direct measurements in abdominal SCAT, most of the increase in adipose tissue fatty acid mobilization requires only low-intensity exercise (27, 28) with only modest (28) or no additional increase when exercise intensity is increased further (27). Therefore, low-intensity physical activity provides a more than adequate stimulus for increased abdominal adipose tissue fatty acid mobilization. Interestingly, since whole body fat oxidation continues to increase up to ~65%VO2max (23), this indicates that alternative stores of fat are used as exercise intensity increases (e.g., other adipose sites or intramuscular fat). It should be noted that most research on exercise-induced fatty acid mobilization has been conducted using young lean (mostly active) subjects who have a relatively high VO2max and who were studied in the post-absorptive state. Ra NEFA in the circulation using tracers was greater in older women when they worked at the same absolute intensity as younger women but, as the authors pointed out, this was probably because this represented greater relative exercise intensity (29). When these older women exercised at the same relative intensity as the younger women, then the Ra NEFA was lower, probably because the absolute workload was lower (29). Clearly, a better understanding of exercise intensity (absolute and relative) and fatty acid mobilization is required, since this plays an important role in the regulation of fat mass. An exercise-induced increase in adipose tissue lipolysis has been classically attributed to elevated catecholamine concentrations and a small decrease in insulin concentration (8, 30). Even low-intensity exercise at 40–45% VO2max increases epinephrine concentration about three-fold (31, 32). One study in paraplegic patients indicated that adipose tissue lipolysis during exercise is largely activated by circulating mediators and not sympathetic outflow (28), although other studies in similar patients indicate that neural activation of lipolysis can play an important role (33).

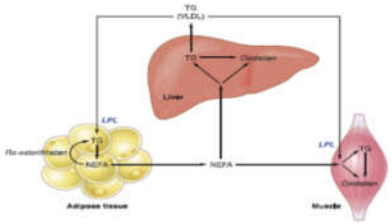

Fig 2. Pathways of fatty acid trafficking between tissues in the fasted state. Triacylglycerol (TG) stored in adipose tissue is mobilized to release non-esterified fatty acids (NEFA) into the circulation. The rate of NEFA release is also modulated by the re-esterification of fatty acids within adipose tissue. NEFA are taken up by, among other tissues, skeletal muscle and liver. In each of these tissues, they may enter the pathway of β-oxidation, or they may be used for synthesis of TG. There is some evidence that fatty acids for oxidation are drawn from the intracellular TG pool (35, 36). The liver, in addition, may secrete fatty acids in the form of very-low-density lipoprotein (VLDL)-TG, from which fatty acids may be taken up for esterification in adipose tissue and for oxidation or esterification in muscle via the lipoprotein lipase (LPL) pathway.

Selective blocking of β-adrenergic receptors in abdominal and gluteal subcutaneous adipose tissue at rest and during 30 min exercise at 66%

VO2max in young lean men and women markedly reduced (but did not abolish) lipolysis during exercise (8). Several other studies have confirmed that while circulating epinephrine is primarily responsible for exercise-induced lipolysis, even after blocking the action of epinephrine, there is still an increase in lipid mobilization (34). This suggests that other circulating mediators must play an important role in the stimulation of lipolysis during acute exercise. There is evidence that atrial natriuretic peptide (ANP) is secreted during exercise in an intensity-dependent manner, and this is a putative alternative candidate (35). When β-adrenergic receptors are blocked during exercise in overweight men, the increase in lipid mobilization from abdominal SCAT during exercise remained unchanged, and this led to the conclusion that epinephrine is not the primary lipolytic stimulus in overweight men and that ANP might be more important (34). The same investigation showed that blocking β-adrenergic receptors in lean men produced a~50% reduction in lipolysis during exercise, and it is therefore possible that ANP may be more important with increased adiposity (34). As the duration of fixed-intensity exercise increases, there is an increase in both whole body lipolytic rate (23) and also directly determined regional adipose tissue lipolysis (26, 28). This may be the product of slow-acting hormones such as growth hormone and cortisol (36, 37). The increase in hormones such as growth hormone is influenced by various factors including exercise intensity and duration (38), although it should be noted that a direct relationship between growth hormone-induced lipolysis and increased fat oxidation during exercise has been questioned (37). In young men, lipolysis is greater in a second bout of exercise performed 60 min after a first bout, and this raises the possibility that the system is perhaps “primed” in some way (26). there is an age-related decline in growth hormone secretion in response to exercise performed at the same relative intensity (39), and it is possible that this could carry over into different adipose tissue lipolytic response to prolonged exercise in older and younger people.

8. During and after exercise: fatty acid uptake

Low-level physical activity is a powerful stimulus for lipid mobilization in the fasted state, and the physical activity that accumulates throughout the day has considerable potential to mobilize large amounts of lipid over time (dependent on an individual’s physical activity profile). The net delivery of dietary fat to adipose tissue (arterial triacylglycerol) is reduced by prior exercise (40). The modification of postprandial responses appears to be largely governed by the total energy expenditure of physical activity (41). Acute exercise has long-lived effects (10–20 h) on the oxidation of exogenous dietary fat (42). So, in addition to enhanced lipolysis and fatty acid mobilization during and after acute physical activity in the fasted state, some of the regulation of adipose mass with regular physical activity is likely to be mediated through an acute exercise-meal interaction and a net reduction in adipose fat

storage because fat has been removed by other tissues such as muscle (42).

9. During exercise: adipose glucose and lactate metabolism

Glucose is necessary for triacylglycerol formation within adipocytes by provision of glycerol 3-phosphate and can act as a precursor for fatty acid synthesis via de novo lipogenesis. The release of glycerol during adipose tissue lipolysis could contribute to the generation of glucose via hepatic gluconeogenesis (43). There are few studies available that have examined glucose metabolism in human adipose tissue during and after acute exercise. One investigation reported that glucose uptake is reduced and becomes negligible across abdominal SCAT (a–v difference) during cycling, although the difference was not significant with the six subjects in this experiment (27). The same investigation also reported an increase in SCAT lactate output (a–v difference) during cycling at 40% VO2max but a nonsignificant decrease in lactate output (and possibly lactate uptake) during cycling at 60% VO2max (27).

10. During Exercise: Adipose Tissue Blood Flow (ATBF)

Fatty acid mobilization during exercise relies not only on an increased rate of lipolysis (assuming similar or reduced fatty acid re-esterification) but also on adequate ATBF. In addition, the delivery of biologically relevant mediators to adipose tissue (e.g., circulating hormones) is a function of both concentration and blood flow (delivery = concentration × blood flow). Two main methods have been used to measure ATBF during exercise: washout of radioactive 133Xenon (Xe) and washout of an indicator (usually ethanol) from Microdialysis. There is some evidence that this effect of exercise may be region-specific, with an increase in subcutaneous abdominal ATBF in response to cycling exercise but no change in femoral ATBF (44). However, other studies have shown that femoral ATBF does respond to a leg extension exercise model (45). It appears that there is an increase in ATBF during low- to moderate-intensity exercise even in adipose tissue that is distant from working skeletal muscle. It is unclear what causes an increase in ATBF during exercise. Some of the response may simply be a consequence of increased cardiac output, but other mediators such as epinephrine and ANP increase during exercise and have active vasodilatory properties (46). Adenosine is a potent vasodilator in many tissues (47) and is present extracellularly in human adipose tissue (48). At least in swine, extracellular adenosine concentrations in adipose tissue increase markedly during exercise (49). It is also possible that the relative suppression of NEFA mobilization from adipose tissue during vigorous intensity exercise, discussed earlier, might reflect the antilipolytic effects of extracellular adenosine (50). It is has been hypothesized that vigorous intensity exercise leads to a catecholamine-induced vasoconstriction of

adipose tissue and subsequent fall in ATBF and that this might explain the well-documented fall in fatty acid mobilization from adipose tissue at higher exercise intensities (25, 50). It remains unclear whether very demanding exercise leads to a reduction of ATBF during exercise or whether ATBF simply fails to keep up with an intensity-related increase in adipose tissue lipolysis.

11. Post-exercise: fatty acid metabolism and adipose tissue blood flow

In lean young men, fatty acid mobilization and ATBF remain elevated for several hours after moderate-intensity exercise (27, 51). Generally, it appears that immediately after exercise there is a transient decrease in fatty acid mobilization (determined directly in adipose tissue by a–v difference) followed by a steady increase over the following 3 h (27, 51). Recent evidence from tracer studies suggests that fatty acid mobilization (Ra NEFA) is maintained for 24 h after exercise but declines progressively until it is close to resting values at this time point (52). It appears that growth hormone plays an important role in post-exercise lipolysis, since blocking the exercise-induced secretion of growth hormone (using octreotide infusion) suppresses post-exercise lipolysis (a–v difference) and ATBF (133Xe washout) in adipose tissue but does not affect these parameters during exercise (51). During vigorous intensity exercise, fatty acid mobilization from adipose tissue may be suppressed and ATBF may fall or fail to increase with increased intensity. Fat oxidation during exercise appears to be maximal at around 60–65% VO2max (53). Whether there is a subsequent increase in fat oxidation and fatty acid mobilization in the post-exercise period after more vigorous intensity exercise remains unclear, but would make sense from a physiological perspective. One recent study found that there was a correlation between exercise intensity (absolute energy expenditure) and post-exercise fatty acid mobilization (Ra NEFA) (52), which supports a role for exercise intensity being an important determinant of fatty acid mobilization after exercise has ceased. In support of a post-exercise "correction" in fat utilization with high-intensity exercise, the total oxidation of fat over 24 h determined using a respiration chamber is similar when obese men perform high or low-intensity exercise with equivalent energy expenditure (54). Clearly, fat balance ultimately depends on total fat oxidation, and this is the sum of fat oxidation both during and after a bout of exercise.

12. Sex-specific variation in fatty acid mobilization during and after acute exercise

At the whole body level (using tracers plus indirect calorimetry), young lean women show greater fatty acid mobilization during low- and moderate-intensity exercise than men (31). It has been proposed that this difference is partly because of the significantly greater fat stores found in women and that, when expressed for a given mass of adipose tissue, there is no such sex-related difference (55). In overweight women,

catecholamines make only a minor contribution to lipid mobilization from abdominal SCAT during exercise at low to moderate intensities (30–50% VO2max), whereas blocking β2-adrenergic receptors potentiates lipolysis at all intensities in abdominal SCAT in young overweight men (35). Women show evidence of greater lipolysis during exercise at the same relative intensity in spite of the fact that they have lower concentrations of catecholamines in arterialized blood (35). These comparisons are complicated by the fact that men tend to have a higher VO2max than women, so the absolute intensity of exercise will be different when relative intensity is controlled. Post-exercise fat oxidation is greater than at rest in men but not in women, even the day after exercise (31). Therefore, at least at the whole body level, it appears that sex-related differences observed during exercise are reversed in the hours after exercise.

13. Acute exercise and Adipokines

An acute bout of exercise leads to an increase in the concentration of adipokines in the blood, and many of these molecules can exert effects in other tissues (56). For example, leptin and adiponectin increase fatty acid oxidation and glucose uptake in skeletal muscle (56). Changes in concentrations of tumor necrosis factor (TNF) - α in venous blood have been reported but these are inconsistent, whereas an increase in circulating interleukin (IL)-6 is a well-established response to demanding exercise (57). One of the adipokines that has been most studied directly in adipose tissue in response to acute exercise is IL-6. There is consistent evidence that long-duration moderate-intensity exercise (3 h) leads to an increase in IL-6 mRNA in adipose tissue in young lean men (58). Interestingly, Lyngso et al 2002, showed that there was no increase in IL-6 secretion from abdominal SCAT during shorter duration (60 min) exercise at 60% VO2max (using a–v difference), but that there was an increase in IL-6 secretion over 3 h post-exercise so that it was 15-fold higher than in the control trial (59). It appears that while the increase in circulating IL-6 during exercise is primarily the result of release from skeletal muscle and probably not adipose tissue (57), adipose tissue may make a quantitatively significant contribution to systemic IL-6 concentrations in the post-exercise period. Therefore, there is consistent evidence that long-duration moderate- intensity exercise has the capacity to transiently increase both adipose tissue IL-6 expression and secretion in the short term. There are some clues as to the physiological significance of an increase in adipose IL-6 during and after exercise. IL-6 may play a role in the regulation of liver metabolism to promote greater hepatic uptake of the fatty acids that are mobilized in the post-exercise period (59, 60). Alternatively, IL-6 might be actively secreted by adipose in an attempt to increase fatty acid mobilization in the face of a significant metabolic challenge (59, 60). There have been a few isolated reports of other adipokines measured directly in SCAT before and after an acute bout of exercise. One investigation showed no change in SCAT leptin mRNA before

or after 3 h of moderate-intensity exercise even though plasma concentration was lower over the 5 h post-exercise observation period (61). The observation that carbohydrate ingestion countered the exercise-induced decrease in leptin prompted the authors to suggest that there was post-transcriptional regulation of leptin secretion (61), and this makes perfect sense based on other findings (62). Interestingly, as was the case for IL-6, it is possible that hormones such as epinephrine might be responsible for the fall in plasma leptin seen during sustained exercise (61). In support of this observation, β-adrenergic stimulation using local infusion of isoproterenol in subcutaneous adipose tissue reduces leptin concentration in microdialysate (63). We know very little about the effect of acute exercise on other adipokines. One hour of cycling at 55% VO2max has been shown to generate a transient increase in adipose tissue interstitial adiponectin concentration in both lean and overweight young men, although interestingly adiponectin SCAT mRNA actually fell during and after exercise (64). These authors reported no change in TNF-α in adipose tissue interstitial fluid, but there was an increase in TNF-α mRNA in both lean and overweight men which was most pronounced in the post-exercise period (64). They also found that leptin mRNA was reduced in both lean and overweight men, whereas there was no change in resistin mRNA (64). There has been one report that 3 h of moderate- intensity exercise increases SCAT visfatin mRNA in young lean men (65), although the time course and the magnitude of the effect was highly variable between subjects. Visfatin is an insulin-mimetic peptide that is preferentially expressed in visceral fat (66). Finally, acute exercise in young lean women (2 h at 60% VO2max) or young lean men (1.5 h at 70% VO2max) did not change adipose tissue IL-18 mRNA (67).

14. Chronic exercise (Training) and adipose tissue function

Basal fatty acid mobilization and lipolysis after training

Basal (nonstimulated) lipolysis in adipocytes studied ex vivo has been found to be similar (68), lower (69), and higher (61) in trained men and women compared with sedentary controls. There has been one report that weight loss from caloric restriction alone reduces basal lipolysis in adipocytes from obese postmenopausal women, whereas the same energy deficit and weight loss from combined caloric restriction and exercise maintains basal lipolysis (20). Various investigators have measured intercellular glycerol with microdialysis to examine training-induced changes in regional lipolysis in situ. One cross-sectional study reported that basal adipose tissue lipolysis is similar in trained young men compared with sedentary controls when this was corrected for differences in adipose tissue blood flow (70). Most intervention (training) studies that have used adipose tissue microdialysis show no change in basal regional lipolysis with training. Two studies reported a training-induced decrease in basal regional lipolysis in abdominal SCAT but, as pointed out in one of these studies and mentioned

above, the decrease in glycerol in microdialysate may actually reflect an increase in adipose tissue blood flow with training (46). Training intervention studies that have used stable isotopes have reported lipolysis at rest to increase (71), decrease (72), and not change (71, 73). Body mass did not change in any of these studies; diet was not deliberately manipulated, and follow-up measures were taken between 36–64 h (71, 73). It is possible that the different intensity of exercise and perhaps poorer fitness and baseline activity in some study participants (72) may play a role in explaining these variable findings.

15. Stimulated and exercise-induced fatty acid mobilization and lipolysis after training

There is evidence that the lipolytic response to stimulation is increased after training. Cross-sectional studies indicate that isolated adipocytes from active men and women examined ex vivo have a greater response to lipolytic agents per cell or per gram of lipid than sedentary controls (17, 69). It should be noted that these lipolytic assays tend to use very high (supraphysiological) concentrations of lipolytic agents such as epinephrine. Studies using microdialysis have reported that regional epinephrine- stimulated lipolysis is similar in trained and sedentary young men (70), whereas the suppression of lipolysis by insulin is greater than sedentary controls (74). Studies using stable isotopes have reported no difference in Ra glycerol between trained and sedentary subjects when exercising at the same absolute workload, even though there were large differences in total fat oxidation (75). In contrast, the Ra glycerol is higher in endurance-trained men compared with untrained controls during exercise at the same relative intensity of 70% VO2max (76). Friedlander and co-workers (77, 78) showed that 10 -12 wks. of training in young lean men and women increased the Ra NEFA during exercise at a given relative or absolute intensity (but not Ra glycerol). In contrast, 12 weeks of training in lean (44) and obese women did not change the Ra NEFA during exercise at the same absolute intensity (73), although whole body fat oxidation increased ~20%. Horowitz et al 1999 also found that 16 wks. of training in five young lean men did not change the Ra glycerol or NEFA in response to epinephrine infusion (79). There is some (inconsistent) evidence that there is an increase in stimulated or exercise-induced regional lipolysis with training (and possibly greater whole body lipolysis). The intriguing observation that adipose tissue achieves similar or greater lipolysis in spite of lower circulating concentrations of lipolytic agents during exercise (71) points towards an increase in the sensitivity of the regulation of adipose tissue lipolysis.

16. Regulation of fatty acid mobilization after training

Adipose tissue seems to maintain fatty acid mobilization during exercise in the face of reduced lipolytic signals such as epinephrine after training. Microdialysis studies show that adipose tissue is more responsive to local infusion of β-

agonists after training, which may indicate better β-adrenergic responsiveness (46, 80). In one investigation, blocking the action of α2-adrenergic receptors removed the training-induced increase in lipolysis during a standardized bout of exercise in young overweight men, and it was proposed that this indicated a less pronounced antilipolytic effect from α2-adrenergic activation as a result of training (81). In contrast, 12 weeks of training in obese women did not improve α2-adrenergic activity (82). Microdialysis also shows a greater lipolytic response to ANP infusion after 16 weeks training in overweight men (46). Taken collectively, these results indicate that after exercise training, adipose tissue is more sensitive to lipolytic agents at a local level (e.g., post-receptor events affecting lipase expression and/or activity).

17. Fatty acid uptake after training

Exercise and physical activity have a profound effect on postprandial lipid metabolism (41). Adipose tissue LPL seems to be either reduced with training (18), or remain unchanged (82). Therefore, the tissue-specific response of LPL favors the view that long-term exercise training diverts dietary fat to other tissues such as muscle for oxidation rather than being stored in adipose tissue, although ultimately much of this is a short-lived (up to 3 days) response to recent exercise rather than a sustained (persistent) effect of training per se.

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