

Review Article

Benefits of Physical Activity in Weight Reduction - Therapeutic Approaches from a Metabolic and Energetic Point of View: A Systematic Review

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***Corresponding author:** Prof. Dr. med Aloys Berg, Faculty of Medicine, University of Freiburg, Germany, Email: aloys.berg@klinikum.uni-freiburg**Received:** December 14, 2017; **Accepted:** January 08, 2018; **Published:** January 15, 2018**Abstract**

Overweight adults mostly show not only an abnormal body composition, but a decreased muscular and metabolic fitness which might be responsible for associated risk factors and mechanisms provoking cardiovascular and metabolic diseases. If the reduction in body weight is realized by an associated increase of leisure time physical activity (LTPA), significant benefits can be expected in metabolic flexibility. These benefits are related to the improved transmembranous transport and utilization of glucose as well as increased fatty acid oxidation and the kinetics of intramuscular triglycerides (IMTG). These mechanisms induce a more effective reduction in insulin resistance and a more significant improvement of the lipid profile than by caloric restriction alone. Finally, it should be recognised that exercise may also influence appetite regulation and eating behaviour. For effective weight loss and weight maintenance, it is confirmed that a combination of increased physical activity and calorie restriction is essential.

Keywords: Physical activity; Diet and exercise; Metabolic syndrome; Energy expenditure; Obesity treatment; Eating behaviour; Appetite regulation

Background

Although excess weight and obesity are primarily a problem of body composition, it is essential to recognise that not only weight management but also metabolic fitness are necessary parameters for both the prevention and treatment of obesity. This also makes the need for physical activity and exercise significant because overweight subjects usually do not only have a problem in physical activity, but also they have limitations in their muscular and metabolic competence [1-4]; this is because the pathogenic effects of an unhealthy lifestyle are particularly evident with the simultaneous occurrence of obesity and lack of physical activity [5]. In a study of nearly 17,000 subjects with moderate obesity (BMI 30-34.9) compared to those of a healthy weight (BMI 18.5-24.9), the prevalence of type 2 diabetes (T2DM) was increased five-fold and, hypertension more than doubled, while dislipoproteinemia increased more than 30% [6]. Therefore, keeping body weight within the normal weight range and managing any weight changes appropriately are necessary to remain metabolically healthy. Indeed, the recommendations of both national and international medical societies for lifestyle management not only focus on a change in eating habits, but also the promotion of an increased level of physical activity [7-10].

It is clear that sport and exercise are regulatory variables for metabolic fitness and flexibility. Precisely what advantages increased physical activity has in addition to reducing body weight, and what these advantages can be attributed to, is the focus of the following overview.

Approach 1: Effects on Triglycerides and Insulin Resistance

Epidemiological data clearly shows that metabolic disorders such as insulin resistance are associated not only with obesity but also with muscular deficits [11]. Therefore, obesity is not the only driver of insulin resistance. Of greater importance, are the intracellular triglyceride status and the intra-abdominal to subcutaneous fat ratio [12,13]. These factors are related to reduced size of functional fat cells and thus a lower capacity to handle fat intake, it has combined with increased fat release. There is a noticeable increase in triglycerides and free fatty acids in the circulation, and triglycerides are also deposited in organs outside of the fat deposits [4].

In skeletal muscle, which is the peripheral tissue mainly responsible for the disposal of triglycerides and regulation of energy reserves, an increased fat content leads to a reduction of muscular glucose uptake and the conversion of glucose into stored glycogen. Since skeletal muscle is responsible for most of the insulin-mediated glucose uptake from the circulation (approx. 80%), these glucose metabolism disorders have a particularly severe effect on insulin resistance [14]. In addition, while the activity of key enzymes of fat oxidation in T2DM is also reduced, the muscle cell is less geared towards oxidation rather than the storage of fatty acids [13,15]. The significance of this phenomenon can be demonstrated convincingly in the offspring of T2DM patients. There is evidence that, at an early age and without symptoms, there is a 30% reduction in insulin sensitivity; at the same time the concentration of intramuscular fatty

acids is increased by more than 80% [16]. In addition, a key function of the mitochondria, to produce energy through fat oxidation, is clearly limited. This shows that intramuscular fat accumulation, in its storage form of triglyceride, is an important metabolic trigger in development of insulin resistance [15,17].

A differentiation has to be made between insulin-dependent and insulin-independent glucose uptake by skeletal muscle. Physiologically, elevated glucose levels lead to the binding of insulin to its receptor to form a complex signal cascade, which triggers the translocation of the glucose transport protein (GLUT-4) from the cytoplasm into the muscle membrane. Only then, glucose can be taken up into the muscle cell; in this case the glucose usage and storage enzymes also show increased activity [13]. In impaired fat cell function with subsequent intramuscular fat accumulation, this signalling cascade is disturbed and the key function of this metabolic process (PI 3-kinase) is suppressed via intermediate products of lipid metabolism. Under physical exercise, insulin-independent intracellular signals (calcium concentration-dependent, activated AMP kinase) and GLUT-4 translocation, as well as acute transcription are increased, enabling improved glucose uptake and also increased glucose metabolism [18].

With this in mind, the statements from several medical scientific societies uniformly agree on the importance of physical activity in the therapeutic intervention for insulin resistance and T2DM [13]. They refer to a number of controlled studies and meta-analyses, and to evidence for the effectiveness of both endurance and strength training. For example, the American Diabetes Association (ADA) supported the therapeutic influence of glycemic metabolism through physical exercise at evidence level A [19]. Important pathophysiological mechanisms of peripheral insulin resistance in muscle cells can be positively influenced both through aerobic endurance training as well as strength training exercise. Weight loss, however, is not the main focus in this metabolic conception.

In this way, the HbA_{1c} value as a clinical indicator of a disturbed T2DM metabolic state may significantly decrease on the scale of oral anti diabetic mono therapy [19,20].

The T2DM management guidelines published in 2006 recommend more physical activity (from a metabolic perspective, and particularly for overweight subjects with a T2DM predisposition [13,19].

- For endurance exercise: at least 150 minutes per week at 40 - 60% VO_{2max} or 90 minutes per week at > 60% VO_{2max} at least 3 days per week with less than 2 consecutive days without exercise. Where possible and medically reasonable, both higher volumes and intensities, up to 80% are meaningful, since this can positively influence cardiovascular morbidity and mortality in particular.

- For strength training: at least 3 times a week, involving all the major muscle groups (3 passes with 8-10 repetitions with submaximal intensity). An improvement of glycemic metabolic state can be seen even in the absence of weight loss. This suggests that an important stimulus for the reduction in muscle insulin resistance is represented by muscle contraction per sec.

Approach 2: Effects on Fatty Acid Oxidation and Lipid Profile

Important for the effectiveness and efficiency of sport and exercise on overweight and obesity, is not only the physical fitness per sec or the degree of aerobic capacity, but the extent of mitochondrial oxidation of fatty acids during the physical activity period [21]. Accordingly, Intervention programmes designed to improve body weight and body composition in overweight individuals should be related to the increased activity levels aimed to improve the lipoprotein profile and the classic cardiovascular risk factors. Consequently, not only the raising of physical fitness (VO_{2max}) but the increase of physical activity as a measure of increased leisure-time energy expenditure should be considered [21]. Therefore, sports medicine concepts are agreed on moderate intensity aerobic level for effective weight loss [21,22].

This aerobic workout intensity level, induces both acute and chronic metabolic effects, benefiting the metabolism of obese subjects by primarily engaging the oxidative muscle fibres (type I muscle fibres, ST fibres) [23,24]. Muscle cellular glucose uptake will also be increased by the translocation of glucose transport proteins (GLUT-4) from the microsomal pool to the cell surface (see below). Circulating insulin levels also decrease due to the α-adrenergic inhibition of insulin secretion during exercise-induced physical stress. In this case, lipolysis in adipose tissue is promoted, and the supply of free fatty acids in the plasma increased significantly.

An additional benefit is the associated increase in activity of the endothelial and intracellular lipoprotein lipase (LPL) in type I muscle fibres [25]. As a result of increased LPL activity, triglycerides from circulating VLDL particles and triglycerides from intramuscular storage (IMTG) can now be hydrolysed and used in muscle cellular β-oxidation [23,26,27]. In relation to the muscular energy demand, after an exercise period of about 30 minutes, the optimal use of lipids in working muscles can be expected. Fatty acids, which are released primarily as palmitic acid during this period of exercise (particularly from adipose tissue, but in measurable portions also from the circulating lipoproteins and intramuscular triglyceride depots via hydrolysis), constitute the energetically preferred substrate for the mitochondrial energy supply within the muscle fibre [17,26,28]. As a consequence of this metabolic adaptation, the sustained requirement for free fatty acids for the recovery of muscular deposits in the regeneration phase leads to a sustained reduction in plasma triglycerides as a reduction of triglyceride content in circulating plasma lipoproteins (VLDL).

It can therefore be assumed that an endurance-oriented physical activity with preferential use of β-oxidation, accelerates the conversion of intra- and extra-muscular triglycerides, and also favourably influences the partitioning of body mass in favour of muscle mass and at the expense of fat mass in overweight individuals [21,29]. This has important consequences for the expression of risk factors that accompany obesity and determine the extent of the conditions such as: hyperinsulinemia, peripheral insulin resistance and hypertension, decreased peripheral responsiveness to catecholamines and androgens, increased proportion of atherogenic

low density lipoproteins and increased lipid peroxidation [5,12,21,29-31]. In addition, weight loss induced by adaptation to physical training favourably influence antioxidative regulation and subsequent immunological reactions (e.g. the secretion of anti-inflammatory cytokines and adhesion proteins) and the endothelial function.

From the clinical and therapeutic perspective, a physical training intervention is significantly able to improve the reduced metabolic flexibility in overweight and untrained subjects relating to decreased HDL cholesterol, elevated triglycerides, and an increased proportion of small-dense LDL particles [21,23,32]. It is not necessarily the ergometric performance that is important for the effect of sport and exercise on this unfavourable lipid profile, but the muscular energy supply during the period of physical activity. In this context, a minimum duration of 30 minutes per workout and the moderate intensity of the exercise should be emphasised. This can be explained by the mobilisation of fat and the activation of fat metabolism which is induced by the associated increased oxidation of fatty acids in working muscles [24,26,27].

Therefore, intervention programmes designed for improving the lipoprotein profile and other cardiovascular risk factors should not only be measured based on increasing physical fitness (VO_{2max}), but also on the increase in physical activity as a measure of the increased leisure-time energy expenditure or the total daily energy expenditure [33]. Furthermore, the quantitative measurement of the exercise-associated metabolic rate as a component of the increased energy metabolism shows a closer negative correlation with metabolic risk factors compared with the improvement of physical fitness. Also, in regard to the influence of the amount and intensity of exercise stress on blood lipid levels, the quantity of physical activity, and not the intensity or increase in the VO_{2max} is most closely associated with the improvement in the lipid profile [21,32]. It is understood that the effect of physical activity and weight loss complement the desired change in the lipid profile synergistically; this is clearly shown by the triglyceride and LDL cholesterol levels in the context of sport-oriented exercise programs for weight loss.

In regard to lipid utilisation and lipid profile, the following facts have to be summarised accordingly for increased activity in overweight subjects:

- Lipid oxidation is indeed determined by muscular characteristics (proportion of high-oxidative ST fibres and their enzymatic capacities), which can however be trained at any age, including in overweight subjects.
- In order to optimise the supply of endogenous fat (lipolysis) and the FA metabolism (β -oxidation), moderate exercise intensities (50% VO_{2max}) are suggested.
- Fats are burned in muscle even at rest and immediately after the onset of exercise; however, the proportion of energy supply from IMTG increases with increasing exercise duration; therefore, sessions of at least 30 minutes are preferable, but not mandatory.
- The IMTG depots are crucial not only for fat balance, clearance rate of TG and free FAs after exercise, but also for insulin sensitivity.
- It should be noted that exercise performed following

consumption of a carbohydrate-rich meal, results in the suppression of fat oxidation for energy production induced by increased insulin levels.

Approach 3: Effects on Energy Consumption

Depending on the composition of the training programme, the caloric usage of physical activity and its share of the daily calorie balance is often overestimated both by the person concerned as well as the advising physician and physical therapist [34]. Nevertheless, it is important when assessing the energy balance to know that during endurance exercise, energy turnover can be increased continuously, expressed as a multiple of resting metabolic rate: In untrained subjects, this equates to about 4-5 times and in trained subjects by as much as 8-10 fold [22]. For the respective energy cost of physical work or oxygen consumption knowledge of both the exercise intensity and the duration of exercise is necessary. In a 'usual' nutritional state with a mixed fatty acid and glucose oxidation, 5kcal are expended per litre of oxygen consumption. Since about 11.5ml of oxygen per watt minute is required based on the watt power in addition to resting metabolic rate, energy turnover can be estimated and given using a calorie calculator for most types of exercise and training regime [22].

Experience has shown that at 100 watts per hour, and at 200 watts per hour about 350kcal and 700kcal respectively can be consumed in addition to the resting metabolic rate. This should be considered as calories burned per week or as negative energy balance in debate on the benefits of leisure-time activities effects on obesity and weight management [1,2,22]. With increasing body weight, the same level of physical activity requires more energy to be expended and is perceived as a correspondingly greater physical stress [34]. Overweight subjects should choose lower exercise intensity than those with a normal weight in order not to become prematurely tired and frustrated, leading them to abandon their exercise plans.

Example: Energy expenditure of people with varying fitness levels and health.

	Weight	VO_{2max}	Endurance performance	Energy metabolism
	(kg)	(ml/kg/min)	(%)	(kcal/h)
Trained	70	65	80	1,092
Untrained	100	30	45	405

The difference in daily activity metabolism between what is physiologically possible for trained endurance athletes and what is individually feasible for overweight subjects may thus constitute a factor of 10 or more calorie output (see the table example). For example, a trained subject during a usual activity, burns approximately 2000kcal within two hours. In contrast, an untrained overweight subject uses approx. 200kcal in a 30-minute period. In reality for therapeutic sport practices, this means that untrained subjects with a reduced exercise capacity cannot achieve a considerable reduction in their fat mass only to the extent of physical activity. This requires a lot of discipline and a strong will. Therefore, in most cases, a reduction in weight only by changing activity behaviour in the short and medium term cannot be achieved [35].

Since the desired weight loss is essentially impossible without achieving a negative energy balance, for successful weight loss both principles are always used: Energy consumption through targeted physical activity and lower energy consumption through a targeted

calorie restriction with changes in energy and nutrient supply [1,8,35]. The two principles do not compete with each other, but are independent components of the weight loss programme.

With regard to the statement “losing weight through sport”, it is not unexpected that successful weight loss and weight maintenance after successful weight loss is more related to leisure-time activity which requires considerable effort [35]. It has already been emphasised that the energy cost of physical activity and its share of the daily calorie balance are generally overestimated.

Regular physical activity as a part of a recommended programme for losing weight and stabilising achieved weight loss, remains unchanged and unchallenged [1,8,35]. In this regard, it is evident that a failure to target exercise, significantly reduces the success of sustained weight loss [36]. For overweight subjects, generally 150 minutes of moderate exercise or an additional energy use of 1,500 kcal per week is recommended [37]. While exercise in the range of 250-300 kcal per day can be quite favourable, in order for a meaningful and verifiable supplement to calorie restriction through dieting, (e.g. via meal replacements), exercise workouts such as strolling, walking or jogging for 5 x 30 minutes per week are insufficient to stabilise any weight loss achieved with a normal diet, i.e. without sustained calorie restriction [7]. However, even the mentioned level of physical activity is better than nothing in terms of raising motivation and quality of life.

Longitudinal studies show that the effort required to maintain a long-term healthy weight is significantly greater than 5 x 30 minutes per week of exercise [38,39]. A sustained decrease in weight of more than 10% of initial body weight was only seen in a multi-year period of investigations in leisure activities, with the moderate range of about 60 minutes per day or more (21 or more MET hours per week). Compared to the recommended activity levels of 150 minutes per week as 5 x 30 minute blocks, this equates to a large scale increase to 420 minutes per week - an increase of additional 180 percent. Clearly, for the previously untrained individual, it is also certainly achievable with a positive exercise experience and with a high degree of discipline to complete more than 60 minutes of daily physical activity. However, for the majority of individuals who have become overweight, it seems unlikely that these activity levels will be sustained. In practice, and in the management of obesity, this means that despite the change in activity behaviour within a reasonable framework, without a concomitant reduction in caloric intake, long-term stabilisation of a reduced weight cannot be achieved [35,40].

Approach 4: Effects on Eating Behaviors and Appetite Regulation

The ability of exercise to create a negative energy balance (EB) relies not only directly on its impact on energy expenditure (EE), but also indirectly on its potential to modulate energy intake (EI) by effecting appetite regulation or even food choices [41,42]. It has been suggested that a larger reduction in physical activity levels, together with an inability of the organism to down regulate EI to a similar extent to match the reduced EE, are the dominant factors in promoting obesity [43]. This uncoupling between EI and EE is likely to result from a breakdown in the normal mechanisms regulating appetite and eating behavior [44]. Eating behavior can be described as a complex, comprising the selection of specific food items,

the size of food portions consumed and the frequency of eating, which together determine not only the total energy intake but also micro- and macronutrient intake [45]. However, the motivation to eat and consume food in response to acute exercise is known to be additionally modulated by gender, body weight and eating behavior among a number of other factors [46]. Unfortunately, there is less research on how exercise-induced responses in appetite-regulating hormones differ between sexes or different age groups. A better understanding of how exercise intensity and workload affect appetite across the sexes and life stages will be a powerful tool in developing more successful strategies for managing weight [47].

There are several studies which have attempted to explain the association between exercise and food intake. Exercise intensity is one important variable mediating the exercise effects on appetite [48]. An exercise intervention has been shown to improve appetite control in previously sedentary individuals. However, the mechanisms whereby exercise improves this short-term appetite control remain obscure. The hypothesis of changes in the postprandial release of satiety peptides such as bioactive peptides (BAP's) “Leu-Pro-Tyr-Pro-Arg” and “Pro-Gly-Pro” is still unproven [44,49].

In the long-term, there is some evidence to suggest that physical activity is associated with an increase in carbohydrate intake, but it is uncertain whether these changes are biologically driven or as a result of changes of a psychological nature. Contrary to a popularly held view, food selection and nutrient intake constitute patterns of behavior held in place by environmental factors and short-acting post-ingestive physiological responses; these patterns of behavior are relatively immune to modulation by the metabolic effects of exercise [50]. It is clear that both inactivity and exercise have an effect on eating behavior in general and appetite in particular, both in short and long term studies, from the motivation to eat and food intake in a broader perspective EB and body weight [44].

In a study on male participants [48], feelings of hunger were briefly suppressed under a high-intensity exercise condition compared to a low-intensity exercise and control group, whereas the intake of a liquid-source of energy and carbohydrate was higher after the exercise sessions. However, the total energy intake remained unchanged. Similar to male subjects, exercise in females had no significant short-term effect on energy intake. These results showed that there are both similarities and differences between males and females in the appetite response to foods varying in macronutrient composition following vigorous exercise. These differences may help to explain why exercise so often produces a less than satisfactory effect on weight control in females [51,52].

In addition to the statement above relating to a more difficult weight reduction in females, the effect of exercise on various body systems suggests that it will have numerous physiological effects in addition to an increase in EE. Some studies have proposed that the fat-free mass (FFM, the largest contributor to resting metabolic rate), but not BMI or fat mass (FM), is closely associated with self-determined meal size and daily energy intake. Several models of appetite regulation have described the role of leptin (as a signal from adipose tissue) in influencing hypothalamic neuropeptide pathways that modulate the stimulation and inhibition of food intake [53,54]. With most attention directed towards the role of adipose tissue (or FM),

it can be considered that FFM has become the ‘forgotten variable’, even though it is clearly important under some conditions [55]. It is therefore interesting that detailed analyses of body composition and appetite variables using a multi-level platform have demonstrated that the FFM, but not FM or BMI, is strongly correlated with meal size and daily EI [56]. The strong implication of this relationship is that some signaling molecule(s) arising from the FFM, or some physiological consequences that reflect the activity of FFM, act as a driver of food intake. Vigorous exercise (high-intensity cycling or running) has been found to significantly reduce hunger and a delay to the onset of eating, a phenomenon that has become known in its consequence as exercise-induced anorexia [57]. A better short-term appetite control has been described in physically active compared to sedentary men, and an exercise intervention has been shown to improve appetite control in previously sedentary individuals [44].

Understanding of the impact of an acute bout of exercise on the hormones involved in appetite regulation may provide insight into some of the mechanisms that regulate energy balance. For example, in resting conditions, acylated ghrelin is known to stimulate food intake, whereas hormones such as peptide YY (PYY), pancreatic polypeptide (PP) and glucagon-like peptide 1 (GLP-1) are known to suppress food intake [58]. However, exercising prior to food intake has been shown to decrease appetite via suppressed plasma ghrelin concentrations [47]. No response to the timing of exercise relative to food intake on plasma leptin concentration was detected. These data indicated the timing of exercise in relation to meal consumption may influence appetite and its hormonal regulators. In addition, post-meal exercise may extend the suppressive effects of meal consumption on appetite [59].

In order for exercise to have a significant impact on weight control, it is important to consider the energy density of the accompanying diet. Results of a study by King et al, 1995 indicated that consuming high-fat foods can prevent exercise inducing any (short-term) negative energy balance [57]. Therefore, the combination of physical activity and a low-fat diet could be used advantageously to control appetite, prevent overconsumption and protect against the development of obesity [52,57]. In a study by Verger et al (1994) [60] a buffet-type meal was presented to 28 young men after participation in various athletic activities and to 30 subjects who remained at rest. The food choices after exercise yielded an energy intake from proteins that were significantly larger than after rest, but not of carbohydrate or fat. So far, it was hypothesized [44] that the beneficial impact of exercise on appetite regulation can contribute to its well-established efficacy in the prevention of weight regain in obese individuals. However, more studies are needed in the obese population to clearly establish the role of exercise on appetite control.

Conclusion

It can be concluded that leisure-time physical activity and training are more than just a “fat burner”, and in their health effects, they should not be only viewed as energy conversion of calories [1,29,34,35]. The calculation of energy use is possible at any time via the measured increase in oxygen consumption, in relation to the intensity and duration of physical activity. This observation alone does not account for the energy balance of the complex physical activity effects in the individual as a whole. Despite a comparable influence

on energy balance, increased energy deficit via targeted physical activity and reduced energy intake through dietary restriction as well as a changed eating behaviour all has different mechanisms of action. This indicates why they are independent but integral components of a successful weight management intervention.

Authors' Contributions

S. Koohkan: Writing of the manuscript, conceive and coordination. D.H. McCarthy: Editing the manuscript. A. Berg: Project leader, guiding and supervising of manuscript writing, decision to submit. All authors read and approved the final manuscript.

Acknowledgment

We would like to thank all of researchers of original papers we used and referenced because their committed work gave us the material for writing this review. Additionally, the authors confirm that they have no ethical or commercial conflict by publishing this paper.

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