Science & Sports (2020) xxx, xxx—xxx

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ORIGINAL ARTICLE

Effects of 2 years endurance training targeted at the level of maximal lipid oxidation on body composition

Effets sur la composition corporelle de 2 ans d'entraînement en endurance ciblé au niveau maximal d'oxydation des lipides

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Received 5 November 2019; accepted 18 November 2019

KEYWORDS
LIPOX max;
Exercise;
Endurance;
Weight loss;
Obesity

Summary
Introduction. — The main problem in obesity management is weight regain that occurs after all currently used slimming procedures. Regular physical activity remains the most effective measure to stop this weight regain. Among the varieties of training that can be offered, endurance exercise at low to moderate intensities targeted at the level of maximum lipid oxidation (LIPOX max) is one of the easiest to implement and has well-documented effects on glucose metabolism, blood lipids, eating behavior, and body composition. Our purpose in this study was to study the effect of this type of exercise on body composition over 2 years.
Methods. — Nonrandomized controlled longitudinal study. Forty-five obese subjects (14 men, 31 women, age = 20—85 years old) were re-trained with LIPOXmax (3 × 45 min/week at home with regular follow-up after induction in hospital) over 2 years. They were compared to a matched control group of 26 subjects. Exercise calorimetry and segmental bioelectric impedance were performed at the beginning and at the 24th month.
Results. — Trained group lost weight (− 6 ± 1.44 kg) over 2 years. This is explained by a loss of fat mass (− 5 ± 1.26 kg), affecting truncal fat mass (− 2.66 ± 0.62 kg $P < 0.0001$), and appendicular fat mass (1.38 ± 0.72 kg $P < 0.01$). There is also a reduction in lean body mass (− 2.41 ± 0.86 kg, $P < 0.01$). Controls gain 3 ± 0.85 kg ($P < 0.001$). In the trained group, the ability to oxidize lipids increased ($P < 0.001$) and there was a positive correlation between weight changes and mean arterial blood pressure at 24 months ($R = 0.37$ $P = 0.02$).

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https://doi.org/10.1016/j.scispo.2019.11.003
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Conclusion. — The weight loss effectiveness of endurance training targeted at the LIPOXmax is maintained for 24 months. This weight loss affects both trunk and appendicular fat mass but also lean mass. It associated with a decrease in blood pressure and an improvement in the ability to oxidize lipids during exercise.
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MOTS CLÉS
LIPOX max ;
Exercice ;
Endurance ;
Perte de poids ;
Obésité

Résumé

Introduction. — Le grand problème de l'obésité est la reprise pondérale qui peut s'observer après toutes les thérapeutiques actuellement utilisées. L'activité physique régulière reste la mesure la plus efficace permettant d'enrayer cette reprise de poids. Parmi les types d'entraînement proposés, l'endurance à des intensités faibles à modérées ciblée sur le niveau d'oxydation lipidique maximale (LIPOX max) est une des plus faciles à mettre en œuvre et a des effets bien documentés sur le métabolisme gluco-lipidique, le comportement alimentaire, et la composition corporelle. Nos objectifs dans cette étude ont été d'étudier l'effet de ce type d'exercice sur la composition corporelle sur 2 ans.

Méthodes. — Étude longitudinale contrôlée non randomisée. Quarante-cinq sujets obèses (14 hommes, 31 femmes, âge = 20—85 ans) ont été réentraînés au LIPOXmax (3 × 45 min/semaine à la maison avec suivi régulier, après induction en milieu hospitalier) sur 2 ans. Ils ont été comparés à un groupe témoin apparié de 26 sujets. La calorimétrie d'exercice et l'impédance bioélectrique segmentaire ont été réalisées au début et au 24^{e} mois.

Résultats. — Le groupe réentraîné a perdu du poids (− 6 ± 1,44 kg) sur 2 ans et − 6 ± 2,2 kg après 5 ans. Cela s'explique par une perte de masse grasse (− 5 ± 1,26 kg), affectant la masse grasse tronculaire (− 2,66 ± 0,62 kg p < 0,0001), et la masse grasse appendiculaire (1,38 ± 0,72 kg p < 0,01). Il y a aussi une réduction de masse maigre (− 2,41 ± 0,86 kg, p < 0,01). Les contrôles gagnent 3 ± 0,85 kg (p < 0,001). Dans le groupe réentraîné, la capacité à oxyder les lipides a augmenté (p < 0,001) et on retrouve une corrélation positive entre les changements de poids et la pression artérielle moyenne à 24 mois (r = 0,37 p = 0,02).

Conclusion. — L'efficacité amaigrissante de l'entraînement en endurance au LIPOX Max est maintenue à 24 mois et l'on observe que cette perte de poids affecte la masse grasse tronculaire et appendiculaire mais aussi la masse maigre et s'accompagne d'une diminution de la pression artérielle et d'une amélioration de la capacité à oxyder les lipides à l'exercice.
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1. Introduction

The importance of exercise training in the management of obesity is now well recognized [1], although its effects on weight loss, considered alone, are generally described as rather moderate [2]. It is well established that it improves the efficiency of weight reducing procedures and prevents weight regain [3]. Even more, it is clear that high amounts (15 hrs/wk or more) of endurance and/or resistance exercise, can induce an important weight loss together with a host of beneficial biological alterations [4]. The issue is more controversial with low volumes of exercise training. Numerous studies investigate the promising effects of sophisticated strategies based on interval training [5], but there is also some literature on the effects of low volumes of endurance training [6]. Surprisingly, low volumes (eg: 3 × 45 min/week) of low-to-moderate intensity endurance exercise have proven to be an efficient tool for reducing body fat stores and improving carbohydrate metabolism, while at higher intensities the metabolic benefit is less obvious [7]. This paradox is explained by the fact that exercise is not only a mean to induce an energy deficit, but exerts additional effects on metabolism that are obvious at low volume, and that low intensity exercise involves more lipid oxidation than high intensity [8]. Even more, low volumes of exercise targeted at an intensity that privilegiates carbohydrate oxidation often induce a paradoxical weight gain [9] explained by the fact that they increase hunger and food intake [10].

Therefore, there is a rationale to target low volumes of exercise at the intensities where lipids are oxidized [11,12] rather to higher intensities. This approach has been demonstrated to induce weight loss by its own [13] and to have a prolonged effect over more than 3 years [14].

Therefore, it is clearly established that exercise targeted on lipid oxidation is an easy and efficient way to obtain a weight loss on the long term. However, little is known until now on the tissues affected by this weight loss. Weight loss strategies that maximize fat mass loss — while minimizing lean mass loss — are generally assumed to provide the greatest health benefit for this demographic, although evidence from well-designed trials is needed to guide recommendations [15]. Actually, over a short period (3 months), several studies have shown that training targeted on lipid oxidation induced a decrease in fat mass associated with a maintaining or even an increase in fat-free mass [13]. This protective effect on fat-free mass consists with the effect of high intensity which may, on the opposite, decrease fat-free mass [16].

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Presumably, maintaining a greater fat-free mass is likely to be beneficial for metabolism and for health. However, recent studies suggest that this issue is more complex and that the higher fat-free mass observed in obese sedentary patients is associated with insulin resistance [17]. Therefore, it is not sure that the maintaining or the increase of this fat-free mass during a weight-loss strategy is beneficial.

It is clear on the other hand that exercise training is an efficient technique for maintaining fat-free mass in people involved in a weight-loss strategy [18]. This is true even for moderate intensity exercise [19].

Therefore, the purpose of this study was to assess on the long term (2 years) the effects of low volumes of exercise targeted on lipid oxidation on fat mass and fat-free mass in obese subjects.

2. Materials and methods

2.1. Subjects

We investigated in this study the weight loss of a cohort of 45 subjects that continued LIPOXmax training over 2 years (14 men, 31 women, age: 20—85 years, body mass index: 22—43 kg/m^2) was compared to a matched control group. Controls were subjects that did not start any change in their diet or exercise habits despite repeated advice, but still attended regularly outpatient consultations. Patients' characteristics are shown in Table 1. The 2 cohorts were matched for weight and body mass index.

2.2. Bioelectrical impedance measurements

Prior to the exercise-test, subjects' body composition was assessed with bioimpedance analysis with a six terminal impedance plethismograph BIACORPUS RX 4000 Biacorpus RX4000, (SoAGIL DEVELOPPEMENT, 8 avenue Jean-Jaurès F-92130 Issy-les-Moulineaux, France) with data analysis with the software BodyComp 8.4. This device measures total resistance of the body to an alternative electric current of 50 kHz [20,21].

Body fat mass, fat-free mass were calculated in each segment of the body according to manufacturer's database-derived disclosed equations, and total water with published equations using the classical cylindric model and Hanai's mixture theory [21]. Muscle mass was assessed with Janssen's equation from hand-foot resistance at 50 kHz [22].

2.3. Bioelectrical impedance measurements

All subjects were asked to come and perform test in the morning after an overnight fast (12 hours). The test consisted of five six-minute steady-state workloads theoretically set at 20, 30, 40, 50, and 60% of Pmax. However, these intensity levels can be modified during the test according to the evolution of the respiratory exchange ratio (RER = VCO2/VO2) in order to obtain values of RER below and above 0.9 which is the level of the Crossover Point (COP) which is defined below. The subjects performed the test on an electromagnetically braked cycle ergometer (Ergoline Bosch 500). Heart rate and electrocardiographic parameters were monitored continuously throughout the test by standard 12-lead procedures. Metabolic and ventilatory responses were assessed using a digital computer-based breath to breath exercise analyzing system (COSMED Quark CPET). Thus, we could measure VO2, VCO2 mL/min) and calculate the non-protein RER. Lipid oxidation (Lipox) and carbohydrate utilization (Glucox) rates were calculated by indirect calorimetry from gas exchange measurements according to the non-protein respiratory quotient technique as previously reported [23]. This technique provided carbohydrate and lipid oxidation rates at different exercise intensities. Additionally, after smoothing the curves, we calculated the two parameters quantifying the balance between carbohydrates and lipids induced by increasing exercise intensity: the maximal lipid oxidation point (LIPOXmax) and the Crossover Point (COP). The LIPOXmax is the exercise intensity at which lipid oxidation reaches its maximal level before decreasing while carbohydrate utilization further increases. It is calculated as previously reported after smoothing of the curve plotting lipid oxidation as a function of power.

2.4. Coaching and follow-up of patients

Each subject included in the exercise group was enrolled in eight exercise sessions of 45 min at the LIPOXmax determined with the exercise test in order to include in his/her everyday life at least 3 similar bouts of low intensity endurance exercise per week. Subjects were followed monthly in outpatient unit for the first year and then every 3 or 4 months [24].

2.5. Statistical analysis

Descriptive statistics were performed. A two-way analysis of variance (ANOVA) was used to determine whether there was an effect of training vs. non training over time and whether it was different between the two groups. A *P*-value less than 0.05 was used to assess statistical significance.

3. Results

On the average there was a gradual weight loss in the trained group (-6 ± 1.44 kg after 2 years $P < 0.0001$) while in the control group there was a trend to weight increase. Among trained subjects, 39 lose weight (from 1 to 36.9 kg) e.g. 86.7%, while 6 lose no weight or actually gained weight (13.3%). The Fig. 1 shows the difference between the two groups showing an increasing difference among non trained individuals who gain weight on the average while trained subjects lose weight.

The Fig. 1 shows the average evolution of body weight over 2 years. While controls gained weight over this period, LIPOXmax group lose weight. Weight loss at 1 year was observed in exercise and controls group, but at 2 years there was a weight regain ($P < 0.01$) in controls so that results were better ($P < 0.0001$) in the exercise group who maintained weight loss in 86.7% of subjects. Average weight loss was -6 ± 1.44 kg after 2 years for the LIPOX max group.

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Table 1 Study subjects (mean ± SEM).

	Gender (F/M)	AGE (yr)	Weight (kg)	BMI (kg/m^2)
LIPOXmax (*N* = 45)	31F/14M	52 ± 2	88 ± 3.22	31 ± 4.81
Controls (*N* = 26)	18F/8M	49 ± 2	90 ± 3.29	32 ± 0.83

Comparison: LIPOXmax and control groups are matched for age, weight and body mass index. No significant difference between the two groups.

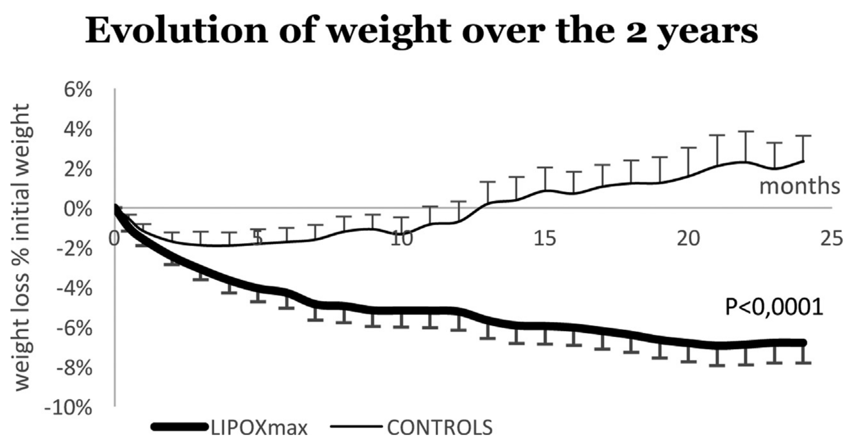

Figure 1 Respective evolution of weight (in kg) over the 2 years. It can be seen that controls gained weight over this period, while LIPOXmax group lose weight. Weight loss at 1 year was observed in exercise and controls group, but at 2 years there was a weight regain ($P < 0.01$) in controls so that results were better ($P < 0.0001$) in the exercise group who maintained weight loss in 86.7% of subjects. Average weight loss was − 6 ± 1.44 kg after 2 years for the LIPOX max group.

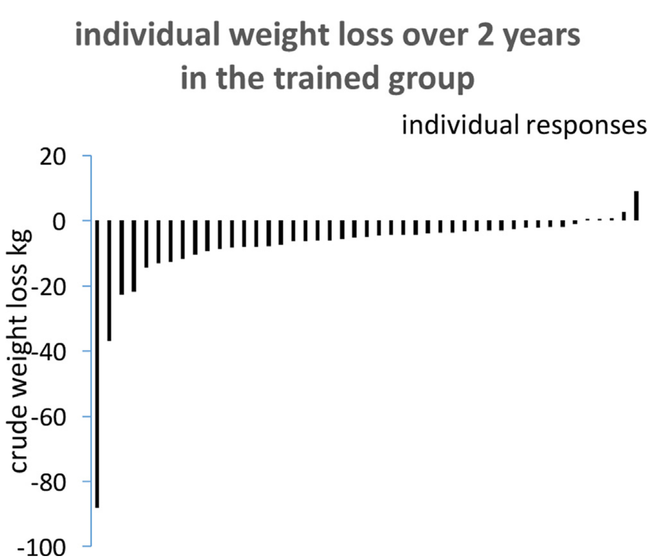

Figure 2 Individual weight loss responses in the LIPOXmax group. There are 86.7% responders (among whom 20% are good responders losing more than 10% of the initial weight), and 13.3% non responders who lose no weight or even gain weight.

The Fig. 2 shows the individual responses to the exercise strategy over 2 years. It can be seen that there are 86.7% responders (among whom 20% are good responders losing more than 10% of the initial weight), and 13.3% non responders.

As shown on Fig. 3, the body composition changes over 2 years. The LIPOX max group loses fat mass (FM) (− 5 ± 1.26 kg, $P < 0.001$) and loses lean mass (− 2.41 ± 0.86 kg, $P < 0.01$), while controls gain fat mass with an average of 3 ± 0.85 kg ($P < 0.001$).

Although there was an overall effect of training on fat-free mass, analysis of the various components of fat free mass especially the muscular mass assessed by Janssen's equation (Fig. 4) did not change over the 2 years in either of the two groups. By contrast, the effect on fat mass (FM) is shown on Fig. 5. It can be seen that the two components of FM are significantly decreased. The LIPOX max group lost 2.66 ± 0.62 kg of truncal fat mass ($P < 0.0001$), and 1.38 ± 0.72 kg of appendicular fat mass ($P < 0.01$) over 2 years of re-training. By contrast, there is no significant change in the body composition of fat mass in the control group.

The Fig. 6 shows the evolution of fat oxydation of the trained (LIPOX max) group. There is a better fat oxydation ($P < 0.001$) over 2 years of training.

4. Discussion

This study confirms that low intensity exercise training targeted at the LIPOXmax has a long-term efficiency on weight loss, and evidences for the first time that this weight loss comprises a decrease in both truncular and appendicular fat stores together with a decrease in fat-free mass.

The main limit of this study is obviously that this is an observational study, without initial randomization. However, this is a controlled study since the cohort of LIPOXmax trained subjects is compared to a control group. The groups

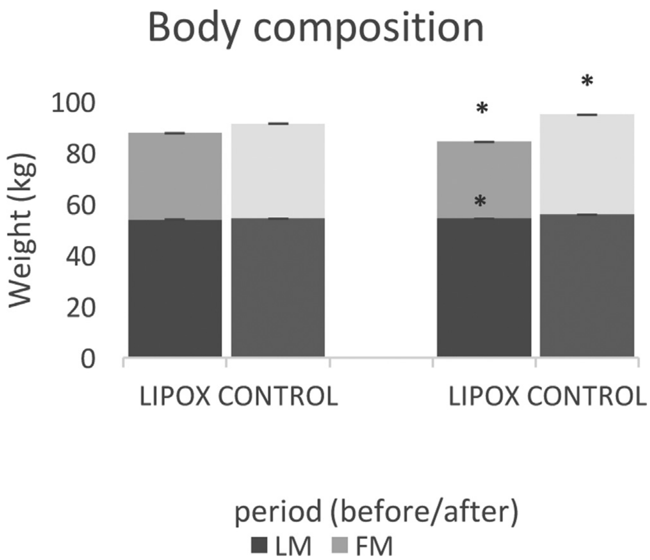

Figure 3 Body composition of the 2 groups after 2 years. There is a significant decrease ($P < 0.01$) withan average of 2.41 ± 0.86 kg of lean mass (LM) for the Lipox group after 2 years of re-training, with also a significant decrease ($P < 0.001$) with an average of 5 ± 1.26 kg fat mass (FM). Whereas, there is a significant increase ($P < 0.001$) with an average of 3 ± 0.85 kg fat mass (FM) after 2 years in the control group. The comparison of the 2 groups by ANOVA test reveals a significant difference ($P < 0.0003$) between the groups.

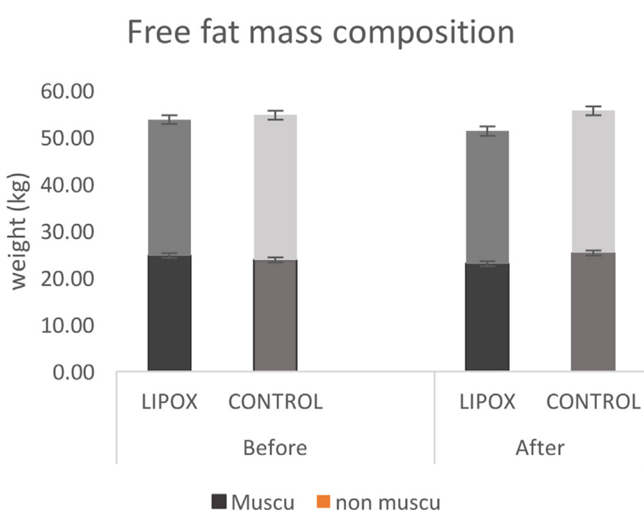

Figure 4 Evolution of free fat mass and its two components (muscle and non-muscle FFM) over 2 years. There is an overall decrease in FFM in trained subjects but neither muscle nor non-muscle FFM is significantly modified.

LIPOXmax and control have the same BMI and age and are thus well matched for possible confounding factors. Another limitation is the fact that only patients that were still followed are included in the analysis, which is thus not performed in ''intention to treat''. One can assume that a significant proportion of subjects that discontinued the procedure are people who were deceived by its efficacy and thus were poor responders, so that a study in intention to treat would yield on the average a lower weight loss. By

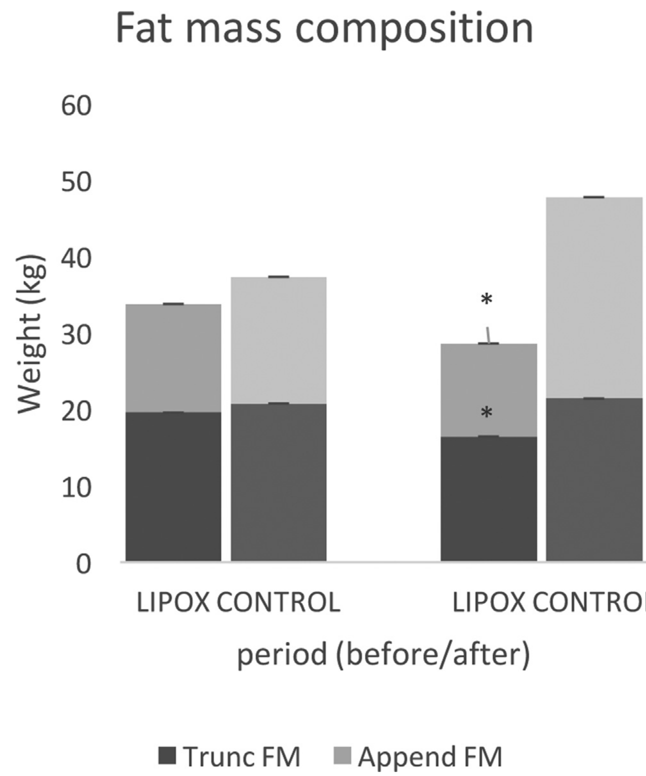

Figure 5 Fat mass body composition (Truncular FM, Appendicular FM) of the two groups. There is a significant decrease ($P < 0.0001$) with an average of 2.66 ± 0.62 kg of truncal fat mass, as well as an average of loss of 1.38 ± 0.72 kg of appendicular fat mass ($P < 0.01$) in the group LIPOX after 2 years of re-trainig. By contrast, there is no significant change in the control group.

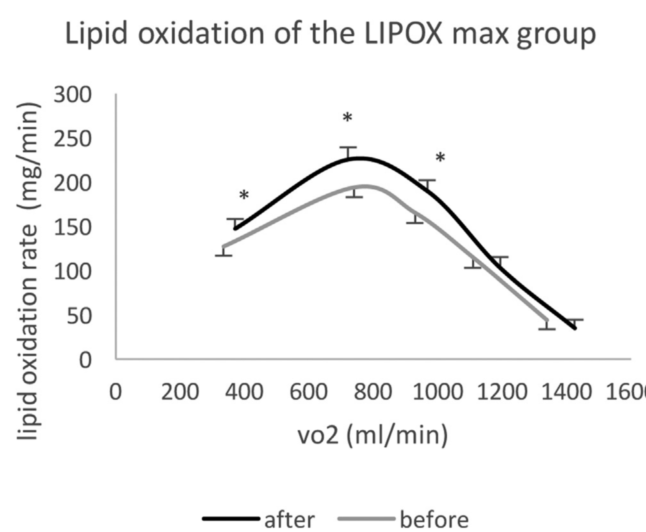

Figure 6 Lipid oxidation during exercise calorimetry in the LIPOX group before and after 2 years of training. There is a significant ($P < 0.001$) increase in lipid oxidation at rest, at the first level ($P < 0.001$) and at second level of the stress test ($P < 0.01$) after 2 years of re-training.

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contrast a strength of this study is to show a sample of subjects in conditions of ''true life'', continuing their training over 2 years or more with on the average persisting weight-reducing effects.

A randomized control trial of similar groups will be useful to do, but such a study will probably be extremely expensive and difficult to manage. The control group is not a series of patients randomized and assigned to a non-treatment follow up, but a sample of subjects that still wanted to be followed but were unable to start a weight reducing procedure, expecting to do so in a next future. The evolution of weight in this control group is similar to that reported in STRRIDE [25], which is $+1.0 \pm 2.7\%$ of initial body weight. In our series, it is interesting to see that in the control group, weight gain increases after time: 2.4 ± 5.12 kg over two years. This finding clearly shows that continued physical inactivity results in progressive weight gain, as pointed out by the authors of STRRIDE [25].

A major originality of this study on LIPOXmax compared to other studies on low intensity exercise is that training is targeted on the basis of exercise calorimetry. Most studies assume that low intensity below 50% VO2max involves to a large extent fat oxidation [25], but when large series of exercise calorimetries are performed it is clear that there is a large interindividual variability [26] so that a theoretical value calculated with a fixed percentage of VO2max may fall outside of the zone of maximal lipid oxidation in 60—70% of patients [27]. Therefore, the use of exercise calorimetry helps to precisely target exercise on lipid oxidation while the use of a theoretical percentage of VO2max is far less precise.

Some methodological aspects of the study need to be discussed. Concerning exercise calorimetry, the protocol employed for calculating lipid oxidation is Pérez—Martin's one [11] which uses 6 min steps, while other teams prefer 3 min steps. We have previously published that the 3 min steps used by most authors are too short to achieve a steady state in obese patients [23]. In addition, our protocol is based on the derivation of the equation of lipid oxidation, the point of maximal lipid oxidation being actually calculated as the point where the derivative of the equation plotting lipid oxidation against power intensity becomes equal to zero [28]. Therefore, this procedure called LIPOXmax is not fully equivalent to the FATmax procedure described by A. Jeukendrup and coworkers [29] and based on 3 min steps without such a calculation.

On the whole, whatever its methodological limits due to the lack of randomization, this study unequivocally demonstrates that many patients included in such a protocol gradually lose weight for at least 2 years, and therefore that low intensity endurance exercise targeted on the zone of maximal lipid oxidation is efficient for losing weight on the long term in a significant percentage of obese subjects. This approach is not the most widely used but it has been proposed since almost twenty years as a promising strategy against obesity [11,29—34]. When targeted with exercise calorimetry at levels where lipid oxidation is maximal (LIPOXmax), it has been shown to improve mitochondrial respiration [35], blood glucose control and blood lipids, low grade inflammation and body composition, even at low weekly volume [12].

Surprisingly, this approach generated less literature, perhaps because its weight-reducing effects over the short term, although significant, were not spectacular. However, its prolonged use has already been shown to result in a sustained weight loss [24,12] which contrasts with the quite constant weight regain observed in almost all classical strategies [3].

The weight reducing effects found in study over 2 years are in agreement with those of our previous study with the same methodology on 3 years [14,37]. The average weight loss after 2 years (-6 kg) and the rate of positive results (86.7%) are quite the same as the weight loss at 3 years in our preceding study (5.31 kg, efficacy in 80% of subjects). Therefore, LIPOXmax training has a slow effect but this effect becomes quite interesting on the long term. In a recent presentation, we showed that weight loss was actually maintained over more than 4 years, resulting at this time into a body weight at $-9.16 \pm 3.4\%$ of initial weight [36,37].

Interestingly, both truncular and appendicular fat mass, which have different pathophysiological relevance [15], exhibit a significant decrease in the LIPOX max group over 2 years of training. Thus, clearly, this training procedure decreases fat stores in various locations in the body.

It is more surprising to observe that there is also a significant decrease in fat-free mass. This finding contrasts with the effect of short term LIPOXmax training as presented in Romain's meta-analysis [13] which showed on the average a preservation or an increase in fat free mass. On the long term, the picture is thus different. Since the treatment of obesity aims at reducing fat mass and not fat-free mass, the decrease of the latter which is commonly observed in most procedures is generally considered as a concern and the need to preserve fat-free mass is emphasized [38]. However, a paradox of fat-free mass has been recently pointed out by the team of I.J. Dionne who reported that in sedentary obese patients this parameter was not associated with a beneficial metabolic profile but was, on the other way about, an independent determinant of insulin resistance and thus of the metabolic syndrome [14,39]. Therefore, in such patients, there are compounds of fat-free mas that are not beneficial for metabolism and that can be losen during weight reduction without harm. Interestingly, in this study, muscle mass as determined by Janssen's equation is not decreased by training, indicating that the loss of fat free mass affects another component but not muscle mass. The exact effect of this loss of fat free mass after long term LIPOXmax training requires further studies to understand its pathophysiological relevance.

5. Conclusion

In conclusion, our study clearly demonstrates that for the group of patients included in the LIPOXmax procedure there is still losing weight after 2 years of endurance training at low intensity. This long-term effect is not usual in obesity studies and will require to be further investigated. One of the next steps of this study is to investigate whether this weight loss persists in the future years or if there is a later tendency to weight regain as observed with almost all other slimming procedures. In addition, the alterations in body composition evidenced here require to be further analyzed, since beside the expected decrease in fat mass there is also a decrease in fat-free mass which is likely to be not deleterious in this context, but remains poorly understood.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE 2015;10(4):e0119017.
[2] Wu T, Gao X, Chen M, van Dam RM. Long-term effectiveness of diet-plus-exercise interventions vs. diet-only interventions for weight loss: a meta-analysis. Obes Rev 2009;10(3):313—23.
[3] Svetkey LP, Stevens VJ, Brantley PJ, Appel LJ, Hollis JF, Loria CM, et al. Comparison of Strategies for Sustaining Weight Loss: The Weight Loss Maintenance Randomized Controlled Trial. JAMA 2008;299:1139—48.
[4] Dutheil F, Lac G, Lesourd B, Chapier R, Walther G, Vinet A, et al. Different modalities of exercise to reduce visceral fat mass and cardiovascular risk in metabolic syndrome: the RESOLVE randomized trial. Int J Cardiol 2013;168:3634—42.
[5] Gillen JB, Gibala MJ. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? Appl Physiol Nutr Metab 2014;39(3):409—12.
[6] Johnson J, Slentz C, Houmard JA, Samsa GP, Duscha BD, Aiken LB, et al. Exercise training amount and intensity effects on metabolic syndrome: STRRIDE. Am J Cardiol 2007;100:1759—67.
[7] McGarrah RW, Slentz CA, Kraus WE. The effect of vigorous- versus moderate-intensity aerobic exercise on insulin action. Curr Cardiol Rep 2016;18(12):117.
[8] Brun JF. Exercise makes more than an energy deficit: toward improved protocols for the management of obesity? EBioMedicine 2015;18:1862—3.
[9] Brun JF, Romain AJ, Sferlazza A, Fédou C, Raynaud de Mauverger E, Mercier J. Which individuals become fatter when they practice exercise? Science & Sports 2016;31:214—8.
[10] Guiraudou M, Chérif A, Richou M, Fidani T, Romain AJ, Mercier J, et al. Effects over 24Hr of exercise targeted on lipid versus carbohydrate oxidation on eating behaviour in normal weight volunteers. Int J Sports Sci Med 2018;2(2):031—5.
[11] Pérez-Martin A, Dumortier M, Raynaud E, Brun JF, Fédou C, Bringer J, et al. Balance of substrate oxidation during submaximal exercise in lean and obese people. Diabetes & Metabolism 2008;27(4):466.
[12] Besnier F, Lenclume V, Gérardin P, Fianu A, Martinez J, Naty N, et al. Individualized exercise training at maximal fat oxidation combined with fruit and vegetable-rich diet in overweight or obese women: the LIPOXmax-Réunion randomized controlled trial. PLoS One 2015;10:e0139246.
[13] Romain AJ, Carayol M, Desplan M, Fedou C, Ninot G, Mercier J, et al. Physical activity targeted at maximal lipid oxidation: a meta-analysis. J Nutr Metab 2012;2012:285395.
[14] Drapier E, Cherif A, Richou M, Bughin F, Fedou C, Mercier J, et al. Long term (3 years) weight loss after low intensity endurance training targeted at the level of maximal muscular lipid oxidation. Integr Obesity Diabetes 2018;4:4, http://dx.doi.org/10.15761/IOD.1000201.
[15] Beavers KM, Ambrosius WT, Rejeski WJ, Burdette JH, Walkup MP, Sheedy JL, et al. Effect of exercise type during intentional weight loss on body composition in older adults with obesity. Obesity (Silver Spring) 2017;25(11):1823—9.
[16] Brandou F, Savy-Pacaux AM, Marie J, Bauloz M, Maret-Fleuret I, Borrocoso S, et al. Impact of high- and low-intensity targeted exercise training on the type of substrate utilization in obese boys submitted to a hypocaloric diet. Diabetes Metab 2005;31(4 Pt 1):327—35.
[17] Ghachem A, Lagacé JC, Brochu M, Dionne IJ. Fat-free mass and glucose homeostasis: is greater fat-free mass an independent predictor of insulin resistance? Aging Clin Exp Res 2019;31(4):447—54, http://dx.doi.org/10.1007/s40520-018-0993-y.
[18] Weinheimer EM, Sands LP, Campbell WW. A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. Nutr Rev 2010;68(7):375—88.
[19] Chomentowski P, Dubé JJ, Amati F, Stefanovic-Racic M, Zhu S, Toledo FG, et al. Moderate exercise attenuates the loss of skeletal muscle mass that occurs with intentional caloric restriction-induced weight loss in older, overweight to obese adults. J Gerontol A Biol Sci Med Sci 2009;64(5):575—80.
[20] Brun JF, Guiraudou M, Mardemootoo C, Traoré A, Raingeard I, Chalançon A, et al. Validation de la mesure segmentaire de la composition corporelle en comparaison avec la DEXA: intérêt de la mesure de la masse grasse tronculaire. Science & Sports 2013;28:158—62.
[21] Guiraudou M, Maimoun L, Dumas J-M, Julia M, Raingeard I, Brun J-F. Composition corporelle mesurée par impédancemétrie segmentaire (BIAS) et performance de sprint chez les rugbymen/Body composition measured by bioimpedance segmental (BIAS) analysis and sprint performance in rugby players. Science & Sports 2015;30:298—302.
[22] Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol (1985) 2000;89(2):465—71.
[23] Brun JF, Varlet-Marie E, Romain AJ, Mercier J. Measurement and physiological relevance of the maximal lipid oxidation rate during exercise (LIPOXmax). INTECH book. Sports Medicine and Sports Injuries 2011 [Kenneth R. Zaslav (Ed.) « An International Perspective on Topics in Sports Medicine and Sports Injury » INTECH open, 2012, ISBN: 978-953-51-6793-8. https://www.intechopen.com/books/an-international-perspective-on-topics-in-sports-medicine-and-sports-injury/measurement-and-physiological-relevance-of-the-maximal-lipid-oxidation-rate-during-exercise-lipoxmax. BN 979-953-307-096-3].
[24] Guiraudou M, Fédou C, Romain AJ, Sferlazza A, Calas E, Brun JF. Effects over one year of low-intensity endurance exercise targeted at the level of maximal lipid oxidation. Science & Sports 2015;30:e127—31.
[25] Slentz CA, Aiken LB, Houmard JA, Bales CW, Johnson JL, Tanner CJ, et al. Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. J Appl Physiol 2005;99:1613—8.
[26] Maunder E, Plews DJ, Kilding AE. Contextualising maximal fat oxidation during exercise: determinants and normative values. Front Physiol 2018;9:599.
[27] Brun JF, Halbeher C, Fédou C, Mercier J. Quelles sont les limites de normalité du LIPOXmax ? Peut-on le prédire sans effectuer de calorimétrie d'effort ? Science & Sports 2011;26:166—9.
[28] Bordenave S, Flavier S, Fedou C, Brun JF, Mercier J. Exercise calorimetry in sedentary patients: procedures based on short 3 min steps underestimate carbohydrate oxidation and overestimate lipid oxidation. Diabetes Metab 2007;33(5):376—84.
[29] Achten J, Jeukendrup AE. Optimizing fat oxidation through exercise and diet. Nutrition 2004;20:716—27.

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[30] Perez-Martin A, Mercier J. Stress tests and exercise training program for diabetics — Initial metabolic evaluation. Ann Endocrinol 2001;62:291—3.
[31] Dériaz O, Dumont M, Bergeron N, Després JP, Brochu M, Prud'homme D. Skeletal muscle low attenuation area and maximal fat oxidation rate during submaximal exercise in male obese individuals. Int J Obes Relat Metab Disord 2001;25:1579—84.
[32] Achten J, Gleeson M, Jeukendrup AE. Determination of the exercise intensity that elicits maximal fat oxidation. Med Sci Sports Exerc 2002;34:92—7.
[33] Brandou F, Dumortier M, Garandeau P, Mercier J, Brun JF. Effects of a two-months rehabilitation program on substrate utilization during exercise in obese adolescents. Diabetes Metab 2003;29:20—7.
[34] Venables MC, Jeukendrup AE. Endurance training and obesity. Med Sci Sports Exerc 2008;40: 495—502.
[35] Bordenave S, Metz L, Flavier S, Lambert K, Ghanassia E, Dupuy AM, et al. Training-induced improvement in lipid oxidation in type 2 diabetes mellitus is related to alterations in muscle mitochondrial activity. Effect of endurance training in type 2 diabetes. Diabetes Metab 2008;34(2):162—8.
[36] Javernaud E, Brun J-F, Richou M, Bughin F, Mercier J. Les effets du réentraînement ciblé au LIPOXmax sur le comportement alimentaire et la composition corporelle sont précoces et se prolongent au moins 4 ans. Nutr Clin Metab 2018;32(4):260.
[37] Brun JF, Chérif A, Richou M, Bughin F, Raynaud de Mauverger E. Effets précoces et tardifs d'un entrainement régulier au LIPOXmax dans l'obésité. 11ème congrès commun de la Société française de médecine de l'exercice et du sport (SFMES) et de la Société française de traumatologie du sport (SFTS) au Havre du 20 au 22 Septembre 2018. Volume des résumés (communication PO47), in: Barrault D, Gleizes-Cervera SD, Courage O (Eds); 2018. p. 54.
[38] Dixon JB, Lambert EA, Grima M, Rice T, Lambert GW, Straznicky NE. Fat-free mass loss generated with weight loss in overweight and obese adults: what may we expect? Diabetes Obes Metab 2015;17(1):91—3.
[39] Perreault K, Lagacé JC, Brochu M, Dionne IJ. Association between fat free mass and glucose homeostasis: common knowledge revisited. Ageing Res Rev 2016;28:46—61.

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