Substrate oxidation during exercise at moderate and hard intensity in middle-aged and young athletes vs sedentary men

Jérôme Manetta, Jean-Frédéric Brun, Christian Prefaut, Jacques Mercier

Abstract

This study investigated the combined effects of endurance training and aging on substrate oxidation during exercise. Thirty-one healthy male subjects in 4 groups (8 middle-aged trained cyclists, 8 young trained cyclists, 7 middle-aged sedentary men, and 8 young sedentary men) performed 2 50-minute cycle ergometer exercise tests, below and above (±15%) their individual ventilatory threshold (VT). Substrate oxidation was evaluated by indirect calorimetry during the steady-state tests. Aging decreased carbohydrate (CHO) use (P < .05) in all subjects regardless of fitness status or exercise intensity. However, it declined 2-fold less in the trained men (P < .05) and was associated with a stronger epinephrine response (P < .05). During hard-intensity exercise, endurance training increased by 100% CHO use in the older men (P < .05). In the younger men, training increased fat oxidation but did not change CHO oxidation, resulting in a marked decrease in the ratio between CHO and fat used at high-intensity exercise (~93%; P < .05). These data suggest an age-related decline in the use of CHO as an energy source in exercising men, independent of intensity level. This decline, however, is attenuated in well-trained men for exercise intensities above the VT. In view of these findings, we hypothesize that cycling training performed at a specific exercise intensity (ie, 15% above VT) may improve CHO mobilization and use in middle-aged men.

1. Introduction

Aging is associated with several deleterious changes in body composition and whole body energy metabolism. These modifications include increased adiposity [1], muscle loss [1], and an altered glucose metabolism [2], all of which are due in part to decreased energetic expenditure [3] and a decline in physical activity [4]. The mechanisms that determine the age-associated changes in metabolic functions in relationship with body composition are not well defined, but evidence so far demonstrates that the loss of fat-free mass is at least partially attributable to physical inactivity [5].

Regular exercise is therefore frequently proposed to older adults as a means of maintaining or improving body composition and glucose disposal and enhancing energy expenditure.

The mobilization and use of endogenous substrates during exercise are important for energetic metabolism and athletic performance. Moreover, exercise intensity and endurance training are known to be the 2 main factors in determining the balance of substrate use during exercise [6]. Endurance training enhances the ability to consume lipids during mild-to-moderate exercise intensity, but the transition to hard exercise appears to result in a crossover to predominantly carbohydrate (CHO) use [7]. In agreement, several authors have shown that regular exercise decreases CHO use and increases lipid use [8,9] during moderate-intensity exercise, whereas others have shown a higher ability to use glucose [2,10,11] and CHO preferentially during hard-intensity exercise [12-15].

Although few studies have been performed specifically in aged populations, marked alterations in the pattern of substrate use seem to occur with aging. Sial et al [16] showed that CHO oxidation was lower in elderly subjects than in young subjects during moderate-intensity exercise performed at the same relative intensity. We recently showed that endurance training resulted in increased CHO use during exercise.
The mechanism of balancing the use of CHO- and lipid-derived substrates during exercise, however, has not yet been clearly evidenced. Carbohydrate disposal is also disturbed in older subjects, as evidenced by lower glucose effectiveness and insulin sensitivity [2,17]. This finding is particularly relevant for the middle-aged population because this insulin resistance of aging is initiated as early as the third decade of life [17,18].

The extent to which training counteracts these metabolic effects of aging has been incompletely elucidated. More specifically, the combined effects of training and aging on substrate oxidation balance at hard- vs moderate-intensity exercise are not known. This study was thus undertaken to investigate in both young and middle-aged subjects (1) the effect of aging on the balance of substrate oxidation and (2) as to what extent and at which intensity level (moderate- or hard-intensity or both) training modifies this balance. We investigated substrate use during both moderate- and hard-intensity exercise in young and middle-aged sedentary and trained men. Substrate oxidation rates were determined by indirect calorimetry during exercise [19,20].

2. Materials and methods

2.1. Subjects

A total of 31 healthy male subjects in 4 groups (8 middle-aged trained cyclists [TrA], 8 young trained cyclists [TrY], 7 middle-aged sedentary men [SedA], and 8 young sedentary men [SedY]) participated in this study. None had a family history of diabetes or hypertension. Smokers or those currently using medication for the control of blood arterial pressure or lipid or CHO metabolism were excluded. No subject exhibited electrocardiogram abnormalities at rest or during a maximal cycle ergometer test. The physical characteristics of the subjects are shown in Table 1. Body composition was assessed with a 4-terminal impedance plethysmograph Dietosystem Human IM-Scan [21]. All middle-aged cyclists were on the same cycling team and their training program amounted to nearly 9 hours of cycling per week (290 ± 13 km); this team had been cycling together for 12.3 ± 1.6 (SE) years. The young cyclists were also on the same team and their training program totaled nearly 14 hours per week (430 ± 19 km); this team had been cycling together for the past 6.4 ± 1.2 (SE) years.

After receiving a complete and accurate verbal description of the procedure and the risks and benefits associated with the study, the subjects provided written consent. The experimental protocol was approved by the Committee on Research for the Medical Sciences.

2.2. Protocol

The subjects came to the laboratory on 3 separates days for (1) a maximal aerobic capacity test from which the ventilatory threshold (VT) was determined (day 1) and (2) 2 50-minute steady-state exercise tests, below (−15%) and above (+15%) their individual VT, performed in random order (days 2 and 3).

The tests were separated by at least 4 days and never more than 7 days. All subjects were requested to refrain from exercise and consumption of cola drinks and coffee for the 3 days before testing. Prior to study enrolment, a brief interview was conducted [22] to ascertain that all subjects had approximately the same dietary habits.

2.3. Incremental maximal exercise test

The subjects’ maximum oxygen consumption (V̇O2max) was measured during 8 to 12 minutes of exercise performed on an electronically braked cycle ergometer (550 ERG, Bosch, Berlin, Germany). Fractions of oxygen and carbon dioxide in the expired air were measured by a mass spectrometer (Marquette MGA 1100, Marquette, Blagnac, France). The calibration of the mass spectrometer was checked before each test with standard calibration gases. A 3-L syringe was used to calibrate the volume turbine using flow rates similar to subject ventilation. During exercise, gas exchanges were measured breath-by-breath using a mass spectrometer (Marquette MGA 1100, Marquette). Heart rate was monitored throughout the exercise test. Exercise testing started with a 3-minute warm-up at 40 W. The workload was increased by steps of 20 W for the sedentary group and 30 W for the trained group every minute until maximal exercise was reached, which was evaluated in terms of maximal heart rate, respiratory exchange ratio (RER) values (>1.15), and oxygen consumption per unit time (V̇O2) stability. The
results of this test were used to determine the VT according to the method of Beaver et al [23].

2.4. Steady-state exercise test

Subjects arrived at the laboratory at 8:00 AM after an overnight fast (ie, 12 hours). A Teflon catheter was inserted in the cephalic vein at the level of the cubital fossa for blood sampling at various times. At 8:30 AM, resting blood sample was drawn for subsequent analysis and subjects then exercised either below (−15%) or above (+15%) their VT for 50 minutes on an electronically braked cycle ergometer (550 ERG, Bosch). Water was given ad libitum during exercise tests. During the 50 minutes of exercise, the subjects were instructed to maintain a pedaling rate of 75 rpm and ventilatory flow rate (VE), RER, VO2, and carbon dioxide production (VCO2) were measured continuously, as described above. During this period, the VO2 and VCO2 varied by less than 0.1 L/min and VE varied by less than 0.5 L/min.

2.5. Indirect calorimetry and substrate oxidation measurements

The percentages of CHO and lipid oxidation were calculated by using the following equations [19]. The RER value was the average of every 5-minute period throughout the entire 50 minutes of exercise.

\[
\text{% lipid} = \frac{1}{0.29} (1 - \text{RER}) \\
\text{% carbohydrate} = \frac{0.71}{0.29} (\text{RER} - 0) \\
\]

The rates of substrate oxidation of CHO and fat were calculated from gas exchange measurements according to the table of nonprotein respiratory quotient [20].

\[
\text{carbohydrate} = 4.585 \times \text{VCO2} - 3.226 \times \text{VO2} \\
\text{lipid} = 1.695 \times \text{VO2} - 1.701 \times \text{VCO2}
\]

with mass expressed in grams per minute and gas volume in liters per minute.

The VO2 and VCO2 values were the averages of every 5-minute period throughout the entire 50 minutes of exercise.

2.6. Sample collection and analysis

Blood samples were drawn at rest (t0) and at 5, 15, 30, 45, and 50 minutes during exercise. Samples were immediately placed in a tube containing lithium heparin (glucose, insulin, catecholamines) or EDTA (lactate). The plasma was immediately separated by centrifugation at 4°C and was stored at −80°C until analysis. Plasma glucose (Sigma Diagnostics, Saint Quentin, France) and lactate (Boehringer Mannheim, Grenoble, France) concentrations were determined by specific enzymatic methods adapted to the spectrophotometer (Beckman DU 640, Beckman, France). Plasma insulin (Insik-5, Sorin Biomedica, Vercelli, Italy) was measured by radioimmunoassay. Plasma catecholamine concentration was determined using reverse-phase high-performance liquid chromatography procedures (460 Electrochemical Detector, Waters, Oklahoma City, Okla). All these biochemical measurements were performed in a hospital laboratory submitted to a close regular quality control.

2.7. Statistical analysis

Data are expressed as means ± SE. To detect differences between training status and age groups, a 2-way analysis of variance was performed. If the analysis of variance indicated significant differences, these were located by a pairwise multiple comparison procedure (Student-Newman-Keuls). To detect differences between parameters represented by a single measurement, nonparametric tests for unpaired (Mann-Whitney) and paired (Wilcoxon) data were used as appropriate. A P value less than .05 was considered significant.

3. Results

Subjects were matched for height, weight, body mass index, and fat (%) in each category of age (Table 1). The VO2max was higher in the cyclists than in the sedentary subjects independently of age and in the younger than in the older subjects (Table 1).

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**Fig. 1. Comparison of total CHO use (grams) in middle-aged men (SedA and trained TrA) and in young men (SedY and TrY). **P < .05, TrY vs SedY; \*P < .05, TrA vs SedA; \#P < .05, SedY vs SedA; **P < .05, TrY vs TrA.**
3.1. VO₂ measurement

When exercise intensity during both exercises (VT and +VT) was expressed as a percentage of VO₂max, the percentages were quite similar for TrA, TrY, SedA, and SedY (respectively, 50.6% ± 3.2%, 52% ± 1.6%, 51.2% ± 3.1%, 53% ± 3.5% below VT and 72.1% ± 1.6%, 70.3% ± 2.7%, 73.2% ± 2.2%, 73.1% ± 3.2% above VT). However, when reported in absolute intensity as a power output, these values differed between middle-aged men (SedA vs TrA) (respectively, 84 ± 3.9 vs 125 ± 5.6 W below VT [P < .05] and 119 ± 5.6 vs 186 ± 8.2 W above VT [P < .05]) and between young men (SedY vs TrY) (respectively, 118 ± 6.1 vs 156 ± 7.3 W below VT [P < .05] and 162 ± 7.4 vs 212 ± 9.3 W above VT [P < .05]).

3.2. Substrate oxidation during steady-state exercise

3.2.1. Effect of age

3.2.1.1. Sedentary group. During steady-state exercise performed below VT, the percentage of substrate oxidation did not differ between SedA and SedY. Total CHO oxidation was lower in SedA than in SedY (−62%; P < .05; Fig. 1), and CHO oxidation rates were lower in SedA as well (P < .05; Fig. 2). During steady-state exercise performed above VT, the percentages of CHO oxidation and total CHO use were lower in SedA than in SedY (respectively, −22% [Fig. 3] and −40% [Fig. 1]; P < .05). Carbohydrate oxidation rates were also lower in SedA (P < .05; Fig. 2), and total fat oxidation was higher in SedA (+76%; Fig. 3).

3.2.1.2. Trained groups. During steady-state exercise performed below VT, the percentage of CHO oxidation was lower in TrA than in TrY (−28%; P < .05; Fig. 3). The total CHO use was lower in TrA (−25%; P < .05; Fig. 1), and CHO oxidation rates were also lower (P < .05; Fig. 2). During steady-state exercise performed above VT, the percentage of substrate oxidation did not differ, but total CHO use was lower in TrA than in TrY (−20%; P < .05; Fig. 1). Carbohydrate oxidation rates were also lower in TrA (P < .05; Fig. 2).

3.2.2. Effect of training

3.2.2.1. Middle-aged men. During steady-state exercise performed below VT, the percentage of substrate oxidation and CHO oxidation rates did not change in the middle-aged subjects, whereas total fat use was higher in TrA than in SedA (+100%; P < .05; Fig. 1). However, during steady-state

![Diagram](image-url)
**Fig. 4.** Plasma lactate, glucose, and insulin concentrations at rest and during 50 minutes of cycle ergometer exercise below (−VT) and above (+VT) the VT in TrA (n = 7; open triangle), in SedA (n = 7; open circle), in TrY (n = 7; filled triangle), and in SedY (n = 7; filled circle). Values are means ± SE. *P < .05, TrY vs SedY; # P < .05, TrA vs SedA; & P < .05, SedY vs SedA; **P < .05, TrY vs TrA.

**Fig. 5.** Plasma catecholamine concentrations at rest and during 50 minutes of cycle ergometer exercise below (−VT) and above (+VT) the VT in TrA (n = 7; open triangle), in SedA (n = 7; open circle), in TrY (n = 7; filled triangle), and in SedY (n = 7; filled circle). Values are means ± SE. § P < .05, middle-aged men vs young men; # P < .05, TrA vs SedA.
exercise performed above VT, both percentage of CHO oxidation and total CHO use were higher in TrA than in SedA (respectively, +14% [Fig. 3] and +41% [Fig. 1]; \( P < .05 \)). Carbohydrate oxidation rates were higher in TrA than in SedA (\( P < .05 \); Fig. 2).

3.2.2.2. Young men. During steady-state exercise performed below VT, the percentage of substrate oxidation and CHO oxidation rates did not change in the young subjects, whereas total fat use was higher in TrY than in SedY (+64%; \( P < .05 \); Fig. 1). During steady-state exercise performed above VT, the percentage of CHO oxidation was lower (−93%; \( P < .05 \); Fig. 3) and total fat use was higher (+113%; \( P < .05 \); Fig. 1) in TrY than in SedY.

3.3. Plasma substrates and hormones at rest and during exercise

Baseline plasma glucose concentration was higher in TrY than in SedY. Plasma glucose concentrations were higher during exercise performed below VT in TrY than in SedY (\( P < .05 \); Fig. 4). Furthermore, glucose concentration was higher in SedA than in SedY in baseline state and during both exercise intensities (\( P < .05 \); Fig. 4).

Baseline plasma lactate concentrations were not different among groups, whereas these concentrations were lower in all groups when exercise was performed below VT (\( P < .05 \); Fig. 4). Furthermore, plasma lactate concentrations were lower in TrA than in SedA during exercise below VT (\( P < .05 \); Fig. 4).

Baseline plasma insulin concentration was lower in TrA than in SedA (\( P < .05 \); Fig. 4). However, this concentration, which averaged 12 \( \mu \text{U/mL} \) in the young subjects, decreased significantly during exercise at both intensities (\( P < .05 \); Fig. 4).

Baseline plasma epinephrine (Epi) concentration did not differ among groups, whereas baseline norepinephrine (Nor) concentration was higher in the middle-aged subjects than in the young subjects, regardless of training status (\( P < .05 \); Fig. 5). During exercise, Epi concentration was higher in TrA than in SedA from 15 minutes to the end of exercise above VT (\( P < .05 \)) and Nor concentration was higher in the middle-aged subjects than in the young subjects during both exercise intensities (\( P < .05 \); Fig. 5). Furthermore, Epi and Nor concentrations were higher during exercise performed above VT than below VT in TrA but not in the other groups (Fig. 5).

4. Discussion

The purpose of this study was to characterize the effect of an interaction between aging and endurance training on substrate oxidation during moderate and hard exercise intensities. The cross-sectional data demonstrate clearly that CHO use was lower in middle-aged men than in young men regardless of fitness status and exercise intensity. However, this age-related decline was less important in the trained subjects and was associated with a higher Epi response. Cycling training increased CHO use during hard exercise in the older men. In the younger men, training was not associated with an improvement in CHO oxidation but, rather, with a marked decrease of the percentage of CHO used for oxidation during high exercise caused by a marked increase in the use of lipids.

Indirect calorimetry has been used in many studies to determine substrate oxidation during high-intensity exercise [12-15] and is now a well-recognized method. Its main potential cause of mistake has been well studied and its effect appears to be negligible. During high-intensity exercise, the accelerated lactic acid production increases plasma lactate concentrations and requires increased use of the bicarbonate buffering system to maintain a neutral pH. This phenomenon results in elevated CO\(_2\) production that may, in turn, induce an increase in the RER unrelated to substrate balance, which could have disturbed our calculation. However, it has been reported that this bicarbonate-derived CO\(_2\) production exerts a quite moderate effect on V\(\text{CO}_2\) because it increases it by approximately 1%, which seems rather negligible [24]. Moreover, a good concordance between net fuel oxidation measured with stable isotope techniques and indirect calorimetry during submaximal exercise even at hard intensity (ie, 85% of V\(\text{O}_{2\text{max}}\)) has been demonstrated by Romijn et al [25]. In addition, when prolonged exercise protocols are used (eg, 50 minutes), CO\(_2\) production is reduced from the beginning of exercise.

During exercise, both absolute and relative (ie, % of maximal oxygen uptake) exercise intensities play important roles in the regulation of substrate metabolism. The absolute work rate determines the total quantity of fuel required by the muscles during effort, whereas relative intensity plays a major role in determining the balance of substrates (ie, CHO and fat) oxidized by the working muscle [26]. In accordance, we calculated substrate oxidation during exercise at 15% below and above the VT, which corresponded to a nearly identical percentage of V\(\text{O}_{2\text{max}}\) (almost 50% and 70%) for each group of subjects.

4.1. Effect of age

We show clearly in the present study that the older men had lower CHO use than the younger men during exercise at both exercise intensities (ie, moderate and hard). These findings are in agreement with those of Sial et al [16], who reported that, in 73-year-old individuals who performed at similar relative intensities during exercise (ie, 56% ± 3% of maximal oxygen uptake), CHO oxidation rates were substantially higher in the young adult group than in the elderly group. These authors concluded that this increase was related mostly to the increased energy requirements from glycogen. This is consistent with our data measured below VT. Nevertheless, they did not find any significant difference in the percentage of oxidized CHO, which contrasts with the present results. One explanation for this
The discrepancy is the difference in age (73 vs 52 years in our study). On the other hand, they did not match subjects for sex. The propensity for women to use more lipid than men during exercise [27] may thus explain part of this difference in findings.

The difference in CHO oxidation between the middle-aged and young groups may have been the result of alterations in the use of muscle glycogen as a fuel in older subjects. Diminished baseline muscle glycogen stores have been noted in elderly subjects [28], and this decline may have influenced the use of muscle glycogen in our middle-aged subjects because the rate of glycogenolysis during exercise is closely related to initial content [29]. Thus, the higher CHO oxidation in our younger groups may have been supplied mostly by higher muscle glycogen use. Actually, these age-related differences in the ability to oxidize CHO at exercise seem to be an aspect of a more general impairment of CHO metabolism related to aging and worsened by sedentariness, which also includes a decrease in insulin sensitivity [2,17] that may impair glucose tolerance, a lower GLUT-4 protein concentration in skeletal muscle [30], and a lower insulin-mediated glucose uptake [2]. In the present study, SedA showed higher blood glucose levels during both exercise intensities than SedY, which agrees with this concept of a less efficient glycoregulation [2].

On the whole, aging affected substrate metabolism, as reflected by declining CHO oxidation during both moderate- and hard-intensity exercises, independently of fitness status. However, this decline was less important (ie, 2-fold less) in the trained subjects, indicating that endurance training attenuated the effect of aging on CHO oxidation at exercise, consistent with its overall beneficial effects on glucose disposal [2].

4.2. Effect of endurance training

Endurance training induced opposite results in the 2 age groups. Training increased CHO use during hard-intensity exercise in the older men and decreased it in the younger men.

Above VT, the trained middle-aged men had higher RER at steady state at the end of each exercise session compared with the sedentary control subjects, suggesting that they oxidized more CHO during hard-intensity exercise. This result is in agreement with several studies [13-15]. In 70-year-old individuals, a longitudinal analysis of the effects of training [31] has found a similar effect. A more precise analysis of gas exchange data confirmed these observations, showing that the quantity of CHO used was significantly higher in TrA.

Concerning our young subjects, endurance training led to a decrease in the ratio between CHO and fat used for oxidation during hard-intensity exercise. This finding is surprising and contrasts to some extent with several studies performed in young subjects [13,14]. We can, however, also explain these opposite results by a difference in training status. In a recent longitudinal study [13], we showed that trained young subjects had higher CHO use during hard-intensity exercise than sedentary matched subjects only after several months of intensified training. Thus, the present data for our trained young subjects suggest that the quantity of training was insufficient to induce CHO dependence at this level of intensity. Moreover, our young subjects had been cycling for far fewer years than our middle-aged subjects (6 vs 12 years). The metabolic adaptations of training may thus have been more effective in the older cyclists, suggesting that, in addition to training status [13], the number of years of training may be an important secondary factor in determining the balance of substrate use during exercise.

4.3. Catecholamines

Catecholamine measurements in our 4 groups may help to understand at least in part the physiological mechanisms underlying these age- and training-related differences in CHO oxidation. Although we observe similar values of plasma Epi at rest, baseline Nor is higher in the middle-aged subjects than in the young subjects, regardless of the training status. During exercise above VT, Epi response is higher in TrA than in SedA. Norepinephrine response is higher in the middle-aged subjects than in the young subjects at both exercise intensities. The classic power dependence of both catecholamine responses at exercise is to some extent hidden by all those differences. Actually, it is significantly evidenced only in the subgroup of middle-aged trained individuals, in whom both Epi and Nor responses are higher when exercise is performed above VT than below it.

In aged subjects, an increase in the rate of Nor appearance has been reported to occur as a result of training and to be associated with an increased ability to oxidize fat [32]. In our subjects, who are markedly younger (50 rather than 70 years old), we did not clearly evidence this fact. By contrast, we found an obvious effect of training status on Epi response. Despite its inhibitory effects on glucose transport and glucose uptake, Epi is known to accelerate glycogenolysis and CHO oxidation in muscle. Consistent with this property, the rise in Epi response during hard-intensity exercise has been reported to be associated with increased CHO oxidation [12,33]. This fact is found again in our study.

In this respect, it is striking to observe, in our study, that the responses in catecholamines are stronger in middle-aged subjects and are so weak in young subjects that they do not reach statistical significance. This may be assumed to indicate that at middle age, a catecholamine response is needed to sustain substrate use at exercise, whereas in young subjects, at similar relative intensities, fuel supply does not require this hormonal effect. However, such a homeostatic explanation remains fully speculative.

What our catecholamine data clearly show is that regular training at middle age is associated with an increase in both
Epi response and CHO oxidation during high-intensity exercise. On the other hand, middle age, whatever the training status, is also associated with stronger responses in Nor. The physiological relevance of the latter finding is less obvious. It may be involved in lipid metabolism as reported in older (70 years old) individuals [32], but this role is not clearly evidenced in our sample of subjects. Because alterations in adrenoreceptor sensibility may also occur during exercise, training, and aging and may therefore modify lipid metabolism during muscular activity [34,35], all these questions remain incompletely resolved.

On the whole, endurance training (eg, cycling) appears to induce different modifications in the balance of fuel oxidation during hard-intensity exercise depending on age. These alterations seem closely linked to several other factors, however, such as sex, catecholamine response during exercise, and prior training status. For example, it has been shown in older patients that the ability to oxidize fat at rest is higher in men than in women. However, despite a markedly higher Nor response at exercise, fat oxidation during a prolonged workload was similar in men and women [36]. In addition, it is known that whatever training status and whatever the balance of substrate oxidation at exercise, exercise by itself is able to increase lipid oxidation at rest [37]. Our understanding of how exercise-induced and endurance training–induced responses interact to affect substrate use over the course of aging remains limited and further investigation is necessary.

In summary, the results of this cross-sectional study demonstrate that CHO oxidation at exercise is decreased at middle age independently of exercise intensity and fitness level. Nevertheless, this alteration in CHO metabolism is less important (ie, almost 2-fold less) in trained subjects and is then accompanied by a higher Epi response. Endurance training increases CHO oxidation during hard-intensity exercise in middle-aged subjects, contrasting to some extent with its effect on young subjects. These findings may have clinical relevance because they suggest that endurance training performed at a specific exercise intensity (ie, 15% above the VT) may be a way to restore CHO use in middle-aged adults. However, this latter assumption will require additional investigations.

References

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