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Repeated prolonged whole-body low-intensity exercise: effects on insulin sensitivity and limb muscle adaptations

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Abstract

This study investigates the effect of prolonged whole-body low-intensity exercise on insulin sensitivity and the limb muscle adaptive response. Seven male subjects (weight, 90.2 ± 3.2 kg; age, 35 ± 3 years) completed a 32-day unsupported crossing of the Greenland icecap on cross-country skies pulling sleighs. The subjects were studied before and 3 to 4 days after the crossing of the icecap. Subjects came in overnight fasted, and an intravenous glucose tolerance test (IVGTT) was done. A biopsy was obtained from the vastus lateralis and deltoid muscle. On a separate day, a progressive test was performed to establish maximal oxygen uptake. During the crossing, subjects skied for 342 ± 41 min/d. Peak oxygen uptake (4.6 ± 0.2 L/min) was decreased ($P < .05$) by 7% after the crossing and body mass decreased ($P < .05$) by 7.1 ± 0.2 kg, of which 4.4 ± 0.5 kg was fat mass and 2.7 ± 0.2 kg lean body mass. Glycosylated hemoglobin (5.6% ± 0.01%) was not affected by the crossing. The IVGTT data revealed that insulin sensitivity (7.3 ± 0.6 mU · L^{-1} · min^{-1}) and glucose effectiveness (0.024 ± 0.002 min^{-1}) were not changed after the crossing. Similarly, the IVGTT data, when expressed per kilogram of lean body mass or body mass, were not affected by the crossing. Citrate synthase activity was higher ($P < .05$) in the leg (29 ± 1 μmol · g^{-1} · min^{-1}) than in the arm muscle (16 ± 2 μmol · g^{-1} · min^{-1}) and was unchanged after the crossing. Muscle GLUT4 protein concentration was higher ($P < .05$) in the leg (104 ± 10 arbitrary units) than in the arm (54 ± 9 arbitrary units) and was not changed in the leg, but was increased ($P < .05$) by 70% to 91 ± 9 arbitrary units in the arm after the crossing. In conclusion, the increased glucose transporter expression in arm muscle may compensate for the loss of lean body mass and the decrease in aerobic fitness and thereby contribute to the maintenance of whole-body insulin sensitivity after prolonged low-intensity exercise training.

1. Introduction

The appearance of insulin resistance and the subsequent lifestyle diseases have reached epidemic proportions in the Western world, and lifestyle changes such as increased physical activity are promoted as a means to combat this phenomenon. Regular physical activity and thus training is generally considered to lead to marked improvement in whole-body insulin sensitivity [1,2]. In addition, there is evidence that regular strength training leads to improved insulin sensitivity, most likely because of an increase in muscle mass [3,4]. However, it is less clear to what degree aerobic training performed at lower intensities, where aerobic fitness is not improved, will also improve insulin sensitivity. When low-intensity training was performed for 2 weeks with a limited muscle mass, the one-leg kicking model, total muscle GLUT4 protein content was increased and aerobic fitness was unchanged [5]. Albeit insulin sensitivity was not measured, an increased glucose transport capacity is believed to mediate an increased insulin sensitivity [6,7]. We studied prolonged whole-body low-intensity exercise in a

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small number of subjects (n = 4) and found an increased homeostatic model assessment (HOMA) insulin resistance index (HOMA-R_{mod}) after 7 weeks of training [8]. The observed increased HOMA-R_{mod} was present despite the repetitive 6 to 7 hours of daily physical activity, but coincided with a decreased lean body mass and a decreased aerobic fitness, both of which would parallel an increased insulin resistance. However, in our study, the number of subjects was limited, and the determination of insulin resistance not performed by either intravenous glucose tolerance test (IVGTT) or euglycemic clamp technique. Therefore, one aim of the present study was to further investigate the effect of prolonged low-intensity whole-body exercise on insulin sensitivity and aerobic fitness.

During whole-body exercise, as in cross-country skiing, upper and lower body muscles demonstrate marked differences in both fiber type and blood flow distribution [9]. In line with this, Schantz and colleagues [10] found that 8 weeks of prolonged low-intensity cross-country skiing increased oxidative capacity and capillarization in the triceps brachii muscle, but had no effect on oxidative capacity or capillarization in the vastus lateralis muscle. Our previous study revealed a similar different adaptation pattern in arm and leg muscles after prolonged low-intensity training [8]. However, in the previous study, we did not measure muscle GLUT4 concentration, and only limited information is available on the GLUT4 protein content in arm vs leg muscles. Daugaard and colleagues [5,11] used the single-fiber technique to demonstrate that muscle GLUT4 protein content was not uniformly distributed between fiber types in different skeletal muscles, but that the total muscle GLUT4 content in soleus, vastus lateralis, and triceps brachii muscles was similar. However, the fiber type distribution of the triceps brachii muscle is markedly different from that of the soleus and vastus lateralis, and it may therefore reflect a completely different recruitment and substrate use pattern. The second aim of this study was therefore to investigate the effect of prolonged low-intensity whole-body exercise on insulin sensitivity and GLUT4 content in arm and leg muscle exhibiting more similar fiber-type distribution.

2. Methods

2.1. Subjects

Seven moderately trained male subjects (age, 35 ± 3 years; height, 185 ± 3 cm; weight, 90.2 ± 3.2 kg, and maximal oxygen uptake 4.57 ± 0.20 L of O_2/min) participated in the study. The subjects were all physically active in outdoor sports, and all had a broad experience in sports, challenging both upper and lower body muscles. Furthermore, in the last 6 months before the crossing, all subjects prepared for the experiment by doing regular (twice a week) "nonsnow" cross-country training. Subjects were fully informed of the nature and the possible risks associated with the experimental part of the study before they volunteered to participate. The planning, handling, and financial burden of the tour across the icecap was completely organized and controlled by the subjects. The experimental procedure achieved ethical approval from the Copenhagen and Fredriksberg Community Ethical committee (KF), and all subjects volunteered to participate and provided ethical consent (KF 01-218/02).

The subjects commenced the crossing from Kangerlussuag on the west coast of Greenland on April 12, 2003, and finished in Isortoq on the east coast on May 13. The subjects traveled a total of 32 days. However, 4 days were spent resting in the tents because of harsh weather conditions and a case of snow blindness. The total distance covered on ice was approximately 570 km, and an altitude of approximately 2500 m above sea level was reached. The peak altitude was reached after approximately 400 km, and the skiing was until this point performed with "skins" under the skies. In this situation, the friction from the direction of the hairs on the skin mounted under the ski (mohair or synthetic) prevents the ski from sliding backward. Furthermore, the forward motion of the ski is easier if the ski is slightly lifted during the forward motion. Each subject pulled a sledge weighing initially 115 to 120 kg, declining toward 75 to 80 kg at the end of the expedition. During the passage the day temperature ranged between −30°C and 0°C, and some wind was experienced. On average, the subjects spent 342 ± 42 min/d on the cross-country skies pulling the sledges. The subjects took turns leading the other members of the expedition making snow tracks, and breaks were taken throughout the day. Because of the cold conditions, most breaks lasted less than 10 minutes, and only the lunch break was slightly longer (~15-25 minutes). The food consumed during the passage was prepacked and carried by the subjects. The diet was a standard diet consisting of a breakfast, lunch, and an evening meal, and a variety of snacks for consumption during the day. Based on the composition of the prepacked food, the calculated nutrient composition was 11% ± 1% protein, 39% ± 1% fat, and 50% ± 1% carbohydrate, expressed as a percentage of the consumed energy. During the first part of the expedition, the subjects were not able to consume their calculated daily ration. However, during the later part, food intake was increased, and subjects were able to consume their full daily ration, and in addition, the food that was not consumed during the first part. Based on individual descriptions of the average daily consumption of food, the average daily energy consumption was calculated to be 18.0 ± 1.1 MJ. The daily consumed amount of carbohydrate provides approximately 6.1 ± 0.5 g of carbohydrate per kilogram of body weight. During the early part of the crossing of the icecap, the heart rate was measured during the skiing by conventional Polar heart rate system (Polar 620i, Polar Electro, Oulu, Finland). Because of generator problems on the ice, the acquired data could not be loaded onto a portable PC, and thus, heart rate measurements are limited to the storing capacity of the heart

rate equipment. Thus, stored heart rate data are only available for 2 days for each subject.

2.2. Experimental protocol

On 2 separate days before departure and again after arrival from Greenland 3 and 4 days after the last expedition day, the subjects came overnight fasted to the laboratory. The subjects were asked to refrain from vigorous physical activity on the preceding day. After an initial rest period, a needle biopsy was obtained with suction from the vastus lateralis muscle and from the deltoid muscle. Before exercise, body composition was determined both by bioelectrical impedance technique (Omron BF 300, Matoukasa Co Ltd, Japan) and by traditional skinfold measurements [12]. After this procedure, a standard progressive exercise test was performed to measure maximal oxygen uptake. The pulmonary oxygen uptake ($\dot{V}O_2$) and carbon dioxide release were measured by an automated online system (AMIS 2001, Innovision, Odense, Denmark). On the following day, subjects performed a standard IVGTT as described by Vessby and colleagues [13]. In brief, venous blood samples were collected at −5, 0, 2, 4, 8, 19, 22, 40, 50, 70, 90, and 180 minutes. At time point 0, an intravenous injection of 0.3 g glucose per kilogram of body weight was administered (maximum, 25 g), and at 20 minutes, an intravenous insulin injection of 0.3 IU/kg body weight was administered. Emphasis was placed on subjects performing a minimum of physical activity during the IVGTT procedure.

2.3. Analytical procedures

Blood was transferred into tubes containing 0.3 mol/L EDTA (10 μL/mL blood) and immediately centrifuged at 4°C for 10 minutes. A small fraction of the blood was transferred into tubes containing ethyleneglycol bis(aminoethylether) tetraacetic acid reagent, and this was later used for the insulin determinations. The plasma was stored at −80°C until analysis. Plasma glucose and lactate were analyzed on an automatic analyzer (Cobas Fara, Roche, Saint-Louis, France). Insulin in venous plasma was determined using a radioimmunoassay kit (Insulin RIA100, Pharmacia, Uppsala, Sweden). Blood hemoglobin level was measured on an Advia 120 hematology system (Bayer, Leverkusen, Germany), and glycosylated hemoglobin level was measured using high-performance liquid chromatography (Tosoh, Eurogenetics, Tessenderlo, Belgium). Plasma interleukin 6 (IL-6) and plasma tumor necrosis factor α (TNF-α) were measured with high-sensitivity enzyme-linked immunosorbent assay kits from R&D Systems (Minneapolis, MN).

The muscle tissue from the biopsies was frozen in liquid nitrogen within 10 to 15 seconds of sampling. Before freezing, a section of the samples was cut off, mounted in embedding medium, and frozen in isopentane cooled to its freezing point in liquid nitrogen. Both parts of the biopsy were stored at −80°C until further analysis. Before biochemical analysis, muscle biopsy samples were freeze-dried and dissected free of connective tissue, visible fat, and blood under a stereomicroscope. In serial transverse muscle sections, fiber types were stained for myofibrillar ATPase as described previously [14]. The maximal activity of the enzyme citrate synthase was determined fluorometrically as previously described [15]. Total muscle GLUT4 protein content was analyzed by Western blotting as previously described [4].

2.4. Calculations

Body density was determined from the skinfold measurements, and subsequently, body fat (%) was calculated from the body density according to Ref. [16]. The IVGTT data were analyzed by the MINMOD Millenium program (MinMod, ver 6.02, Minmod; Richard M. Bergman, Los Angeles, CA). A number of variables relating to the glucose insulin dynamics can be estimated by the above physiological modeling program, the acute insulin response to glucose (AIR_g), the disposition index (DI), the insulin sensitivity, and the glucose effectiveness [17]. In addition, the HOMA-R_{mod} described originally by Matthews and colleagues [18] and modified by Jenkins and colleagues [19] was calculated according to the latter. In brief, fasting plasma insulin and fasting plasma glucose values were used to calculate an index of insulin resistance (HOMA-R_{mod}) and insulin secretion (HOMA-β_{mod}) [19]. The average exercise intensity during the cross-country skiing was calculated using the observed work heart rate on the available days and the laboratory-measured maximal heart rate of the subjects. Furthermore, individual curves for the relation between oxygen uptake and heart rate were generated from the exercise tests performed before and after the crossing, and based on these, the observed heart rate during the crossing was used to estimate the average oxygen uptake during the crossing.

Table 1
Anthropometric, maximal oxygen uptake, and fiber type data before and after crossing the Greenland icecap on cross-country skies

	Before	After
BMI (kg/m^2)	26.5 ± 0.7	24.4 ± 0.6*
Body mass (kg)	90.2 ± 3.2	83.1 ± 3.0*
Fat (%)	19.4 ± 1.3	15.7 ± 1.3*
LBM (kg)	72.8 ± 3.1	70.1 ± 3.0*
$\dot{V}O_2$max (L/min)	4.57 ± 0.20	4.26 ± 0.21*
Fiber type (%)		
Arm		
Type I	54.7 ± 6.6	66.9 ± 6.4*
Type IIA	22.1 ± 3.4	17.7 ± 2.9*
Type IIX	23.2 ± 6.8	15.4 ± 4.9
Leg		
Type I	61.4 ± 4.1	69.4 ± 4.2*
Type IIA	31.0 ± 3.7	16.4 ± 2.1*
Type IIX	7.5 ± 2.4**	14.2 ± 1.8*

Values are mean ± SEM (n = 7). BMI indicates body mass index; LBM, lean body mass.
* $P < .05$, arm vs leg.
** $P < .05$, before vs after.

Table 2
Blood values at rest before and after crossing the Greenland icecap on cross-country skies

	Before	After
Blood hemoglobin level (mmol/L)	8.96 ± 0.16	9.11 ± 0.17
Plasma glucose (mmol/L)	4.66 ± 0.09	4.98 ± 0.15
Plasma insulin (pmol/L)	19.0 ± 5.1	24.5 ± 5.9
HbA_{1c}	0.056 ± 0.001	0.057 ± 0.001
Plasma TNF-α (pg/mL)	1.53 ± 0.59	1.41 ± 0.53
Plasma IL-6 (pg/mL)	0.82 ± 0.64	0.97 ± 0.43

Values are mean ± SEM (n = 7). HbA_{1c} indicates glycosylated hemoglobin.

2.5. Statistics

Two-way repeated measures analysis of variance was used to analyze for differences due to the factors intervention and/or muscle type. Student-Newman-Keuls test was used as post hoc test. In all cases, statistical significance level was set at .05. The statistical analysis was performed using Sigma Stat 2.03 (Sigmastat, SPSS, Ekrath, Germany). Results are given as mean ± SEM.

3. Results

After the crossing of the icecap, a decrease was observed in body mass, body mass index, lean body mass, and content of body fat (Table 1). On average, the subjects had a mean weight loss of 7.1 ± 0.7 kg, of which 64% ± 4% was fat and the remaining was lean body mass. Similar body composition data were obtained by bioelectric impedance analysis and the skinfold method; therefore, only data from the latter analysis are shown. During the crossing, the daily exercise intensity averaged approximately 62% ± 2% of maximal heart rate (estimated to approximately 42% ± 3% of $\dot{V}O_2max$). The maximal whole-body oxygen uptake was decreased by 7% during the passage (Table 1). Before the passage, there was no difference in the number of types I and IIA muscle fibers, but there is a lower number of type IIX fibers in the vastus lateralis compared with the deltoid muscle. After the passage, a significant increase in type I and a decrease in type IIA muscle fiber type expression were observed in both arm and leg muscle. In the leg muscle, an increase in type IIX fibers was also observed after the crossing (Table 1).

In the fasted condition, plasma glucose concentration and insulin concentration were not significantly changed during the passage (Table 2). Similarly, we did not observe any changes in glycosylated hemoglobin, TNF-α, or plasma IL-6 concentrations during the passage.

The insulin sensitivity, determined by the IVGTT, did not change during the passage of the icecap (Table 3). The same result was apparent when the calculated HOMA-R_{mod} was compared before and after the passage of the icecap (Table 3). In addition, we observed no changes in other variables estimating the AIR_g, that is, the DI, indicating the capacity of glucose to stimulate its own disposal, or the

Table 3
Insulin resistance data before and after skiing across the Greenland icecap

	Before	After
AIR_g (mU · L^{-1} · min^{-1})	351 ± 59	296 ± 64
DI (10^3)	2.41 ± 0.32	2.43 ± 0.71
Insulin sensitivity (mU · L^{-1} · min^{-1})	7.31 ± 0.62	7.67 ± 1.11
Glucose effectiveness (min^{-1})	0.024 ± 0.002	0.025 ± 0.004
HOMA-R_{mod}	12.4 ± 1.0	15.2 ± 1.3
HOMA-β_{mod}	0.57 ± 0.04	0.62 ± 0.05

Values are mean ± SEM (n = 7). The IVGTT data were analyzed by the MINMOD Millenium program (MinMod, ver 6.02). The AIR_g, the DI, the insulin sensitivity, and the glucose effectiveness were generated from the MINMOD Millennium program, and the formulas used are described by Boston and colleagues [17].

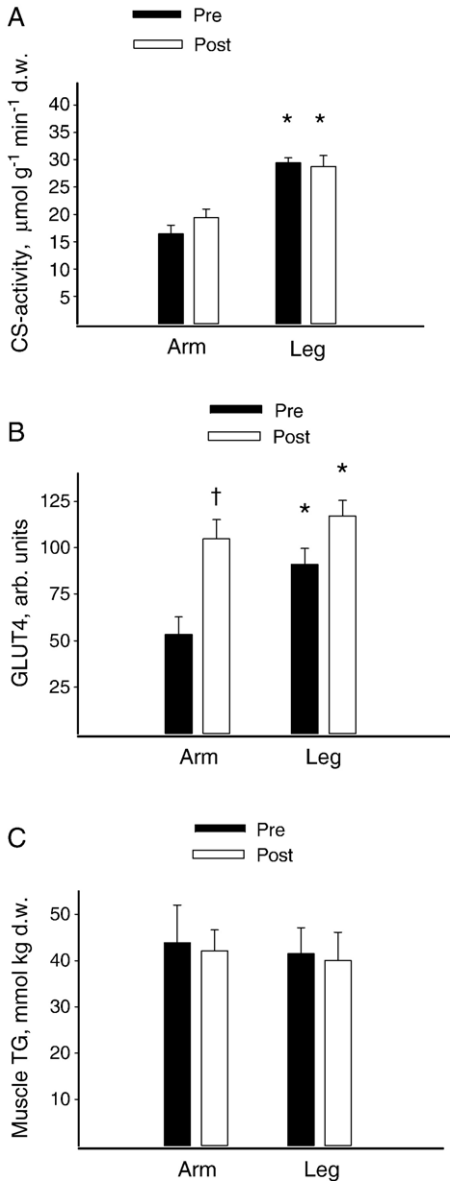

Fig. 1. Citrate synthase activity (A), total muscle GLUT4 protein (B), and muscle triacylglycerol (C) in deltoid and vastus lateralis muscles before and after crossing the Greenland icecap on cross-country skies. *$P < .05$, arm vs leg; †$P < .05$, before vs after.

HOMA-β_{mod} during the passage (Table 3). Despite the observed decrease in lean body mass and body weight after the crossing, the insulin sensitivity and glucose effectiveness did not become significantly different when expressed either per kilogram of lean body mass or per kilogram of body mass before and after the passage. Muscle citrate synthase activity was higher in the vastus lateralis than in the deltoid muscle, both measured before and after the passage, but citrate synthase activity was unchanged after the passage (Fig. 1A). Total muscle GLUT4 protein content was markedly lower in the arm compared with the leg muscle both before and after the passage of the icecap (Fig. 1B). Interestingly, a marked increase was observed in total GLUT4 protein content in the arm, whereas the total leg GLUT4 protein content remained unchanged (Fig. 1B). Finally, we observed no difference in muscle triacylglycerol content between the arm and leg muscles, and no change was observed after the passage (Fig. 1C).

4. Discussion

In this study, we observed a lower GLUT4 protein expression in the deltoid muscle compared with the vastus lateralis muscle despite their almost similar composition of types I and II muscle fibers. Furthermore, we observed that prolonged low-intensity training leads to a marked increase in the total muscle GLUT4 protein concentration in the arm, whereas in the leg, total GLUT4 protein remained unchanged. In addition, we observed that insulin sensitivity was unchanged after prolonged low-intensity exercise despite a decreased aerobic fitness and loss of lean body mass. A possible scenario could be that the increased muscle glucose transporter expression in the arms compensated for the loss of lean body mass and the decrease in aerobic fitness and thereby contributed to the maintenance of whole-body insulin sensitivity.

In 2 studies, Daugaard and colleagues [5,11] used the single-fiber technique to demonstrate that GLUT4 protein content was not similarly distributed between muscle fiber types in different human skeletal muscle and that total muscle GLUT4 protein content in soleus, vastus lateralis, and triceps brachii was similar. In contrast to our expectations and the similar GLUT4 protein content in arm and leg muscle observed by Daugaard and Richter [11], we observed a lower GLUT4 protein expression in the deltoid muscle compared with the vastus lateralis muscle. In this study, the deltoid and the vastus lateralis have approximately similar muscle fiber-type composition, and the difference in GLUT4 content between the deltoid and the vastus lateralis muscles indicates that muscle GLUT4 protein content may not be uniformly distributed between muscle fiber types and/or that arm and leg muscle exhibited a different training status [11]. The observed difference in citrate synthase activity between arm and leg muscle provides some support for the latter option. There is strong evidence that one effect of regular training is an increase in total muscle GLUT4 content [20,21], and in the present study, we observed a marked increase in total GLUT4 content in arm muscle, but not in the leg muscle, after prolonged whole-body low-intensity exercise. Interestingly, the increase in GLUT4 protein in the arm muscle occurred without a concomitant increase in oxidative capacity. However, Houmard and colleagues [22] observed that muscle GLUT4 protein remained unchanged, whereas citrate synthase activity decreased significantly after 14 days of training cessation indicating that changes in oxidative capacity and muscle GLUT4 protein expression are not always tightly coupled.

The lack of an increase in the muscle citrate synthase activity and the presence of a significant decrease in whole-body maximal oxygen uptake occurred despite the very prolonged daily physical activity. However, this is not surprising because the physical activity was performed at rather low exercise intensity, as indicated by the heart rate. The determination of exercise intensity during the crossing was unfortunately not optimal because of technical problems in the cold environment. However, other studies of ultraendurance exercise indicate that very prolonged exercise cannot be sustained at more than approximately 50% to 55% of $\dot{V}O_2$max in elite-trained subjects [23-25], and given the nonelite training status of our subjects and the fact that the exercise in the present study was repeated day after day, this is in good agreement with the slightly lower intensity observed in the present study.

The finding of a different training response in arm and leg muscle is in line with prior studies where a positive adaptation pattern in oxidative enzyme activity and capillarization was seen in arm and not leg muscle after prolonged whole-body exercise [8,10]. When the effect of endurance training was studied separately in arm and leg muscle, there were similar improvements in oxidative capacity and muscle mitochondrial volume, although the changes were brought about by different mechanisms [26]. The implication of these findings is that muscle localization/function may influence the muscle adaptation pattern during whole-body training. Thus, the questions arise if the training load was similar in the upper and lower body during the intervention and if both muscles were recruited. With regard to the latter, both the deltoid and the vastus lateralis muscles are of prime importance for cross-country skiing [27], and particularly considering that the skiing in this case also included pulling a heavy sledge and using skins through most of the crossing (HC Holmberg, personal communication). With regard to the similarity of the training load on upper and lower body, the observation of an unchanged citrate synthase activity in both muscles is an indication that the TCA cycle enzymes were similarly influenced by the intervention. Therefore, we believe that the upper and lower body was similarly affected by the intervention. However, although we consider it unlikely, it is not possible to exclude that other upper and/or lower body muscles may exhibit an adaptation pattern that is

different from that observed in the deltoid and vastus lateralis muscles. In addition, we cannot completely exclude that the 3- to 4-day delay from the termination of the crossing to the measurements performed could have affected the measured variables.

In the present study, we also observed a significant shift toward more type I muscle fibers and less type IIA fibers in both muscles after the intervention. In most longitudinal training studies in humans, an increased content of type IIA muscle fibers occurred at the expense of type IIX muscle fibers, and only minimal changes in type I fiber content were present [28]. In the present study, the amount of prolonged low-intensity exercise training was markedly higher compared with previous studies of low-intensity exercise, and the findings of the present study are therefore not in disagreement with prior findings. However, the number of subjects is limited, and because there is some variation in muscle fiber-type determination, further studies should investigate the presence of a significant muscle fiber-type shift with very prolonged low-intensity exercise.

Regular training exert an overall positive effect on metabolic capacity through a number of mechanisms, of which one of the more important is a marked improvement in whole-body insulin sensitivity [1,2]. In the present study, no effect of prolonged regular whole-body low-intensity training was observed on insulin sensitivity, measures of insulin glucose dynamics, or glycosylated hemoglobin. Only a few studies have used regular low-intensity training and measured insulin sensitivity by either the IVGT or euglycemic clamp technique. In several studies, Dela and colleagues [1,29,30] have found that one-leg cycle training, which can be categorized as low or moderate whole-body intensity exercise, induced a marked increase in insulin sensitivity determined by the clamp technique. However, in these latter studies, aerobic fitness was increased and lean body mass was unchanged or increased, whereas in the present study, lean body mass and aerobic fitness were decreased. Therefore, it is likely that the decreased aerobic fitness and the loss of lean body mass may explain the difference in training response observed compared with these prior studies. Moreover, as in the studies mentioned above, we did observe an overall increase in total muscle GLUT4 concentration (arm and leg together), and this may have counterbalanced the loss of lean body mass and aerobic fitness decrease, leading to an overall unchanged insulin sensitivity after training in the present study. In a prior study, we found an increased HOMA-R_{mod} after a similar crossing of the icecap [8]. The application of the IVGTT and, in addition, also the HOMA-R_{mod} in the present study did not support this finding. However, compared with our prior study, the crossing was done 10 days faster, and the diet consumed contained less carbohydrate, 50% in the present and 60% in our previous study. Several studies, both epidemiological [31] and intervention studies [32,33], have linked consumption of simple sugars to an attenuation of insulin sensitivity. These differences in diet intake and duration may thus explain the observed different effects of prolonged low-intensity exercise on insulin sensitivity.

In recent years, many studies have linked muscle triacylglycerol stores to insulin resistance [34,35]. In morbidly obese subjects undergoing bariatric surgery, a marked increase in insulin sensitivity paralleled a significant drop in intramyocellular triacylglycerol after 6 months [36], but although impressive, this still does not provide a direct evidence for causal coupling between muscle triacylglycerol storage and insulin resistance. In the present study, no change was observed in muscle triacylglycerol content in arm or leg muscle after the crossing, which is consistent with the observation of an unchanged insulin resistance. The cytokines TNF-α and IL-6 have both been linked to insulin resistance, with TNF-α inducing insulin resistance and IL-6 counteracting the effects of TNF-α and thus attenuating insulin resistance [37,38]. The cytokines IL-6 and TNF-α are, in addition to other tissues, both produced in adipose tissue. In the present study, the crossing of the icecap resulted in a daily energy deficit of approximately 6 MJ/d, indicated by a loss of 7.1 kg of body mass, of which approximately 60% was fat. Despite this fat mass loss, no change was observed in plasma IL-6 and TNF-α measured at rest. Thus, prolonged low-intensity training did not lead to changes in plasma IL-6 and TNF-α at rest.

In conclusion, a novel finding is the lower total GLUT4 protein expression in the deltoid muscle compared with the vastus lateralis muscle despite their similar fiber-type composition. Furthermore, the total muscle GLUT4 protein concentration was increased only in the arm but not in the leg muscle after whole-body low-intensity training, which suggests that arm and leg limb muscle may not necessarily show the same response to physical activity. The increased glucose transporter expression in the arm may have compensated for the loss of lean body mass and the decrease in aerobic fitness and could thereby contribute to the observed maintenance of whole-body insulin sensitivity.

The current physical activity recommendation is 30 minutes of exercise a day and, if possible, 1 or 2 exercise bouts at a higher intensity per week. However, it is not clear how much inclusion of physical activity with a higher intensity, to achieve an increase in aerobic fitness, will influence the effects of physical activity on insulin sensitivity. Thus, further studies should investigate to what extent changes in insulin sensitivity are linked to changes in aerobic fitness.

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