

Effect of a Prolonged Altitude Expedition on Glucose Tolerance and Abdominal Fatness

Mu-Tsung Chen, Wen-Chih Lee, Shih-Chang Chen, Chiu-Chou Chen, Chung-Yu Chen, Shin-Da Lee, Jørgen Jensen, and Chia-Hua Kuo

In the present study, we investigated the effect of a long-term mountain expedition on glucose tolerance and insulin action. Twelve registered mountaineers ages 31 years (SD = 1.1) participated in a 25-day expedition at a 2,200–3,800-m altitude with an average duration of 8 hr per day. Arterial oxygen saturation (SaO₂) was substantially reduced during hiking. Glucose tolerance and insulin responses were measured prior to and twice during the expedition period. Maximal oxygen consumption increased from 43.0 ± 2.7 to 49.1 ± 2.2 mL/kg/min. Percentage of body fat decreased from 19.4 ± 6.8% to 16.9 ± 5.9%. The area under the curves for insulin and glucose during the oral glucose tolerance test were also reduced in Days 3 and 25. The present study demonstrated that altitude hiking activity is an effective lifestyle intervention to improve insulin action.

Key words: diabetes, hypoxia, insulin resistance, mountain hiking

Insulin resistance is a pathogenic condition that plays a central role in the development of several age-related metabolic disorders, particularly type 2 diabetes mellitus (Reaven, 1988). During the preclinical stage, fasting blood glucose concentrations may be well below 100 mg/dL. However, the postprandial blood insulin concentration becomes progressively higher than normal before the

onset of clinical syndromes. Because skeletal muscle is the main tissue responsible for postprandial glucose disposal (Defronzo, Ferrannini, Sato, & Wahren, 1981), factors that enhance skeletal muscle insulin sensitivity could directly improve whole body glucose tolerance (Rothman et al., 1995). The beneficial effect of physical activity in treating type 2 diabetes and improving insulin sensitivity has been well established (Ivy, Zderic, & Fogt, 1999; Peirce, 1999).

Most studies investigating the effect of exercise training on insulin sensitivity were performed at sea level (Ivy et al., 1999). In isolated skeletal muscle, energy stress produced by muscle contraction and hypoxia has been found to increase glucose uptake across the plasma membrane (Winder, 2001). Therefore, high-altitude hiking may cause a physiological adaptation leading to improved glucose tolerance. However, studies with short-term (less than 1 week) altitude exposure reported mixed results (Larsen, Hansen, Olsen, Galbo, & Dela, 1997; Lee et al., 2003; Schobersberger et al., 2003). Short-term high altitude exposure (above 4,500 m) can stimulate stress hormone releases (cortisol and growth hormone), which can antagonize insulin action (Larsen et al., 1997). In this study, we investigated the effect of a prolonged altitude expedition (at 2,200–3,800 m) on glucose tolerance and abdominal fatness and measured the stress hormones.

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Mu-Tsung Chen is with the School of Liberal Education at Shih Chien University. Wen-Chih Lee is with the Committee for General Studies at Shih Hsin University. Shih-Chang Chen, Chiu-Chou Chen, Chung-Yu Chen, and Chia-Hua Kuo are with the Laboratory of Exercise Biochemistry at Taipei Physical Education College and Department of Rehabilitation Science at China Medical University. Shin-Da Lee is with the Department of Physical Therapy at China Medical University. Jørgen Jensen is with the Department of Physiology at the National Institute of Occupational Health and Norwegian School of Sport Sciences.

Method

Participants

Twelve healthy volunteers ($Mage = 31$ years, $SD = 1.1$; 10 men and 2 women) participated in the 25-day hiking activity. None of the participants had a history of diabetes, and none took any medication during the investigation period. All participants were registered mountaineers in the Republic of China Alpine Association. The 25-day hiking plan and experimental procedure were explained to all participants before they signed a consent form. The Human Subject Committee of Taipei Physical Education College provided ethical approval for the study.

Mountain Expedition Program

All participants hiked daily for 25 days in the central ridge mountain area of Taiwan. At Day 1, they were bused from Taipei (sea level) to a 2,200-m altitude base camp. The first 3 days of altitude hiking were confined to the mountain area close to the base camp to ensure their capability of completing this expedition. During the 25 days, participants hiked at altitudes between 2,200 and 3,800 m for 8–9 hr per day (~5 hr hiking + ~3 hr rest/eating) with a backpack load of 0.33 kg per kilogram of body weight. On Day 3, participants returned to base camp for blood sample collection. Samples were stored in crushed dry ice immediately after collection and transported to the laboratory in ~3–4 hr. They were stored at -80° C until analysis.

Food and water were supplied *ad libitum* throughout the entire period. The hiking intensity was an average of 63% maximal heart rate (HR_{max}). A heart rate monitor (Polar S810i™; Polar Electro Oy, Kempele, Finland) was used to measure heart rate during the expedition. To estimate the actual hypoxia level in circulation during the hiking activity, arterial oxygen saturation (SaO₂) was recorded during a 5-min step test using a portable oxygen saturation monitor (OxiMax®, Pleasanton, CA). Participants performed the test with backpack load (0.33 kg per kilogram of body weight) at 3,100 m. Each participant stepped up and down a 35-cm step for 5 min at a rate of 96 steps per min. Heart rates and SaO₂ after the test are shown in Table 1.

Oral Glucose Tolerance Test and Insulin Response. We administered the oral glucose tolerance test (OGTT) and measured the insulin response during OGTT (Hsu et al., 2008) at sea level 1 week before the activity and on Days 3 and 25 of the hiking expedition. On the day of the OGTT, participants reported to the experimenters between 6–7 a.m. after an overnight fast. We collected blood samples from their fingertips after a 75-gm oral glucose load (500 ml glucose solution) under sedentary conditions. We collected blood samples at 0 (fasting value), 50, and 80 min. A glucose analyzer (Lifescan, High Wycombe, UK) was used

to determine glucose concentration using the glucose oxidase method. Plasma samples from approximately 200 μ l of fingertip blood were used for insulin determination (Lee et al., 2006) by the ELISA method following procedures established by the Diagnostic Systems Laboratories (Webster, TX).

Stress Hormone Levels. We collected venous blood samples immediately before OGTT to measure stress hormone levels. Plasma testosterone, cortisol, and growth hormone (GH) were quantified on a TECAN Genios ELISA analyzer (Salzburg, Austria) using the ELISA kit.

Aerobic Capacity. We measured maximal oxygen consumption 1 week before the mountain expedition and at sea level 2 days after the altitude activity. All participants performed a modified Bruce protocol with a backpack load of 0.33 kg per kilogram of body weight on a treadmill. A MetaMax I system (Leipzig, Germany) was used to continuously record oxygen consumption. This test was conducted at 24 – 26° C and 55% humidity. Participants started with a 3-min fast walk (1.7 mph) at a 5° grade. Intensity increased every 3 min by increasing the grade 2° and the speed 0.3 mph until participants reached exhaustion (respiratory exchange ratio greater than 1.10). The reliability coefficients of maximum oxygen uptake (VO₂max) and HR_{max} were 0.89 and 0.87, respectively, indicating high test reliability. The validity coefficient of VO₂max and HR_{max} were 0.90 and 0.88, respectively.

Body Composition. We measured waist (umbilical level) and hip (maximum at buttocks) circumferences to the centimeter and calculated the waist-to-hip ratio (WHR) to estimate the degree of central fat distribution. We measured muscle, fat, and water masses by bioelectrical impedance analysis (BIA) using InBody 3.0 (Biospace Co., Seoul, South Korea).

Statistical Analysis. A paired *t* test was used to compare the mean difference to all measured values before and after the 25-day altitude hiking activity. We performed an analysis of variance with a repeated measure for sea level, Day 3, and Day 25 for glucose, insulin, and stress hormones. Fisher's protected least significance test, which

Table 1. Heart rate and arterial O₂ saturation (SaO₂) at sea level and at altitude after a 5-min step test

	Sea level		Altitude (3,100 m)	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
HR rest	63.1	1.6	79.1	3.7*
HR 5-min step test	153.6	5.8	164.0	4.6*
SaO ₂ rest	98.1	0.1	91.0	2.2*
SaO ₂ 5-min step test	96.1	0.4	79.6	1.7*

Note. *M* = mean; *SD* = standard deviation; HR = heart rate; participants performed the test with a weight load of 0.33 kg per kg body weight.

**p* < .05 significant difference against sea level.

holds the value of type I errors to .05 for each test, was used to distinguish significant differences between pairs of groups; $p < .05$ was considered statistically significant. All values were expressed as means and standard errors.

Results

To estimate arterial O₂ saturation level during altitude hiking condition, participants performed a 5-min step test at sea level and at an altitude of 3,100 m. The results are shown in Table 1. Both resting and stepping HR were significantly elevated at altitude, while resting and stepping SaO₂ were significantly lowered at altitude.

OGTT and Insulin Concentrations

Figure 1 shows glucose and insulin concentrations during OGTT. The fasting glucose level at altitude was slightly elevated at Day 3 (4.54 ± 0.14 mmol/L) and Day 25 (4.83 ± 0.12 mmol/L) compared to sea level (4.31 ± 0.09 mmol/L). Glucose tolerance after a 75-g oral glucose ingestion was significantly improved on Days 3 and 25. Fasting insulin concentration was not significantly altered at altitude (see Figure 2). Insulin responses under the oral glucose challenged condition were significantly lower on Days 3 and 25 compared to sea level.

Body Composition

Table 2 shows body weight, fat mass, and percentage of body fat. WHR significantly decreased after the 25-day activity compared to sea level. Fat mass and percentage of body fat were significantly lower at Day 25. Because fat tissue is not the major portion of body weight, reduction in body weight was not significant during the 25 days.

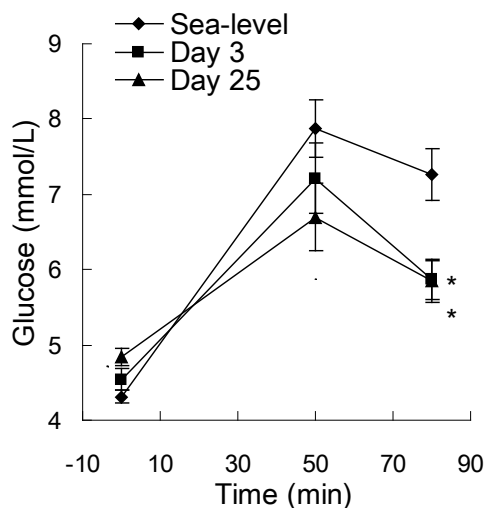


Figure 1. Effect of 25-day altitude hiking activity on glucose tolerance; * $p < .05$ significant difference against sea level.

Table 3 shows aerobic capacity, which was measured 1 week before the activity and at sea level 48 hr following cessation of the altitude activity. VO₂max, oxygen pulse, and hiking performance (Bruce Stress Test) were significantly improved following the 25-day altitude activity. Resting oxygen consumption was slightly lower after the 25-day altitude activity.

Stress hormone values are displayed in Table 4. We measured three stress hormones under sedentary and overnight-fasting conditions. The average plasma cortisol, testosterone, and GH concentrations for participants were significantly elevated at altitudes above their sea level.

Discussion

Skeletal muscle is an important target in preventing and treating insulin resistance. Both exercise and hypoxia are known to enhance glucose permeability across the plasma membrane in skeletal muscles (Winder, 2001).

Table 2. Effect of 25-day altitude hiking activity on body composition

	Sea level		Day 25	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Body weight (kg)	69.6	12.8	68.2	12.4
% Body fat	19.4	6.8	16.9	5.9*
Fat mass (kg)	13.7	6.4	11.6	5.3*
Waist-to-hip ratio	0.83	0.05	0.81	0.04*

Note. *M* = mean; *SD* = standard deviation.

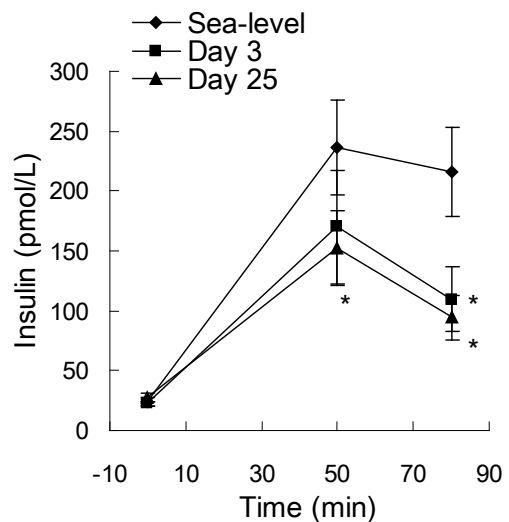


Figure 2. Effect of 25-day altitude hiking activity on insulin levels during the oral glucose tolerance test; * $p < .05$ significant difference against sea level.

In this study, we determined the effect of a long-term hiking activity at moderate altitudes on whole-body glucose tolerance, insulin sensitivity, and body composition for healthy adults. Although their fasting glucose was slightly elevated, their glucose tolerance improved during and after the altitude activity. This improvement was associated with enhanced insulin sensitivity, as evidenced by lower insulin levels. More importantly, the WHR circumference reduced significantly over the 25-day period.

Insulin sensitivity associates closely with body fatness (Jonk et al., 2007). However, the improvement in glucose tolerance and insulin sensitivity at Day 3 at altitude, suggests this improvement was not solely attributed to reduced body fat. This improvement was most likely due to the combined effects of increased skeletal muscle insulin and lowered body fat percentage along with lower WHR. There is evidence that acute exercise increases glucose tolerance and insulin sensitivity until muscle glycogen levels are replenished (Chou et al., 2005; Lai, Lin, & Jensen, 2009; Lai, Stuenkel, Kuo, & Jensen, 2007). Participants in this study used the same muscle groups daily. The muscle glycogen would have not been fully replenished in the overnight period prior to the subsequent exercise bout. Therefore, the exercised muscle would be sensitive to circulating insulin for glucose uptake, which could explain the improvement in OGTT at Days 3 and 25.

Most exercise training studies demonstrating significant fat-reducing effect were performed at sea level for more than 3 months (Toth, Beckett, & Poehlman, 1999). The present study demonstrated that only 1 month of mountain expedition could significantly lower body fat, as indicated by the reduction in WHR. Living in a mountain environment demands more physical activity. In this study, participants hiked daily ~5 hr per day, 7 days a week with a backpack load. If hiking requires approximately 8 metabolic equivalents (or 28 ml/kg/min) for approximately 5 hr, then daily exercise energy expenditure would be 2,925 kcal/day (based on an average body weight of 69.6 kg). If another 2,000 kcal were required each day for nonexercise metabolism, then participants could have been at a potentially significant energy deficit throughout the study. Therefore, a higher energy expenditure than

general living conditions at sea level could explain the reduction in fat storage. Furthermore, reduced sedentary time, such as television watching, using motorized transportation, and computer usage (Brownson, Boehmer, & Luke, 2005; Fotheringham, Wonnacott, & Owen, 2000), could also account in part for the fat-reducing effect of the mountain expedition.

Previous studies reported that 21 days of high-altitude physical activity could reduce body weight due to both fat and muscle weight reduction (Rose et al., 1998; Tanner & Stager, 1998). However, in the current study body weight and muscle weight at Day 25 were not significantly changed. One major difference between these studies was that they reported an insufficient energy intake, whereas food was supplied *ad libitum* in our study. Our result is consistent with evidence from animal studies showing no change in muscle weight after chronic hypoxia (Deveci, Marshall, & Egginton, 2001).

The effect of a mountain expedition on body composition could also be associated with change in stress hormone levels, as evidenced by the fact that exogenous treatment with testosterone (Marin, 1995) or growth hormone (Richelsen et al., 1994) reduces abdominal fat storage and increases muscle mass. The current data show that baseline testosterone and GH significantly increased during the 25-day activity when resting SaO₂ reduced from 98.1 ± 0.1 to 91.0 ± 2.2. Because hypoxia enhances exercise-induced growth hormone and testosterone releases (Chen et al., 2006), the combined effects of the hiking activity and moderate altitude hypoxia could cause greater stress hormone releases to affect body composition.

Wilmore et al. (2001) reported a significant correlation between changes in VO₂max and glucose uptake after 6 weeks of endurance training. In the present study, we found a similar result in improvement in insulin sensitivity, increased maximal oxygen consumption, and run time to exhaustion. Favorable cardiorespiratory fitness and longer treadmill running time have been shown as predictors for a low prevalence of insulin resistance (Lee, Sui, Church, Lee, & Blair, 2009; Nagano et al., 2004). It is likely that

Table 3. Effect of 25-day altitude hiking activity on aerobic capacity

	Sea level		Day 25	
	M	SD	M	SD
Run time to exhaustion (min)	16.5	0.6	17.2	0.5*
VO ₂ max (mL/kg/min)	43.0	2.7	49.1	2.2*
HRmax	184.3	2.1	192.0	2.8

Note. M = mean; SD = standard deviation; VO₂max = maximum oxygen uptake; HRmax = maximal heart rate.

*p < .05 significant difference against sea level.

Table 4. Stress hormone levels^a

	Sea level		Day 3		Day 25	
	M	SD	M	SD	M	SD
Testosterone (mg/dL)	6.1	1.3	10.2	1.3*	10.5	1.1*
Growth hormone (mg/mL)	1.1	0.4	0.7	0.2	1.6	0.4*
Cortisol (mg/dL)	17.9	0.8	20.7	2.2*	23.9	1.6*

Note. M = mean; SD = standard deviation.

^aTestosterone and cortisol were significantly elevated on Day 3 in altitude. All stress hormones were significantly elevated on Day 25 in altitude.

cardiovascular fitness enhanced glucose tolerance in part by promoting favorable changes in body composition.

The increased red blood cell count could in part explain the improvement in maximal oxygen consumption. Increased testosterone levels may help to stimulate erythropoiesis and could partially explain the increase in maximal oxygen consumption (Coviello et al., 2008; Lee et al., 2006). Additionally, reduced body weight, which is normally observed after exercise training, could also contribute to the increased relative maximal oxygen consumption (ml/kg/min) if "absolute" oxygen consumption (L/min) remained the same. However, participants' body weight was not significantly altered in the present study.

Although participants' glucose tolerance improved with the altitude hiking activity, their fasting glucose was significantly elevated. The high glucose level could be related to hypoxia, as most of the exercise training studies demonstrated a glucose-lowering action (Ho et al., 2008; Ivy et al., 1999). Increased baseline stress hormone levels and sympathoadrenal activity could mediate an increased glucose level at altitude (Lee et al., 2006; Louis & Punjabi, 2009). In this study, cortisol and heart rate were elevated at altitude. Cortisol level is generally known to increase with altitude and functions to accelerate the rate of hepatic glucose output (Larsen et al., 1997).

Previously, Mazzeo et al. (1998) found increases in both epinephrine and norepinephrine levels during altitude exposure. In their study, plasma epinephrine increased significantly and peaked on Day 4, whereas norepinephrine continuously increased during a 12-day altitude exposure. The effect of sympathoadrenal signaling on body composition is well evidenced by prolonged administration of sympathoadrenal agonist in rat and human studies (Kamalakkannan et al., 2008; Rothwell & Stock, 1987). Catecholamine acts as a powerful substrate mobilizer while countering the effects of insulin (Kopelman, 2000). Thus increased sympathoadrenal activity may explain the favorable outcome in body composition and clarify the high fasting glucose in altitude.

One limitation of the study was the inability to estimate energy expenditure accurately at altitude. Although heart rate can predict energy expenditure at sea level (Keytel et al., 2005), altitude hypoxia, which elevates baseline heart rate and intensifies heart rate during hiking, can confound reliability. Under hypoxia, the heart rate must increase to compensate oxygen and glucose deliveries to peripheral tissues. Furthermore, energy reliance on anaerobic metabolism is elevated under altitude hypoxia (Chen et al., 2009; Lin et al., 2008). Such a condition could confound the relationship between energy expenditure and heart rate. Another limitation was in using BIA to estimate body fat content, which is not the most accurate method. We obtained a group difference of 2.5%, which is less than the error of estimation for most body fat evaluation procedures. Thus, WHR appears to be

a more reliable parameter to reflect the effect of lifestyle intervention on body fat changes.

Conclusion

The present study demonstrated that a prolonged mountain expedition at moderate altitudes is an effective lifestyle intervention to improve whole-body insulin sensitivity, aerobic capacity, and body composition. Although body fat distribution is strongly correlated with insulin sensitivity, its favorable effect on body composition cannot solely explain the beneficial effect of the 25-day expedition on insulin sensitivity and glucose tolerance. The improvement in insulin sensitivity appears to be related to the acute effect of altitude hiking on exercised skeletal muscle. Moreover, reduced body fat after the expedition would be expected to sustain the beneficial effect on glucose tolerance for a longer period of time.

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Authors' Notes

The Republic of China Alpine Association supported this study in part. Please address correspondence concerning this article to Chia-Hua Kuo, 101 Zhongcheng Rd. Sec. 2, Shih-Lin District, Laboratory of Exercise Biochemistry, Taipei Physical Education College, Taipei 111, Taiwan.

E-mail: kuochiahua@gmail.com