BODY COMPOSITION AT HIGH ALTITUDE: A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF DIETARY CARBOHYDRATE SUPPLEMENTATION

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ABSTRACT
Background: Body mass loss is inevitable with chronic hypoxic exposure. However, the exact body-composition changes, their causes, and possible treatments remain unknown.

Objective: The objective was to investigate body composition during a high-altitude expedition by using non–empirically derived methods, experimentally manipulating energy intake, and investigating the influence of initial body composition.

Design: Forty-one participants completed a 21-d expedition in the Himalayas. Energy intake was manipulated with a double-blind, placebo-controlled, randomized trial of carbohydrate energy supplementation. Body composition was assessed before and after the expedition by using a 4-component model including fat mass, total body water, bone mineral mass, and residual mass (principally protein and glycogen). Data were analyzed by repeated-measures analysis of variance.

Results: Participants allocated to receive carbohydrate were given an additional 15,058 ± 6211 kcal over the 21-d expedition (>6 kcal·kg⁻¹·d⁻¹). Nevertheless, the functionally important residual mass decreased in both groups by 6% (main effect of time: P = 0.021), with no effect of allocation (interaction effect: P = 0.116). Similar decreases were observed for fat mass (11%) and total body water (3%), which were also unabated by allocation. Furthermore, high initial fat mass (by median split) did not preserve residual mass (high-fat compared with low-fat participants: residual loss = 5% compared with 8%; P = 0.990).

Conclusions: High-altitude exposure decreased body mass, including the functionally important residual component. These losses were not abated by increasing energy intake or an initially high fat mass. Factors other than negative energy balance must contribute to body-composition changes with chronic hypoxia. This trial was registered at clinicaltrials.gov as NCT00731510. Am J Clin Nutr 2009;90:1193–202.

INTRODUCTION
With exposure to chronic hypoxia, body mass loss is inevitable. Field studies at high altitude (1–3) and experimental studies in hypobaric chambers (4, 5) suggest significant body-composition changes, including loss from the functionally important fat-free mass component. Because these changes include muscle loss and decreased protein stores, they likely contribute to the decreased physical performance (6–10) and the increased infection rate and slow wound healing reported with chronic hypoxic exposure (11).

Despite these important consequences, hypoxia-associated body mass loss remains poorly understood and whether it can be prevented is unknown. The precise body-composition changes associated with high-altitude exposure are contradictory (12, 13), and the causes of body mass loss are also incompletely defined. Most previous studies have relied on observational designs. Nevertheless, the presumed primary cause of body mass loss is negative energy balance due to increased energy expenditure (increased basal metabolic rate and physical activity level) and decreased energy intake (anorexia) (14). Chamber studies suggest that a deficit of 400 kcal/d occurs as a result of hypoxia per se (4, 5). Associated with this energy deficit is the depletion of glycogen, which leads to the increased oxidation of amino acids for production of energy and depletion of protein pools such as muscle (8).

Consequently, reviews and guidelines suggest that negative energy balance and glycogen depletion should be avoided during high-altitude sojourns (8, 15–19) and that those with recent weight loss should avoid subsequent altitude exposure (16). However, few palatable yet practical dietary interventions to increase energy and carbohydrate intake have been conducted in extreme high-altitude environments, and, surprisingly, sugar-sweetened beverages have received little attention despite their known weight-increasing effects at sea level (20). Moreover, the


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influence of initial body composition, and thus initial body energy stores, on body mass loss has not been adequately explored, despite the known influence of initial fat mass on the loss of fat-free mass at sea level (21).

Hence, the objective of this study was to investigate factors affecting body composition at high altitude. Specifically, we first aimed to accurately describe body-composition changes during a typical high-altitude expedition. Second, we aimed to determine whether a simple dietary intervention, carbohydrate energy drink supplementation, could reverse body mass loss. This randomized, double-blind, placebo-controlled trial also allowed experimental investigation of whether body mass loss at high altitude is primarily due to negative energy balance. Finally, defining participants into high or low initial fat and fat-free mass groups also explored the influence of initial body composition on subsequent body-composition changes. We hypothesized that body mass loss would primarily (but not exclusively) consist of fat mass and that, because of increased energy availability, both those subjects allocated to carbohydrate and those with a higher initial fat mass would better preserve their functionally important fat-free mass.

SUBJECTS AND METHODS

Participants

Forty-one participants were recruited by JHM from the Medical Expeditions 2008 Hidden Valley Expedition to Nepal. This expedition was “open to all with a healthy enthusiasm for the outdoors and/or a passion for research in remote and difficult circumstances.” The study was approved by both the North West Wales Research Ethics Committee and the Nepal Health Research Council, and all participants provided written informed consent.

Study design and intervention

This study had a prospective, experimental, randomized group design with outcome measures obtained serially. The study schematic is shown in Figure 1. The primary outcome measure was the functionally important body-composition component of residual mass (principally protein and glycogen). The quality of the measurement of outcomes was enhanced with extensive training of assessors, including completion of a 5-d pilot expedition at low altitude in the United Kingdom (22). All participants were familiarized with the assessments 1 mo before departure for Nepal. One-time nonreturnable deposits were received, and the participants were randomly assigned within their expedition group, stratified by sex, to receive either a 10% carbohydrate solution (PSP22; Science in Sport, Blackburn, United Kingdom) or placebo solution. Carbohydrate was principally maltodextrin and provided 10 g carbohydrate/L and 37 kcal/L. The placebo consisted principally of natural flavorings and aspartame; the nutrient content was negligible. The flow of participants through the study is shown in Figure 2. Randomization and assignment of participants to groups was completed by a researcher, independent of the study and without knowledge of the participants’ baseline characteristics, using a randomly permuted blocks design obtained with a pseudo random number generator (www.randomization.com). The expedition cooks were not blinded to enable dosing of solutions during the expedition. The participants, data collectors, and data analyzers remained blinded until all intention-to-treat analyses had been completed (confirmed by a manipulation check after the expedition). The expedition cooks made up the indistinguishable solutions in kettles with boiled water, and the participants drank them ad libitum either from mugs at meal times or from personal water bottles during the day. The amount drunk was recorded (see Secondary outcome measures: diet).

Primary outcome measures: molecular-level body composition

The participants had fasted and voided and wore standard minimal clothing (swimsuit) for all measurements, which were made at the same time of day. A nonempirically derived measure of body composition was provided by a 4-component model that included bone mineral mass, total body water (TBW), fat mass,
and the functionally important residual component (protein and glycogen) (23). This hydrodensitometry method was chosen because other techniques (such as dual-energy X-ray absorptiometry) are less valid and would have involved a delay before posttesting while transfer to the laboratories was completed. Bone mineral mass was obtained by measuring bone mineral content with dual-energy X-ray absorptiometry (QDR1500, software version 5.72; Hologic, Waltham, MA) and applying a correction factor of 1.0436 (24). Values were assumed not to change during the study (a period of 3 mo) (25). Residual lung capacity was determined by helium dilution (Zan310, nSpire Health Inc, Hertford, United Kingdom). The participants were tested in a crouch position to simulate the conditions experienced during the underwater weighing procedure (see below). This value was assumed not to change because lung volume is unaffected by hypoxia (26).

TBW was determined by deuterium oxide dilution. After a sample of saliva was obtained before dosing to determine initial enrichments at each of the time points, an oral dose of \( \approx 0.07 \text{ g} \ 2\text{H}_2\text{O/kg body mass} \) was administered. All dosing materials were weighed before and after administration to obtain exact doses, which were recorded. A sample of the dosing solutions was stored for later analysis of the samples. Additional saliva samples were then collected 4.5 and 5.5 after dosing. Two different methods for calculating TBW (plateau and interpolation) were used (27). The pre-expedition doses collected for the mid- and postexpedition TBW measurements also formed the last daily samples for plateau determinations in the first and second determinations, respectively. All samples of saliva were measured at the Medical Research Council Human Nutrition Research Laboratories, Cambridge, United Kingdom, by using isotope ratio mass spectrometry as previously

**FIGURE 2.** Flow of participants throughout the study. Sample size refers to the primary outcome measure (residual mass) and all other measures unless specifically stated otherwise in Subjects and Methods. *These 2 subjects were also counted in the “lost to follow up” category.
described (27). TBW was calculated by using the following equation:

\[
TBW = \frac{1}{1.04} \times \left[ \frac{D \times \frac{T}{d} \times (Ed - Et)}{d \times (Es - Ep)} \right] \times \frac{1}{1000}
\]

where TBW is in kg, \(D\) is the amount of oral dosing solution administered to the subject (g), \(T\) is the amount of bottled water (g) used to dilute a sample of the dosing solution \(d\) (g), \(Ed\) is the enrichment of the diluted dose \(d\) in \(T\) (%), and \(Es\) is the enrichment of the bottled water diluent (%). With the plateau method, \(Es\) is the mean enrichment of saliva samples at 4.5 and 5.5 h (%), and \(Ep\) is the enrichment of each predose sample (%). For the interpolation method (where predose values were subtracted from all postdose samples before time versus logged enrichment was plotted; \(Es - Ep\)), enrichment was determined by back extrapolation to time = 0 of the disappearance curve of \(^2\)H over the measurement period (%).

Body volume was obtained from hydrostatic weighing. Body mass was measured in air by using a calibrated electronic scale (InBody 230; Biospace, Seoul, Korea). The participants then entered a swimming pool or a 1000-L water container to sit submerged on a suspended calibrated scale (Seca, Birmingham, United Kingdom) for the measurement of body mass under water after full expiration. The following equations were used to determine body volume and hence body fat (23):

\[
BV = \left( \frac{BM - UWM}{D} \right) - (RV + GIG)
\]

\[
FM = 2.748 \times BV - 0.699 \times TBW + 1.129 \times Mo - 2.051 \times BM
\]

where \(BV\) is body volume (kg), \(BM\) is body mass (kg), \(UWM\) is underwater mass (kg), \(RV\) is residual lung volume (L), \(GIG\) is gastrointestinal gas (assumed to be 0.1 L), \(FM\) is fat mass (kg), \(TBW\) is in kg, and \(Mo\) is bone mineral mass (kg).

From these calculations, fat-free mass (kg) and residual mass (kg) (principally protein and glycogen) were determined by subtracting fat mass and TBW from total body mass. Fat and residual mass indexes were calculated by dividing respective body components by the square of height (m). Internal validity of this technique was suggested by the good intraclass correlation and limits of agreement between the bioelectrical impedance–determined appendicular lean mass and the dual-energy X-ray absorptiometry–determined appendicular lean mass [ICC\(_{(3,1)}\) = 0.986, limits of agreement = 1.4 kg], although a consistent and significant negative bias of 1.9 kg was observed. Ultrasound with integral calipers (180 plus; Sonosite Inc, Bothell, WA), depth of the vastus lateralis muscle, and overlying subcutaneous fat were measured at the midpoint of a line drawn between the iliac crest and the tibial tuberosity while the participant lay supine (site confirmed by palpation). On repeat testing, correct positioning of the probe was ensured by using traced clear plastic of anatomical landmarks. Participants were removed from the analysis if their images were too unclear to enable differentiation between tissues or if the results changed by >0.5 cm between tests (\(n\) removed = 4; total \(n\) analyzed = 37). Internal validity of this measure was not determined because gold standard tissue-level body composition was not obtained; however, in our hands the CV was 8% (tested on 3 occasions before, during, and after a 5-d wilderness expedition at low altitude).

Secondary outcome measures: diet

Dietary composition (including fluid from food) was calculated by using computer software (Dietmaster; Lifestyles Technologies Inc, Phoenix, AZ). Diet was made up of European and Nepali foods typical of Himalayan kitchen tent-supported expeditions (31). Carbohydrate or placebo supplements and alternative drinks were provided as requested. Food diaries were recorded at 2 time points (see Figure 1) to enable investigation of interactions between supplementation and altitude. At each time point, food diaries were recorded for 24 h at all meal times by each participant under supervision of a group researcher. Three-day diaries were not recorded to reduce participant load, because minimal interday and interindividual variability in diet was possible and because access to food other than that provided by the expedition cooks was negligible. Portion sizes were measured with weighing scales at the same time that food was served. Leftovers and seconds were subtracted and added as required. Extra snacks and all drinks consumed were also recorded. Participants with incomplete diaries were removed from the analysis (\(n\) removed = 2; total \(n\) analyzed = 39).

Additionally, intake of supplements was self-recorded every day by using drink bottles of known volume and head counters to record refills. Self-recorded supplement intake was checked against actual supplement intake by recording the mass of supplement consumed by each group (data not shown). Furthermore, internal validity of recorded supplement intake was suggested by comparison with food diaries on days when both were obtained. The ICC\(_{(3,1)}\) between the 2 methods was 0.991, the bias was 0.01 L, and the limit of agreement was 0.5L.

Secondary outcome measures: harms

Gastrointestinal upsets were self-reported daily according to the Bristol Stool Scale (number of motions per day and consistency of motions on a 1–7-point Likert scale) (32).
Statistics

All data are presented as means ± SDs. All analyses were performed by using a statistical computer package (SPSS version 15; SPSS Inc, Chicago, IL). Statistical significance was set at P ≤ 0.05 (2-tailed). After relevant assumptions were checked for, baseline demographic characteristics were compared by using Student’s t and chi-square tests. Then, an intention-to-treat analysis detailed the overall efficacy of supplementation. Trial participants were analyzed within the group to which they were randomly assigned, regardless of how much treatment they actually received. Because of the before and after test design, missing data were treated by removing the participant from the analysis (rather than by using a last observation carried forward method). A per-protocol analysis detailed the effects of carbohydrate supplementation in compliant individuals. Participants from the carbohydrate group were included in the per-protocol analysis only if all outcome data were available and if they had consumed sufficient supplement to receive >5.7 kcal · kg body mass⁻¹ · d⁻¹ of carbohydrate. This value was chosen because it equated to the 400-kcal/d energy deficit observed in previous chamber studies (4, 5). Providing all outcome data were obtained, all participants were included from the placebo group regardless of compliance because the placebo supplement had negligible nutritional value.

To investigate the influence of altitude exposure and energy intake, body-composition data were first analyzed by 4-factor repeated-measures analysis of variance with a within factor of time [before, mid- (if collected), or after expedition] and between factor of allocation (carbohydrate or placebo), and the randomization stratification variables of sex (men or women) and expedition trekking group (1, 2, 3, or 4). No interactions were noted between stratification variables and response to treatment of any outcome measure. Therefore, for clarity and to reduce manuscript length, all data were reanalyzed by 2-factor repeated-measures analysis of variance with a within factor of time [before, mid- (if collected), or after expedition] and between factor of allocation (carbohydrate or placebo). To investigate the influence of altitude and initial body composition, body-composition data were also analyzed by 3-factor repeated-measures analysis of variance with a within factor of time (before or after expedition) and between factors of initial fat mass index (low or high following a median split) and initial fat-free mass (low or high following a median split). Dietary data were analyzed by 2-factor repeated-measures analysis of variance with a within factor of altitude (low or high) and between factor of allocation (carbohydrate or placebo), whereas harms (stools) were analyzed by 2-factor repeated-measures analysis of variance with a within factor of time (day) and a between factor of allocation (carbohydrate or placebo). Assumptions such as normal distribution and sphericity of data were checked by using Mauchley’s test and Box’s M in SPSS. Greenhouse-Geisser correction to the df was applied when violations to sphericity were present (33). Significant main effects and interactions were followed up with a test of simple main effects, Tukey’s test, or step-down Holm-Bonferroni procedures (34) as appropriate to control for multiple comparisons. Effect size (ES; partial η²) values are provided for main outcome measures and were interpreted as small (0.05), medium (0.1), or large (0.2) (35). ES describes the proportion of the total variability attributable to a factor—for within, between, and interaction effects—and is calculated as follows:

$$\eta^2 = \frac{SS_{\text{between}}}{SS_{\text{between}} + SS_{\text{error}}}$$  \hspace{1cm} (4)

where SS is relevant type III sum of squares.

Because no data on the effects of increased energy intake on residual mass at high altitude are available, sample size was determined from a pilot study completed by our group using similar outcome measures of body composition after a wilderness expedition at low altitude (22). Using Hopkins’ method of estimating sample size for magnitude-based inferences (36), a minimum sample size of 11 participants per group was calculated as follows: the smallest important difference in change in means for body mass was assumed to be 2 kg (Cohen’s smallest important effect, or 0.2 × between subject SD), the within-subjects’ SD (typical error) was calculated as 1.87 kg, and the maximum chances of type I and II errors were chosen as 5%.

RESULTS

In the intention-to-treat analyses, no significant differences were observed at baseline between the carbohydrate and placebo groups, respectively, in age (35 ± 13 y compared with 34 ± 15 y; P = 0.829), sex (65% men compared with 64% men; P = 0.996), height (175 ± 7 cm compared with 174 ± 7 cm; P = 0.815), or body mass (74 ± 13 kg compared with 72 ± 10 kg; P = 0.496). Similarly, in the per-protocol analyses, no significant differences were observed at baseline between the carbohydrate and placebo groups, respectively, in age (30 ± 13 y compared with 34 ± 15 y; P = 0.413), sex (73% men compared with 64% men; P = 0.653), height (176 ± 8 cm compared with 174 ± 7 cm; P = 0.611), or body mass (71 ± 9 kg compared with 72 ± 10 kg; P = 0.971).

Effect of altitude and supplementation on body-composition change

Body-composition analyses showed that body mass decreased (significant main effect of time) because of an 11% decrease in fat mass, a 6% decrease in residual mass (principally protein and glycogen), and a 3% decrease in TBW (Figure 3). The total body water loss was 2.4 kg and was composed of 45% fat, 20% residual mass (principally protein and glycogen), and 35% TBW. Hydration of the fat-free mass remained remarkably constant at 73% (P = 0.321, ES = 0.03). Intention-to-treat analysis suggested that allocation to carbohydrate or placebo did not affect body mass loss or molecular-level body composition (Figure 3). Per-protocol analysis confirmed that, even in compliant individuals, allocation still had no significant effect on body mass loss or on body-composition components (P = 0.816–0.102, ES = 0.01–0.11). Consistent with these results, bioelectrical impedance data confirmed significant main effects of time (ES = 0.23–0.60), (Table 1) but a lack of effect of allocation (P = 0.308–0.107, ES = 0.03–0.08) on regional body composition. Bioelectrical impedance data also suggested that lean mass loss was greater from the arms (8% decrement) than from the legs (3% decrement).

Vastus lateralis muscle depth (ES = 0.09), but not overlying fat depth (ES = 0.09), also decreased significantly during the
expedition (Table 2). Depth of the vastus lateralis by ultrasound initially showed a significant interaction, but these findings were not confirmed by the per-protocol analysis ($P = 0.106$, ES = 0.09), which suggested that factors other than supplementation may explain this result.

**Effect of initial body composition on body-composition change**

With the functionally important residual mass (principally protein and glycogen) as the dependent variable, a lack of a triple interaction ($P = 0.514$, ES = 0.02) and a lack of a double interaction for initial fat mass index by time (Figure 4, top left panel) showed that the initial fat mass index had no influence on loss of residual mass. In contrast, a significant double interaction for initial residual index by time (Figure 4, top right panel) showed that those with a lower initial residual mass preserved their residual component, whereas those with a higher initial residual mass lost significantly more. Conversely, with fat mass as the dependent variable, a lack of a triple interaction ($P = 0.617$, ES = 0.01) and a lack of a double interaction for initial residual mass index by time (Figure 4, bottom right panel) showed that initial residual mass had no influence on loss of fat mass. In contrast, a significant double interaction for initial fat mass index by time (Figure 4, bottom left panel) showed that those with a lower initial fat mass preserved their fat mass

**FIGURE 3.** Mean (±SD) molecular-level body composition of participants before and after a high-altitude expedition. Two-factor repeated-measures ANOVA was used to compare the carbohydrate (-----; $n = 20$) and placebo (--; $n = 14$) groups. For all outcome measures, there were no significant main effects of allocation: $P = 0.806$–0.384; effect size [partial $\eta^2$; ES, interpreted as small (0.05), medium (0.1) or large (0.2)] = 0.00–0.02. Body mass: *significant main effect of time ($P < 0.001$, ES = 0.68), nonsignificant interaction ($P = 0.658$, ES = 0.00). Total body water: *significant main effect of time ($P < 0.001$, ES = 0.49), nonsignificant interaction ($P = 0.867$, ES = 0.00). Residual mass: *significant main effect of time ($P = 0.021$, ES = 0.16), nonsignificant interaction ($P = 0.116$, ES = 0.08). Fat mass: *significant main effect of time ($P < 0.001$, ES = 0.47), nonsignificant interaction ($P = 0.096$, ES = 0.08).

**TABLE 1**

<table>
<thead>
<tr>
<th></th>
<th>Leg lean mass</th>
<th>Arm lean mass</th>
<th>Skeletal muscle mass</th>
<th>Fat-free mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before expedition²</td>
<td>$18.4 \pm 3.1$</td>
<td>$6.5 \pm 1.5$</td>
<td>$32.9 \pm 6.0$</td>
<td>$58.3 \pm 9.8$</td>
</tr>
<tr>
<td>Mid-expedition²</td>
<td>$17.8 \pm 2.9$</td>
<td>$6.1 \pm 1.4$</td>
<td>$31.2 \pm 5.4$</td>
<td>$55.6 \pm 8.9$</td>
</tr>
<tr>
<td>After expedition²</td>
<td>$17.8 \pm 2.9$</td>
<td>$6.0 \pm 1.4$</td>
<td>$31.4 \pm 5.8$</td>
<td>$55.6 \pm 9.4$</td>
</tr>
<tr>
<td>Change²</td>
<td>$-0.6 \pm 0.9$</td>
<td>$-0.5 \pm 0.5$</td>
<td>$-2.0 \pm 2.2$</td>
<td>$-3.4 \pm 3.5$</td>
</tr>
<tr>
<td>Statistical significance²</td>
<td>$P &lt; 0.001$</td>
<td>$&lt;0.001$</td>
<td>$&lt;0.001$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Effect size²</td>
<td>0.23</td>
<td>0.41</td>
<td>0.58</td>
<td>0.60</td>
</tr>
</tbody>
</table>

¹ All values are means ± SDs.
² Intention-to-treat analyses.
³ Two-factor repeated-measures ANOVA.
⁴ Partial $\eta^2$, interpreted as small (0.05), medium (0.1), or large (0.2).
component, whereas those with a higher initial fat mass lost significantly more. To further clarify which body composition type lost most of the functionally important residual mass, these data were also expressed as ES and absolute and relative change (Table 3). Residual mass loss was greatest in the participants with initial high residual mass and lowest in the participants with a low residual mass and was unaffected by initial fat mass. Consistent relative (%) changes support that this interpretation was not confounded by scaling effects.

Effect of supplementation on dietary intake

Although body composition was unaffected by allocation, dietary analysis confirmed a substantial increase in energy intake.

![Figure 4](https://academic.oup.com/ajcn/article-abstract/90/5/1193/4598094)

**FIGURE 4.** Mean (±SD) body-composition changes during a high-altitude expedition as influenced by initial body composition (n = 34). Three-factor repeated-measures ANOVA was used for comparisons. Influence of initial fat mass index [fat mass (kg)/height$^2$ (m); ———, high initial fat mass index (>5.1); ——, low initial fat mass index (≤5.1) by median split] on loss of the functionally important residual mass [nonsignificant interaction: $P = 0.990$, effect size [partial $\eta^2$; ES, interpreted as small (0.05), medium (0.1), or large (0.2)]] = 0.00] and on loss of fat mass (significant interaction: $P = 0.031$, ES = 0.15). Influence of initial residual mass index [residual mass (kg)/height$^2$ (m); ———, high initial residual mass index (>3.9); ——, low initial residual mass index (≤3.9) by median split] on loss of the functionally important residual mass (significant interaction: $P = 0.003$, ES = 0.28) and on loss of fat mass (nonsignificant interaction: $P = 0.355$, ES = 0.03).
in the carbohydrate group, especially in compliant individuals. Participants allocated to the carbohydrate group received an additional 1.8 ± 1.1 g · kg body mass⁻¹ · d⁻¹, which equated to an extra 8.1 ± 5.0 kcal · kg body mass⁻¹ · d⁻¹ (intention-to-treat analysis). In those who were compliant (the 57% of participants allocated to the carbohydrate group who achieved an intake >5.7 kcal · kg body mass⁻¹ · d⁻¹ as carbohydrate), the additional carbohydrate received was 2.4 ± 1.1 g · kg body mass⁻¹ · d⁻¹, or 11.2 ± 4.5 kcal · kg body mass⁻¹ · d⁻¹ (per-protocol analysis). This extra intake decreased the energy deficit by 83% [calculated as additional energy intake from carbohydrate/(sea-level normal dietary energy intake – high-altitude normal dietary energy intake)]. In total, during the expedition, the carbohydrate group received an extra 10,885 ± 7021 kcal (intention-to-treat analysis) or 15,058 ± 6707 kcal (per-protocol) from supplement drinks.

Despite this substantial increased energy intake from supplement drinks, allocation to the carbohydrate group did not reduce normal dietary intake of carbohydrate (P = 0.365–0.355), protein (P = 0.800–0.614), or fat (P = 0.869–0.680), as evidenced by the lack of main effects of group and the lack of interactions. However, normal dietary intake of all 3 macronutrients (and consequently energy intake) was lower at high than at low altitudes in both groups (Table 4). Nevertheless, the relative macronutrient composition of the remaining diet was unaltered during the expedition (carbohydrate intake: 54 ± 1% compared with 52 ± 1%, P = 0.333; fat intake: 37 ± 1% compared with 39 ± 1%, P = 0.123), although the relative protein content tended to decrease (12 ± 1% compared with 10 ± 1%; P = 0.078). These intention-to-treat analyses were confirmed by per-protocol analysis (nonsignificant main effects of group and nonsignificant interactions: P = 0.896–0.621; significant main effects of time: P = 0.028 to <0.001).

**Effect of supplementation on harms**

Lack of interactions (P = 0.892–0.594) and lack of main effects suggested that gastrointestinal upsets were not affected by allocation (P = 0.805–0.127) or time (P = 0.226–0.085). One subject allocated to receive placebo stopped consuming the supplement because of diarrhea (confirmed with removal and reintroduction of treatment with consequent cessation and initiation of symptoms).

**DISCUSSION**

Sojourners to high altitude are in negative energy balance, which has been proposed to be the principal cause of the commonly observed body mass loss (12). Hence, guidelines recommend increasing energy intake during high-altitude exposure (8, 15–19). Our findings refute that increasing energy intake will abate the loss of fat and fat-free mass. Our data thus contradict our hypotheses: body-composition changes were due to a greater decrement in fat-free mass than in fat mass and neither increased energy intake nor an initially high fat mass prevented loss from the functionally important residual component (principally protein and glycogen).

Specifically, our study extends previous findings by precisely detailing the composition of body mass loss during a typical high-altitude expedition. Previous field studies (2, 3, 37) have generally relied on small samples and methods that may be confounded by fluid retention (13). Our data seem robust to this potential confounding factor, because TBW assessment was confirmed by 2 methods (plateau and interpolation). Our observed body mass loss of ~110 g/d was made up of 45% fat, 35% TBW, and 25% residual mass (principally protein and glycogen), which is remarkably consistent with chamber studies that show greater loss from the fat-free mass component (4, 38). Consequences of these body-composition changes remain unknown but may include detrimental to physical performance (8) and health (39).

**TABLE 3**

<table>
<thead>
<tr>
<th>Sample site</th>
<th>Carbohydrate</th>
<th>Protein</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low altitude</td>
<td>4.8 ± 1.8</td>
<td>1.1 ± 0.6</td>
<td>1.7 ± 1.3</td>
</tr>
<tr>
<td>High altitude</td>
<td>3.8 ± 1.6</td>
<td>0.7 ± 0.3</td>
<td>1.1 ± 0.5</td>
</tr>
</tbody>
</table>

Statistical significance

- **P**²: 0.001 <0.001 0.025 0.002
- **Effect size**: 0.30 0.40 0.30 0.25

1 Values are overall group means ± SDs from intention-to-treat analyses.
2 Main effect of time from 2-factor repeated-measures ANOVA.
3 Partial η²; interpreted as small (0.05), medium (0.1), or large (0.2).
We also investigated regional and tissue body-composition changes. Bioelectrical impedance and ultrasound suggested that the loss of leg muscle was less than the loss of arm muscle. These regional body-composition differences are discordant with previous findings obtained with computed tomography and magnetic resonance imaging (4, 13). Assuming no confounding effect of subclinical fluid retention, it is possible that there was sparing of the leg muscles in the present study because of the greater physical activity on our expedition (12); prior studies were completed in a chamber (4) or included air transport to moderate altitude (13).

Some authors have claimed that body mass loss, such as reported above, can be prevented by simple dietary intervention (40–43), but whether this claim is justified is debatable. First, studies that have successfully matched energy intake to energy expenditure have used enforced feeding (42) or used experimental conditions not applicable to field environments with “a large choice of palatable food in comfortable conditions” (41). In any case, even when solid food is offered in plentiful supply, it is often not consumed because of anorexia (4, 44). Previously investigated diets have often been unpalatable and caused significant gastrointestinal distress (10, 45). Second, weight loss was often not actually prevented (42, 43); mean losses averaged 70–188 g/d, and a high proportion of participants continued to lose significant body mass (42). Third, body mass loss is difficult to interpret, and whether loss of the functionally important body components was abated is not clear. Finally, these studies did not use randomized controlled designs, which makes the determination of diet efficacy difficult.

In contrast, our dietary intervention was provided ad libitum, was palatable, caused no harm (ie, gastrointestinal distress was not increased in the carbohydrate group), and was easy to carry, prepare, and consume in an extreme environment. The use of energy drinks to supplement diet successfully increased energy intake: an extra 10,000 kcal was provided during the expedition, energy drinks to supplement diet successfully increased energy intake, and was easy to carry, palatable, caused no harm (ie, gastrointestinal distress was not increased in the carbohydrate group), and was easy to carry, prepare, and consume in an extreme environment. Energy drinks to supplement diet successfully increased energy intake: an extra 10,000 kcal was provided during the expedition, energy drinks to supplement diet successfully increased energy intake, and was easy to carry, palatable, caused no harm (ie, gastrointestinal distress was not increased in the carbohydrate group), and was easy to carry, prepare, and consume in an extreme environment. Moreover, the time course of acclimatization varies considerably between physiologic systems and individuals. Our ascent profile of ≈300 m/d was designed to allow adequate acclimatization, but 25% of participants still reported acute mountain sickness at day 16, including symptoms of nausea that will have reduced nutrient intake. By day 22, all participants were acclimatized, as suggested by cessation of symptoms and stabilization of oxygen saturations. Thus, the results presented herein are particularly relevant to those people similarly acclimatizing to altitudes of ≈5500 m. Admittedly, higher calorie intake can be obtained with a high-fat supplement, but palatability would be poor. Interestingly, alternative macronutrient dietary manipulations at a high altitude have also been unsuccessful; studies of increased protein intakes have failed to abate body mass loss and have even had detrimental effects, including decreases in carbohydrate intake and in physical performance (47–49). Another study used a solid food carbohydrate supplement, but total energy intake did not increase (44). On the contrary, we increased carbohydrate and energy intakes, but still failed to reverse body mass loss. Thus, interventions to reverse body mass loss at a high altitude and the mechanisms responsible for the current lack of efficacy remain unknown.

In summary, at high altitudes, increases in energy intake with a palatable and practical carbohydrate dietary intervention does not preserve residual mass (protein and glycogen). Also, there is no sparing of a body-composition component via utilization of stored energy (ie, being fatter at the start of an expedition will not preserve your residual mass). These data suggest that mechanisms other than energy availability must be responsible (at least in part) for the loss of the functionally important residual mass (protein and glycogen). Our findings suggest that preparation for high-altitude exposure should involve increases in fat-free mass without increases in fat mass. Anabolic exercise, as opposed to increases in nutrient intake, seems essential.

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The authors’ responsibilities were as follows—JHM and SJO: designed the study, collected the data, and interpreted most of the data; JHM: analyzed the data; JHM: interpreted and collected the data; SJO: funded the study.
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