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Cold exposure increases adiponectin levels in men

Pascal Imbeault*, Isabelle Dépault, François Haman*

Behavioural and Metabolic Research Unit (Montfort Hospital), School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ontario, Canada K1N 6N5

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Abstract

Sympathetic nerve activation is recognized at the adipose tissue level during cold exposure. Adiponectin is a key protein produced by adipose tissue, but its acute modulation remains unknown in humans exposed to cold. The aim of this study were (1) to examine the acute effects of cold exposure on circulating adiponectin and (2) to determine whether the changes are modulated by (*a*) an acute glucose ingestion as well as (*b*) a short-term modulation in carbohydrate (CHO) availability. Using a random crossover design, 6 healthy men were exposed to cold for 120 minutes with ingestion of beverages containing low (Control, 0.04 g/min) or high (High, 0.8 g/min) amounts of glucose during the course of the experiment (study 1). In study 2, 6 healthy men were exposed twice to cold for 120 minutes after equicaloric low-CHO diet and exercise and high-CHO diet without exercise. Plasma adiponectin concentrations were quantified before and during cold exposure. In study 1, adiponectin levels did not change during High, whereas a 20% rise was observed during Control (condition × time interaction, $P = .06$). In study 2, adiponectin levels increased by approximately 70% during cold exposure after both low- and high-CHO diets (effect of time, $P < .05$). A 120-minute period of cold exposure is accompanied by a significant increase in adiponectin levels in young healthy men. The rise in adiponectin levels observed during shivering is inhibited with glucose ingestion but not after diets varying in CHO content.

1. Introduction

Apart from providing mechanical and thermal insulation, white adipose tissue has classically been viewed as a tissue for storing and releasing nonesterified fatty acids. This tissue is now well recognized as a critical source of many endocrine signals termed *adipokines*. Of those, adiponectin has been identified as a protein with antidiabetic and antiatherosclerotic properties [1]. In humans, a number of studies have shown increases in circulating adiponectin after insulin-sensitizing (thiazolidinediones) therapies [2-5] or weight loss (reviewed by Imbeault [6]). Acutely, no changes have been found in the levels of this protein during exercise [7,8] or after a meal [9-11]. To our knowledge, insulin infusion through a hyperinsulinemic euglycemic clamp is one of the few known conditions that have an acute inhibitory effect on circulating adiponectin in humans [3,12,13]. Consequently, the acute modulation of adiponectin levels remains to be investigated in humans.

At the adipose tissue level, cold exposure is accompanied by an increased noradrenaline turnover through an activation of the sympathetic nerves [14]. This cold-induced increase in noradrenaline turnover activates the β-adrenergic receptors and, in turn, raises the mobilization of nonesterified fatty acids from the white adipose tissue [15]. In 3T3-L1 adipocytes, stimulation of the β-adrenergic receptors reduced adiponectin gene expression [16]. The administration of a β-adrenergic stimulant was also shown to decrease adiponectin gene expression and levels in mice, suggesting a role of the sympathetic system in the modulation of this adipokine [17]. Conflicting results have nonetheless been reported relative to the effect of cold exposure in rodents; one study showed no change [18], one a decrease [19], and another an increase [20] in adiponectin levels. No information is available on the effect of cold exposure on adiponectin levels in humans. Studies in humans showed that total heat production is increased during acute cold exposure and that this increase is derived primarily from fat oxidation [21,22]. Animal studies support that adiponectin increases muscle lipid oxidation [23,24]. Whether or not changes in adiponectin levels are linked with the acute cold-mediated effect on

* Corresponding author. Tel.: +1 613 562 5800x4269; fax: +1 613 562 5149.
E-mail addresses: imbeault@uottawa.ca (P. Imbeault), fhaman@uottawa.ca (F. Haman).

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energy metabolism is beyond the scope of this article. However, based on the antidiabetic and antiatherosclerotic properties of adiponectin [1], the acute cold-mediated rise of the levels of this protein could be of clinical significance. Consequently, one purpose of this study was to quantify changes in plasma adiponectin levels in humans during cold exposure.

Modifying carbohydrate (CHO) intake is known to influence insulin sensitivity [25]. Using a combination of stable isotope tracers and stable-label intravenous glucose tolerance test, Sunehag et al [26] reported that, in the short term, a high CHO intake increases insulin levels and insulin sensitivity in young men. Adiponectin is a well-accepted marker for systemic insulin sensitivity in that significantly lower levels are found in the plasma of individuals with type 2 diabetes mellitus compared with insulin-sensitive individuals [27]. Plasma adiponectin levels are also known to be acutely reduced by insulin in humans [3,12,13]. During cold exposure, it remains unknown whether acute glucose ingestion or short-term dietary interventions causing modifications in insulin levels/sensitivity also affect potential changes in adiponectin levels. Therefore, the second and third objectives of this study were (1) to determine whether the changes in adiponectin levels are modulated by glucose ingestion and (2) to examine whether adiponectin levels are differently modulated by changes in CHO availability during sustained low-intensity shivering.

2. Research design and methods

2.1. Subjects

Twelve non–cold-acclimatized men gave their written consent to participate in these studies that were approved by the Research and Ethics Board of the University of Ottawa. All subjects were healthy, as determined by a medical history questionnaire; and none of them were smokers. Table 1 presents the physical characteristics of subjects who were all young men with normal body weight.

2.2. Anthropometric measurements

Body weight was determined with a standard beam scale (HR-100, BWB-800AS; Tanita, Arlington Heights, IL), and height was measured with a tape. In study 1, body composition was determined using dual-photon x-ray absorptiometry (Lunar Prodigy; General Electric, Madison, WI). In study 2, body density was determined by hydrodensitometry; and the Siri [28] formula was used to estimate body composition.

Table 1
Physical characteristics of subjects in study 1 (n = 6) and study 2 (n = 6)

	Study 1	Study 2
Age (y)	24.0 ± 2.0	22.2 ± 0.3
Weight (kg)	71.7 ± 2.1	70.6 ± 3.2
BMI (kg/m^2)	22.8 ± 1.6	23.3 ± 1.5
Body fat (%)	12.1 ± 1.4	11.5 ± 1.0

Data are means ± SE. BMI indicates body mass index.

2.3. Protocol: study 1

Six men participated in 2 randomly assigned experimental conditions, each separated by at least 7 days. Each trial consisted of a 120-minute baseline period followed by 120 minutes of shivering at an intensity equivalent to approximately 2.5 times that of the resting metabolic rate (data not shown). Subjects ingested drinks containing trace amounts of glucose (Control) or a 20% glucose solution (High).

Experiments were conducted between 8 AM and 12 PM, after 36 hours without heavy physical activity. The last evening meal was standardized (3220 kJ or 770 kcal; 42% CHO, 28% fat, and 30% protein), and subjects were asked to report to the laboratory at 8:00 AM the next morning after a 12- to 14-hour fast. Upon their arrival in the laboratory, subjects wearing only shorts were instrumented with thermal probes, an indwelling catheter (22G, 25.4 mm; Medex, Oakdale, CA) was placed in an antecubital vein for blood sampling, and subjects were fitted with a "liquid-conditioned suit" (3-piece LCS; Med-Eng Systems, Ottawa, Ontario). Subjects were then asked to empty their bladder (time = 0 minute) and remain seated for 120 minutes at ambient conditions (~23°C-25°C). Resting blood samples were collected 30 minutes prior and at the end of the baseline period. After this habituation period, a 4°C water perfusion was started through the LCS using a temperature-controlled circulation bath (Endocal, NESLAB, and Model 200-00; Micropump, Vancouver, WA). During the Control condition, participants ingested 100-mL solutions containing only trace amount of glucose at 30-minute intervals from the beginning of the baseline period through to the termination of the trial. At the onset of cold exposure during the High condition, an initial bolus of 200 mL of a glucose beverage was given followed by 100 mL at 30-minute intervals throughout the remainder of the experimental trial. The solutions delivered 0.042 and 0.83 g/min of glucose in the Control and High conditions, respectively. Blood samples continued to be collected every 30 minutes throughout cold exposure. Body and skin temperatures were measured (detailed below) at baseline before cooling and during the subsequent 120 minutes of cold exposure.

2.4. Protocol: study 2

Six participants were exposed to cold on 2 separate occasions after following (1) a diet low in CHO and heavy exercise bouts (Lo) and (2) a diet high in CHO without exercise bouts (Hi), as previously described [29]. A brief description of the diet and exercise regimen is given below. Upon their arrival at the laboratory (8:00 AM; 12 hours postabsorptive), subjects were instrumented with thermal probes, an indwelling catheter (18G, 32 mm; Medical, Arlington, TX) was placed in an antecubital vein for blood sampling, and they were fitted with LCS. After voiding their

bladder, subjects remained seated for the next 120 minutes at 23.2°C ± 0.01°C (758 ± 2 mm Hg, 39.8% ± 3.6% relative humidity). Resting blood samples were collected at the end of the baseline period. After this period, they were transferred to an environmental chamber (10.5°C ± 0.01°C, 755 ± 3 mm Hg, 61% ± 2% relative humidity); and the perfusion of the LCS with 10°C water was started using a temperature-controlled circulation bath (Endocal, NESLAB, and Model 200-00; Micropump). The shivering intensity was equivalent to approximately 2.5 times that of the resting metabolic rate (data not shown). Blood samples were collected at 60, 90, and 120 minutes of cold exposure. Body and skin temperatures were measured (detailed below) at baseline before cooling and during the subsequent 120 minutes of cold exposure.

2.5. Lo and Hi diet and exercise regimen

In an attempt to modify CHO reserve, a combination of exercise and dietary manipulations was used within a 7-day period. Total caloric intake was similar for both diets and was adjusted for differences in body weight between subjects (~170 $kJ \cdot kg^{-1} \cdot d^{-1}$). Lo diet was composed of 10% calories as CHO, 66% as lipids, and 24% as proteins, whereas Hi diet was composed of 71% calories as CHO, 13% as lipids, and 16% as proteins. Three days before the Lo experiment, the glycogen depletion phase began with subjects performing upper and lower body exercises for 2 hours at 65% maximum oxygen consumption on a cycloergometer and a hand crank ergometer (alternating every 30 minutes between legs and arms). After these exercises, subjects were prescribed a Lo diet for the next 3 days until the evening of Lo experiment. During this phase, additional 1-hour exercises were performed each day (days 2 and 3) with upper and lower body (30 minutes each at 65% maximum oxygen consumption). Immediately after Lo experiment (day 4), subjects began a Hi diet for the next 2.5 days and were asked to refrain from exercising during this period. Hi experiments were performed on the morning of day 7.

2.6. Body and skin temperatures

Tympanic (T_{ty}) (study 1) or esophageal (T_{es}) (study 2) temperature and mean skin temperatures ($\overline{T}_{skin}$)were monitored continuously before and during cold exposure. A tympanic thermocouple or pediatric esophageal probe (Mon-a-therm Tympanic or Mon-a-therm General Purpose; Mallinckrodt Medical, St Louis, MO) was used for measuring T_{ty} or T_{es}. $\overline{T}_{skin}$ was averaged from 12 sites using heat flux transducers (ie, forehead, chest, biceps, forearm, abdomen, lower and upper back, front and back calf, quadriceps, hamstrings, and finger tip) and calculated by using an area-weighted equation [30].

2.7. Blood analyses

All blood samples were drawn after an overnight fast of at least 12 hours from an antecubital vein before and after each intervention period. Plasma catecholamine levels were determined (study 1 only) on alumina-extracted samples (100 μL) using high-performance liquid chromatography with electrochemical detection. The high-performance liquid chromatography incorporated a Varian ProStar 410 solvent delivery system (Varian Chromatography Systems, Walnut Creek, CA) coupled to a Princeton Applied Research 400 electrochemical detector (EG & G Instruments, Princeton, NJ). Concentrations were calculated relative to appropriate standards, using 3,4-dihydroxybenzalamine hydrobromide as an internal standard.

Because cold exposure has a strong diuretic effect that can result in a 20% to 25% decrease in plasma volume [31,32], we quantified changes in plasma volume using hematocrit (Hct) measurements (study 1 only). Blood samples were transposed in a glass microhematocrit heparinized tube (Fisher Scientific, Nepean, Ontario) and spun with a microhematocrit centrifuge. Hematocrit was calculated and corrected for 4% plasma trapped with the packed red cells, as previously suggested [33]. No significant change in Hct during cold exposure was observed in Control (48.9% ± 2.6% and 50.7% ± 2.3%, before and after 120 minutes of cold exposure, respectively). A significant increase in Hct was noted in High (pre-Hct = 43.8% ± 1.6% vs post-Hct = 50.7% ± 2.3%; $P < .05$, before and after 120 minutes of cold exposure, respectively).

Plasma glucose concentrations were assayed using spectrophotometric analysis after conversion of glucose to glucose 6-phosphate by hexokinase. Laboratory-grade reagents (Sigma-Aldrich Canada, Oakville, Ontario; Fisher Scientific) were used for preparing a standard hexokinase reaction; and after 30-minute incubation of prepared samples at room temperature, spectrophotometric analysis of resultant nicotinamide adenine dinucleotide (reduced form) (NADH) light absorbance was performed in duplicate using a Synergy HT Series Multi-Detection Reader (Bio-Tek Instruments, Highland Park, Winooski, VT), with absorbance readings of 340 nm wavelength emissions. The intraassay coefficient of variation was 3.4%. A commercially available enzyme-linked immunosorbent assay kit (Linco Research, St Louis, MO) was used to measure plasma insulin levels, and the intraassay coefficient of variation was 3.5%. Leptin levels were measured (study 2 only) using a commercially available radioimmunoassay kit (Linco Research), and the intraassay coefficient of variation was 2.5%. Plasma adiponectin was assessed using a commercially available enzyme-linked immunosorbent assay (study 1) and a radioimmunoassay kit (study 2) (Linco Research). The intraassay coefficient of variation was 2.9% and 3.1% for study 1 and study 2, respectively. It should be noted that plasma samples from the same individuals were analyzed within the same run.

2.8. Statistical analyses

Repeated-measures analysis of variance with 2 within-subjects factors (effects of condition [ie, study 1: Control and High; study 2: Lo and Hi diet] and effects of time) were used

for plasma analyses. Univariate associations between variables were quantified using Pearson product moment correlation coefficients. α was set at .05. All analyses were performed using SPSS Software 16.0 (SPSS, Chicago, IL). All values in text are presented as mean ± SD; and those in figures, as mean ± SE.

3. Results

3.1. Study 1

3.1.1. Temperature responses

Changes in T_{ty} and $\overline{T}_{skin}$ before and during cold exposure were not different between Control and High, as presented in Fig. 1. T_{ty} did not change during cold exposure (36.1°C ± 0.2°C), whereas $\overline{T}_{skin}$ decreased from 33.3°C ± 0.3°C at ambient temperature to 23.9°C ± 0.5°C after 90 minutes of cold exposure ($P < .05$) and remained constant until the end of the experiment.

3.1.2. Plasma concentrations

Changes in plasma norepinephrine and epinephrine levels are depicted in Fig. 2. At ambient temperature, plasma norepinephrine and epinephrine levels did not differ between Control and High. A mean 4-fold increase in norepinephrine levels was observed after 120 minutes of cold exposure ($P < .05$) in both Control and High. Conversely, there was no change in epinephrine levels during cold exposure in both Control and High.

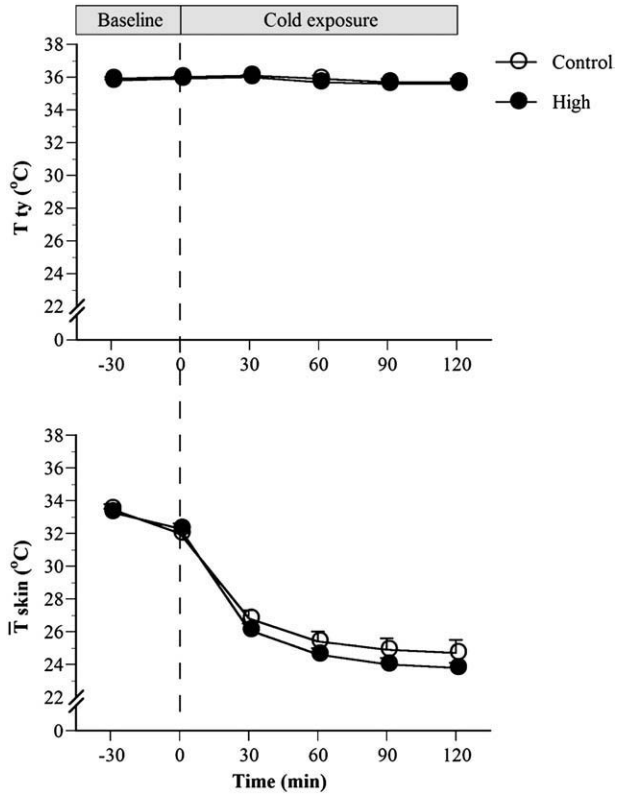

Fig. 1. Changes in T_{ty} and $\overline{T}_{skin}$ before and during cold exposure for Control and High. Values are means ± SE. Significant effect of time for $\overline{T}_{skin}$ ($P < .05$).

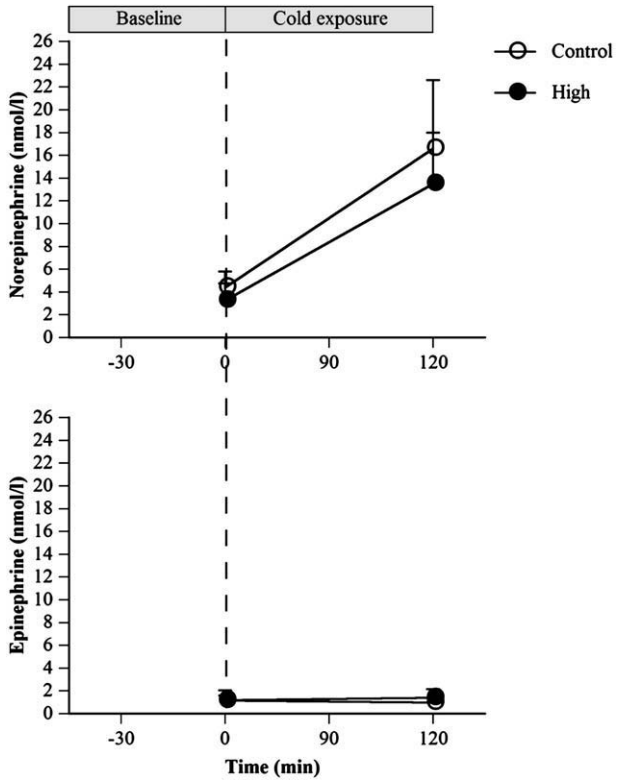

Fig. 2. Changes in norepinephrine and epinephrine levels before and during cold exposure for Control and High. Values are means ± SE. Significant effect of time for norepinephrine ($P < .05$).

Changes in circulating glucose, insulin, and adiponectin are shown in Fig. 3. At ambient temperature, glucose levels were not different between Control and High. Glucose levels did not change during cold exposure in Control but significantly increased in High (condition × time interaction, $P < .05$). Insulin levels did not differ between conditions at ambient temperature. During cold exposure, insulin levels increased in both conditions but to a greater extent in High (condition × time interaction, $P < .05$). Cold exposure was accompanied by a rise in adiponectin levels during High, whereas no significant changes were observed during Control (condition × time interaction, $P = .06$).

3.2. Study 2

3.2.1. Temperature responses

Changes in T_{es} and $\overline{T}_{skin}$ before and during cold exposure were not different between Lo and Hi, as presented in Fig. 4. T_{es} did not change during cold exposure (36.5°C ± 0.3°C), whereas $\overline{T}_{skin}$ decreased from 33.6°C ± 0.4°C at ambient temperature to 27.4°C ± 0.5 °C after 90 minutes of cold exposure ($P < .05$) and remained constant until the end of the experiment.

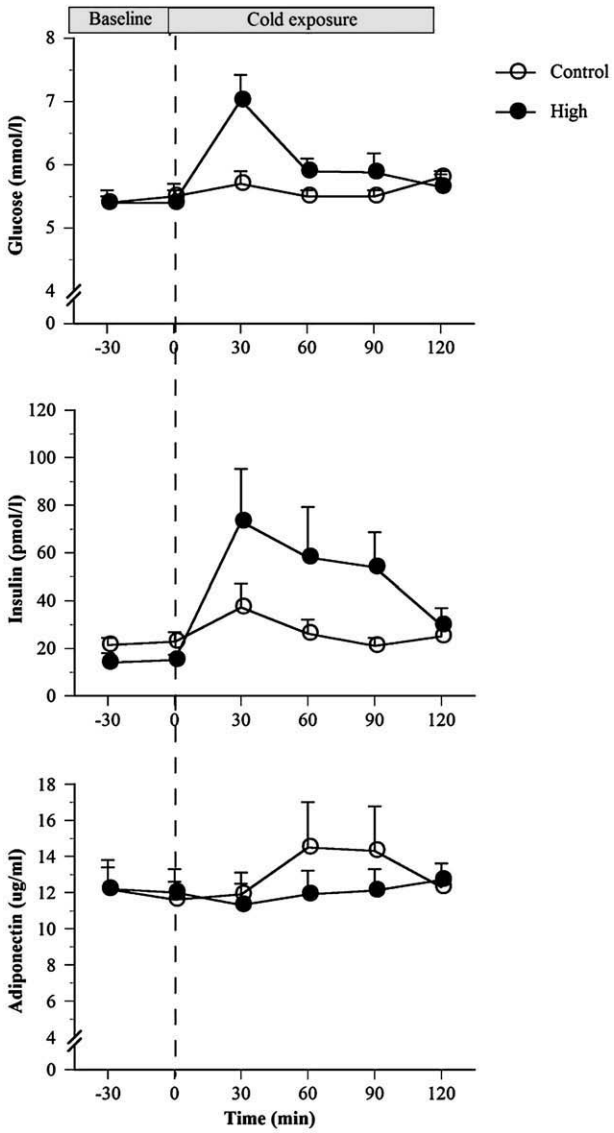

Fig. 3. Changes in plasma glucose, insulin, and adiponectin levels before and during cold exposure for Control and High. Values are means ± SE. Significant condition × time interactions for glucose, insulin, and adiponectin ($P < .05$). See "Results" for specific statistical effects.

3.2.2. Plasma concentrations

Changes in circulating glucose, insulin, and adiponectin are illustrated in Fig. 5. At ambient temperature, glucose levels were not different between Lo and Hi but increased during cold exposure in both conditions (time effect, $P < .05$). Insulin levels were greater after Hi as compared with Lo (condition effect, $P < .05$) at ambient temperature and did not change during cold exposure. Adiponectin levels were greater after Hi as compared with Lo (condition effect, $P < .05$) at ambient temperature. Circulating adiponectin increased significantly during cold exposure for both Lo and Hi (effect of time, $P < .05$). The mean relative increase (eg, increment over the adiponectin levels measured at ambient temperature) of adiponectin at 120 minutes was 76% ± 3.8% and 70% ± 3.8% for Lo and Hi, respectively. It is important to mention that we only measured total circulating levels of adiponectin. Adiponectin circulates under various oligomeric states, the high–molecular weight (HMW) complex being the more active [34]. Despite the fact that relative levels of HMW adiponectin are generally proportional to total levels [34], future studies examining the levels of the low–molecular weight and HMW forms of adiponectin will further contribute to our understanding of the role of this protein during cold exposure.

As a reference point to cold exposure, leptin was measured before and at 90 minutes of cold exposure. There was no difference in leptin levels at ambient temperature between Lo and Hi (0.53 ± 0.2 and 0.71 ± 0.4 ng/mL for Lo and Hi, respectively). After 90 minutes of cold exposure, the mean plasma levels of leptin in both interventions decreased by 22% ± 53%; and this fell short of statistical significance ($P = .07$).

In view of the heterogeneity observed in changes of adiponectin levels during cold exposure within the 12 studied participants, a correlation analysis was performed to examine whether the initial levels of adiponectin could be associated with the relative change of the circulating protein at the end of cold exposure. As depicted in Fig. 6, the lower the adiponectin

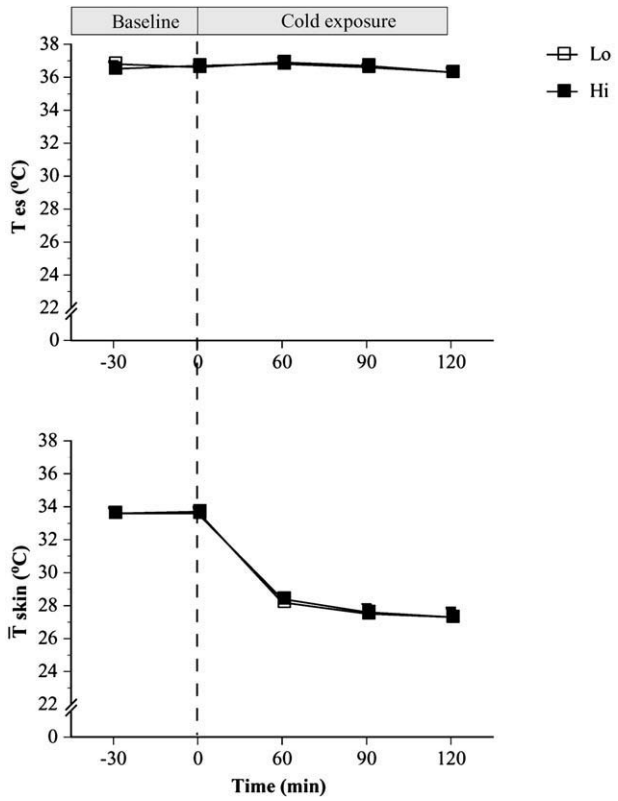

Fig. 4. Changes in T_{es} and $\overline{T}_{skin}$ before and during cold exposure for Lo and Hi. Values are means ± SE. Significant effect of time for $\overline{T}_{skin}$ ($P < .05$).

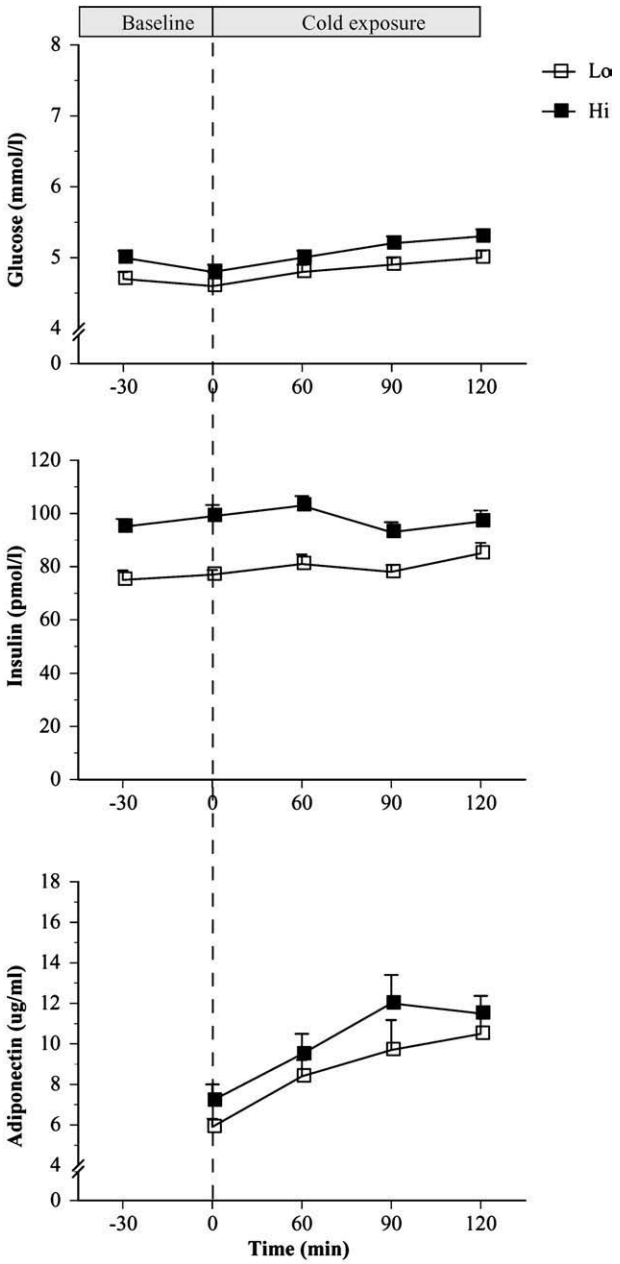

Fig. 5. Changes in plasma glucose, insulin, and adiponectin levels before and during cold exposure for Lo and Hi. Values are means ± SE. Significant effect of time for glucose ($P < .05$). Significant effect of condition for insulin ($P < .05$). Significant effect of condition ($P < .05$) and time ($P < .05$) for adiponectin. See "Results" for specific statistical effects.

levels were before cold exposure, the greater the relative increase in levels of circulating adiponectin was in response to cold exposure ($r = -0.74$, $P < .05$).

4. Discussion

The aims of the present study were (1) to examine the acute effects of cold exposure on circulating adiponectin and (2) to determine whether changes are modulated by (*a*) an acute glucose ingestion as well as (*b*) a short-term modulation in CHO availability. Results show that a 120-minute period of cold exposure is accompanied by a significant increase in adiponectin levels in young healthy men. The rise in adiponectin levels observed during shivering is inhibited with glucose ingestion (study 1, High) but not after a low-CHO or a high-CHO diet (study 2). It is also important to note that the intensity of cold exposure used in these experiments is far from extreme. In both studies, cold exposure did not alter core temperature (~36.5°C); consequently, shivering was solely induced by modifying skin temperature (from ~34°C to ~25°C after 90 minutes in the cold). As compared with the available literature on cold exposure in humans, *shivering intensity* is defined as a low-shivering intensity; that is, cold exposure induced heat production relatively expressed to the resting metabolic rate less than 2.5 and then sustained during several hours to days [35].

This is the first study to report an acute increase in adiponectin levels in humans. Several studies have explored whether plasma adiponectin levels are acutely modulated in response to the consumption of a meal or to an exercise session [6], but none found any effect. Our results show that adiponectin levels increased from 11.6 ± 1.0 μg/mL at ambient temperature (time 0) to 14.3 ± 2.4 μg/mL after 90 minutes of cold exposure in the Control condition of study 1. In study 2, circulating adiponectin increased from 6.5 ± 0.5 μg/mL at ambient temperature to 10.8 ± 1.9 μg/mL after 90 minutes of cold exposure (average of the Hi and Lo conditions). What factors could be related to the approximately 20% to 70% rise in adiponectin levels observed here during cold exposure? Although there is a paucity of

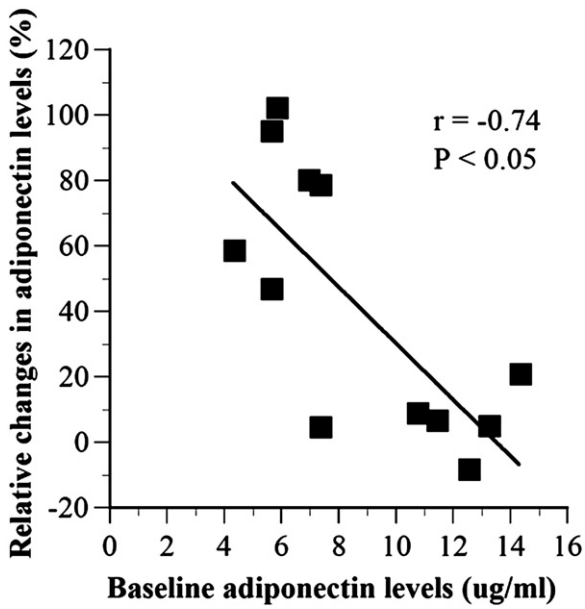

Fig. 6. Association between plasma adiponectin levels at ambient temperature and the relative changes of circulating adiponectin induced at the end of 120 minutes of cold exposure in 12 healthy men.

evidence currently available on the underlying mechanisms of adiponectin regulation in vivo, we can speculate that a number of factors could be responsible for modulating circulating levels of this protein.

4.1. Potential influence of insulin secretion

The inhibitory effect of insulin on adiponectin levels have been confirmed by a number of in vitro [36] and in vivo [3,12;13] experiments. The only condition that supports the inhibitory role of insulin on adiponectin levels in the present studies is when glucose is ingested during shivering (study 1, High). In the Control condition, insulin levels slightly increased throughout cold exposure even if glucose was not ingested. Despite this small but significant increase in insulin levels, our results still show an increase in circulating adiponectin during shivering. Taken together, these results suggest that a 2-fold increase in insulin does not inhibit the rise in circulating adiponectin, whereas a 4-fold increase totally inhibits the rise in adiponectin levels.

In study 2, fasting insulin levels were significantly greater after short-term high-CHO (Hi) than low-CHO (Lo) diet. These results are concordant with those of Sunehag et al [26], who showed that a 7-day high-CHO diet (60% calories as CHO) induced a significant increase in fasting insulin levels. In the same study, changing from low- to high-CHO diet also resulted in increased insulin sensitivity in adolescents. Adiponectin levels are good markers for systemic insulin sensitivity [1]. This may explain the higher levels of fasting adiponectin observed after Hi as compared with Lo diet. Despite the fact that our manipulations of CHO availability had a significant impact on fasting circulating adiponectin, the mean increase of this adipokine during cold exposure did not differ between Hi and Lo diet (mean increase of 70% vs 76%, respectively). These findings suggest that the potential improvement in insulin sensitivity derived from the passage of a low- to a high-CHO diet does not influence the relative increase in circulating adiponectin during shivering.

4.2. Potential effects of catecholamine release

Catecholamine levels were measured as index of sympathetic nervous system activation. Previous work has shown that the concentration of plasma norepinephrine is markedly increased during acute cold exposure in humans [37-40]. Norepinephrine has high affinity for the β-adrenoceptors of human adipocytes [41,42]; and in this context, Fasshauer et al [16] reported that adiponectin gene expression is inhibited by β-adrenergic stimulation in 3T3-L1 adipocytes. This inhibitory effect of β-adrenergic stimulation on adiponectin messenger RNA levels has also been demonstrated in mice in vivo and in human adipose tissue explants [17]. With this in mind, one would predict that cold exposure would be accompanied by a significant decrease in adiponectin levels. However, as stated above, results from our study show quite the opposite, where 2 hours in the cold increases adiponectin levels. In animals, effects of acute cold exposure remain controversial. For example, researchers have found that cold exposure increases [20], does not change [18], or decreases [19] levels of adiponectin. Clearly, much work remains to fully understand the effects of cold exposure on adiponectin levels.

4.3. Clinical relevance

Over the last decade, a number of health benefits have been linked with increased levels of adiponectin [1]. For example, this adipokine has been reported to present antidiabetic and antiatherosclerotic properties. Again, our current study is, to our knowledge, the first to report acute increase in adiponectin levels in humans. Interestingly, however, these observed changes in adiponectin concentrations seem to depend to a large extent on the initial level of this protein even in morphologically similar individuals. In Fig. 6, we plotted the baseline adiponectin levels against the relative change in the cold. This association indicates that the lower the initial levels of adiponectin are, the greater the rise in this protein will be during cold exposure. The exact reasons for this link remain to be explored. Of even greater clinical importance, we previously analyzed the association between the relative changes in body mass and total adiponectin levels after weight loss induced by traditional interventions and bariatric surgery in adults [6]. This exercise showed that a 10% to 40% body weight reduction is required to induce the 20% to 70% increase in adiponectin levels observed here in the cold. This emphasizes the substantial stimulatory effect of cold exposure on circulating adiponectin found in the present study (20% to 70% increase). Future work will need to evaluate the duration of this rise in circulating adiponectin during or after cold exposure.

In summary, the results of these studies demonstrate that (1) adiponectin levels significantly increase during a 2-hour period of cold exposure in young healthy men, (2) the rise in adiponectin appears to be regulated by the level of insulin levels during shivering, and (3) manipulating CHO availability before cold exposure does not alter the increase in circulating adiponectin during shivering. Additional work will be required to elucidate the exact mechanisms responsible for modulating the release of this adipocyte-derived protein and to characterize its metabolic roles in the human shivering response.

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