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ORIGINAL ARTICLE

Do changes in gastro-intestinal blood flow explain high-altitude anorexia?

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ABSTRACT

Background Gastrointestinal symptoms are common on acute exposure to high-altitude (HA). Underlying mechanisms are not understood, but vascular shunting away from the gut could be responsible. Therefore, blood flow in the superior mesenteric artery (SMA) and hepatic portal vein (HPV) was examined at sea level (SL) and after ascent to 4392 m (HA).

Materials and methods Twelve subjects [eight male, mean age 40 (22–72) years] were studied following an overnight fast and a standard meal. Cross-sectional vessel area and blood velocity were measured by ultrasound, systolic and diastolic flow calculated for the SMA (HR × vessel area × velocity, $cm^3\ min^{-1}$) and mean flow for the HPV.

Results All subjects experienced reduced appetite at HA. Blood flow in the SMA and HPV increased following food at SL (mean SMA systolic flow 1024 vs. 3316 $cm^3\ min^{-1}$, $P < 0{\cdot}001$; HPV 505 vs. 1789, $P < 0{\cdot}001$) and at HA (2020 vs. 3767, $P < 0{\cdot}001$; HPV 708 vs. 1727, $P < 0{\cdot}001$). Pre-prandial flow in the SMA and HPV was significantly increased at HA compared with SL. The changes were due to increased vessel diameter and increased flow velocity. There was no difference in post-prandial flow between SL and HA in the HPV, although the increase in post-prandial flow was greater at SL than HA (254% increase vs. 144%).

Conclusions These results show that resting blood flow in the gastrointestinal tract is increased during exposure to high-altitude hypoxia, and that the vascular response of increased blood flow following food ingestion is maintained. Therefore, reduced flow is unlikely to cause gastrointestinal symptoms and reduced appetite at HA.

Keywords Acute mountain sickness, blood flow, gut, high altitude, hypoxia, superior mesenteric artery.

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Introduction

High altitude (HA) has diverse effects on human physiology resulting from hypobaric hypoxia. Gastrointestinal (GI) manifestations of hypobaric hypoxia are significant, with both short and long-term effects. Acute exposure to HA results in anorexia, nausea and vomiting [1]. Longer-term exposure to HA (days to weeks) results in progressive weight loss, which is related to the altitude reached and duration of exposure [2,3]. However, the underlying pathophysiological mechanisms of HA anorexia and weight loss remain incompletely understood.

Investigation into the causes of HA weight loss have focused on reduced energy intake, increased basal metabolic rate (coping with cold conditions), earlier satiation, gastrointestinal malfunction and nutrient malabsorption, changes in body composition and body water, and difficulty accessing fresh and palatable food [2,4]. Energy balance studies at 6542 m showed inadequate intake rather than malabsorption to be the main cause of energy deficit resulting in weight loss [4]. However, other work has found malabsorption of carbohydrate [5]. There is also evidence that changes in endocrine signalling occur. Tschop *et al.* [6] found that plasma leptin levels were raised at HA [3,6], and that increased leptin levels were associated with loss of appetite and AMS [6]. Cholecystokinin, a satiety-signalling hormone [7,8], has been reported to rise on exposure to high altitude, especially in those suffering from loss of appetite [9].

It has been previously proposed that a reduction in blood flow to the GI tract may contribute to the GI symptoms suffered at high altitude [10]. Loshbaugh *et al.* [10] studied the effect of a 2-h exposure to hypoxia equivalent to 4800 m, using a

hypobaric chamber, on blood flow in the superior mesenteric artery (SMA). A significant reduction in SMA blood flow compared with flow at normoxia, both before food ingestion and in response to a high calorie test meal, was found [10]. The authors hypothesize that if reductions in blood flow were maintained during prolonged exposure they might be responsible for reduced appetite and weight loss. Whether his phenomenon occurs on longer exposure to HA hypoxia is not currently known.

This study aimed to test the hypothesis that a reduction in blood flow to the GI tract occurs in response to hypobaric hypoxia experienced on ascent to high altitude in subjects experiencing loss of appetite. It was further hypothesized that a reduction in blood flow occurs at rest and the normal increased blood flow response to a meal is blunted, providing evidence for a novel mechanism of gut dysfunction and HA weight loss.

Methods

Subjects

Twelve healthy volunteers [eight men, mean age 40 (22–72) years] were studied. Written informed consent was obtained from all subjects. All were non-smokers, normotensive, on no medication, physically fit, living at 50–150 m and with no recent exposure to high altitude. A power calculation based on Loshbaugh's study [10] demonstrated that 10 subjects would provide 80% power to detect a difference at $P < 0{\cdot}05$ significance. The study was approved by South Birmingham Research Ethics committee.

Ascent profile

Subjects spent 3 days at sea-level (SL, 0 m, Arica, Northern Chile), followed by two nights acclimatizing at 3300 m, before ascending to Parinacota (4392 m, HA). All ascent travel was undertaken by road. Measurements were taken at SL and after 24 h at 4392 m.

Data collection

Two sets of data were collected at 0 and at 4392 m: (i) pre-prandial measurements after an overnight fast (min 8 h, max 11 h); (ii) post-prandial measurements 45–60 min after a standard breakfast meal of 1000 kCal (Enshake, Abbott Nutrition, Maidenhead, UK). This protocol was based on that used by Loshbaugh [10]. Weight (kg) and heart rate (HR) were recorded. AMS symptoms were documented using the Lake Louise score system before the standard meal. To expand the range of possible responses, we created a standalone visual analogue scale to ask about appetite on a 0–10 scale. Blood pressure was recorded using a standard cuff on the brachial artery and mean blood pressure (MBP) calculated from diastolic pressure + 1/3 (systolic pressure − diastolic pressure). Finger-pulse oximetry (arterial oxygen saturation, SaO_2) was measured using an Ohmeda Biox 3740 Pulse Oximeter (Omron Healthcare, Milton Keynes, UK). For all data four measurements were taken both pre- and post-prandially, from which a mean was calculated. These measurements took approximately 10–15 min per subject. Haemoglobin (g dL^{-1}) was determined by analysis of EDTA-anticoagulated venous blood with a HemoCue 201 + haemaology analyser (Hemocue, Lake Forest, CA, USA).

Gut blood flow haemodynamics

Following a 5-min rest subjects were examined in supine position using a portable duplex Doppler ultrasound machine (Sonosite MicroMaxx C60e with 5-2 MHz 60-mm broadband curved array; Sonosite, Hitchin, UK). Vessel area (cm^2) was calculated from measurement of the radius of the SMA and the HPV (πr^2, assuming that the vessel is cylindrical). Systolic and diastolic flow velocity (cm s^{-1}) was recorded in the SMA and maximum and minimum flow velocity (cm s^{-1}) was recorded in the HPV. Volume of flow is derived from area and velocity according to: m^2 x m/s = m^3/s, and a standard formula [11] was used to calculate peak systolic or diastolic flow [HR × vessel area × systolic *or diastolic* flow velocity (cm s^{-1})] for the SMA (cm^3 min^{-1}). Because the HPV has a venous sinusoidal flow pattern with no systolic or diastolic peaks or troughs, maximum and minimum flow was recorded. The formula for calculating SMA flow (HR × vessel area × velocity) was adapted to calculate HPV flow by multiplying by time (60 s × vessel area × velocity; cm^3 min^{-1}). An average of maximum and minimum flow was calculated for the HPV. This estimation does not take account of vessel wall resistance or changes due to any turbulent flow. Oxygen delivery (mL O_2 min^{-1}) was calculated from the formula: blood flow (L min^{-1}) × Hb concentration (g L^{-1}) × 1·39 (mL O_2 g^{-1} Hb).

SMA and HPV measurements were performed by two trained sonographers. The Doppler tracings for the HPV were obtained via a right lateral intercostal approach in order to ensure that the beam/vessel angle (insonation angle) was < 20°. The SMA was investigated by placing the probe under a subject's xiphisternum. Measurements were taken with the subject's breath held during a moderate inspiration to reduce disturbance from respiratory movement [12]. The angle of insonation for the SMA was < 60°. Validation of SMA and HPV measurements was achieved by blinded re-assessment at 0 and at 4392 m. Comparison of data between sonographers showed the intra-subject coefficient of variation (standard deviation/mean × 100) to be 12% in the SMA and 14% in the HPV. This is similar to that previously reported [12–14].

Statistical analysis

Data was tested using SPSS software (SPSS Inc., Chicago, IL, USA). Paired data was analysed using the Wilcoxon signed

rank test. Subject demographic and cardio-respiratory data is presented as mean ± standard deviation. Blood velocity and blood flow data is presented as mean ± standard error of the mean. Significance was set at $P < 0{\cdot}05$. Reporting of the study conforms to STROBE [15].

Results

Subject demographics, AMS and gastro-intestinal symptoms

Mean age was 40 (22–72) years, height 175 ± 8 cm (150–186), weight 74·2 ± 9·3 kg (61·7–89·6) and BMI 24 ± 2 kg m^{-2} (19–27). There was a non-significant fall in mean weight during the study (Table 1, $P > 0{\cdot}05$). No subjects experienced gastro-intestinal symptoms or AMS symptoms at SL (Table 1). LLS scores were significantly higher at 4392 m than at 0 m and four subjects had a score of ≥ 3. On ascent to 4392 m all subjects experienced loss of appetite. One subject experienced severe gastro-intestinal discomfort (nausea, vomiting). LLS appetite scores ranged from 1 to 3 at 4392 m. Visual analogue scale scores for appetite (0 = normal appetite, 10 = no appetite) ranged from 0 to 2 at 0 m and 2 to 7 at 4392 m ($P < 0{\cdot}001$). The r^2 correlation between LLS appetite and VAS scores was 0·548.

Cardiorespiratory data

There was a post-prandial increase in HR at 0 and 4392 m ($P < 0{\cdot}01$, Table 1). Both resting (pre-prandial) and post-prandial HR was increased at 4392 m compared with 0 m ($P < 0{\cdot}01$). There was no difference in MBP pre- and post-prandial at 0 or 4392 m ($P > 0{\cdot}1$), but MBP did fall significantly pre- vs. post-prandially at 4392 m ($P < 0{\cdot}01$). There was no significant change in haemoglobin concentration at 4392 m (15·6 ± 1·7 at 0 m to 16·3 ± 1·9 g dL^{-1} at 4392 m, $P > 0{\cdot}05$). Arterial oxygen saturation fell at 4392 m compared to 0 m ($P < 0{\cdot}001$) and calculated blood oxygen content fell from 20·2 ± 2·2 to 18·4 ± 2·6 mL O_2 dL^{-1} ($P < 0{\cdot}01$).

Table 1 Cardiorespiratory and AMS data

	0 m		4392 m	
	Pre-prandial	Post-prandial	Pre-prandial	Post-prandial
HR	56 (8)	68 (12)*	64 (9)†	76 (11)*†
MBP	96 (7)	94 (6)	96 (12)	91 (11)
SaO_2	98 (1)	99 (1)	86 (4)†	85 (4)†
Hb	15·6 (1·7)		16·3 (1·9)	
Weight (kg)	74·2 (9·3)		73·6 (8·9)	
LLS (total)	0 (0–1)		2 (0–7)*	
LLS (appetite)	0 (0–0)		1 (1–3)*	
VAS	0 (0–1)		3 (1–7)*	

Values are mean (SD) except LLS and VAS which are median (range).
VAS, visual analogue scale for appetite.
*Significantly different from pre-prandial value at same altitude.
†Significantly different from the corresponding values at the other altitude.

SMA haemodynamics

No technical difficulties were experienced operating the sonography equipment. However, a problem with the memory function of the machine prevented the recording of mean volume flow. Increase in diameter of the SMA occurred in all subjects following a meal at SL and at 4392 m ($P < 0{\cdot}001$, Table 2). There was significant increase in vessel diameter at rest at 4392 m compared with 0 m ($P < 0{\cdot}001$). Peak systolic and diastolic flow velocity showed a significant post-prandial increase at 0 and at 4392 m ($P < 0{\cdot}001$). Pre-prandial peak systolic and diastolic flow velocity was greater at 4392 m than at 0 m ($P < 0{\cdot}01$). There was no significant difference in post-prandial peak systolic or diastolic flow velocity ($P > 0{\cdot}1$).

When HR, vessel area and flow velocity were combined to calculate flow, similar trends were seen (Fig. 1). There was a significant increase in peak systolic and diastolic flow after the test meal at 0 and at 4392 m ($P < 0{\cdot}001$). Pre- and post-prandial peak systolic flow and diastolic flow were all increased at 4392 m compared with 0 m ($P < 0{\cdot}001$).

The post-prandial increase (Δ) in flow, although significant at 0 and 4392 m was lower at 4392 m (Δ in systolic flow 1747 ± 350 at 4392 m vs. 2291 ± 440 cm^3 min^{-1} at 0 m). This represented an increase of 86% of pre-prandial flow at 4392 m and of 224% at 0 m.

Oxygen delivery (mL min^{-1}) was calculated from the product of flow (L min^{-1}) and blood oxygen content (1·39 × Hb × SaO_2/100). Diastolic oxygen delivery did increase significantly post-prandially at 0 m (20·2 ± 3·4 to 80 ± 15·3 mL min^{-1}, $P < 0{\cdot}001$) and at 4392 m (24·1 ± 5·9 to 110·2 ± 19·2, $P < 0{\cdot}001$). Systolic oxygen delivery showed the same trend (data not shown). Resting diastolic oxygen delivery was not significantly different between 0 m (20·2 ± 3·4) and 4392 m (24·1 ± 5·9, $P > 0{\cdot}05$).

Regression analysis showed no relationship between degree of loss of appetite (determined using the VAS score and by LLS appetite score) and change in resting pre-prandial blood flow (systolic or diastolic) between 0 and 4392 m ($P > 0{\cdot}1$).

HPV haemodynamics

Post-prandial vessel dilation was seen at 0 and 4392 m ($P < 0{\cdot}001$, Table 3). As in the SMA, pre-prandial vessel calibre was greater at 4392 m than at 0 m ($P < 0{\cdot}001$). Both maximum and minimum flow velocity was increased post-prandially at 0 and at 4392 m ($P < 0{\cdot}01$). There was no significant difference between pre- and post-prandial flow velocity.

Table 2 SMA data

	0 m			4392 m		
SMA	**Pre-prandial**	**Post-prandial**	**Difference (4392–0 m)**	**Pre-prandial**	**Post-prandial**	**Difference (4392–0 m)**
Radius (cm)	0·28 (0·02)	0·41 (0·02)*	0·13*	0·37 (0·02)†	0·42 (0·02)	0·05*
Peak systolic flow velocity (cm s^{-1})	67 (5)	116 (12)*	49*	87 (6)†	119 (13)	32*
Peak systolic flow (cm^3 min^{-1})	1025 (114)	3316 (399)*	2291*	2020 (169)†	3767 (482)†	1747*
Diastolic flow velocity (cm s^{-1})	6 (1)	15 (3)*	9*	7 (1)	19 (3)	12*
Diastolic flow (cm^3 min^{-1})	92 (16)	397 (74)*	305*	163 (33)†	616 (100)†	453*

Values are mean (SEM).
*Significantly different from pre-prandial value at same altitude.
†Significantly different from the corresponding values at the other altitude.

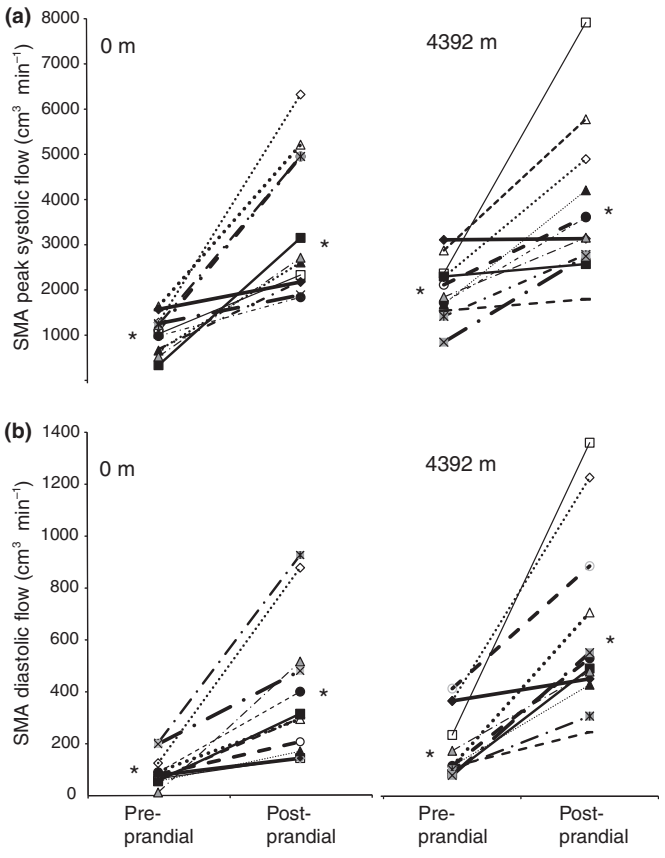

Figure 1 Individual peak systolic and diastolic flow in the SMA at 0 and 4392 m. The post-prandial change in diastolic and peak systolic blood flow was significant at both 0 and 4392 m ($P < 0·001$). Pre-prandial flow and post-prandial flow were both increased at 4392 m compared with 0 m ($P < 0·001$). *Average values. Symbols represent individual subject data, and are consistent between graphs.

Changes in flow observed in the HPV were similar to those in the SMA (Fig. 2). Post-prandial increases in flow were seen at 0 and at 4392 m ($P < 0·001$). Pre-prandial flow was greater at 4392 m than at 0 m ($P < 0·001$). There was no significant difference in post-prandial flow.

Although the post-prandial increase in flow in the HPV was significant at both 0 and 4392 m, the amount of increase in flow was lower at 4392 m (Δ average flow of 1019 ± 210 at 4392 m vs. 1285 ± 230 cm^3 min^{-1}, $P < 0·001$). This represented an increase of 254% of pre-prandial flow at 0 m and of 144% at 4392 m.

Discussion

These results show for the first time that the SL response to a food challenge – an increase in arterial and venous blood flow in the gut – was maintained on exposure to high altitude hypoxia, although it is noteworthy that the increase in flow was reduced at HA. Furthermore, the data demonstrate that resting arterial and venous blood flow was increased following a 3-day exposure to hypobaric hypoxia.

These findings have several implications for high altitude gastrointestinal physiology. Firstly, all subjects in this study experienced loss of appetite on ascent to 4392 m. Therefore, gut dysfunction and high altitude symptoms (including anorexia) are unlikely to be primarily caused by gross hypoperfusion from vessels supplying the gastrointestinal tract. Other factors, such as neurohormonal satiety signalling, may be more important. Furthermore, microcirculatory changes, which could include shunting, vasoconstriction and mucosal oedema, might also occur.

Secondly, the weight loss seen on exposure to high altitude is not likely to be due to GI dysfunction resulting from a blunted vascular response to food ingestion. There was a significant raised blood flow response following food challenge

Table 3 HPV data

	0 m			4392 m		
HPV	**Pre-prandial**	**Post-prandial**	**Difference (4392–0 m)**	**Pre-prandial**	**Post-prandial**	**Difference (4392–0 m)**
Radius (cm)	0·35 (0·02)	0·46 (0·01)	0·11*	0·40 (0·02)†	0·45 (0·02)	0·05*
Maximum velocity (cm s^{-1})	24 (3)	50 (3)	26*	25 (2)	51 (3)	26*
Maximum flow (cm^3 min^{-1})	612 (82)	1961 (125)	1349*	761 (88)†	1959 (467)	1198*
Minimum velocity (cm s^{-1})	16 (2)	41 (3)	25*	22 (2)†	38 (2)	16*
Minimum flow (cm^3 min^{-1})	395 (60)	1616 (256)	1221*	654 (78)†	1495 (223)	841*
Average flow (cm^3 min^{-1})	505 (65)	1789 (135)	1284*	708 (69)†	1727 (150)	1019*

Values are mean (SEM).
*Significantly different from pre-prandial value at same altitude.
†Significantly different from the corresponding values at the other altitude.

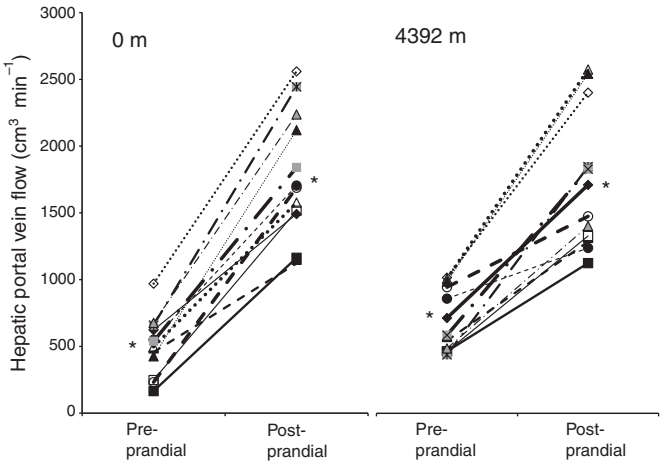

Figure 2 Individual flow in the HPV at 0 and 4392 m. Post-prandial flow was increased compared with pre-prandial flow at both 0 and 4392 m. Pre-prandial flow was greater at 4392 m than at 0 m ($P < 0·001$). There was no significant difference in post-prandial flow ($P > 0·05$). *Average values. Symbols represent individual subject data, and are consistent between graphs.

at SL and at high altitude in both vessels, although the magnitude of this increase was lower at altitude than at SL (144% vs. 254% in the HPV and 86% vs. 224% systolic flow in the SMA). The smaller increase following food at HA was due to significantly raised resting blood flow rather than lower post-prandial flow in both the SMA and HPV. Although similar post-prandial changes in blood flow would not be required if the increased flow at HA was sufficient to meet metabolic needs (reducing the need for increased vessel diameter), a smaller degree of post-prandial increase in vessel diameter at HA contributed to the relatively smaller increase in flow following the meal in the SMA and the HPV. Whether this difference could cause impaired gut function in response to food is not known. However, increased Hb (a minor contribution) and increased SMA blood flow (a major contribution) compensate for decreased SaO_2 at HA to maintain oxygen delivery both at rest and following food. It is also possible that the significantly raised resting flow seen at HA in the SMA could cause mucosal oedema, resulting in impaired mucosal oxygen delivery.

Although the data presented do disprove the hypothesis that grossly impaired blood flow in the GI tract is a pathogenic factor in HA gastrointestinal dysfunction and anorexia we cannot determine if the increased flow observed at HA in the SMA was a reflection of a widespread hyperdynamic state or was restricted to the GI tract. Cardiac output increases in acute hypobaric hypoxic conditions [10] and simultaneous measurements of systemic blood flow in other arteries will be required in future studies.

The novel observation that blood flow in the SMA at rest is increased at high altitude follows similar findings in other vascular systems, including the brain [16], and likely represents an adaptive response to hypoxic impaired tissue oxygen delivery. The increase in resting (pre-prandial) blood flow in both the SMA and the HPV was due to a combination of increased vessel diameter, increased velocity of blood flow and increased heart rate. There was no increase in blood pressure at HA, and MBP fell after the meal at 4392 m. Further study is required to determine whether the changes found in this study are maintained during longer exposure to HA.

The blood flow calculated for the SMA and the HPV was consistent with values previously reported in the literature and with findings that food ingestion results in increased SMA systolic and diastolic blood flow [12,14,17–19].

These findings differ from Loshbaugh *et al*. [10], who found exposure to hypobaric hypoxia in a chamber equivalent to 4800 m resulted in (i) a decrease in pre-prandial blood flow in the SMA, and (ii) a blunted response to a standard meal [10]. However, Loshbaugh's study used an ascent rate of 1000 ft min^{-1}, a very short exposure (2 h) to hypobaric hypoxia and used subjects resident at ~1750 m. The present study aimed to investigate whether the findings of Loshbaugh *et al*. were also seen on longer exposure to hypobaric hypoxia using a slower ascent rate. Therefore a similar test protocol was employed, testing after an overnight fast and 45–60 min after the same 1000 kCal standard meal. Direct comparison between Loshbaugh *et al*. (which measured SMA time average flow) and this study (which measured SMA systolic and diastolic flow) was not possible, but the trends in change may be compared due to the similar altitudes and test meal. In future studies time average flow will be measured. It is likely that the findings of Loshbaugh *et al*. represent the short-term response to acute exposure to hypobaric hypoxia, whereas the data presented here demonstrates that after time (3 days) the GI tract adapts by increasing resting SMA blood flow and maintaining an increased blood flow response to food.

We were unable to demonstrate any relationship between changes in blood flow in either vessel and appetite loss. Regression analysis between changes in resting blood flow and VAS appetite scores or LLS appetite scores were not significant. Indeed, rather than hypoperfusion resulting in anorexia and possible impaired GI function, resting blood flow was increased by approximately 40% in the HPV and by more than 80% in the SMA. Furthermore, the arterial and the venous vascular response to food ingestion remained after three days HA hypoxia, when appetite was reduced, although the amount of increase in blood flow was reduced. Alternative mechanisms must be sought to explain HA GI symptoms, and further studies at higher altitudes and over longer periods of time are required. This would be of particular importance in the study of weight loss at high altitude.

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Contributions

NK, CC, AW and CHI designed the study. Data collection was carried out by NK, FH and AJD. The paper was written by NK, AW and CHI.

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References

1 Maggiorini M, Muller A, Hofstetter D, Bartsch P, Oelz O. Assessment of acute mountain sickness by different score protocols in the Swiss Alps. *Aviat Space Environ Med* 1998;**69**:1186–92.
2 Hamad N, Travis SP. Weight loss at high altitude: pathophysiology and practical implications. *Eur J Gastroenterol Hepatol* 2006;**18**:5–10.
3 Lippl FJ, Neubauer S, Schipfer S, Lichter N, Tufman A, Otto B *et al*. Hypobaric hypoxia causes body weight reduction in obese subjects. *Obesity (Silver Spring)* 2010;**18**:675–81.
4 Westerterp KR, Kayser B, Wouters L, Le Trong JL, Richalet JP. Energy balance at high altitude of 6,542 m. *J Appl Physiol* 1994;**77**:862–6.
5 Dinmore AJ, Edwards JS, Menzies IS, Travis SP. Intestinal carbohydrate absorption and permeability at high altitude (5,730 m). *J Appl Physiol* 1994;**76**:1903–7.
6 Tschop M, Morrison KM. Weight loss at high altitude. *Adv Exp Med Biol* 2001;**502**:237–47.
7 Lieverse RJ, Jansen JB, Masclee AM, Lamers CB. Satiety effects of cholecystokinin in humans. *Gastroenterology* 1994;**106**:1451–4.
8 Lieverse RJ, Jansen JB, Masclee AA, Lamers CB. Satiety effects of a physiological dose of cholecystokinin in humans. *Gut* 1995;**36**:176–9.
9 Bailey DM, Davies B, Milledge JS, Richards M, Williams SR, Jordinson M *et al*. Elevated plasma cholecystokinin at high altitude: metabolic implications for the anorexia of acute mountain sickness. *High Alt Med Biol* 2000;**1**:9–23.
10 Loshbaugh JE, Loeppky JA, Greene ER. Effects of acute hypobaric hypoxia on resting and postprandial superior mesenteric artery blood flow. *High Alt Med Biol* 2006;**7**:47–53.
11 Rutherford R. *Vascular Surgery*. Philadelphia: W B Saunders, 2000.
12 Perko MJ. Duplex ultrasound for assessment of superior mesenteric artery blood flow. *Eur J Vasc Endovasc Surg* 2001;**21**:106–17.
13 Perko MJ, Just S. Duplex ultrasonography of superior mesenteric artery: interobserver variability. *J Ultrasound Med* 1993;**12**:259–63.
14 Tai DI, Chuah SK, Chen CL, Lo SK, Changchien CS, Li IT. Interobserver variability of portal hemodynamics measured by Doppler

ultrasound on three different locations of portal vein. *J Clin Ultrasound* 1996;**24**:61–6.
15 Simera I, Moher D, Hoey J, Schulz KF, Altman DG. A catalogue of reporting guidelines for health research. *Eur J Clin Invest* 2010;**40**:35–53.
16 Imray CH, Myers SD, Pattinson KT, Bradwell AR, Chan CW, Harris S *et al*. Effect of exercise on cerebral perfusion in humans at high altitude. *J Appl Physiol* 2005;**99**:699–706.
17 Moneta GL, Taylor DC, Helton WS, Mulholland MW, Strandness DE Jr. Duplex ultrasound measurement of postprandial intestinal blood flow: effect of meal composition. *Gastroenterology* 1988;**95**:1294–301.
18 Lilly MP, Harward TR, Flinn WR, Blackburn DR, Astleford PM, Yao JS. Duplex ultrasound measurement of changes in mesenteric flow velocity with pharmacologic and physiologic alteration of intestinal blood flow in man. *J Vasc Surg* 1989;**9**:18–25.
19 O'Donohue J, Ng C, Catnach S, Farrant P, Williams R. Diagnostic value of Doppler assessment of the hepatic and portal vessels and ultrasound of the spleen in liver disease. *Eur J Gastroenterol Hepatol* 2004;**16**:147–55.