ORIGINAL RESEARCH

Hydration and the Physiological Responses to Acute Normobaric Hypoxia

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Objective.—The effect hydration status has on exposure to hypoxia is unclear. The purpose of the study was to identify how hydration status, above and below euhydrated levels, affects the physiological responses and onset of acute mountain sickness symptoms during acute normobaric hypoxia.

Methods.—Eight males completed intermittent walking tests under normobaric hypoxic conditions (FIO₂ = 0.13) after controlled hyperhydration, hypohydration, and euhydration protocols. A range of physiological, psychological, and altitude illness markers were monitored throughout the 125-minute exposure.

Results.—Heart rate, core temperature, peripheral arterial oxygen saturation, urine osmolality, and mean self-reported Lake Louise Questionnaire acute mountain sickness scores were significantly different between euhydration, hypohydration, and hyperhydration, respectively, and closely correlated with environmental symptoms questionnaire, Lake Louise questionnaire, and headache scores (P < .05). Other measures of ventilation and lung function were also significantly different between hydration conditions (P < .05).

Conclusions.—Hydration state above and below euhydration has detrimental consequences on physiological strain and onset of acute mountain sickness symptoms when exposed to acute normobaric hypoxia.

Key words: hypohydration, hyperhydration, physiological strain index, acute mountain sickness

Introduction

The physiological responses to acute normobaric hypoxia, hypobaric hypoxia, and altitude have been widely researched, with many studies showing a range of physiological variables that contribute to the onset of altitude illness. Acute hypoxia can cause a decline in oxygen delivery, a rise in sympathetic activity, peripheral vasconstriction, and a consequent decline in aerobic capacity and rise in heat storage. Acute mountain sickness (AMS) is experienced when ascending to high altitude too rapidly. Symptoms include headache, gastrointestinal symptoms, insomnia, dizziness, and lassitude or fatigue.

Risk of dehydration is greater at altitude due to increased water vapor loss, energy expenditure, and ventilation. High-altitude backpackers have been shown to be hypohydrated (HYPO) at the start of a day’s hike and progressively dehydrate with each day, and mountain-eers can dehydrate by 5.5% over 3 weeks. At sea level, >2% HYPO reduces endurance performance, and further HYPO can have a significant effect on health and cognitive function. Hypohydration causes hypovolemia, vasconstriction, compensatory rise in heart rate, and consequential decline in oxygen delivery and heat dissipation. However, little research has investigated the effect of hydration status during hypoxia in adult and pediatric populations, causing much debate within the scientific community. The only study to control hydration at simulated altitude found no evidence to support hydration maintenance as a countermeasure to the observed effects. In a retrospective study, Basnyat et al found that drinking <3000 mL per day increased the risk of AMS by 60% and suggested that drinking up to 5 L·day⁻¹ would reduce AMS incidence.

In contrast, fluid retention through antidiuresis has also been linked to the onset of AMS symptoms. Overhydrating may increase extracellular fluid volume and
induce greater intracranial pressure and headache. Conversely, hyperhydration (HYPER) may reduce the physiological stress of hypoxia through increased stroke volume, vasodilation, and heat dissipation. Sea level studies report contrasting findings, with some that support the use of HYPER to improve endurance and others that have found no effect.

The purpose of this study was to determine the effect of hydration, above and below a euhydrated (EU) state, on the physiological responses to hypoxia and onset of AMS symptoms during a 125-minute acute normobaric hypoxic intermittent walking test.

Methods

PARTICIPANTS

Eight physically active males 20 ± 1 years of age (mean ± SD), height 182 ± 4 cm, weight 89 ± 13 kg, body fat 13% ± 3%, and maximal oxygen uptake (V\textsubscript{O2max}) 43 ± 7 mL·kg\textsuperscript{-1}·min\textsuperscript{-1} participated in the study. Participants were informed of the procedures and possible risks of the study, which had the approval of the University of Brighton research ethics committee, before giving their written informed consent. Participants had not performed exhaustive exercise in the 2 days prior to each trial and had not consumed alcohol or caffeine during a period of at least 24 hours immediately preceding the study. Participants were nonsmokers and had not spent time above 2000 m in the preceding 2 months.

EXPERIMENTAL DESIGN

The study required participants to attend the laboratory on 4 separate occasions, first for a familiarization session involving anthropometric tests and cardiovascular fitness assessment; the next 3 visits involved an intermittent walking test in a hypoxic environment under 3 different hydration states (EU, HYPO, HYPER). The order of the tests was randomized, determined by a Latin squares design. Each test was separated by a 7-day washout period.

LACTATE THRESHOLD TO V\textsubscript{O2max} TEST

Participants attended the laboratories prior to hypoxic testing for a familiarization session and assessment of body composition, using the Jackson and Pollock\textsuperscript{22} 7-site skinfold body fat assessment. Participants completed a lactate threshold and V\textsubscript{O2max} test using a previously validated incremental running protocol.\textsuperscript{23} Walking speed that would result in exertion of 50% V\textsubscript{O2max} on a 10% gradient was predicted using a 10-minute steady-state walking test with heart rate, indicating intensity based on the heart rate:oxygen uptake relationship.

INTERMITTENT WALKING TEST

The intermittent walking test involved testing a range of physiological markers over the 125-minute test duration, which involved a 35-minute rest followed by three 20-minute exercise phases separated with three-minute rest intervals and a final 20-minute recovery phase, as shown in Figure 1. Exercise involved participants’ walking on a treadmill (PP55Sport, Woodway, Steinackerstrasse, Germany) at a predetermined speed equal to 50% V\textsubscript{O2max} while at a gradient of 10%.

HYDRATION PROTOCOLS

Euhydration

Participants completed 1 hour of moderate intensity running 15 hours prior to the intermittent walking test while wearing warm clothing (hat, gloves, sweater, pants). Participants were then encouraged to rehydrate over the 15 hours by consuming 150% of sweat lost during the hour exercise. Sweat lost was quantified by the decline in body mass from normal to current values. “Normal body mass” was taken as the mean postmorning void body mass over 7 consecutive days.

Hypohydration

Participants completed the exercise as described for the EU trial but with complete fluid restriction during exercise and for 15 hours preceding the intermittent walking test.

Hyperhydration

Participants completed the exercise and consumed fluid as described for the EU condition, but on arrival to the laboratory participants were asked to consume a bolus of water equal to 28 mL·kg\textsuperscript{-1} body mass over a period of 40 minutes. This method has been widely used within one laboratory,\textsuperscript{24} which reported nausea or other adverse side effects only when performing the protocol with glycerol instead of water alone. Participants were then allowed a further 20-minute rest before pretest measurements were undertaken.

URINE MEASURES

The urine volume of participants was measured throughout the testing period. Urine specific gravity was as-
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Figure 1. Schematic of the intermittent walking test (EX = exercise).

Assessed using a refractometer (Atago, Bellevue, WA). Urine color was assessed using the urine color chart. Urine osmolality was measured using a micro-osmometer (Micro-osmometer 3300, Advanced Instruments Inc, Norwood, MA). Free water clearance \(\text{CH}_2\text{O}\) was calculated using urine flow \(V\), urine osmolality \(U_{\text{osm}}\), and plasma osmolality \(P_{\text{osm}}\) in the following equation: 
\[
\text{CH}_2\text{O} = V - [(U_{\text{osm}}/P_{\text{osm}}) \times V].
\]

**GAS MEASURES**

Gas samples were collected in Douglas bags over approximately 40 seconds during the rest and exercise periods. Ambient \(O_2\) and \(CO_2\) values were measured constantly through sample tubing linked to a gas analyzer (Servomex 1400, Servomex Group Ltd, Crowbrough, England). Breathing frequency was measured and tidal volume calculated from minute ventilation. Peripheral arterial oxygen saturation \(\text{SpO}_2\) estimated using a finger pulse oximeter (Nonin 2500, Nonin Medical Inc, Plymouth, MI) was recorded every fifth minute. Lung function (Gold Standard Vitalograph, Vitalograph Ltd, Maids Morton, England) was measured pre- and post-test. Hypoxic ventilatory response (HVR) was calculated using the change in \(\text{SpO}_2\) against the change in minute ventilation \(V_e\); 
\[
\text{HVR} = \Delta \text{SpO}_2/\Delta V_e.
\]

**ASSESSMENT OF ACUTE MOUNTAIN SICKNESS**

A modified 65-question Environmental Symptoms Questionnaire (ESQ), with the sleep-based questions removed, was used. Environmental Symptoms Question-
Hydration Status in Hypoxia

naire change (ΔESQ) was calculated using pre- and post-values. Environmental Symptoms Questionnaire cerebral score (ESQc) was also calculated.\textsuperscript{28} The Lake Louise Questionnaire (LLQ)\textsuperscript{29} was used with the sleep question extracted. Acute mountain sickness symptoms were calculated using the sum of 4 questions scored 0 to 3, including headache, gastrointestinal upset, fatigue or weakness, dizziness, or lightheadedness. The mean of the 5 LLQ scores over the walking test duration (LLQ\textsubscript{MEAN}) was also calculated. Feeling state was assessed from 4 visual analogue scales related to LLQ questions, as previously described.\textsuperscript{30} Thermal sensation,\textsuperscript{31} perceived thirst,\textsuperscript{32} and rating of perceived exertion\textsuperscript{31} were monitored every fifth minute during the intermittent walking test.

BLOOD MARKERS

Blood, pre- and post-test, was taken from the antecubital fossa using a 10-mL syringe. Blood for plasma osmolarity was spun in ethylenediaminetetraacetic acid tubes and measured using a micro-osmometer. Finger tip blood samples (Accuchek Softclix Pro, Roche, Lewes, England) were collected in triplicate heparinised capillary tubes, triplicate slides, and single microvettes to measure hematocrit (Hct), hemoglobin (Hb), blood lactate, and blood glucose, respectively. Peripheral oxygen blood content (Cpo\textsubscript{2}) was calculated from Hb and Sp\textsubscript{O2} and heart rate using the following equation: Cpo\textsubscript{2} = Hb × Sp\textsubscript{O2} × 1.34.\textsuperscript{26} Change in plasma volume (PV) was calculated from Hct and Hb between each time point using the following equation of Dill and Costill,\textsuperscript{34} where ‘A’ was the first blood sample and ‘B’ was the second: ΔPV\% = 100[(Hct\textsubscript{A}(1 – Hct\textsubscript{B} × 10\textsuperscript{-2}))]/[(Hb\textsubscript{B}(1 – Hct\textsubscript{A} × 10\textsuperscript{-2}))] – 100.

PHYSIOLOGICAL STRAIN

Rectal core temperature, measured using a probe (Henleys Medical Supplies Ltd, Lancing, Lewes, England) inserted 10 cm past the anal sphincter, and heart rate (HR) were used to calculate physiological strain index (PSI) using the equation PSI = 5(T\textsubscript{ret} – T\textsubscript{ref}) × (39.5 – T\textsubscript{ref})\textsuperscript{-1} + 5(HR\textsubscript{t} – HR\textsubscript{0}) × (180 – HR\textsubscript{0})\textsuperscript{-1}, where T\textsubscript{ret} and HR\textsubscript{t} are simultaneous measurements taken at any time during the exposure and T\textsubscript{ref} and HR\textsubscript{0} are the initial measurements.\textsuperscript{35} Hypoxic cardiac response (HCR) was calculated from change in Sp\textsubscript{O2} and HR: HCR = ΔSp\textsubscript{O2}/ΔHR.\textsuperscript{26}

STATISTICAL METHODS

Data were checked for normality, and sphericity was adjusted using the Huynh-Feldt method. One-way analysis of variance with repeated measures and Tukey’s honestly significantly different posthoc analysis were used to make comparisons between test conditions. Pearson’s product moment correlation coefficient was used to determine correlation between selected variables. All data were analyzed using a standard statistical package (SPSS version 14 for Windows, 2005). All data are reported as mean ± SD, with the significance level set at \( P < .05 \).

Results

Hydration protocols induced different pretest body mass and hydration markers, causing hydration of approximately 0%, –2%, and +2% of normal body mass for the EU, HYPO, and HYPER conditions, respectively, as shown in the Table.

Heart rate, core temperature, and PSI were found to be significantly different between hydration conditions (\( P < .01 \)) over time (\( P < .001 \)) (Figure 2). Heart rate and PSI were higher in the HYPO and HYPER conditions but not different from each other. Core temperature was significantly lower throughout the HYPER trials, compared with either the EU or HYPO conditions. None of the time points correlated with AMS symptom markers.

Perceptual markers of strain, including rating of perceived exertion (EU 12.9 ± 1, HYPO 14.2 ± 2, HYPER 14.1 ± 1) and thermal sensation scale (at rest (EU 4.5 ± 0.5, HYPO 4.3 ± 0.6, HYPER 4.2 ± 0.4) and during exercise (EU 5.5 ± 0.7, HYPO 6.1 ± 0.2, HYPER 6 ± 0.8)), were found to be greater in HYPO and HYPER than in EU conditions (\( P < .05 \)). As expected, perceived thirst [pretest (EU 2.5 ± 0.9, HYPO 6.8 ± 2, HYPER 0.8 ± 0.3) and post-test (EU 4.8 ± 1, HYPO 8.7 ± 3, HYPER 3.6 ± 1)] was increased with an increased water deficit (\( P < .0001 \)).

Peripheral arterial oxygen saturation was different between conditions (\( P < .002 \)), with HYPER (75 ± 1%) significantly less than EU (79 ± 3%) and HYPO (80 ± 3%) during all exercise time points (\( P < .001 \)). Derivatives of Sp\textsubscript{O2}, such as hypoxic cardiac response and hypoxic ventilator response, were not found to be different between conditions. However, hypoxic ventilator response during the second and third bout of exercise positively correlated with mean LLQ scores (\( r = .510, P = .013; r = .498, P = .016 \), respectively). Minute ventilation during exercise (EU 38.2 ± 4.1; HYPO 40.5 ± 6.2; HYPER 44.4 ± 6.2 L·min\(^{-1}\)) was significantly different (\( P < .027 \)), while other ventilatory markers, such as breathing frequency and tidal volume, showed no difference with hydration.

Urine measures showed pretest differences between conditions (Table). Post-test values for urine specific
Table. Mean ± SD pre and posthydration markers for euhydrated (EU), hypohydrated (HYPO), and hyperhydrated (HYPER) conditions

<table>
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<tr>
<td>Body mass (kg)</td>
<td>89.73 ± 0.6</td>
<td>89.77 ± 1.3^a</td>
<td>102.9 ± 1.9</td>
<td>104.4 ± 1.9</td>
<td>86.91 ± 1.9</td>
<td>87.61 ± 1.9</td>
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<tr>
<td>Body mass loss from baseline (%)</td>
<td>-2.1 ± 0.1</td>
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<tr>
<td>Urine specific gravity</td>
<td>1.003 ± 0.001^†</td>
<td>1.051 ± 0.005</td>
<td>2.062 ± 0.006</td>
<td>2.086 ± 0.006</td>
<td>1.015 ± 0.001</td>
<td>1.013 ± 0.001</td>
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<tr>
<td>Urine osmolality (mosm·kg^-1)</td>
<td>1.10.2 ± 0.1</td>
<td>1.13.4 ± 0.1</td>
<td>2.283 ± 0.014</td>
<td>2.283 ± 0.014</td>
<td>1.10.2 ± 0.1</td>
<td>1.13.4 ± 0.1</td>
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<tr>
<td>Urine color</td>
<td>2.25 ± 0.4</td>
<td>2.25 ± 0.4</td>
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<tr>
<td>Plasma osmolality (mosm·kg^-1)</td>
<td>9.4 ± 0.1</td>
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<td>9.4 ± 0.1</td>
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<tr>
<td>Urine flow (L·h^-1)</td>
<td>0.075 ± 0.001</td>
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<tr>
<td>Sweat rate (L·h^-1)</td>
<td>0.183 ± 0.01</td>
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<tr>
<td>Forced expiratory volume in 1 second (FEV1)</td>
<td>4.84 ± 0.31</td>
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<tr>
<td>Forced vital capacity (FVC)</td>
<td>101.0 ± 0.1</td>
<td>101.0 ± 0.1</td>
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<tr>
<td>Blood oxygen content</td>
<td>94.0 ± 0.1</td>
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<tr>
<td>Hb</td>
<td>13.9 ± 0.2</td>
<td>13.9 ± 0.2</td>
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<tr>
<td>Hct</td>
<td>41.0 ± 0.1</td>
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* Denotes significant difference between conditions.
† Denotes significant difference between pre- and postvalues (P < .05).

Discussion

This study aimed to identify the effects of hydration status on the physiological responses to intermittent exercise under hypoxic conditions. The results clearly show greater physiological strain, hypoxemia, AMS symptoms, and change in feeling states in hydrations above and below EU.

Hyphdration and HYPER showed higher and lower heart rates, respectively, than EU conditions, as has been previously noted.36 Elevated HR during HYPO, as compensation for a decline in end diastolic ventricular volume and thus maintenance of cardiac output,37 was only notably different between conditions at rest. This may
Figure 2. Heart rate, rectal core temperature, and physiological strain index time course for the 3 hydration conditions. The three 20-minute exercise phases are indicated above the X axis.
be due to a significant decline in HYPER SpO$_2$ during hypoxic exercise, causing significant strain and sympathetic adrenergic response. Consequently, HR would rise to meet oxygen delivery demands, negating the reductions in cardiovascular strain, which was previously noted with HYPER during exercise in hot environments.$^{24}$ In HYPO, a rise in sympathetic activity induced metabolic heat production, while low plasma volume caused peripheral vasoconstriction’s cumulatively increasing heat storage, resulting in HYPO’s producing the greatest rest and exercising core temperatures. This may also be responsible for the HR drift noted in HYPO, while other conditions maintained in a steady state after 10 minutes of exercise. Core temperatures for HYPER were maintained constantly lower than EU or HYPO throughout the test, in response to elevated PV’s promoting vasodilation and enhanced heat dissipation. The general trend for reduced and increased core temperatures has been previously reported with hyperhydration$^{38}$ and hypohydration,$^{39}$ respectively, in all conditions, except hypoxia. From this study, hypoxic exercise seems to have similar detrimental effects as exercise in the heat.$^{40}$ Continual rise in core temperature for all conditions shows an inability to dissipate heat at such intensity in hypoxia, irrespective of hydration state.

Perceptual scales highlight these physiological changes, with rating of perceived exertion raised above EU values for both HYPO and HYPER. In contrast, the thermal sensation scale was not different between conditions, even with constant differences in core temperature of ~0.4°C throughout the trials. Visual analogue scales and AMS symptom scores showed both HYPO and HYPER to elicit similar adverse effects on feeling state and particularly headache, compared with EU. Although initially HYPO induced worse symptoms that continued to develop over the test, HYPER from 60 minutes onwards caused the most severe headache and LLQ scores (Figure 3). Mechanisms behind headache development are not proved here. Yet it is conceivable that this headache may be due to the resultant increase in intracellular fluid and thus cell swelling within the brain, notably increasing 60 to 80 minutes postfluid ingestion. Increases in cerebral arteriole constriction with hypoxic exercise would aggravate cerebral hypoxia, but no differences in ventilation were noted between hydration conditions. It is unclear whether headache severity was exacerbated due to hypoxia, because previous sea level HYPER studies have presented similar findings,$^{24}$ although headaches have not been reported in hyponatremia.$^{41}$ Clearly, mechanisms causing this acute headache are not related to the chronic fluid retention–based AMS pathophysiology that Roach and Hackett$^{19}$ describe. However, it is clear that over drinking while at altitude may induce headache and exacerbate AMS symptoms. Hence, for
diagnosis of AMS, patients should be in an established state of EU, as previously suggested. Peripheral arterial oxygen saturation is thought to be the main predictor of wellness or performance during hypoxia, although hydration differences suggest that it may only be reliable when individuals are in a state of EU.

Suggested fluid intake values of up to 5 L·day\(^{-1}\) seem sensible based on EU exercising sweat rates of 0.6 L·hour found in this study. However, the intake of the 5 L clearly needs to be spread throughout the day in order to maintain a state of EU and optimal fluid balance, which may or may not have a detrimental effect on physiological strain and onset of AMS symptoms when exposed to hypoxia for longer duration.\(^{18}\) The HYPO level used in this study may only replicate the deficits induced over a day. It remains unclear as to whether physiological responses to hypoxia are altered with severity of HYPO or whether a critical HYPO level exists whereby tolerance and performance within hypoxia are significantly reduced from EU values.

This study used a small sample of young physically active adult males who were unrepresentative of the general population. Also, the study did not use a normoxic control to compare the effects of hydration states on normoxic exercise. However, much work\(^{11,35,39}\) has been published in this area, and the sole purpose of the study was to identify the effect of hydration states above and below EU during hypoxic intermittent exercise.

Although AMS tends to occur over a period of hours and may be the result of multifactorial processes, induction of greater physiological strain is only likely to exacerbate AMS symptoms.\(^{43}\) Likewise, overhydration may induce symptoms of headache and gastrointestinal discomfort. This study clearly shows that hydration state above and below EU has detrimental consequences on physiological responses, psychological feeling states, and self-reported AMS symptoms. Correlation of urine measures highlights the ease at which hydration status can be evaluated. Maintaining urine color at ~2, specific gravity <1.015, or osmolality <400 mosm·kg\(^{-1}\) with small but regular fluid intakes should reduce the physiological strain during acute hypoxic exposure. Furthermore, well-controlled research using a greater sample size is required to ascertain whether hydration state is influential over a chronic exposure. The mechanistic association between HYPO and hypoxia also needs further exploration.

References

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