Original articles

Effect of hypercapnia on spleen-related haemoglobin increase during apnea

Matt X Richardson, Harald K Engan, Angelica Lodin-Sundström and Erika Schagatay

Abstract

(Richardson MX, Engan HK, Lodin-Sundström A, Schagatay E. Effect of hypercapnia on spleen-related haemoglobin increase during apnea. *Diving Hyperb Med*. 2012;42(1):4-9.)

Background: Splenic contraction associated with apnea causes increased haemoglobin concentration and haematocrit (Hct), an effect that may promote prolonged breath-holding. Hypoxia has been shown to augment this effect, but hypercapnic influences have not been investigated previously.

Methods: Eight non-divers performed three series of apneas on separate days after inspiration of oxygen with different carbon dioxide (CO_2) levels. Each series consisted of three apneas 2 minutes apart: one with pre-breathing of 5% CO_2 in oxygen (O_2, 'Hypercapnia'); one with pre-breathing of 100% O_2 ('Normocapnia'); and one with hyperventilation of 100% O_2 ('Hypocapnia'). The apnea durations were repeated identically in all trials, determined from the maximum duration attained in the CO_2 trial. A fourth trial, breathing 5 % CO_2 in O_2 for the same duration as these apneas was also performed ('Eupneic hypercapnia'). In three subjects, spleen size was measured using ultrasonic imaging.

Results: Haemoglobin concentration increased by 4% after apneas in the 'Hypercapnia' trial ($P = 0.002$) and by 3% in the 'Normocapnia' trial ($P = 0.011$), while the 'Hypocapnia' and 'Eupneic hypercapnia' trials showed no changes. The 'easy' phase of apnea, i.e., the period without involuntary breathing movements, was longest in the 'Hypocapnia' trial and shortest in the 'Hypercapnia' trial. A decrease in spleen size was evident in the hypercapnic trial, whereas in the hypocapnia trial spleen size increased, while only minor changes occurred in the other trials. No differences were observed between trials in the cardiovascular diving response.

Conclusion: There appears to be a dose-response effect of CO_2 on triggering splenic contraction during apnea in the absence of hypoxia.

Key words

Breath-hold diving, carbon dioxide, hypercapnia, haematology, respiration, physiology

Introduction

Apneic diving is associated with several physiological adjustments in order to maintain brain and heart function during interrupted gas exchange with the environment, the best described of which is the cardiovascular 'diving response' consisting of bradycardia and peripheral vasoconstriction.[1] The human diving response has been found to be oxygen-conserving, likely owing to both the reliance of non-perfused areas on anaerobic metabolism, and to the bradycardia, limiting the oxygen demand of the myocardium.[2,3] The diving response is initiated by apnea and may be modified by face immersion and possibly by chemoreceptor input.[4,5]

Recent work suggests that splenic contraction may also be a protective response which serves to increase body gas storage capacity by elevating circulating red cell mass.[6,7] Increases in haemoglobin concentration (Hb) and haematocrit (Hct) have been demonstrated during both single and repeated apneas performed within short intervals.[7–9] The increases in Hb and Hct are related to contraction of the spleen, an effect that is maximised after three to five apneas and reversed within 8–9 minutes after cessation of the series of apneas.[6,7,10] These changes may increase oxygen-carrying capacity and carbon dioxide (CO_2) buffering during apnea and have been shown to prolong breath-hold time across a series of apneas.[7]

The correlation between changes in Hb and Hct and splenic contraction is strong, and it is estimated that approximately 60% of the change in these parameters during apnea can be directly attributed to the emptying of the spleen's stored contents.[7,11] This response does not appear to be affected by face immersion, which makes it different to the cardiovascular diving response, which is fortified by face immersion.[12,13] It has been shown that the magnitude of the spleen-related Hb increase is augmented by hypoxia,[14] but there may be other apnea-related components that cause some contraction even in the absence of hypoxia. Of these, hypercapnia is a strong candidate as it is a largely unavoidable consequence of cessation of breathing.[14] In a recent study, we found that apnea or hypoxic breathing resulted in different levels of splenic contraction despite similar levels of arterial oxygen saturation (S_aO_2), with the response to apnea being twice that of hypoxia breathing.[15] One explanation for this could be the high partial pressure of carbon dioxide (P_aCO_2) arising from apnea, but other apnea-

induced mechanisms could also be involved. It remains to be tested whether P_aCO_2 has a separate initiation or modifying effect on splenic contraction.

Previous research shows that reaching a threshold level of CO_2 initiates both the 'struggle phase', defined as the onset of involuntary breathing movements, and the end point of apnea, at least in novice apnea subjects.[16] Therefore, hyperventilation can prolong apneic duration by reducing the CO_2 content of the tissues and blood, so that the breaking point of apnea is reached later, which is beneficial for the diver when sufficient O_2 exists. However, if CO_2 has a role in inducing spleen contraction, hyperventilation could prevent the development of this apnea-prolonging response. In order to reveal the separate role of the P_aCO_2 stimulus we examined changes in haematological parameters and splenic volume during apneas conducted at varying P_aCO_2 levels without the influence of hypoxia.

Methods

SUBJECTS

Four male and four female subjects of mean (SD) age 28 (7) years, weight 78 (19) kg and height 176 (11) cm volunteered for the study. Mean vital capacity for the subjects was 5.0 (1.0) L. Subjects signed a consent form after being informed of the experimental protocol, which was in accordance with the Declaration of Helsinki and had been approved by the regional human research ethics board at Umeå University, Sweden. All were non-smokers although one subject used snuff. Subjects were involved in physical exercise for an average of 2.9 (2.7) h per week for general fitness. Subjects had only limited lifetime experience in breath-holding, with no current activity.

EXPERIMENTAL PROCEDURE

The subjects completed four experimental trials spaced by at least 24 hours. Each trial consisted of three apneas spaced by 2 minutes of rest. Hypoxia was eliminated by O_2 breathing and apnea times held constant in all tests allowing the capnic influence to vary independently. In order to reveal any effect of hypercapnia without apnea, a fourth test using eupneic hypercapnia was included. The individual apneic times produced in the hypercapnia trial were repeated in the following trials, which were performed in a randomised order. The four trials were thus:

- Three maximal apneas after first breathing 100% O_2 for 90 s and then 5% CO_2 in O_2 for 30 s ('Hypercapnia');
- Three fixed duration apneas after breathing 100% O_2 at a normal rate for 120 s ('Normocapnia');
- Three fixed duration apneas after first breathing 100% O_2 at a normal rate for 90 s and then 30 s hyperventilation on O_2 ('Hypocapnia');
- Breathing of 100% O_2 at a normal rate for 90 s, breathing 5% CO_2 in O_2 for 30 s and subsequently for a similar period as the apneas in the other trials ('Eupneic hypercapnia').

Subjects were unaware of which gas was being inspired at which time and during which trial.

Subjects reported to the laboratory fasted and without caffeine for at least 2 hours prior to testing. Vital capacity was measured via a spirometer (Compact II, Vitalograph, Buckingham, England) and an intravenous catheter was placed in the antecubital region using sterile technique.

Subjects lay prone for the duration of the trials, beginning with a 20-minute period of prone horizontal rest. A nose clip was placed prior to the first 2-minute countdown and remained in place until 2 minutes after the final apnea. Subjects were administered a normal-fitting mask for breathing the gas mixtures with a flow rate of approximately 10 L min^{-1} during the 2-min countdown periods. At the end of the countdown, the subject was instructed to exhale fully, followed by a deep but not maximal inspiration and begin the apnea. In previous studies, recordings of inspiratory volume after this instruction have documented lung filling to approximately 85% of vital capacity with low inter- and intra-individual variance.[16] Subjects were instructed to avoid hyperventilation, with the exception of the final 30 s of the countdowns in the 'Hypocapnia' trial. Upon completion of the apnea, subjects expired fully into the mask and then resumed normal breathing. In the 'Hypercapnia' trial, apneas were conducted to maximum duration without time cues. In the three time-limited trials, subjects terminated apneas after a 5 s countdown.

Blood samples (2 ml) were taken via the intravenous catheter 2 min before the first apnea, immediately after the first and third apneas and 10 min after the third apnea. Waste samples of 1–2 ml preceded each blood sample and the catheter was rinsed with 2 ml saline following each sample. The total volume of blood (including waste volume) removed from each subject was approximately 15 ml, and the injected saline was approximately 12 ml. Blood samples were analysed for Hb via an automated blood analysis unit (Micros 60 Analyzer, ABX Diagnostics, Montpellier, France).

From 2 min prior to each apnea until 2 min post-apnea, the following parameters were measured continuously: arterial haemoglobin saturation (SaO_2) and heart rate (HR) via a finger pulse oximeter (Biox 3700e, Ohmeda, Madison, WI, USA), mean arterial pressure (MAP) via continuous finger plethysmography (Finapres 2300, Ohmeda, Madison, WI, USA), skin blood flow (SkBF) via laser-Doppler (Periflux System 5000, Perimed, Järfälla, Sweden) on the thumb, and breathing movements via a laboratory-developed pneumatic chest bellows. Breath-by-breath CO_2 was measured before and after each apnea via a Normocap Oxy™ gas analyser, (Datex-Ohmeda, Helsinki, Finland). Data were stored via a BioPac MH100A CE multi-channel data acquisition system

(BioPac Systems Inc., Goleta, CA, USA). The continuous monitoring of the cardiovascular parameters was done to detect the diving response and for safety.

SaO_2 values from the 30 s after each apnea were analysed to determine if any desaturation occurred as a result of apnea, and compared to both control and end-apneic SaO_2 values. Expired CO_2 percentages from the first breath following each apnea (and prior to gas mixture inhalation) were compared between trials. Apneas were divided into an 'easy' phase (prior to the onset of involuntary breathing movements) and a 'struggle phase' (with involuntary breathing movements), and durations compared between trials.[17]

SPLEEN MEASUREMENTS

Three subjects had triaxial measurement of spleen size using ultrasonic imaging (Mindray DP-6600, Shenzhen Mindray Bio-Medical Electronics Compan Ltd, Shenzhen, China) simultaneously with all blood-sampling occasions, for all four trials. Measurements of the maximal diameters of spleen length (L), width (W) and thickness (T) were used to calculate spleen volume according to the Pilström equation:[10]

$$L\ \pi\ (WT\text{-}T^2)/3$$

Splenic volumes after the first and third apnea were compared to the pre-apnea volume and with the 10-minute post-apneic measurement. The ultrasonic imaging technique was not available during the initiation of the study, and so only three subjects were measured.

STATISTICAL ANALYSIS

The Hb values obtained 2 min before the first apnea were used as the control. Mean percentage changes from control were used to compare changes within each trial, and pooled mean changes from apneas were used to compare between trials. Subjects served as their own controls, and effects were expressed as percentage changes from control. All variables were log-transformed before analysis to reduce non-uniformity of error. Excel™ templates were used for the calculations, purpose-designed for analyses using physiological data.[18] Comparisons were done using Student's t-tests with a level for acceptance of significant changes set at $P < 0.05$. A Bonferroni correction was then applied for multiple comparisons and significance was accepted at the respective calculated α level from the correction.

Results are reported as mean (SD) for point values, and as mean (90% confidence intervals, CI) for comparisons. One subject's blood values were lost for the normocapnic trial due to catheter failure, so this subject's data were not included in the blood analyses for this trial. The 'missing' subject was included in the analysis of the remaining trials because the loss of one subject is compensated by a reduction of the degrees of freedom in the calculations. As spleen measurements were obtained from only three subjects, these data are reported without statistical analysis.

Results

DURATION OF APNEA

All subjects successfully repeated the following apnea times (SD) in all trials: 216 (68) s for apnea 1, 222 (80) s for apnea 2, and 245 (55) s for apnea 3. There was a trend ($P = 0.07$) towards prolonged apneic duration from the first to the third apnea. The 'easy' phase of the apneas was shortest in the 'Hypercapnic' trial at 90 (27) s, followed by the 'Normocapnic' trial at 103 (47) s and longest in the 'Hypocapnic' trial at 132 (43) s. The 'easy' phase was significantly longer in the 'Hypocapnic' trial than in the 'Hypercapnic' trial ($P = 0.012$). There were no significant differences in the 'struggle phase' duration: 'Hypercapnic' trial 134 (38) s; 'Hypocapnic' trial 118 (44) s and the 'Normocapnic' trial 112 (48) s.

ARTERIAL HAEMOGLOBIN SATURATION

Mean control values for SaO_2 were above 98% for all trials, and SaO_2 did not change from control levels during any of the apneas, or during post-apneic periods. There were no differences between trials.

HAEMOGLOBIN CONCENTRATION

Baseline values of Hb before the apneas were the same for all conditions. After the first apnea, Hb had increased in the

Figure 1
Changes in mean (SD) Hb from baseline after apnea 1 (A1), after apnea 3 (A3), and 10 minutes following A3. * $P = 0.024$ in 'Hypercapnia', $P = 0.015$ in 'Normocapnia' and ** $P = 0.002$ in 'Hypercapnia', $P = 0.011$ in 'Normocapnia'; for comparisons with control, $n = 7$ for 'Eupneic hypercapnic' trial, $n = 8$ for all other trials

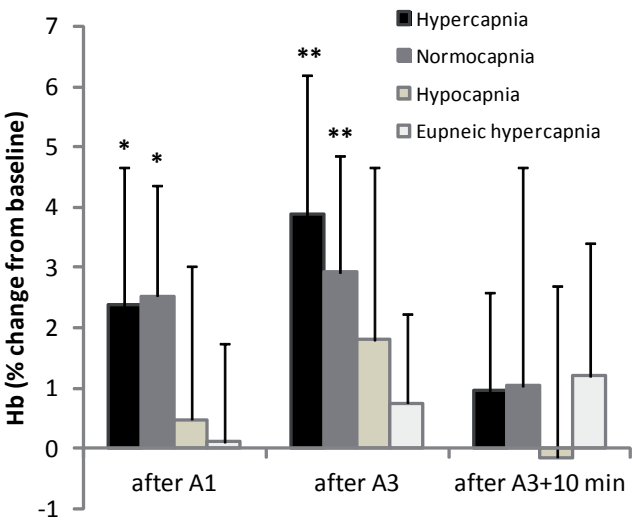
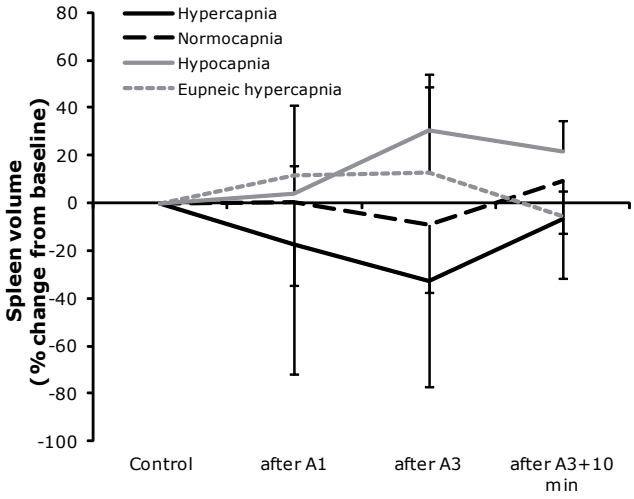


Figure 2
Changes in splenic volume from baseline after apnea 1, after apnea 3 and 10 minutes following apnea 3; mean (SD) values from three subjects



'Hypercapnic' (P = 0.024) and 'Normocapnic' (P = 0.015) trials, while the 'Hypocapnic' and 'Eupneic hypercapnic' trials were similar to control values (Figure 1). After the final apnea, Hb had further increased in the 'Hypercapnic' trial, to 4% above baseline (P = 0.002), and by 3 % in the 'Normocapnic' trial (P = 0.011), while the 'Hypocapnic' and 'Eupneic hypercapnic' trials showed no significant changes. Ten minutes after apneas, Hb values were not different from control values for any of the trials, nor were they different among trials. A comparison of the magnitude of change from baseline revealed no significant difference between trials.

SPLENIC VOLUME

The largest reduction in splenic volume after apnea 3 was seen in the 'Hypercapnia' trial, at -33% from control, followed by the 'Normocapnia' trial at -9% from control (Figure 2). The 'Hypocapnia' and 'Eupneic hypercapnia' trials resulted in increases in spleen size of 30% and 13% from control respectively. Ten minutes following the final apnea, spleen volume tended to be restored in all trials.

CARDIOVASCULAR PARAMETERS

Mean HR and SkBF, two main parameters of the cardiovascular diving response, did not deviate from control values or between trials. MAP was not different between trials, but increased from control in all apnea trials: by 35% in the 'Hypercapnia' trial (P = 0.0012), 15% in the 'Normocapnia trial' (P = 0.06) and by 23% in the 'Hypocapnia' trial (P = 0.034). MAP remained unchanged during the 'Eupneic hypercapnia' trial.

END-TIDAL CARBON DIOXIDE

Post-apneic expired CO_2 was greatest in the 'Hypercapnia' trial at 7.6 (1.3)%, followed by the 'Normocapnia' trial at 7.4 (1.8)%, and the 'Hypocapnia' trial at 7.0 (1.5)%. In the 'Eupneic hypercapnia' trial, the expired CO_2 level following the breathing period equivalent to the apneic duration was 4.6 (1.0)%. Expired CO_2 in the 'Hypercapnia' trial was higher than in the 'Hypocapnia' trial (P = 0.029), and CO_2 in the 'Eupneic hypercapnia' trial was lower than in all other trials ('Hypercapnia' P = 0.001; 'Normocapnia' P = 0.001; 'Hypocapnia' P = 0.001).

Discussion

In the absence of hypoxia ($SaO_2 \geq 98\%$ in all trials), temporary increases in Hb across a series of apneas were greatest in trials with an increased hypercapnic stimulus, suggesting a role for hypercapnia in the elicitation of splenic contraction. The three subjects studied with ultrasound also demonstrated a greater degree of splenic contraction with increased hypercapnic stimulus. This could explain why apnea causes more splenic contraction than that seen with eupneic hypoxia despite similar resulting levels of SaO_2.[15]

A role of the apnea stimulus per se is supported by the lack of response in the 'Eupneic hypercapnia' trial. A greater stepwise influence of CO_2 was also apparent in the relative division of the 'easy' and 'struggle' phases during apnea, where the 'Hypercapnia' trial had the shortest 'easy' phase and the 'Hypocapnia' trial had the longest, further confirming a 'pre-loading' effect of CO_2. Expired post-apnea CO_2 concentrations also indicated a similar, residual stepwise pattern of systemic CO_2 concentration. The lack of change in SaO_2 levels throughout the trials demonstrates that hypercapnia acts as an independent stimulus for splenic contraction during apnea.

The study cannot elucidate the neural or hormonal mechanisms underlying this response. However, the impact of inspired gas concentration just prior to apnea on splenic contraction is likely to be mediated via both central medullary and peripheral carotid body chemoreceptors for CO_2 and O_2 respectively since changes in alveolar CO_2 are reflected in brain extracellular fluid pH over a time course consistent with circulation time, i.e., a few seconds.[19] Nevertheless, there are some 'crossover' effects whereby peripheral receptors respond to CO_2, and hypoxia affects central chemoreception via alterations in cerebral blood flow.[20,21] In most individuals, hyperoxia (PO_2 = 150 mmHg) effectively silences the peripheral response to CO_2.[22,23] Therefore, the likely prevention of significant peripheral chemoreceptor input, because of the sustained normoxia in our protocol, makes it likely that the chemoreceptive stimulus created by CO_2 alone is sufficient to elicit a stimulus leading to splenic contraction during apnea.

Although the mechanisms leading to splenic contraction are, as yet, only partially defined, they almost certainly involve sympathetic innervation. The splenic nerve is mainly adrenergic in composition, and has been shown to respond powerfully to sympathetic discharge and related adrenergic output.[24–26] Hoka and associates also noted marked changes in blood volume following hypercapnia in spleen-intact dogs, whereas this response was considerably decreased in splenectomised dogs.[27] Similar sympathetic activity on the part of the splenic nerve in humans is likely. Bradycardia, a main component of the cardiovascular diving response, was not significant in any trial nor different between trials, suggesting that variations in CO_2 levels do not affect this response. This also illustrates the independent elicitation of the splenic response, in accordance with previous findings.[28]

Both hypoxia and hypercapnia develop upon cessation of breathing, and splenic contraction-induced blood boosting may counteract, to some degree, these effects. Breath-hold divers would likely benefit from a strong splenic contraction, as the increase in circulating Hb would result in increased oxygen storage capacity, increased CO_2 buffering capacity and a speedier recovery from hypoxia between apneas, especially when these haematological effects remain across several minutes between dives, whereas the cardiovascular diving response reverses rapidly.[28] Based on the observations in this study, an increased capnic stimulus during apnea may elicit a stronger or earlier spleen response and subsequent Hb increase than apnea preceded by hyperventilation.

A direction for further research could be to focus on whether there is a true dose-response relationship between arterial CO_2 content and the splenic contraction response, as appears possible from this study. It would also be of interest to compare the individual splenic responses to elevated CO_2 concentration of competition divers who employ hyperventilation during 'warm-up' and divers without 'warm-up' practices before competition.[29]

Conclusions

The enhanced spleen-induced increase in Hb during normoxic hypercapnia suggests a role of hypercapnia as a trigger for splenic contraction during apnea. A separate role of the apnea stimulus is suggested by the lack of response in the 'Eupneic hypercapnia' trial.

Acknowledgements

We thank our subjects for participating in these studies, and the temporary co-worker Robert de Bruijn for valuable help during experiments. The study complies with Swedish laws and ethical standards and was financed by the Swedish National Centre for Research in Sports (CIF), and Mid Sweden University.

References

1 Gooden BA. Mechanisms of the human diving response. *Integr Physiol Behav Sci*. 1994;29;6-16.
2 Andersson J, Schagatay E. Arterial oxygen desaturation during apneas in humans. *Undersea Hyperb Med.* 1998;25:21-5.
3 Schagatay E, Andersson J. Diving response and apneic time in humans. *Undersea Hyperb Med*. 1998;25:13-9.
4 Schuitema K, Holm B. The role of different facial areas in eliciting human diving bradycardia. *Acta Physiol Scand*. 1988;132:119-20.
5 Lin YC, Shida KK, Hong SK. Effects of hypercapnia, hypoxia, and rebreathing on heart rate response during apnea. *J Appl Physiol*. 1983;54:166-71.
6 Hurford WE, Hong SK, Park YS, Ahn DW, Shiraki K, Mohri M, et al. Splenic contraction during breath-hold diving in the Korean Ama. *J Appl Physiol.* 1990;69:932-6.
7 Schagatay E, Andersson JPA, Hallén M, Pålsson B. Selected contribution: role of spleen emptying in prolonging apneas in humans. *J Appl Physiol*. 2000;90:1623-9.
8 Espersen K, Frandsen H, Lorentzen T, Kanstrup I-L, Christensen NJ. The human spleen as an erythrocyte reservoir in diving-related interventions. *J Appl Physiol*. 2002;92:2071-9.
9 Bakovic D, Eterovic D, Saratlija-Novakovic Z, Palada I, Valic Z, Bilopavlovic N, et al. Effect of human splenic contraction on variation in circulating blood cell counts. *Clin Exp Pharmacol Physiol*. 2005;32:944-51.
10 Schagatay E, Haughey H, Reimers J. Speed of spleen volume changes evoked by serial apneas. *Eur J Appl Physiol*. 2005;93:447-52.
11 Richardson MX, Lodin A, Reimers J, Schagatay E. Short-term effects of normobaric hypoxia on the human spleen. *Eur J Appl Physiol*. 2007;104:395-9.
12 Schagatay E, Andersson J, Nielsen B. Hematological response and diving response during apnea and apnea with face immersion. *Eur J Appl Physiol*. 2007;101:125-32.
13 Andersson JP, Liner MH, Runow E, Schagatay EK. Diving response and arterial oxygen saturation during apnea and exercise in breath-hold divers. *J Appl Physiol*. 2002;93:882-6.
14 Richardson MX, de Bruijn R, Schagatay E. Hypoxia augments apnea-induced increase in haemoglobin concentration and hematocrit. *Eur J Appl Physiol*. 2009;105:63-8.
15 Lodin-Sundström A, Schagatay E. Spleen contraction during 20 min normobaric hypoxia and 2 min apnea in humans. *Aviat Space Environ Med*. 2010;81:545-9.
16 Schagatay E. *The human diving response: effects of temperature and training* (dissertation). Lund, Sweden: Lund University; 1996.
17 Moore TO, Hong SK. Physiological and conventional breath-hold breaking points. *J Appl Physiol*. 1974;37:291-6.
18 Hopkins W. *A new view of statistics*. Available from: Internet Society for Sport Science http://www.sportsci.org/resource/stats/
19 Ahmad HR, Loeschcke HH. Fast bicarbonate-chloride exchange between plasma and brain extracellular fluid at maintained PCO_2. *Pflugers Arch.* 1982;395:300-5.
20 Poulin MJ, Liang PJ, Robbins PA. Dynamics of the cerebral blood flow response to step changes in end-tidal PCO_2 and PO_2 in humans. *J Appl Physiol*. 1996;81:1084-95.
21 Vovk A, Cunningham DA, Kowalchuk JM, Paterson DH, Duffin J. Cerebral blood flow responses to changes in oxygen

and carbon dioxide in humans. *Can J Physiol Pharmacol*. 2002;80:819-27.
22 Lloyd BB, Jukes MG, Cunningham DJ. The relation between alveolar oxygen pressure and the respiratory response to carbon dioxide in man. *Q J Exp Physiol Cogn Med Sci*. 1958;43:214-27.
23 Mohan R, Duffin J. The effect of hypoxia on the ventilatory response to carbon dioxide in man. *Respir Physiol*. 1997;108:101-15.
24 Ayers AB, Davies BN, Withrington PG. Responses of the isolated, perfused human spleen to sympathetic nerve stimulation, catecholamines and polypeptides. *Br J Pharmacol*. 1972;44:17-30.
25 Davies BN, Powis DA, Withrington PG. The differential effect of cooling on the responses of splenic capsular and vascular smooth muscle to nerve stimulation and noradrenaline. *Pflugers Archiv*. 1978;377:87-94.
26 Herman NL, Kostreva DR, Kampine JP. Splenic afferents and some of their reflex responses. *Am J Physiol. Regul Integr Comp Physiol*. 1982;242:R247-54.
27 Hoka S, Arimura H, Bosnjak ZJ, Kampine JP. Regional venous outflow, blood volume, and sympathetic nerve activity during hypercapnia and hypoxic hypercapnia. *Can J Physiol Pharmacol*. 1970;70:1032-9.
28 Schagatay E, Andersson JP, Nielsen B. Hematologial response and diving response during apnea and apnea with face immersion. *Eur J Appl Physiol*. 2007;101:125-32.
29 Schagatay E. Predicting performance in competitive apnea diving. Part II: dynamic apnea. *Diving Hyperb Med*. 2010;40:11-22.

Submitted: 08 April 2011
Accepted: 18 October 2011

Matt X Richardson, PhD, Harald K Engan, MSc, Angelica Lodin-Sundström, MSc, Erika Schagatay, PhD,
Environmental Physiology Group, Department of Engineering and Sustainable Development, Mid Sweden University, Östersund, Sweden.
Professor Schagatay also works at the National Winter Sports Research Centre, Östersund, Sweden.

Address for correspondence:
Harald K Engan
Environmental Physiology Group, Mid Sweden University
Department of Engineering and Sustainable Development
Akademigatan 1, SE 831 25
Östersund, Sweden.
Phone: *+47-(0)73-558954*
Fax: *+46-(0)63-165700*
E-mail*: <Harald.Engan@miun.se>*