Cerebrovascular reactivity to hypercapnia is unimpaired in breath hold divers

Vladimir Ivancev1, Ivan Palada1, Zoran Valic1, Ante Obad1, Daria Bakovic1, Niki M. Dietz2, Michael J. Joyner2 and Zeljko Dujic1

1Department of Physiology, University of Split School of Medicine, Split, Croatia
2Department of Anaesthesiology, Mayo Clinic College of Medicine, Rochester, MN, USA

Hypercapnic cerebrovascular reactivity is decreased in obstructive sleep apnoea and congestive heart disease perhaps as a result of repeated apnoeas. To test the hypothesis that repeated apnoeas blunt cerebrovascular reactivity to hypercapnia, we studied breath hold divers and determined cerebrovascular reactivity by measuring changes in middle cerebral artery velocity (MCAV, cm s−1) per mmHg change in end-tidal partial pressure of CO2 (PET,CO2) in response to two hyperoxic hypercapnia rebreathing manoeuvres (modified Read protocol) in elite breath-hold divers (BHD, n = 7) and non-divers (ND, n = 7). In addition, ventilation and central (beat-to-beat stroke volume measurement with Modelflow technique) haemodynamics were determined. Ventilatory responses to hypercapnia were blunted in BHD versus ND largely due to lower breathing frequency. Cerebrovascular reactivity did not differ between groups (3.7 ± 1.4 versus 3.4 ± 1.3% mmHg−1 PET,CO2 in BHD and ND, respectively; P = 0.90) and the same was found for cerebral vascular resistance and MCAV recovery to baseline after termination of the CO2 challenge. Cardiovascular parameters were not changed significantly during rebreathing in either group, except for a small increase in mean arterial pressure for both groups. Our findings indicate that the regulation of the cerebral circulation in response to hypercapnia is intact in elite breath-hold divers, potentially as a protective mechanism against the chronic intermittent cerebral hypoxia and/or hypercapnia that occurs during breath-hold diving. These data also suggest that factors other than repeated apnoeas contribute to the blunting of cerebrovascular reactivity in conditions like sleep apnoea.

(Received 24 January 2007; accepted after revision 4 April 2007; first published online 5 April 2007)

Corresponding author Z. Dujic: Department of Physiology, University of Split School of Medicine, Soltanska 2, 21000 Split, Croatia. Email: zdujic@bsb.mefst.hr

Elite breath-hold divers are able to sustain breath-holds in spite of significant hypercapnia and hypoxia. During descent and at the nadir of field dives breath-hold divers are faced with hyperoxic hypercapnia, due to increased ambient hydrostatic pressure (Liner et al. 1993; Ferretti, 2001). The largest danger of hypoxia occurs during the last portion of the dive or immediately after surfacing due to rapid reduction in the hydrostatic pressure and oxygen consumption during the dive. By contrast, breath-hold divers are exposed to hypercapnia during most of the dive. Ventilatory responses to hypercapnia are generally reduced in assisted-diving Ama (Masuda et al. 1982), underwater hockey players (Davis et al. 1987), Royal Navy divers (Florio et al. 1979), elite breath-hold divers (Grassi et al. 1994) and in trained divers (Delapille et al. 2001), although in some studies normal responses have been seen (Masuda et al. 1981; Bjurstrom & Schoene, 1987). These differences in ventilatory response to CO2 may be due to differences in chemical stimuli (hypoxic hypercapnia versus hyperoxic hypercapnia), sex differences (e.g. progesterone-induced hyperventilation in the postovulatory phase) or methods for investigating chemosensitivity (ramp versus steady-state protocols). However, as a whole they are consistent with the idea that repeated exposure to hypercapnia blunts the ventilatory response to CO2.

Blunted ventilatory responses to hypoxia and hypercapnia have also been reported in obstructive sleep apnoea (OSA) patients (Garcia-Rio et al. 2002), since these patients may experience recurrent episodes of obstruction of airflow during sleep resulting in significant hypercapnia and arterial desaturation. Intermittent hypoxia and hypercapnia during obstructive episodes may alter autonomic function with chronically increased
Table 1. Anthropometric characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>Breath hold divers (BHD)</th>
<th>Non-divers (ND)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 7)</td>
<td>(n = 7)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>29.7 (6.3)</td>
<td>31.4 (2.8)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>188 (8.5)</td>
<td>182.6 (8.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>92.4 (14.3)</td>
<td>86.9 (13.1)</td>
</tr>
<tr>
<td>BMI</td>
<td>26.1 (3.4)</td>
<td>26.1 (3.5)</td>
</tr>
<tr>
<td>Body fat index (%, body fat/kg)</td>
<td>18.8 (8.3)</td>
<td>19.9 (6.1)</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>111.9 (18.1)</td>
<td>97.2 (9.3)</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
<td>118.4 (19.6)</td>
<td>102.7 (13.0)</td>
</tr>
<tr>
<td>Duration of breath-hold diving (years)</td>
<td>7 (4)</td>
<td>—</td>
</tr>
<tr>
<td>PB depth constant weight (meters)</td>
<td>34 (6)</td>
<td>—</td>
</tr>
<tr>
<td>PB static breath-hold (seconds)</td>
<td>284 (34)</td>
<td>—</td>
</tr>
</tbody>
</table>

Values are means (s.d.); BMI, body mass index; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; PB, personal best.

daytime sympathetic efferent nerve activity (Spicuzza et al. 2003) causing systemic hypertension due to increased total peripheral resistance (Wolk & Somers, 2003).

Daytime hypercapnic cerebrovascular reactivity is impaired in OSA (Placidi et al. 1998; Diomedi et al. 1998; Loepky et al. 1984; Qureshi et al. 1999) and congestive heart disease (Georgiadis et al. 2000), whereas morning (Ameriso et al. 1994; Meadows et al. 2005) and sleep (Meadows et al. 2003) attenuation to hypercapnia was reported even in healthy subjects. In these subjects, the morning cardiovascular response to hypoxia was intact (Meadows et al. 2005). Following continuous positive airway pressure (CPAP) treatment in OSA patients, cerebrovascular reactivity to hypercapnia was normalized (Diomedi et al. 1998). Since the ventilatory response to hypercapnia is blunted in both OSA patients and breath-hold divers, and because both groups undergo periods of repeated apnoeas, we reasoned that cerebrovascular reactivity might also be blunted in apnoea divers. However, breath-hold divers may not fully model OSA patients due to differences in duration, frequency (shorter and more frequent apnoeas in OSA) and type (end-expiratory in OSA versus end-inspiratory in divers) of apnoeas. However, apnoea divers might also have normal cerebrovascular reactivity as an adaptive response and the protective mechanism against intermittent hypercapnia and hypoxia. Finally, OSA patients frequently have other coexisting conditions that might also influence vascular reactivity in comparison to breath hold divers who are robustly healthy. Thus, the present study aimed to test the hypothesis that breath-hold divers have unchanged cerebrovascular reactivity to hypercapnia. By testing this hypothesis we hoped to gain insight into the role of repeated bouts of hypercapnia on cerebrovascular reactivity in the absence of coexisting disease, as a first step in understanding factors that might contribute to the blunted cerebrovascular reactivity to hypercapnia in sleep apnoea.

Methods

Subjects

All experimental procedures in this study were performed in accordance with the Declaration of Helsinki and were approved by the ethical committee of the University of Split School of Medicine. Each method and potential risks were explained to the participants in detail and they gave their written informed consent before the experiment. The anthropometric, lung function data and breath-hold diving history of the study subjects are shown in Table 1.

Protocol

All experiments were carried out in the acclimatized environment in the morning hours with constant temperature and humidity. Participants were instructed not to eat anything at least 4 h before the arrival to laboratory. They were directed to arrive to the laboratory 30 min before the start of the experiment for acclimatization and detailed explanation of the procedures. In each subject we measured height, weight and skinfolds (Harpenden skinfold caliper, England), from which we calculated body fat index, and inquired about diving history. We carried out dynamic spirometry (Quark PFT, Cosmed, Rome, Italy) in the upright posture for all subjects. The investigator who analysed the records was blinded to the subject’s status (divers versus controls).

Rebreathing studies

Carbon dioxide (\(\text{CO}_2\)) sensitivity was assessed using a slightly modified rebreathing method as previously described by Read (1967). Subjects were sitting in a comfortable position while breathing from a mouthpiece with a pneumatic one-way valves connected to breath-by-breath respiratory analyser (Quark b²,
Cosmed, Rome, Italy) and spirometer (Harvard apparatus, Student model, Holliston, MA, USA). The spirometer was filled with 6 l from tank containing 5% CO$_2$ and 95% O$_2$ and connected to inspiratory and expiratory lines, thereby completing rebreathing circuit. Ventilation was continuously (breath-by-breath) measured by analysis of breathing frequency ($B_t$), tidal volume ($V_T$), and ventilation ($V_e$). Subjects were breathing room air normally and quietly at rest for 2 min on the mouthpiece. They were then switched to the spirometer and asked to proceed with normal breathing. End tidal CO$_2$ ($P_{ET,CO_2}$) was measured using an infrared analyser (Poet II, Criticare Systems, Waukesha, WI, USA). The rebreathing protocol lasted until $P_{ET,CO_2}$ values reached 60 mmHg. Each subject performed two rebreathing tests with a recovery period of 15 min between them. The period between successive periods of rebreathing permitted stabilization of cardiovascular parameters.

**Cerebral blood flow measurements**

Cerebral blood flow was estimated by a 2 MHz transcranial Doppler ultrasound probe (Transcranial Doppler, Neurovision System, Multigon, Yonkers, NY, USA) fixed over temporal window to insonate the middle cerebral artery (MCA). The Doppler probe was secured with a headband device (Multigon) to maintain optimal insonation position and angle throughout the protocol. The right MCA velocity (MCAV) was monitored because it was more accessible within our laboratory arrangement. Previous studies have shown no systematic differences in MCAV measured from the right or left sides by use of similar methodology (Klingelhofer et al. 1992; Netzer et al. 1998). Optimization of the Doppler signals from the MCA was performed by varying the sample volume depth in incremental steps and at each depth, varying the angle of insonance to obtain the best-quality signals from the Doppler frequency.

**Instrumentation**

**Cardiovascular variables.** We placed the Finometer cuff around middle finger of the non-dominant hand for continuous, non-invasive monitoring of the heart rate (HR) and blood pressure (Finometer, Finapress Medical Systems, Arnhem, Netherlands). The photoplethysmograph has been previously reported to accurately record changes in mean arterial pressure (MAP) during both exercise and apnoea (Andersson et al. 2004). The photoplethysmograph cuff was positioned at heart level and kept at the same level for the duration of the study. Analog signals of blood pressure, heart rate (HR), $P_{ET,CO_2}$, and cerebral blood flow were continuously recorded and stored on a personal computer (Apple eMac PC) using a PowerLab 16S data acquisition system (ADInstruments, Castle Hill, Australia) at a sampling rate of 100 Hz.

**Stroke volume and total peripheral resistance computation.** From the continuous blood pressure measurement, the arterial pulse wave was analysed by a pulse wave analysis method, which computes changes in left ventricular stroke volume (SV) from the pulsatile systolic area. We used the improved method of Wesseling with the Modelflow program (model-based measurement method based on a nonlinear, 3-element model of the input impedance of the aorta) (Jelkoma et al. 1999). In addition to absolute values, CO is expressed as a change from baseline. CO was computed as SV times HR and total peripheral resistance (TPR) was calculated as MAP divided by CO.

**Data analysis**

The time points for cardiovascular and cerebral perfusion variables of interest were the final 30 s of the baseline period. During the rebreathing data were averaged over five heart beats when $P_{ET,CO_2}$ reached 46, 52 and 60 mmHg. A recovery point of interest was rate when MCAV reached baseline value. The MCAV was computed as the integral of the maximal frequency shifts over 1 beat divided by the corresponding beat interval. Cerebrovascular resistance (CVR) was calculated using the equation CVR = MAP/MCAV. Cerebrovascular reactivity was calculated as percentage change of MCAV divided by $P_{ET,CO_2}$ (mmHg) difference from baseline value to the end of rebreathing. The time points for ventilatory variables of interest were the final 30 s of the baseline period. During the rebreathing phase data were averaged over five breaths (first three breaths when $P_{ET,CO_2}$ reached 46, 52 and 60 mmHg, and two breaths before). A recovery point of interest was in time when MCAV reached baseline value.

**Statistical analysis**

Using Statistica 7.0 software (Statsoft, Inc., Tulsa, OK, USA), comparisons between changes of variables from the control value were first tested with non-parametric Friedman analysis of variance (because of the small sample size). In the case of a significant difference, the Wilcoxon sign rank test was applied for the particular comparison. Intergroup comparison between breath-hold divers (BHD) and non-divers (ND) was done with the Mann–Whitney U test. All data are reported in the text as means (s.d.), and the level of significance was $P < 0.05$.

**Results**

All participants successfully completed the study protocol.
ventilation, cardiovascular and cerebrovascular variables

Table 2. Ventilatory, cardiovascular and cerebrovascular variables

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>46 mmHg</th>
<th>52 mmHg</th>
<th>60 mmHg</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_t$ (l min$^{-1}$)</td>
<td>Non-divers 4.15 ± 3.49</td>
<td>18.42 ± 6.56</td>
<td>36.92 ± 10.91$^*$</td>
<td>54.59 ± 16.00$^+$</td>
<td>35.01 ± 8.21$^+$</td>
</tr>
<tr>
<td></td>
<td>Divers 12.86 ± 3.16</td>
<td>14.71 ± 6.59</td>
<td>23.15 ± 10.75$^+$</td>
<td>37.75 ± 15.21$^*$</td>
<td>29.42 ± 4.72$^+$</td>
</tr>
<tr>
<td>$V_t$ (l)</td>
<td>Non-divers 1.15 ± 0.48</td>
<td>1.62 ± 0.71</td>
<td>2.46 ± 0.40$^+$</td>
<td>2.79 ± 0.54$^+$</td>
<td>1.98 ± 0.42$^+$</td>
</tr>
<tr>
<td></td>
<td>Divers 1.28 ± 0.38</td>
<td>1.64 ± 0.51</td>
<td>2.18 ± 0.63$^+$</td>
<td>2.79 ± 0.73$^+$</td>
<td>2.24 ± 0.48$^+$</td>
</tr>
<tr>
<td>$B_t$ (min$^{-1}$)</td>
<td>Non-divers 14.41 ± 6.38</td>
<td>12.69 ± 4.62</td>
<td>15.83 ± 6.04</td>
<td>19.91 ± 6.09$^+$</td>
<td>18.12 ± 3.16$^+$</td>
</tr>
<tr>
<td></td>
<td>Divers 11.00 ± 4.52</td>
<td>9.42 ± 4.17</td>
<td>10.94 ± 4.58</td>
<td>13.88 ± 4.82</td>
<td>13.95 ± 4.18</td>
</tr>
</tbody>
</table>

Cardiovascular variables

- **MAP (mmHg)**
  - Non-divers 91.33 ± 9.94 | 92.60 ± 10.59 | 95.83 ± 9.26$^*$ | 98.46 ± 11.40$^+$ | 88.33 ± 9.90 |
  - Divers 94.24 ± 3.33 | 96.00 ± 3.75$^+$ | 99.38 ± 5.97$^+$ | 106.08 ± 6.28$^+$ | 92.55 ± 4.03 |
- **HR (bpm)**
  - Non-divers 74.41 ± 13.44 | 69.95 ± 12.51 | 70.49 ± 9.20 | 72.01 ± 9.77 | 75.84 ± 18.00 |
  - Divers 74.58 ± 12.40 | 72.73 ± 11.43 | 70.50 ± 10.41 | 77.11 ± 17.08 | 74.32 ± 20.51 |
- **SV (ml min$^{-1}$)**
  - Non-divers 72.66 ± 16.16 | 78.03 ± 16.48$^*$ | 81.18 ± 12.31$^*$ | 85.70 ± 12.57$^*$ | 92.06 ± 12.68 |
  - Divers 74.89 ± 11.5 | 76.63 ± 14.18 | 75.96 ± 14.95 | 77.69 ± 14.87 | 87.93 ± 13.25$^*$ |
- **CO (l min$^{-1}$)**
  - Non-divers 5.26 ± 0.74 | 5.44 ± 1.01 | 5.63 ± 0.79$^+$ | 6.30 ± 1.09$^+$ | 6.90 ± 1.00$^+$ |
  - Divers 5.64 ± 1.33 | 5.66 ± 1.56 | 5.45 ± 1.48 | 6.08 ± 1.97 | 6.98 ± 1.92$^*$ |
- **TPR (MU)**
  - Non-divers 1.30 ± 0.24 | 1.31 ± 0.31 | 1.31 ± 0.22 | 1.25 ± 0.29 | 0.98 ± 0.19$^+$ |
  - Divers 1.26 ± 0.29 | 1.29 ± 0.30 | 1.38 ± 0.34$^+$ | 1.39 ± 0.37$^+$ | 1.02 ± 0.31$^+$ |

Cerebrovascular variables

- **MCAV (cm s$^{-1}$)**
  - Non-divers 52.52 ± 11.84 | 63.56 ± 12.48$^*$ | 77.67 ± 17.21$^*$ | 86.45 ± 16.02$^+$ | 52.71 ± 11.99 |
  - Divers 52.81 ± 11.53 | 62.68 ± 16.16$^*$ | 75.08 ± 16.16$^*$ | 90.52 ± 18.63$^+$ | 53.73 ± 13.73 |
- **Time (s)**
  - Non-divers — — — — 43 ± 20 |
  - Divers — — — — 36 ± 7 |
- **CVR (mmHg cm$^{-5}$)**
  - Non-divers 1.81 ± 0.42 | 1.50 ± 0.30$^*$ | 1.29 ± 0.32$^+$ | 1.18 ± 0.28$^+$ | 1.76 ± 0.45 |
  - Divers 1.87 ± 0.47 | 1.61 ± 0.38$^*$ | 1.38 ± 0.32$^+$ | 1.22 ± 0.26$^*$ | 1.83 ± 0.50 |

Data are means ± s.d. for all 14 subjects completing the study; differences are reported between baseline versus rebreathing and recovery changes (*P < 0.05) and for differences between groups (non-divers versus divers; |P < 0.05). $V_t$, minute ventilation; $V_t$, tidal volume; $B_t$, breathing frequency; MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; CO, cardiac output; TPR, total peripheral resistance; MCAV, middle cerebral artery mean blood velocity; CVR, cerebral vascular resistance.

Anthropometrical comparisons

The groups of participants were anthropometrically matched. The reported spirometry values correspond to upright posture (Table 1).

Ventilatory variables

During rebreathing BHD and ND showed an increase in $V_t$ ($P < 0.018$). However, BHD had significantly lower increase in $V_t$ than ND ($P = 0.035$) due to lower increase in breathing frequency ($P = 0.048$). There was no significant difference in duration of rebreathing until both groups reached the three target CO$_2$ values.

Cardiovascular variables

Cardiovascular variables are summarized in Table 2. There was no difference in baseline MAP, HR, SV, CO and TPR between BHD and ND. The rebreathing related changes in MAP were similar in both groups: MAP increased in ND due to rise in SV ($P = 0.03$) and in the BHD group MAP increased due to a rise in TPR ($P = 0.04$).

Cerebral blood flow and resistance

Changes in MCAV and CVR are summarized in Table 2 and representative traces for a diver and control are shown in Fig. 1. Both groups showed similar gradual increase in MCAV throughout the rebreathing period above baseline values. The maximum rise in MCAV was ~74% in BHD and ~67% in ND at end of rebreathing, when $P_{ET,CO_2}$ reached 60 mmHg. Cerebrovascular reactivity was not different between the groups (3.7 ± 1.4 versus 3.4 ± 1.3 mmHg$^{-1}$ $P_{ET,CO_2}$ in BHD and ND, respectively; $P = 0.90$) and the similar responses were seen for cerebral vascular resistance and time for MCAV recovery to baseline after termination of the CO$_2$ challenge.

Discussion

The most important finding in this study is that cerebrovascular reactivity to hypercapnia is unchanged in elite breath-hold divers, although they are exposed to repeated bouts of intermittent hypoxia and

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hypcapnia during simulated (‘static’) or field diving and while training for competitions. Ventilatory responses to hypcapnia were blunted, in accordance with previous studies and consistent with the idea that the divers had undergone repeated hypcapnic exposures. Although the mechanism of unchanged cerebrovascular reactivity in elite divers is at present unknown, the contrast to the blunted cerebrovascular reactivity reported in patients with obstructive sleep apnoea suggests that chronic exposure to hypcapnia alone is not responsible.

During last decade elite breath-hold divers have extended considerably the dive duration and depth during ‘static’ and field dives, exposing themselves to greater hypoxia and hypcapnia. Intermittent hypoxia is an effective stimulus for evoking respiratory, cardio-

vascular and metabolic adaptations normally found only in continuous chronic hypoxia (Neubauer, 2001). Some of these adaptations may be beneficial in athletes; although chronic intermittent hypoxia can lead to negative effects such as increased systemic and pulmonary vascular resistance, hypertension, cerebral and coronary vascular disorders and neurocognitive deficits (Neubauer, 2001). Since breath-hold divers are exposed chronically to intermittent hypoxia and hypcapnia similarly to OSA patients, we used them as a human model of intermittent hypoxia/hypcapnia without the coexisting diseases normally seen in the pathophysiological models of hypoxia/hypcapnia. In this way we reasoned that the divers represent a relatively ‘pure’ human model of intermittent hypoxia/hypcapnia. Therefore, the current

Figure 1. Changes in middle cerebral artery velocity (MCAV, cm s$^{-1}$), mean arterial pressure (MAP, mmHg) and ventilation ($V_E$, l min$^{-1}$) for one representative nondiver (ND) and one breath-hold diver (BHD).

Start and stop mark designate rebreathing protocol.
findings suggest that repeated exposures to intermittent hypoxia/hypercapnia in the absence of other risk factors like hypertension, glucose intolerance, hyperlipidaemia or other conditions known to affect microvascular function does not have a markedly negative impact on cerebrovascular reactivity.

The mechanisms responsible for the normal cerebral vascular responses to hypercapnoea in divers in this study are unknown. Intermittent hypoxia and hypercapnoea have been suggested to start a cascade of pathophysiological changes ending in endothelial dysfunction, inflammation and atherosclerosis (Foster et al. 2007). It is thought that intermittent hypoxia leads to increased formation of reactive oxygen species that may diminish the bioavailability of nitric oxide (NO) and thereby reduce NO-dependent vasodilatation (Lavie, 2003). OSA patients have decreased NO that can be reversed by CPAP therapy (Ip et al. 2000). However, hypercapnic cerebral vasodilatation is a local phenomenon with complex and perhaps redundant mechanisms (NO synthase, cyclooxygenase, P-450 oxygenase) (Iadecola & Zhang, 1994; Niwa et al. 2001). In this context, the normal cerebrovascular response to hypercapnia in the divers suggests maintained homeostasis of cerebral blood flow due to adequate concentration of cerebral vasodilators. Our observations also support the idea that repeated hypoxia and hypercapnoea are not sufficient to alter cerebral vascular reactivity in the absence of coexisting metabolic and haemodynamic conditions frequently associated with OSA.

The ventilatory drive to hypercapnia is blunted in different sports related to underwater activities (Florio et al. 1979; Masuda et al. 1982; Davis et al. 1987; Grassi et al. 1994; Delapille et al. 2001) in order to reduce the urge to breathe, despite significant central and peripheral chemical stimulus. Similar respiratory adaptations have also been noted in OSA patients (Garcia-Rio et al. 2002). In this study we found a reduced ventilatory response to a modified Read protocol in elite divers versus non-divers. This finding is in agreement with previous studies. Since the hypercapnic cerebrovascular reactivity is reduced during day in OSA (Loeppky et al. 1984; Placidi et al. 1998; Diomedi et al. 1998; Qureshi et al. 1999) and congestive heart disease (Georgiadis et al. 2000), we reasoned that similar adaptations might occur in breath-hold divers. The diving response is a physiological adaptation to hypoxia and hypercapnia during breath-hold diving in order to conserve the oxygen supply to the vital organs such as the brain and the heart. It is composed in humans of bradycardia, peripheral vasoconstriction, increased arterial blood pressure and decreased cardiac output (Lin et al. 1983). We have shown recently that skeletal muscle desaturates earlier than the arterial blood in breath-hold trained and untrained subjects, providing further support for the oxygen-conserving effect of human diving response (Valic et al. 2006). Recent studies have suggested that splenic contraction is also a part of diving response (Hurford et al. 1990; Bakovic et al. 2003; Schagatay et al. 2005). In addition, the series of breath holds may cause prolonged haemodynamic changes after resumption of normal breathing, composed of increased right ventricular afterload and decreased cardiac output associated with CO2 retention (Bakovic et al. 2006). The finding of normal cerebrovascular reactivity in the divers suggests that this mechanism is also available to ensure that brain blood flow increases adequately during diving.

Limitations
There are several limitations with the current study. First, we estimated cerebral blood flow by measuring with transcranial Doppler blood velocity rather than volume flow. The basic assumption with this method is that relative changes in middle cerebral artery velocity (MCAV) directly represent relative changes in blood flow. The assumption of a stable MCA is challenged (e.g. Dahl et al. 1994); however, most research suggests that MCAV is a reliable index of cortical blood flow (Poilin & Robbins, 1996; Serrador et al. 2000). Poilin & Robbins (1996), using the Doppler signal power as an index of cross-sectional area of the MCA, reported that the calibre of the MCA was unchanged during moderate hypercapnia. Further support comes from a magnetic resonance imaging study by Serrador et al. (2000), who showed that MCA dimensions (measured to within 0.1 mm) are stable under a wide range of end-tidal partial pressure of CO2 (P\text{ET,CO2}) and induced orthostatic stress. Second, it is possible that the divers we studied, while clearly adapted to hypercapnia, do not undergo a daily hypercapnic stimulus that is similar to that experienced by OSA patients. However, field observations suggest that the divers frequently perform 30–50 dives per day of 2–4.5 min in duration over a period of 5–6 h. Additionally, one of the divers we studied operates a breath hold diving school and has held a voluntary apnoea for at least 8 min and this individual, our most extremely trained subject, also showed normal normal cerebrovascular reactivity. Finally, OSA patients should be included in the future investigations to determine the role of more frequent apnoeas in conjunction with coexisting diseases on cerebral vascular responses to hypercapnoea.

In summary, cerebrovascular reactivity to hypercapnia was the same in breath-hold divers in comparison to non-divers (3.7 versus 3.4% MCAV change mmHg$^{-1}$ P\text{ET,CO2}, respectively). The finding of intact cerebral vascular responses in breath-hold divers could be interpreted as a protective mechanism against cerebral ischaemia. Failure of the cerebral circulation to respond to hypercapnia might contribute to hypoperfusion of
the brain during dives. Thus, normal cerebrovascular reactivity to hypercapnia in breath-hold divers in this study could be considered a part of the diving response that has a life saving function. These data also raise important questions about the role of repeated exposures to hypercapnia in the absence of other factors as a major cause of altered cerebrovascular reactivity in conditions like OSA.

References


Acknowledgements

This study was supported by the Croatian Ministry of Science, Education and Sports, grant no. 216006 and 216007. M.J.J. and N.M.D. were supported by the Mayo Foundation. The investigators would like to thank the support staff of the Split University School of Medicine for facilitating this study and the subjects for their enthusiastic participation.