Respiratory Physiology & Neurobiology 192 (2014) 48–54

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Cardio-ventilatory responses to poikilocapnic hypoxia and hypercapnia in trained breath-hold divers

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ARTICLE INFO

Article history:
Accepted 6 December 2013

Keywords:
Breath-holding
Hypoxic ventilatory response
Hypercapnic ventilatory response
Poikilocapnic hypoxia

ABSTRACT

Trained breath-hold divers (BHDs) are exposed to repeated bouts of intermittent hypoxia and hypercapnia during prolonged breath-holding. It has thus been hypothesized that their specific training may develop enhanced chemo-responsiveness to hypoxia associated with reduced ventilatory response to hypercapnia.

Hypercapnic ventilatory responses (HCVR) and hypoxic ventilatory responses at rest (HVR_r) and exercise (HVR_e) were assessed in BHDs ($n = 7$) and a control group of non-divers (NDs = 7). Cardiac output (CO), stroke volume (SV) and heart rate (HR) were also recorded. BHDs presented carbon dioxide sensitivity similar to that of NDs (2.85 ± 1.41 vs. 1.85 ± 0.93 L min^{-1} mmHg^{-1}, $p > 0.05$, respectively). However, both HVR_r (+68%) and HVR_e (+31%) were increased in BHDs. CO and HR reached lower values in BHDs than NDs during the hypoxic exercise test.

These results suggest that the exposure to repeated bouts of hypoxia/hypercapnia frequently experienced by trained breath-hold divers only enhances their chemo-responsiveness to poikilocapnic hypoxia, without altering HCVR.

1. Introduction

Breath-hold divers (BHDs) are exposed to extreme arterial hypoxia and hypercapnia during prolonged breath-holding (BH). It has thus been hypothesized that the repeated exposure to hypoxia/hypercapnia induced by BH training might reset the chemosensitivities for both peripheral and central chemoreceptors. Most studies have noted that the slopes of the ventilatory responses to hypercapnia (HCVR) are usually blunted in underwater hockey players (Davis et al., 1987), Ama divers (Masuda et al., 1982), Royal Navy divers (Florio et al., 1979) and trained breath-hold divers (Delapille et al., 2001; Grassi et al., 1994; Ivancev et al., 2007), although some investigations have shown no significant difference with the control group (Bjurstrom and Schoene, 1987; Dujic et al., 2008; Masuda et al., 1981). Likewise, contradictory results with the hypoxic ventilatory responses (HVR) at rest (HVR_r) and exercise (HVR_e) have been reported in BHDs (Breskovic et al., 2010a; Foster and Sheel, 2005; Grassi et al., 1994).

Human physiological response to BH is called the diving reflex and its main effects are bradycardia, decreased cardiac output and increased arterial blood pressure (Ferretti and Costa, 2003). Several studies have demonstrated that these mechanisms are accentuated in trained BHDs and slow down the depletion of the lung oxygen stores through an oxygen-conserving effect (at rest and exercise), thereby reducing overall oxygen uptake (Lindholm and Lundgren, 2009). The combination of repeated BH-induced hypoxic exposure with the BH-induced oxygen-conserving effect suggests the possibility of BH training as a cost-effective alternative to intermittent hypoxia (Lemaître et al., 2010). Since brief intermittent hypoxia exposures (IHE) have been shown to increase HVR_r (Foster et al., 2005) and HVR_e (Katayama et al., 2001), IHE might therefore be considered as an effective acclimatization strategy to reduce the risk for high-altitude disorders during high altitude exposure (Wille et al., 2012). Recent studies suggest that training with voluntary hypoventilation-induced IHE could be an interesting way for athletes to benefit from intermittent hypoxia without going to altitude or using expensive devices to simulate the hypoxic environment (Woorons et al., 2007, 2010). We thus hypothesized that trained BHDs would have greater HVR_r and HVR_e compared with a control group, due to increases in both minute ventilation (V_E) and arterial oxygen saturation (SaO_2); we further hypothesized that these responses might also be associated with blunted HCVR. We

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http://dx.doi.org/10.1016/j.resp.2013.12.005

assessed the ventilatory and cardiovascular responses to hypercapnia at rest and to poikilocapnic hypoxia during rest and exercise in both BHDs and healthy control subjects.

2. Materials and methods

2.1. Subjects

Fourteen healthy male subjects volunteered to participate in this study and were split into two groups: trained divers ($n = 7$) and non-divers (NDs, $n = 7$). All experimental procedures in this study were performed in accordance with the declaration of Helsinki and were approved by the local research ethics committee. The participants were informed of the objectives and procedures of the study, and all gave written consent prior to the start of the experiment.

2.2. Experimental design

Each subject performed a rebreathing test followed by a hypoxic exercise test, with at least a day's rest between them. All experiments were carried out by the same experimenters in a controlled environment with constant temperature (22 °C).

2.2.1. Rebreathing test

The carbon dioxide (CO_2) sensitivity was assessed using a slightly modified rebreathing method as previously described and explained in greater detail elsewhere (Read, 1967). Briefly, the subjects were comfortably seated, breathing through a mouthpiece connected to a 3-way T-shaped manual directional valve (model 2100, Hans Rudolph, Inc., Kansas City, MO, USA) that allowed switching easily from room air to a 5-L non-diffusing gas bag (model 6005, Hans Rudolph, Inc., Kansas City, MO, USA), which was filled with a hyperoxic/hypercapgnic gas mixture (95% O_2–5% CO_2). After three minutes of breathing in ambient air, the participants were switched to the rebreathing bag mixture at the end of a voluntary exhalation. At the very beginning of CO_2 rebreathing, the subjects were asked to take three deep breaths to ensure that the partial pressures of CO_2 in the bag, lungs and arterial blood quickly equilibrated with the mixed venous partial pressure. After this equilibration phase, the subjects were instructed to breathe spontaneously. Expired gases were collected breath-by-breath in a metabograph (Vmax Encore, CareFusion, SensorMedics, Yorba Linda, CA, USA) to measure V_E, tidal volume (V_T), breathing frequency (F_r) and end-tidal CO_2 pressure ($PetCO_2$). Both V_E and V_T were expressed in units adjusted to body temperature and pressure, saturated with water vapor (BTPS). The rebreathing test ended when $PetCO_2$ reached 70 mmHg, V_E exceeded 100 L min^{-1} or the subject experienced severe discomfort.

2.2.2. Hypoxic ventilatory test

The poikilocapnic hypoxic ventilatory responses (HVR) were determined at both rest and exercise following a standardized protocol modified from Richalet (Lhuissier et al., 2012). Briefly, the test is made up of five consecutive phases of three to five minutes each: rest in normoxia (RN), rest in hypoxia (RH), exercise in hypoxia (EH) and exercise in normoxia (EN). The fifth and last phase was an exercise in normoxia associated with progressive incremental work so that HR reached the same value as during EH (EN+). Acute hypoxic conditions (4.800 m, e.g. FiO_2 = 11.5%) were obtained using an AltiTrainer$_{200}$ (S.M. TEC, Geneva, Switzerland) connected to a nitrogen (N_2) gas bottle. The tests were conducted on an electrically braked cycloergometer (ER 900, Jaeger, Wuerzburg, Germany) at an exercise intensity corresponding to 50% of heart rate (HR) reserve during hypoxic exposures. The workload used during EH was similar than the one applied during EN. The subjects were asked to sustain a constant pedal rate of 70 rpm. V_E and HR were continuously recorded on a breath-by-breath basis. SaO_2 was assessed with a finger probe oximeter (PalmSat 2500, Nonin Medical, Inc., Minneapolis, USA).

2.2.3. Hemodynamic measurements

Throughout both tests, cardiac output (CO), stroke volume (SV) and HR were estimated by bio-impedancemetry (PhysioFlow PF-05, Manatec Biomedical, Macheren, France), a non-invasive method commonly used nowadays to determine cardiodynamic parameters at rest (Charloux et al., 2000; Tonelli et al., 2011) and during exercise (Tordi et al., 2004; Welsman et al., 2005). The relationship between peak CO derived from the impedance-based device and the direct Fick method has been shown to be high at rest ($r = 0.89$, $p < 0.001$), submaximal exercise ($r = 0.85$, $p < 0.001$) and maximal exercise ($r = 0.94$, $p < 0.01$). The PhysioFlow methodology has been described in detail elsewhere (Richard et al., 2001). Briefly, the bio-impedance method for determining CO uses transthoracic impedance changes (dZ) in response to an electrical current administered during cardiac ejection to calculate SV. After shaving and applying a mildly abrasive paste (Reegaponce, Bussy Saint-Georges, France) to the skin, two sets of electrodes, one transmitting and the other receiving, are applied above the supraclavicular fossa (left side) and along the xiphoid process of each subject. Another pair of electrodes is used to measure a single electrocardiogram signal (ECG). After an autocalibration over 30 heart beats, CO is then continuously calculated (beat-to-beat) by multiplying the stroke volume index (SVi) with the body surface area (BSA) and HR, which is obtained from the R–R interval determined on the ECG first derivative:

$$CO(L\,min^{-1}) = HR(beat\,min^{-1}) \times SVi(mL\ m^{-2}) \times BSA(m^2)$$

The same experimenter used this device and performed the hemodynamic recording throughout the study.

2.3. Data analysis

2.3.1. Ventilatory recruitment threshold and CO_2 sensitivity

The data from the rebreathing experiments were analyzed using Sigma Plot software version 12.3 (SPSS, Chicago, IL, USA) to calculate the main parameters describing chemoreflex-mediated ventilatory responses to CO_2 (i.e., the ventilatory recruitment threshold (VRT) and the CO_2 sensitivity (V_ES)). This data analysis was carried out using Duffin's method as a framework (Duffin et al., 2000). First, the three deep breaths used for equilibration as well as any abnormal breaths such as sighs or swallows while rebreathing were ignored in further analysis. On a breath-by-breath basis, V_E was plotted against $PetCO_2$ and the plots were then fitted into a piecewise double-linear regression (i.e., two continuous line segments). The first line segment was a constant representing the subject's basal ventilation (V_EB) and was used to extrapolate the VRT. The second one represented the progressive linear rise in V_E (due to an increase in $PetCO_2$) whose slope was considered to be an estimate of CO_2 responsiveness. The mathematical intersection of the two line segments represented the breaking point (VRT) at which V_E started to increase in a linear manner.

2.3.2. Hypoxic ventilatory responses

V_E, SaO_2 and HR values were averaged over the last minute of each phase. The hypoxic desaturation at rest (ΔSa_r) and exercise (ΔSa_e) were calculated as follows:

$$\Delta Sa_r(\%) = SaO_{2_{RN}} - SaO_{2_{RH}}$$

$$\Delta Sa_e(\%) = SaO_{2_{EN}} - SaO_{2_{EH}}$$