Cardiovascular Regulation During Apnea in Elite Divers


Abstract—Involuntary apnea during sleep elicits sustained arterial hypertension through sympathetic activation; however, little is known about voluntary apnea, particularly in elite athletes. Their physiological adjustments are largely unknown. We measured blood pressure, heart rate, hemoglobin oxygen saturation, muscle sympathetic nerve activity, and vascular resistance before and during maximal end-inspiratory breath holds in 20 elite divers and in 15 matched control subjects. At baseline, arterial pressure and heart rate were similar in both groups. Maximal apnea time was longer in divers (1.7±0.4 versus 3.9±1.1 minutes; \( P<0.0001 \)), and it was accompanied by marked oxygen desaturation (97.6±0.7% versus 77.6±13.9%; \( P<0.0001 \)). At the end of apnea, divers showed a >5-fold greater muscle sympathetic nerve activity increase (\( P<0.01 \)) with a massively increased pressor response compared with control subjects (9±5 versus 32±15 mm Hg; \( P<0.001 \)). Vascular resistance increased in both groups, but more so in divers (79±46% versus 140±82%; \( P<0.01 \)). Heart rate did not change in either group. The rise in muscle sympathetic nerve activity correlated with oxygen desaturation (\( r^2=0.26; P<0.01 \)) and with the increase in mean arterial pressure (\( r^2=0.40; P<0.0001 \)). In elite divers, breath holds for several minutes result in an excessive chemoreflex activation of sympathetic vasconstrictor activity. Extensive sympathetically mediated peripheral vasoconstriction may help to maintain adequate oxygen supply to vital organs under asphyxic conditions that untrained subjects are not able to tolerate voluntarily. Our results are relevant to conditions featuring periodic apnea. (Hypertension. 2009;53:719-724.)

Key Words: baroreflex ■ breath-hold diving ■ chemoreflex ■ diving response ■ sympathetic nervous system

Involuntary sleep apnea episodes trigger sympathetically mediated blood pressure surges and predispose to cardiovascular and cerebrovascular morbidity and mortality. The state of affairs is disturbing, because healthy people, including underwater hockey players, synchronized swimmers, and elite breath-hold divers practice “voluntary” apnea on a regular basis. Freestyle swimmers may hold their breath throughout 50-m sprint competitions. Elite breath-hold divers can hold their breath for several minutes. In these unique individuals, arterial oxygen saturation may decrease to <50%, whereas alveolar carbon dioxide partial pressure increases substantially. Typically, diving fish-catching competitions last for 5 hours with cumulative apnea duration of 1 hour.

Breath holding elicits complex cardiovascular adaptations even before relevant changes in arterial blood gases occur. The response includes bradycardia, reduced cardiac output, and peripheral vasoconstriction through sympathetic activation. The so-called diving response seems to conserve oxygen. Breath holding without water immersion also increases sympathetic vasomotor tone and hypercapnia provide additional stimuli to the sympathetic nervous system through central and peripheral chemoreflex mechanisms. However, in untrained individuals, breath-hold duration is too short to elicit a relevant decrease in arterial oxygen saturation. We tested the hypothesis that the sympathetic vasomotor response to maximal breath holding is increased in apnea divers compared with control subjects.

Methods

Study Population

We recruited 43 young white subjects. Twenty two were active apnea divers. Within the preceding months, they participated in ≥7 diving competitions and ≥70 training sessions, each consisting of 30 to 40 maximal apneas, separated by variable interapneic periods. Matched, untrained subjects served as controls. All of the participants were healthy nonsmokers and ingested no medications. The

Received December 4, 2008; first decision December 27, 2008; revision accepted February 2, 2009.

From the Institute of Clinical Pharmacology (K.H., J.T., J.J.), Hannover Medical School, Hannover, Germany; Department of Neurology (G.D.), Clinical Hospital Split, Split, Croatia; Department of Physiology (I.P., Z.V., D.B., A.O., V.I., T.B., Z.D.), University of Split School of Medicine, Split, Croatia; Autonomic Dysfunction Service (A.D.), Vanderbilt University, Nashville, Tenn; Department of Anesthesiology (M.J.J.), Mayo Clinic College of Medicine, Rochester, Minn; and Experimental and Clinical Research Center (F.C.L.), Charité, Max-Delbrueck-Centrum, Berlin, Germany; and HELIOS Klinikum (F.C.L.), Berlin, Germany.

K.H. and G.D. contributed equally to this work.

Correspondence to Karsten Heusser, Institute of Clinical Pharmacology, Hannover Medical School, Carl-Neuberg-Strasse 1, 30625 Hannover, Germany. E-mail karsten.heusser@gmx.de

© 2009 American Heart Association, Inc.

Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.108.127530

719
The ethical committee of the University of Split School of Medicine approved the study, and written informed consent was obtained.

**Protocol**

The participants arrived at the laboratory in the postabsorptive state and had abstained from caffeine for ≥12 hours. After emptying their bladders, they remained in the supine position throughout the experiments. They were instrumented, including searching for a suitable muscle sympathetic nerve activity (MSNA) recording site. After baseline measurements had been obtained, volunteers performed 2 to 3 bouts of maximal static apnea separated by 5-minute recovery periods. The first bouts were for practice. Apnea was performed with a nose clip and closed lips to avoid air leaks. Immediately before the breath holds, the participants were allowed to perform a maximal inspiration without previous hyperventilation or glossopharyngeal pistoning, a breathing maneuver that is common among experienced apnea divers to maximally increase total lung capacity.

At the end of the experiment we measured the forced vital capacity (FVC) with the subjects still in the supine position.

**Measurements**

Heart rate was determined using a standard ECG. Arterial blood pressure was measured noninvasively using continuous finger-pulse photoplethysmography (Finometer, Finapres Medical Systems). Finger blood pressure was calibrated against brachial arterial pressure. Arterial oxygen saturation (SpO2) was monitored continuously by pulse oximetry (Poet II, Criticare Systems), with the probe placed on the middle finger. Vascular resistance was estimated by the ratio between mean arterial pressure (Finometer) and mean femoral blood velocity (Doppler ultrasound device, Multigun) as described previously, or by impedance cardiography (Cardioscreen, Medis GmbH). A pneumatic chest belt was used to register thoracic and abdominal movements. Especially in divers, involuntary breathing movements are regularly seen during late apnea. Therefore, determination of apnea time was achieved by visual inspection of the subjects.

To measure sympathetic activity, we used the technique of microneurography. We obtained multiunit recordings of postganglionic sympathetic nerve activity with unipolar tungsten microelectrodes inserted selectively into muscle nerve fascicles of the right peroneal nerve in the popliteal space. Nerve activity was amplified with a total gain of 100,000, bandpass filtered (0.7 to 2.0 kHz), rectified, and integrated with a time constant of 0.1 seconds. To improve the signal:noise ratio, we shielded the lower body of the subjects (Waveprotect sheet, Teha Textil GmbH). The sympathetic bursts were identified in the mean voltage neurograms. The rate of sympathetic nerve discharges during baseline was expressed as the number of bursts per minute (burst frequency). During prolonged apnea, every diastolic trough evokes a sympathetic burst (Figure 1, inset). Hence, further sympathetic excitation is not properly reflected by the burst frequency. Therefore, we quantified end-apneic responses also by means of total activity, ie, the cumulated area under the sympathetic bursts in the integrated nerve signal as a surrogate for spike frequency.

Analog signals of the above-mentioned parameters were digitized and stored on a computer. The data files were processed by use of a program written by 1 of the authors (A.D.) that is based on PV-WAVE (Visual Numerics), as described previously.

We determined FVC using spirometry (Quark PFT, Cosmed) and calculated normalized FVC as the ratio between the observed and predicted FVCs of a subject. The calculation depends on height, age, and sex.

**Statistics**

In 8 subjects we were unable to find a stable recording site within the nerve. Thus, only 15 male control subjects and 20 divers (3 women) were included in the statistical analysis.

During apnea, the course of cardiovascular and autonomic reactions is highly dynamic. To trace these responses properly, we...
applied averaging periods of ~20 seconds as a compromise between stable averages and sufficient time resolution. We decided to examine 2 particular periods during apnea: the last 20 seconds of the first minute of apnea and the last 20 seconds of apnea. All of the values are given as means±SDs. Two-tailed unpaired t tests were used to compare baseline data and apnea reactions of the groups. Welch’s correction was applied in case of different variances. We assessed linear association between variables by Pearson or Spearman correlation analysis, depending on the data distribution. A value of P<0.05 was considered statistically significant. Prism 4 for Windows (GraphPad Software, Inc) was used for statistical analyses.

**Results**

Baseline measurements are given in Table 1. Body mass index, hemodynamic variables, and MSNA were similar in both groups. Divers had higher normalized FVC values than control subjects.

Measurements obtained 1 minute into and at the end of breath holding are presented in Table 2. Apnea time varied from 57 seconds in a control subject to 5 minutes and 52 seconds in the best diver. As expected, divers held their breath significantly longer than untrained subjects, leading to a more pronounced oxygen desaturation. The time course of arterial pressure and MSNA is shown in the Figures 1 and 2. In both groups, MSNA and vascular resistance increased during the first minute of apnea and remained elevated until the end of apnea (P<0.01 for all comparisons). Cardiac output showed a fast reduction within the first minute of apnea that was more marked in divers; afterward, it recovered partially. Blood pressure and MSNA continued to increase with prolonged breath holding. Toward the end of breath holding, both measurements increased much more in divers (Figures 2 and 3). The rise in MSNA was correlated with oxygen desaturation (r²=0.26; P<0.01) and with the increase in mean arterial pressure (r²=0.40; P<0.0001; Figure 3). Vascular resistance increased in both groups, but more so in the divers (79±46% versus 140±82%; P<0.01). Total apnea duration was positively correlated with the MSNA increase at the end of the first apnea minute (r²=0.15; P<0.05).

**Discussion**

The important findings in our study are that prolonged apnea in elite divers resulted in profound elevations of MSNA, along with blood pressure, as they decreased their oxygen saturation to 78%. The response was completely different from that of untrained persons. The increase in arterial blood pressure and MSNA was much greater in elite divers with no ceiling on the rise in MSNA, whereas these parameters remained fairly flat throughout the maneuver in control subjects. Compared with baseline, the mean end-apneic sympathetic traffic was <4-fold in the control subjects but...
Within the first 15 to 20 seconds of end-inspiratory apnea, the time course of blood pressure and MSNA resembled the response to a Valsalva maneuver with an initial blood pressure decrease. Thereafter, maintained intrathoracic pressure was then stabilized by moderately increased MSNA, as in previous observations. The vasoconstrictor sympathetic activity at the end of the first minute was greater in the divers, and it correlated with breath-holding duration. It has been shown that training may increase sympathetic responsiveness. However, the phenomenon may be secondary: divers took a deeper breath before apnea, causing higher intrathoracic pressures, resulting in reduced cardiac output and, finally, a more pronounced baroreflex-mediated sympathetic activation. Unloading of low-pressure cardiopulmonary receptors may also contribute to the sustained sympathetic excitation. Thus, in the early, normoxic stage of breath holding, hemodynamic changes appear to drive the increase in sympathetic traffic through baroreflex mechanisms possibly facilitated by central neural mechanisms acquired by training.

Only trained divers attain the late phase of apnea. Chemoreflex engagement through hypoxia, hypercapnia, and the lack of ventilatory MSNA inhibition may all serve to explain the steady MSNA increase. In this period, changes in MSNA and blood pressure were directly correlated with one another. Hence, MSNA appears to drive blood pressure. The observation is consistent with a resetting of the sympathetic baroreflex to higher blood pressure values. Other investigators have argued that baroreflex resetting has priority over ordinary blood pressure regulation to subserve oxygen conservation. Additional studies found that the sympathetic baroreflex maintains its gain under moderate hypoxia despite a higher operational pressure. Hence, it appears that the arterial baroreflex continues to operate during the steady increase in vasoconstrictor outflow. This in contrast to previous suggestions. In the later stage of breath holding, sympathetic activity was not associated with a concomitant increase in leg vascular resistance. It is very likely that the sympathetically mediated vasoconstriction has been attenuated by the direct vasodilator effect that results from hypoxia, as well as from impaired vasoconstrictor transduction induced by hypercapnia. Thus, the rising arterial pressure is presumably attributable to (partially) recovered cardiac output by increased venous return because of involuntary breathing movements backed by sympathetically maintained peripheral resistance.

Hypoxemia in the divers was profound compared with controls. None of the controls had SpO2 values <90% at the end of maximal apnea; in the divers, almost all did. Five divers reached SpO2 levels <70%, which is less than normal mixed-venous blood. Their hypoxemia is necessarily acute, and how they acclimatize to this hypoxia, compared with untrained controls, is uncertain. The values recorded in the divers equal or exceed the hypoxemia observed in severe sleep-apnea patients, who suffer from similar deoxygenation and also have substantially increased MSNA. We found that repeated bouts of hypoxemia in divers did not lead to sustained sympathetic activation or arterial hypertension.

Figure 3. Relationship between changes in mean arterial pressure (MAP) and MSNA at the end of apnea. ○, control subjects; ●, divers. The data suggest that increasing sympathetic activity contributes to the increase in arterial pressure.

Figure 4. Determinants of apnea duration. Schematic drawing of factors that help to cope with the urge to breathe during apnea without previous hyperventilation.
Thus, we have no reason to believe that the repeated apnea episodes in our subjects increase their risk for comorbidities.

Previous studies suggested that water contact of the face during breath holding is the major determinant of peripheral vasoconstriction and that the MSNA increase results from mutual reinforcement of responses to facial receptor activation and apnea. Our findings suggest that face submersion is not necessary to provoke a substantial increase in MSNA with breath holding. On the other hand, we and others did not observe bradycardia, which is characteristic for a complete diving response.

Consistent with previous studies, sympathetic activity was rapidly suppressed when subjects started to breathe again. The response was too fast for a chemoreflex mechanism. Respiration itself and baroreflex mechanisms are a more likely explanation for the first 4 to 5 seconds of suppression. For instance, pulmonary vagal afferents activated by postapneic inhalation contribute to the sympathetic response.

Our study necessarily has limitations. We did not measure expired gas concentrations as subjects resumed breathing. Therefore, we cannot dissect the relative contribution of hypoxia and hypercapnia to late sympathoexcitation. Face immersion in cold water augments the sympathetic response. However, we purposely avoided this maneuver, because it could have affected the response to apnea differently in the 2 study groups.

Even more so, our data do not reflect real diving situations with whole-body immersion in water of certain depth and temperature.

Perspectives

Maximal end-inspiratory dry apnea leads to increased sympathetic vasoconstrictor activity. In elite divers, breath holds for several minutes result in an excessive chemoreflex activation of sympathetic vasoconstrictor activity. The increase is >5 times higher in the elite divers than in untrained control subjects, and it does not reach a ceiling. Such extensive sympathetically mediated peripheral vasoconstriction may help to maintain adequate oxygen supply to vital organs under asphyxic conditions that untrained subjects are not able to tolerate voluntarily. Taken together it appears that, in elite divers, a suite of factors prolongs their ability to resist the urge to breathe, resulting in breath-hold times of several minutes (Figure 4).

In contrast to involuntary apnea in sleep apnea patients, elite divers who reiterate apneas voluntarily do not suffer from sustained sympathetic activation and hypertension. Factors other than frequent apnea, eg, excessive daytime sleepiness and impaired baroreflex function in the patients, may contribute to the discrepancy. The mechanisms deserve further study.

Sources of Funding


Disclosures

None.

References


Cardiovascular Regulation During Apnea in Elite Divers
Karsten Heusser, Gordian Dzamonja, Jens Tank, Ivan Palada, Zoran Valic, Darija Bakovic, Ante Obad, Vladimir Ivancev, Toni Breskovic, André Diedrich, Michael J. Joyner, Friedrich C. Luft, Jens Jordan and Zeljko Dujic

Hypertension. 2009;53:719-724; originally published online March 2, 2009;
doi: 10.1161/HYPERTENSIONAHA.108.127530
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/53/4/719

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/