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Cardiovascular responses to dry apnoeas at exercise in air and in pure oxygen

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ABSTRACT

If, as postulated, the end of the steady state phase (φ2) of cardiovascular responses to apnoea corresponds to the physiological breaking point, then we may hypothesize that φ2 should become visible if exercise apnoeas are performed in pure oxygen. We tested this hypothesis on 9 professional divers by means of continuous recording of blood pressure (BP), heart rate (f_H), stroke volume (Q_S), and arterial oxygen saturation (SpO_2) during dry maximal exercising apnoeas in ambient air and in oxygen. Apnoeas lasted 45.0 ± 16.9 s in air and 77.0 ± 28.9 s in oxygen ($p < 0.05$). In air, no φ2 was observed. Conversely, in oxygen, a φ2 of 28 ± 5 s duration appeared, during which systolic BP (185 ± 29 mmHg), f_H (93 ± 16 bpm) and Q_S (91 ± 16 ml) remained stable. End-apnoea SpO_2 was 95.5 ± 1.9% in air and 100% in oxygen. The results support the tested hypothesis.

1. Introduction

A beat-by-beat analysis of the time course of cardiovascular variables during breath-holding (Costalat et al., 2017, 2013; Fagoni et al., 2017, 2015; Hoiland et al., 2017; Lemaître et al., 2008; Perini et al., 2010, 2008; Sivieri et al., 2015; Tocco et al., 2013, 2012) led to the definition of three distinct phases, which were modelled by Costalat et al. (2017, 2015). These phases are: (i) the first short dynamic phase (φ1); (ii) the steady state phase in which the cardiovascular variables are maintained invariant (φ2); and (iii) the final dynamic phase characterised by a continuous decrease in heart rate (f_H) and increase in blood pressure (φ3).

The φ1 is characterised by a sudden fall of arterial blood pressure and of stroke volume (Q_S) (Andersson and Schagatay, 1998; Fagoni et al., 2017, 2015; Perini et al., 2008). These fall may be due to an immediate fall in venous return related to the high lung volumes at which apnoeas are carried out (Andersson and Schagatay, 1998; Novalija et al., 2007). The concomitant f_H increase in φ1 has been attributed to a baroreflex response (Fagoni et al., 2017, 2015; Sivieri et al., 2015). φ1 has a quite constant duration of less than 30 s and its quantitative characteristics are independent of the metabolic rate (Sivieri et al., 2015) and of the size of lung oxygen stores (Fagoni et al., 2015).

Conversely, the physiological meanings of φ2 and φ3 are still unclear. The current conjecture, which is implicitly included in the model of Costalat et al. (2017, 2015), is that the end of φ2 (Fagoni et al., 2017, 2015; Perini et al., 2010; Sivieri et al., 2015) may correspond to the physiological breaking point of apnoea (Agostoni, 1963; Lin et al., 1974). The observations that φ2 becomes longer in apnoeas performed after breathing pure oxygen (Fagoni et al., 2015) and disappears in apnoeas performed during light exercise (Sivieri et al., 2015) agree with this conjecture. If this conjecture is true, we hypothesize that φ2 should become visible if exercise apnoeas are performed during pure oxygen breathing. The aim of our study was to test this hypothesis by performing a beat-by-beat analysis of the cardiovascular responses to exercising apnoea in pure oxygen.

2. Methods

2.1. Subjects

Nine well trained male divers were enlisted for this study. They were 37 ± 6 years old, 78 ± 7 kg in weight and 176 ± 6 cm tall. All divers were healthy and non-smokers. None of them had previous history of cardiovascular, pulmonary, or neurological diseases, or was taking any medication at the time when the study was carried out. Their

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Table 1
Mean values of cardiovascular variables recorded during steady state exercise before apnoeas (Pre-apnoea), during the steady state phase (only for apnoeas in oxygen), and at the beginning and at the end of the last unsteady phase (mean value over 10 beats). Punctual value of the beginning of the first unsteady phase and in correspondence of the minimum of systolic blood pressure (MSBP) during the same phase. Data are presented as means and standard deviations both for apnoeas performed in air and in pure oxygen. SBP, systolic blood pressure; DBP, diastolic blood pressure; f_H, heart rate; Q_S, stroke volume; $\dot{Q}$, cardiac output; TPR, total peripheral resistances.

		Pre-apnoea	First unsteady phase		Steady state phase	Last unsteady phase	
		mean value	beginning	MSBP	mean value	beginning	end
SBP	air	162 ± 32$^{\#}$	176 ± 39$^{\#}$	102 ± 24	–	173 ± 40$^{\#}$	215 ± 49$^{\#}$
(mmHg)	O_2	166 ± 22$^{\#\S}$	166 ± 43$^{\#\S}$	111 ± 29	185 ± 29$^{\#}$	194 ± 31$^{\#}$	214 ± 36$^{\#}$
DBP	air	74 ± 12	76 ± 11$^{\#}$	51 ± 9	–	82 ± 15$^{\#}$	96 ± 19$^{\#\&}$
(mmHg)	O_2	78 ± 7$^{\#\S}$	81 ± 13$^{\#\S}$	59 ± 13	87 ± 10$^{\#}$	91 ± 11$^{\#}$	104 ± 12$^{\#}$
f_H	air	99 ± 13$^{\&}$	105 ± 14§	109 ± 14§	–	107 ± 15§	76 ± 25
(bpm)	O_2	94 ± 13	102 ± 18§	104 ± 14§	93 ± 16	90 ± 16	78 ± 17
Q_S	air	114 ± 18	83 ± 23*	70 ± 22*	–	78 ± 12*	104 ± 15$^{\#}$
(ml)	O_2	114 ± 18	73 ± 30*	70 ± 16*	91 ± 16	94 ± 17	99 ± 18
$\dot{Q}$	air	11.2 ± 2.3$^{\&}$	8.6 ± 2.4	7.4 ± 1.7*	–	8.3 ± 1.8	7.8 ± 2.4*
($l\,min^{-1}$)	O_2	10.6 ± 2.1	8.0 ± 1.9	7.2 ± 1.5*	8.5 ± 2.2	8.5 ± 2.2	7.6 ± 1.9*
TPR	air	9.2 ± 2.3$^{\S\&}$	12.6 ± 3.5	8.8 ± 1.8$^{\S\&}$	–	13.2 ± 3.5	18.5 ± 7.0
($mmHg\,min\,l^{-1}$)	O_2	10.1 ± 1.8§	11.0 ± 6.9§	10.0 ± 2.1§	14.1 ± 3.1	14.9 ± 4.2	19.1 ± 5.6

*: $p < 0.05$ vs pre-apnoea mean value in the same condition.
$^{\#}$: $p < 0.05$ vs MSBP value during the first unsteady phase in the same condition.
§: $p < 0.05$ vs the end of the last unsteady phase in the same condition.
$^{\&}$: $p < 0.05$ vs the same value in apnoeas performed in pure oxygen.

predicted total lung capacity was 7.0 ± 0.4 l (Stocks and Quanjer, 1995). All gave their informed consent after having received a detailed description of the methods and experimental procedures of the study. The study was approved by the local ethical committee and conformed to the Declaration of Helsinki.

2.2. Experimental procedure

Experiments were carried out in Lindos, Greece, in an air-conditioned room at 23–24 °C, with relative humidity between 60 and 65%. Subjects came to the laboratory on two occasions: one for the tests in air and the other for the tests in oxygen. Air and oxygen were administered in random order. 5 subjects begun with the test in oxygen and 4 subjects with the test in air. At least 2 days separated the 2 tests. Oxygen was administered from a high-pressure tank, via a Douglas bag that was used as pressure buffer. Upon arrival in the laboratory and after instrumentation and familiarization with procedures, the subject was asked to sit on a cycle-ergometer. In oxygen experiments, after connection to the oxygen delivery system, ten minutes were then allowed for alveolar gas equilibration.

The experimental protocol was as follows: the subject performed 40 W exercise at 60 revolutions per minute; after 5 min, which were necessary to achieve steady state conditions, pre-apnoea control values were collected (PRE); then, the subject was asked to perform one maximal apnoea while still exercising. Both in air and in pure oxygen, the subject's pre-dive routine consisted of a couple of deep respiratory acts and was undertaken before breath-holding. A deep inspiration preceded the apnoeas, so that the lung volume at which the apnoeas started was close to the subject's total lung capacity.

2.3. Measurements and data treatment

Arterial blood pressure profiles (Portapres®, TNO-TPD, Amsterdam, The Netherlands) were continuously recorded throughout the experiments. Peripheral blood O_2 saturation (SpO_2) was continuously monitored by infrared spectroscopy (OXY100E module, BIOPAC® System Inc., Goleta, CA, USA) at an earlobe. f_H was continuously measured on a beat-by-beat basis by electrocardiography (ECG100C module, BIOPAC® System Inc., Goleta, CA, USA). The signals were sampled at 100 Hz by using a 16-bit A/D converter (MP150 system, BIOPAC® System Inc., Goleta, CA, USA) and stored on a personal computer for subsequent off-line analysis. The breath-by-breath recording of inspiratory and expiratory flows was performed by an ultrasonic flowmeter (Spiroson®, ECO MEDICS AG, Duernten, Switzerland) calibrated with a three-litre syringe.

Duration of apnoea was obtained from the analysis of respiratory flows. Arterial pressure profiles were analysed off-line, to obtain beat-by-beat values of systolic (SBP), diastolic (DBP), and mean (MBP) arterial pressure using the Beatscope® software (FMS, Amsterdam, The Netherlands). Single-beat Q_S was determined by means of the Modelflow method (Wesseling et al., 1993), applied off-line to the pulse pressure profiles, again using the Beatscope® software package. Beat-by-beat cardiac output ($\dot{Q}$) was then computed as the product of single-beat Q_S times the corresponding single-beat f_H. Total peripheral resistances (TPR) were calculated as the ratio between MAP and $\dot{Q}$.

An automated procedure implemented under MATLAB (version 7.6.0.324, MathWorks®, Natick, MA, USA) was used to identify the three phases of apnoea (Fagoni et al., 2017, 2015; Sivieri et al., 2015) by means of linear regression analysis, allowing the detection of changes in slope between successive phases.

2.4. Statistical analysis

Data are presented as mean and standard deviation (SD). Paired Student T-test was used to compare apnoeas performed in air and in pure oxygen; one-way ANOVA was used to compare cardiovascular data during the time course of apnoeas and Tukey test was used as post-hoc test to isolate the differences when necessary. Differences were considered significant when $p < 0.05$, otherwise they were considered non-significant (NS). The statistical software SPSS (Chicago, USA) was used for this aim.

3. Results

Means and standard deviations of all the cardiovascular variables recorded before and during apnoeas are reported in Table 1. In PRE, they differed between air and oxygen conditions for $\dot{Q}$, that was lower (−5.0 ± 3.2%) in oxygen than in air, due to a lower f_H (−5.3 ± 5.7%) coupled with an unchanged Q_S. Basal SpO_2 was 98.7 ± 1.2% in air and 100% in pure oxygen. Apnoeas lasted 45.0 ± 16.9 s in air and 77.0 ± 28.9 s in pure oxygen ($p < 0.05$).

Examples of the time courses of SBP, DBP and f_H during apnoea