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Original Paper

Effects of Intermittent Breath Holding during Prolonged Exercise on Ventilation and Blood Lactate Responses

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Abstract

In the present study, we examined the physiological response during prolonged exercise with intermittent breath holding (IBH). Eight male subjects performed four series of 5-min exercises at 65% of the peak oxygen uptake with normal breathing (NB) and with IBH. Respiratory variables and the transcutaneous partial pressure of CO_2 ($PtcCO_2$) were continuously recorded during the exercises. Finger blood samples were obtained during the exercises to assess the blood lactate (BLa) levels. Minute ventilation was significantly higher during the IBH condition than during the NB condition ($P < 0.05$). The $PtcCO_2$ level was significantly lower during the IBH condition than during the NB condition ($P < 0.05$). The BLa response was significantly greater during exercise with IBH than during exercise with NB ($P < 0.05$). These findings suggest that compared to exercise with NB, prolonged exercise with IBH induces a hyperventilatory response, resulting in hypocapnia, and using IBH during prolonged exercise induces a greater increase in the BLa level.

1. Introduction

Exercise training at a simulated altitude using a hypoxic chamber improves one's endurance capacity[1,2], and the mechanisms of human adaptation for this kind of training have been clarified[3,4]. However, only a few institutions provide hypoxic chambers for training, and these devices, which create a hypoxic environment, are very expensive; thus, the development of new hypoxic training methods without a hypoxic system is warranted.

Several studies have attempted to induce physiological stimuli, including hypoxia, by respiratory control during exercise as an alternative method for creating a hypoxic condition. It has been reported that

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exercise with hypoventilation at low pulmonary volumes induces severe arterial desaturation[5-8], and muscle deoxygenation[6-8]. Breath holding (BH) is another means for inducing a physiological hypoxic stimulus. BH induces a combined circulatory response called the diving response, which is characterized by bradycardia, peripheral vasoconstriction, and decreased blood flow to peripheral tissue[9-12]. The diving response has an oxygen-conserving effect; previous studies have shown that BH decreases the oxygen uptake ($\dot{V}O_2$) in both resting and exercising states[11,13]. To validate whether BH during exercise is beneficial as a training method, we evaluated the physiological response to short BH performed intermittently during a moderate bicycle exercise[14]. The study showed that exercise with intermittent BH (IBH) induces consistent changes in muscle oxygenation, resulting in lower tissue oxygenation. We also found that IBH during exercise enhances the blood lactate (BLa) response. These findings suggest that exercise with IBH may be a practical method for inducing physiological stimuli, including hypoxia, which may result in enhanced exercise performance.

However, our previous study[14] had limitations. First, we did not measure the partial pressure of CO_2 (PCO_2). BH increases arterial PCO_2 ($PaCO_2$)[13,15]; however, it has been observed as an augmented ventilatory response after the cessation of BH during exercise[16]. We also confirmed that during exercise with IBH, hyperventilation occurred in the normal breathing (NB) phase between each BH episode[14]. The hyperventilatory response induces the excessive expiration of CO_2, which results in hypocapnia. We hypothesized that exercise with IBH induces marked oscillations in $PaCO_2$. Measuring the transcutaneous PCO_2 ($PtcCO_2$) is advantageous because it is a non-invasive monitoring method that provides continuous data[17-19]. It is based on the principle that CO_2 gas diffuses throughout the body tissue and can be detected at the skin's surface. Previous studies have shown good agreement between the estimation of the $PaCO_2$ by the transcutaneous technique, and $PaCO_2$ measured from sampling arterial blood during rest and incremental exercise[19,20]. Hence, the transcutaneous technique is the preferred method for assessing the CO_2 during exercise with IBH. Second, the exercise duration was 5 min, which is too short for a simulated training session. Woorons et al. conducted a series of 5 min exercises with hypoventilation, and each series was separated by 1 min of the same exercise with NB[6,7]. Therefore, we used prolonged exercise with IBH and transition periods of NB.

The present study attempted to elucidate the physiological response during prolonged exercise with IBH and transition periods of NB.

2. Methods

2.1 Subjects

Eight healthy active male subjects participated (mean ± standard deviation [SD]: age = 24.1 ± 4.1 years, height = 172.7 ± 2.7 cm, body weight = 65.5 ± 1.4 kg, body mass index = 22.0 ± 0.90 kg/m^2). All subjects participated in physical activity 3-4 times/w. Informed consent was obtained from each subject after they received a verbal and written explanation about the experimental procedures and possible risks. This study was approved by the Ethics Committee of Kawasaki University of Medical Welfare (no. 315).

2.2 Overview of the experiment

All subjects performed a maximal exercise test on an electrically braked cycle ergometer (Aerobike 75XL, Combi, Tokyo, Japan) to determine their peak $\dot{V}O_2$ ($\dot{V}O_{2peak}$). About 1 week later, each subject performed two submaximal exercise tests (using the same aforementioned ergometer) with IBH (IBH condition) and then with NB (NB condition); these conditions were separated by at least 48 h. The order of the exercise conditions was random and counterbalanced. All tests were performed at the same time of the day and at least 2 h after the subject ate a light meal. Additionally, all subjects were asked to refrain from consuming caffeine-containing beverages and to avoid strenuous exercise for 12 h before each experiment.

2.3 Maximal exercise test

The seat height was adjusted so that there was a slight bend in the subject's knee joint when the foot

pedal was at its lowest point. After a 5-min rest on the cycle ergometer, the exercise test began at an initial power output of 90 W for 4 min, and the load was then increased by 30 W every 2 min until exhaustion. The pedaling rate was maintained at 60 rpm with the aid of a metronome. Subjects were verbally encouraged to perform at maximum effort. The test was terminated when the subject failed to maintain the prescribed pedaling rate. The highest $\dot{V}O_2$ value obtained during the exercise protocol was used as the $\dot{V}O_{2peak}$.

2.4 Submaximal exercise test

The seat height was adjusted in the same manner as described previously for each subject. After a 5-min rest on the cycle ergometer, subjects performed a 4-min warm-up exercise (W-Ex) at 40% $\dot{V}O_{2peak}$ with NB, followed by four series (S1, S2, S3, and S4) of 5-min exercises at 65% $\dot{V}O_{2peak}$ with IBH or NB. Between the series, transition periods with NB (T1, T2, T3, and T4) were included. During these transitions, subjects maintained the same exercise for 1 min. IBH included 10 s of BH after submaximal inspiration, followed by 50 s of NB, and then the sequence was repeated. The minute ventilation ($\dot{V}E$), $\dot{V}O_2$, CO_2 output ($\dot{V}CO_2$), respiratory exchange ratio (RER), heart rate (HR), percutaneous oxygen saturation (SpO_2), and $PtcCO_2$ were recorded during the tests. Lastly, the BLa levels were measured during the final 1 min of the W-Ex, at the end of each series and during the transition period.

2.5 Measurements

Respiratory gases were measured using an automatic gas analyzer (VO2000, MedGraphics, Minneapolis, MN, USA), and the sample time was set at 30 s. HR was recorded at 5-s intervals using a wireless HR monitor (RS800CX; Polar Electro Oy, Kempele, Finland). The BLa level was determined from finger capillary blood samples using an automatic lactate analyzer (Lactate Pro LT-1710, Arkray Inc., Kyoto, Japan).

We assessed the $PtcCO_2$ and SpO_2 by using a combined $PtcCO_2/SpO_2$ monitor (TOSCA 500, Linde Medical Sensors, Basel, Switzerland) with a Stow-Severinghaus-type CO_2 sensor for the earlobe and a pulse oximetry sensor. The accuracy of the TOSCA measurement system has been confirmed previously[17-19]. The $PtcCO_2$ measurement was based on CO_2 gas, which diffuses throughout the body tissue and can be detected by a sensor with a gas-permeable membrane at the skin's surface. Sensor calibrations were automatically performed using one-point dry gas calibration in the system's calibration chamber. The sensor temperature was maintained at 42℃ to induce local vasodilation and enhance skin permeability for CO_2 at the site of the measurement. After the skin and sensor were cleaned with alcohol, the sensor was attached to the right earlobe using a disposable low-pressure adhesive attachment clip. Next, we placed a few drops of contact gel (Linde Medical Sensors, Basel, Switzerland) on the skin at the center of the attachment clip before the sensor was inserted.

The continuous variables were averaged at the last 1 min of the W-Ex. In addition, the average values of each series and transition period were calculated.

2.6 Statistical analysis

Data are presented as mean ± SD. To compare measurement variables between conditions over time, a two-way analysis of variance (ANOVA) was used with the condition and time as factors with repeated measures. As appropriate, the Bonferroni test was performed for post hoc analysis to identify specific significant differences over time between the conditions. SPSS statistical software (version 22.0, IBM, Tokyo, Japan) was used to perform the analyses. The level of statistical significance was set at $P < 0.05$.

3. Results

3.1 Maximal exercise test

Cardiorespiratory variables and workload at exhaustion during the maximal exercise test were as follows: $\dot{V}O_2$ = 3.38 ± 0.22 L/min, 51.6 ± 3.3 mL/kg/min, $\dot{V}E$ = 129.9 ± 11.3 L/min, $\dot{V}CO_2$ = 3.77 ± 0.21 L/min,

RER = 1.12 ± 0.08, HR = 192 ± 11 beats/min, and workload = 288.8 ± 27.5 W.

3.2 Submaximal exercise test

Representative recordings of HR, SpO_2 and $PtcCO_2$ are presented in Fig. 1. In the IBH condition, the HR and SpO_2 showed acute changes for each BH. Although the $PtcCO_2$ level fluctuated, we did not find obvious responses of $PtcCO_2$ to each BH.

Results of the cardiorespiratory variables are shown in Table 1. $\dot{V}E$ was significantly higher in the IBH condition than in the NB condition at S1, T1 and S2 ($P < 0.05$, all), and this trend, although not significant, was maintained throughout the exercise. $\dot{V}O_2$ was significantly higher in the IBH condition than in the NB condition at T2 ($P < 0.05$). $\dot{V}CO_2$ was significantly higher in the IBH condition than in the NB condition at T1, T2, and T4 ($P < 0.05$, all). RER was significantly higher in the IBH condition than in the NB condition at S1, T1, S2, and S4 ($P < 0.05$, all). No significant difference in the HR and SpO_2 was observed during the exercise between the two conditions.

Changes in the $PtcCO_2$ levels are shown in Fig. 2. The $PtcCO_2$ level was significantly lower in the IBH condition than in the NB condition at T1, S2 and T2 ($P < 0.05$, all), and this trend, although not significant, was maintained throughout the exercise.

Changes in the BLa levels are shown in Fig. 3. The BLa level was significantly higher in the IBH condition than in the NB condition at T1, S2, T3, S4, and T4 ($P < 0.05$, all).

4. Discussion

The main findings of the present study were as follows: (1) the $PtcCO_2$ level was significantly lower with significantly higher values of $\dot{V}E$ in the IBH condition than in the NB condition; and (2) the BLa response was significantly greater during exercise with IBH than during exercise with NB.

BH increases the $PaCO_2$ level[13,15]; however, it has been indicated that an augmented ventilatory response is induced after the cessation of BH during exercise[16], which would result in the excessive expiration of CO_2. Therefore, we assumed that exercise with IBH would generate marked oscillations in the $PaCO_2$ level. We found a higher $\dot{V}E$ in the IBH condition than in the NB condition, indicating that an involuntary hyperventilatory response occurred during the NB phase in the IBH condition. Regarding the $PtcCO_2$ response to BH, the $PtcCO_2$ level has been shown to significantly increase when induced by maximal BH during rest. In a preliminary experiment, we confirmed that submaximal static BH (about 2 min) increases the $PtcCO_2$ level. The HR and SpO_2 showed an acute decrease caused by each BH (Fig. 1), which is in agreement with earlier reports that examined the circulatory response to BH during exercise[9,10,12-14]. Regarding the $PtcCO_2$ level, although a fluctuation was observed, obvious responses to each BH were not seen. A potential explanation for this may be associated with the measurement principle of the transcutaneous technique. A previous study reported good agreement between the $PtcCO_2$ and $PaCO_2$ levels during incremental bicycle exercise[21], and the study protocol consisted of increasing the exercise by 10-20 w every 1-2 min. It seems likely that a change in the $PaCO_2$ level under a similar condition would be gradual, and there would be sufficient time for the CO_2 gas to diffuse into the skin from the arterial blood. However, we considered that rapid changes in the $PaCO_2$ level occurred in the IBH condition, and equilibration of the PCO_2 level between arterial blood and the skin surface was slower than the actual kinetics of $PaCO_2$. Consequently, BH may have induced an acute change in the $PaCO_2$ level that could not be detected from the transcutaneous measurement. Overall, the $PtcCO_2$ level tended to be lower in the IBH condition than in the NB condition. Likewise, this trend was observed in averaged data for all the subjects (Fig. 2). These results suggest that exercise with IBH induces hypocapnia overall. Hypocapnia has potentially varied physiological effects such as a leftward shift in the oxyhaemoglobin dissociation curve[22]; decreased blood flow to active muscle[23]; and inhibited activation of the mitochondrial pyruvate dehydrogenase (PDH) which is responsible for oxidizing pyruvate[24]. Although the present study cannot clarify these physiological effects, the findings suggest that IBH-induced hyperventilation had some effects, which will be discussed later.

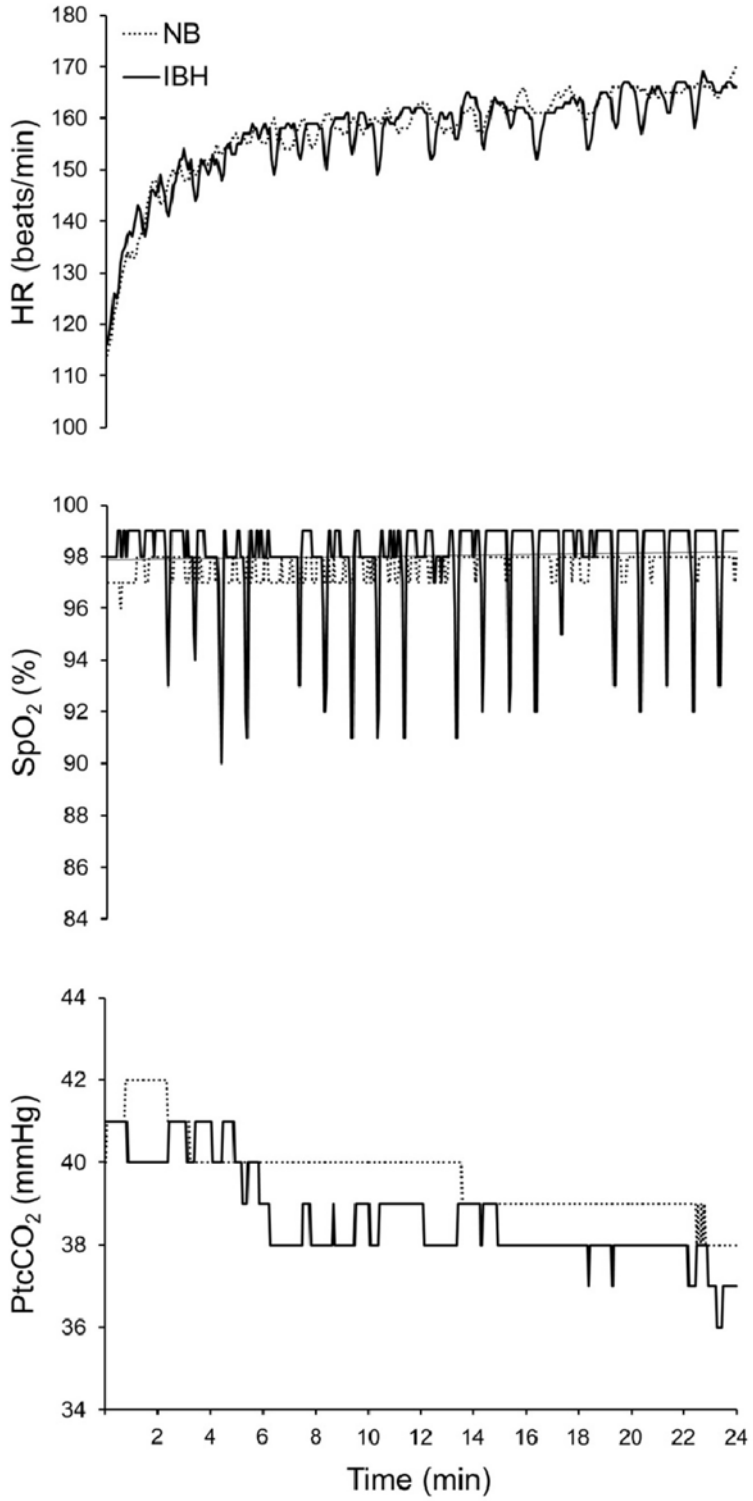

Fig. 1 Representative recordings of heart rate (HR), percutaneous oxygen saturation (SpO_2), and transcutaneous partial pressure of CO_2 ($PtcCO_2$) during exercise with normal breathing (NB) and intermittent breath holding (IBH) conditions.

Table 1 Cardiorespiratory variables during exercise

Variables	Conditions	W-Ex	S1	T1	S2	T2	S3	T3	S4	T4	*P* values
$\dot{V}E$ (L/min)	NB	37.04 ± 5.10	56.33 ± 6.48	63.37 ± 4.57	63.80 ± 6.23	65.08 ± 5.60	64.88 ± 5.76	66.43 ± 4.67	66.51 ± 5.23	65.99 ± 2.67	Condition: 0.084
	IBH	36.87 ± 5.31	64.66 ± 8.28*	71.70 ± 11.08*	71.63 ± 11.57*	74.76 ± 14.03	71.98 ± 12.12	73.30 ± 12.08	71.82 ± 10.78	74.36 ± 12.22	Time: < 0.001
											Interaction: 0.045
$\dot{V}O_2$ (L/min)	NB	1.37 ± 0.11	2.12 ± 0.19	2.32 ± 0.16	2.27 ± 0.17	2.27 ± 0.16	2.26 ± 0.16	2.27 ± 0.14	2.26 ± 0.15	2.25 ± 0.15	Condition: 0.626
	IBH	1.36 ± 0.14	2.11 ± 0.18	2.34 ± 0.16	2.27 ± 0.13	2.36 ± 0.18*	2.21 ± 0.11	2.34 ± 0.21	2.21 ± 0.11	2.29 ± 0.16	Time: < 0.001
											Interaction: 0.040
$\dot{V}CO_2$ (L/min)	NB	1.21 ± 0.04	2.03 ± 0.20	2.19 ± 0.17	2.14 ± 0.17	2.15 ± 0.14	2.14 ± 0.14	2.18 ± 0.10	2.15 ± 0.12	2.15 ± 0.12	Condition: 0.046
	IBH	0.20 ± 0.14	2.08 ± 0.14	2.32 ± 0.14*	2.22 ± 0.09	2.29 ± 0.12*	2.19 ± 0.16	2.26 ± 0.13	2.20 ± 0.14	2.28 ± 0.16*	Time: < 0.001
											Interaction: 0.032
RER	NB	0.89 ± 0.07	0.95 ± 0.10	0.95 ± 0.10	0.95 ± 0.08	0.95 ± 0.07	0.95 ± 0.06	0.96 ± 0.07	0.95 ± 0.06	0.96 ± 0.06	Condition: 0.028
	IBH	0.89 ± 0.08	0.98 ± 0.07*	0.99 ± 0.09*	0.98 ± 0.07*	0.97 ± 0.08	0.99 ± 0.06	0.97 ± 0.08	0.99 ± 0.05*	1.00 ± 0.08	Time: < 0.001
											Interaction: 0.006
HR (beats/min)	NB	113 ± 7	144 ± 10	154 ± 13	158 ± 13	161 ± 13	163 ± 13	164 ± 13	167 ± 13	168 ± 13	Condition: 1.000
	IBH	114 ± 7	146 ± 10	154 ± 11	158 ± 12	161 ± 13	163 ± 12	164 ± 13	166 ± 13	167 ± 13	Time: < 0.001
											Interaction: 0.997
SpO_2 (%)	NB	98.4 ± 0.6	98.2 ± 0.5	98.1 ± 0.5	98.1 ± 0.5	98.2 ± 0.5	98.3 ± 0.4	98.3 ± 0.4	98.4 ± 0.4	98.4 ± 0.4	Condition: 0.316
	IBH	98.5 ± 0.3	98.2 ± 0.4	97.8 ± 0.5	97.8 ± 0.6	97.9 ± 0.6	97.9 ± 0.7	98.2 ± 0.6	98.1 ± 0.6	98.0 ± 0.9	Time: 0.037
											Interaction: 0.067

Values are presented as means ± SD. W-Ex: Warm-up exercise; S1, S2, S3 and S4: series 1, 2, 3 and 4; T1, T2, T3 and T4: transition 1, 2, 3 and 4; $\dot{V}E$: minute ventilation; $\dot{V}O_2$: oxygen uptake; $\dot{V}CO_2$: carbon dioxide output; RER: respiratory exchange ratio; HR: heart rate; SpO_2: percutaneous arterial oxygen saturation; NB: normal breathing; IBH: intermittent breath holding. *: $P < 0.05$ compared to normal breathing values.

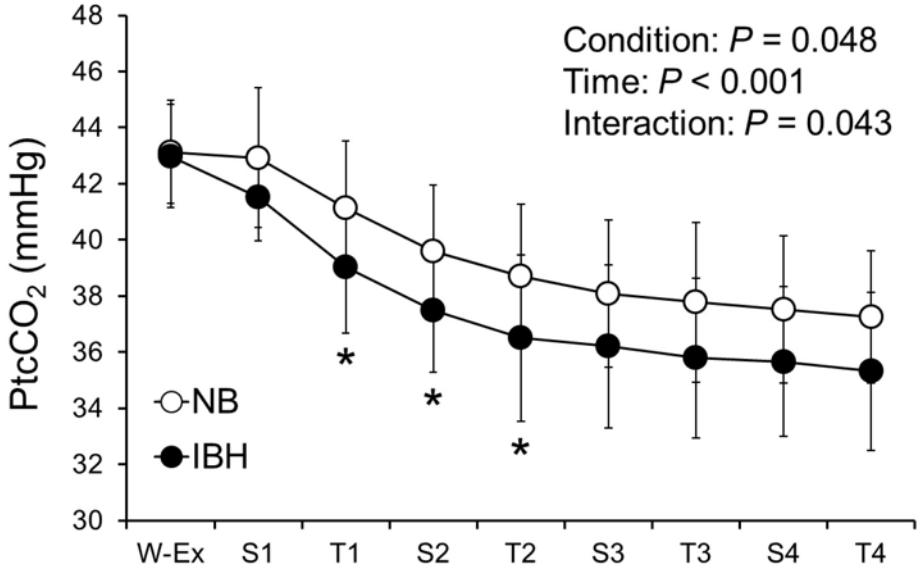

Fig. 2 Changes in the transcutaneous partial pressure of CO_2 ($PtcCO_2$) during exercise with normal breathing (NB) and intermittent breath holding (IBH) conditions. Values are presented as mean ± standard deviation. *: $P < 0.05$ compared to the NB values.

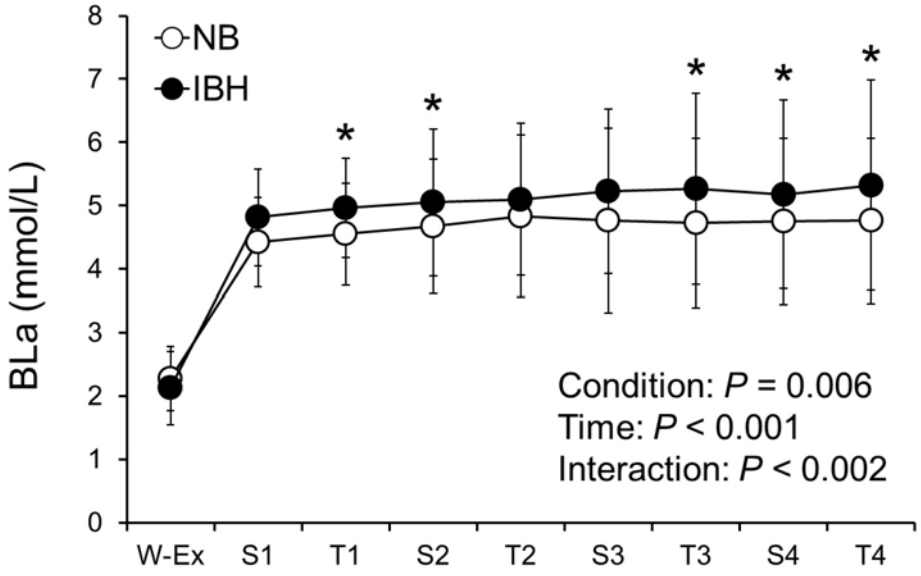

Fig. 3 Changes in the blood lactate (BLa) levels during exercise in normal breathing (NB) and intermittent breath holding (IBH) conditions. Values are presented as mean ± standard deviation. *: $P < 0.05$ compared to the NB values.

In our study, the BLa levels were slightly but significantly higher in the IBH condition than in the NB condition (Fig. 3), suggesting pronounced increases in the BLa levels by IBH during exercise. This result supports our previous study's findings in which a greater BLa response was seen after a 5-min moderate exercise with IBH[14]. There are several possible mechanisms for this. First, there is the possibility that IBH-induced involuntary hyperventilation, which affected the BLa values. Concerning the physiological effects caused by hypocapnia, as mentioned previously, hypocapnia attenuates activation of PDH during exercise, resulting in a potentiated accumulation of lactate in active muscle[24]. Thus, it is highly likely

that the inhibition of PDH activation induced by hyperventilation during exercise increases lactate production because pyruvate oxidation decreases. In fact, several studies on exercise with voluntary hyperventilation observed an enhanced BLa level compared with NB exercise[25,26]. Hence, in our study, IBH-induced hyperventilation may have contributed to the higher BLa values. However, it may be that this hypocapnic effect on the BLa response was not exclusive because an augmented ventilatory response caused by IBH was considerably smaller than that by voluntary hyperventilation in previous studies[24-26]. Second, it is possible that an increased blood epinephrine (EPi) concentration caused pronounced lactate production. Performing BH and hyperventilation increases the EPi concentration[27,28]. An increased blood EPi concentration is associated with accentuated glycogenolysis, resulting in increased BLa levels[29]. Furthermore, a strong correlation has been observed between arterial EPi levels and muscle lactate efflux during exercise under both normoxia and hypoxia[30]. Therefore, in this study, we speculate that the greater BLa response in the IBH condition was likely caused, at least in part, by an increased EPi concentration, although it was not measured. Our current results suggest that prolonged exercise with IBH can contribute to a continuous stimulus to glycolysis.

The findings of this study demonstrated that exercise with IBH induces involuntary hyperventilation, which results in hypocapnia. Moreover, as previously described, earlier findings on the circulatory response to BH during exercise and our previous study have confirmed that BH (and repeated IBH) during exercise can add hypoxic stimuli[9,10,12-14]. Thus, this means that hypoxic and hypocapnia effects are produced alternately during exercise with IBH. Considering previous studies that have shown increased $PaCO_2$ levels induced by BH[13,15], temporary hypercapnia states also occur during exercise with IBH. We propose that exercise with IBH involves unusual physiological stimuli, and its repetition (e.g., IBH training) may have the potential to redound the beneficial physiological adaptation for improving exercise performance. On the basis of the present findings, further studies will be needed to elucidate the effect of IBH training.

5. Conclusion

Our study suggests that prolonged exercise with IBH induces involuntary hyperventilation, leading to hypocapnia. The current observations also show that conducting IBH during prolonged exercise enhances the BLa response.

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