Physiological Effects of Positive Pressure Breathing with Pure Oxygen and a Low Oxygen Gas Mixture

Xiaopeng Liu; Huajun Xiao; Weiru Shi; Dongqing Wen; Lihua Yu; Jianzhang Chen

INTRODUCTION: Positive pressure breathing (PPB) can cause circulatory dysfunction due to peripheral pooling of blood. This study explored a better way at ground level to simulate pure oxygen PPB at 59,055 ft (18,000 m) by comparing the physiological changes during PPB with pure oxygen and low oxygen at ground level.

METHODS: Six subjects were exposed to 3 min of 69-mmHg PPB and 3 min of 59-mmHg PPB with pure oxygen and low oxygen while wearing the thoracic counterpressure jerkin inflated to 1× breathing pressure and G-suit inflated to 3 and 4× breathing pressure. Stroke volume (SV), cardiac output (CO), heart rate (HR), and peripheral oxygen saturation (S_pO_2) were measured. Subjects completed a simulating flying task (SFT) during 3-min PPB and scores were recorded.

RESULTS: HR and SV responses differed significantly between breathing pure oxygen and low oxygen. CO response was not significantly different for pure oxygen and low oxygen, the two levels of PPB, and the two levels of G-suit pressure. S_pO_2 declined as a linear function of time during low-oxygen PPB and there was a significant difference in S_pO_2 response for the two levels of PPB. The average score of SFT during pure oxygen PPB was 3970.5 ± 1050.4, which was significantly higher than 2708.0 ± 702.7 with low oxygen PPB.

CONCLUSIONS: Hypoxia and PPB have a synergistic negative effect on both the cardiovascular system and SFT performance. PPB with low oxygen was more appropriate at ground level to investigate physiological responses during PPB and evaluate the protective performance of garments.

KEYWORDS: positive pressure breathing, hypoxia, stroke volume, cardiac output, heart rate, peripheral oxygen saturation, rapid decompression, G-suit.

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Pilots' life support systems are designed to provide positive pressure breathing (PPB) that delivers high-pressure oxygen and body counterpressure in the event of either loss of cabin pressurization or emergency escape at altitudes above 39,370 ft (12,000 m). PPB can cause respiratory fatigue and circulatory collapse due to peripheral pooling of blood while improving the alveolar partial pressure of oxygen (P_AO_2) to avoid hypoxia, incapacitation, and loss of consciousness.[4,20] The pneumatic counterpressure garments provide support to the chest and lower body to reduce the respiratory difficulties and cardiovascular disturbances. During decompression to altitude above 39,370 ft (12,000 m) subjects become hypoxic, even with PPB. We hypothesized that circulatory dysfunction during PPB above 39,370 ft (12,000 m) is from the combined effects of PPB and moderate hypoxia, and, therefore, it was appropriate to evaluate the efficiency of protective garments when subjects are exposd to hypoxic conditions.

PPB was produced three ways in previous studies. Ground-level PPB with oxygen was produced with a PPB apparatus.[3] Ground-level PPB with normoxic room air was conducted in an altitude chamber by reducing the chamber pressure so that it was less than ambient pressure by designed value.[1,13,15] PPB commenced when a technician opened a valve to the outside of the chamber, allowing atmosphere air to enter the subject`s mask and garments. Altitude PPB with pure oxygen was produced in a hypobaric chamber by rapid decompression to

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49,212 ft (15,000 m) or above[2,6,7] and the positive pressure in the mask and garments was controlled by a breathing regulator anti-G valve.

Altitude PPB with pure oxygen was similar to the real conditions that pilots may encounter, but rapid decompression experiments were more complicated and risky. Compared with altitude PPB with pure oxygen, ground-level PPB with oxygen or normoxic room air does not put the same hypoxic stress on subjects. In this study, we compared the physiological changes during PPB with pure oxygen and low oxygen at ground level and aimed to explore a better way at ground level to simulate altitude PPB with pure oxygen at 59,055 ft (18,000 m).

METHODS

Subjects

Six healthy men (age 19.4 ± 0.6 yr, height 174.2 ± 4.0 cm, weight 69.3 ± 5.9 kg) volunteered for the study. The experimental protocol was approved by the Beihang University Human Ethics Committee. All subjects signed informed consent statements which outlined the purpose of the experiment and the protocols. This form also informed subjects of their rights to withdraw at any time without prejudice. All subjects had extensive experience with PPB and had passed medical examinations prior to participation. Subjects were required to avoid alcohol for 24 h and food for 2 h prior to the experiment. Subjects were fitted with the thoracic counterpressure jerkin and G-suit, together with standard TK-11 flying helmets and YM-9915G oronasal oxygen masks. The fitting of helmets, masks, and garments was performed by the same trained technician.

Equipment

The experiments were conducted with a positive pressure breathing trainer (AVIC Hefei Jianghang Aircraft Equipment Co., LTD, Anhui province, China) at Beijing, China, at an elevation of 144 ft (44 m). The positive pressure breathing trainer could supply the subjects with pressurized breathing gas and also inflate the counterpressure jerkin and G-suit with gas. The proportion of gas pressure in the oxygen mask to that in the jerkin and G-suit could be adjusted according to experimental design. In the experiment, the pressure in the jerkin was equal to the breathing pressure in the oxygen mask, and the pressure in the G-suit was three times or four times the breathing pressure. The counterpressure jerkin and G-suit were used to protect the subjects. The chest bladders of the jerkin cover 20% of the trunk surface above the navel. The G-suit bladders on the abdomen, thigh, and calf cover 60% of the body surface below the navel.

Subjects performed simulating flying tasks (SFT) on a psychological evaluation system (Institute of Aviation Medicine, Beijing, China) during PPB. The SFT required the subjects to keep flying smoothly on a computer screen during latitude changes. The subjects operated the control column with their right hands to compensate for the changes in pitch caused by the latitude changes. The changes were a sine wave whose circle was 20 ms, whose amplitude was from 1/50 to 1/2 of the height of the computer screen (22″), and was divided into 49°. The degree of change increased as the change amplitude increased. The initial degree of the change was 0.10°. The position of the zero parallel was measured every second. If the position of the zero parallel was continuously kept in the central circle for 5 s, the degree of the change increased by 1°. If the position of the zero parallel was continuously kept outside the central circle for 3 s, the degree of the change decreased by 1°. The degrees of change were recorded every second and the sum of 3-min degrees was the score of the task.

Peripheral oxygen saturation (S_pO_2) was measured with a fingertip pulse oximeter (Onyx○R II 9550, Nonin Medical, Inc., Plymouth, MN) with the probe on the index finger. Stroke volume, cardiac output, and heart rate were determined by electrical bio-impedance measurement (MP100WSW for BIOPAC System, Inc., Goleta, CA). Electrocardiogram (ECG) was continuously displayed using three standard limb leads.

Procedure

There were eight experimental conditions in this study, which were two levels of PPB (59 mmHg and 69 mmHg), two levels of G-suit pressure (three times and four times breathing pressure), and two kinds of breathing gas (pure oxygen and low oxygen). The oxygen concentrations in the breathing gas in the low oxygen experiments were 10.0% during 69 mmHg PPB and 8.8% during 59 mmHg PPB. Every subject conducted PPB for 3 min under all eight conditions from 0900 to 1100. There were at least 24 h between any two condition exposures. The order of the eight conditions was randomized.

Prior to the experiments, the subjects were trained on an SFT for over a week. After that week the scores were very stable at baseline. Subjects` bodyweight and height were recorded. A baseline control period of 3 min rest breathing normoxic room air preceded PPB. A technician operated the positive pressure breathing trainer to produce PPB with two levels of pressure, two levels of G-suit pressure, and two levels of oxygen concentration within 10 s. Subjects completed the SFT during the 3-min PPB and scores were recorded. All physiological parameters were measured during the final 10 s of each half-minute except the "0" point, which was calculated from data between 0-10 s after the pressure reached 59 mmHg or 69 mmHg.

PPB and G-suit inflation were initiated immediately after the control period and discontinued when the following presented: breathing fatigue, a fall in heart rate greater than 20% from the baseline, blood oxygen saturation lower than 70%, arrhythmia in the ECG, or presyncopal symptoms. Following the PPB run, a postcontrol period of 3 min was included to monitor the recovery from PPB. A qualified flight surgeon monitored all experiments. Subjects communicated with the experimenters by gesture during PPB.

Statistical Analysis

Values are expressed as means ± SD. For the dependent variables of heart rate (HR), stroke volume (SV), cardiac output (CO), and S_pO_2, the analysis was performed on the difference at minutes 0.0 through 3.0 from an average of the preceding

3-min control period. Differences in HR, SV, and CO were tested by using a four within factors (PPB, G-suit pressure, breathing gas, and time) repeated measures ANOVA. S_pO_2 was tested by using a three within factors (PPB, G-suit pressure, and time) repeated measures ANOVA. The score of the SFT was tested using a three within factors (PPB, G-suit pressure, and breathing gas) repeated measures ANOVA. Paired sample *t*-test was used to determine the differences between the baseline score of the SFT and each experimental condition. All analyses were performed using SPSS 13.0 and all comparisons were carried out using a two-tailed test with $\alpha = 0.05$.

RESULTS

Six subjects completed all 3 min of PPB at 59 and 69 mmHg without presyncopal symptoms. There were significant differences in cardiovascular responses, S_pO_2, and SFT scores between PPB with pure oxygen and PPB with low oxygen.

HR changes were a linear function of time [$F(1,6) = 136.4$, $p < 0.0001$]. There was a significant difference in HR response for the two kinds of breathing gas [$F(1,6) = 28.3$, $p = 0.003$] and two levels of G-suit pressure [$F(1,6) = 21.6$, $p = 0.006$]. There was a significant PPB level × breathing gas interaction [$F(1,6) = 6.8$, $p = 0.048$] and PPB time × breathing gas interaction [$F(6,6) = 27.4$, $p < 0.0001$] (**Fig. 1**). The average increase in HR during 3-min PPB with pure oxygen was 19 bpm above the baseline, while HR increased during PPB with low oxygen by 37 bpm above the baseline.

SV changes were a linear function of time [$F(1,6) = 208.9$, $p < 0.0001$]. There was a significant difference in SV response for the two kinds of breathing gas [$F(1,6) = 15.6$, $p < 0.0001$]. There was a significant PPB time × breathing gas interaction [$F(6,6) = 35.3$, $p < 0.0001$] (**Fig. 2**). The average decrease in SV during 3-min PPB with pure oxygen was 14 ml/beat below the baseline, while SV decreased during 3-min PPB with low oxygen by 20 ml/beat below the baseline.

CO changes were a linear function of time [$F(1,6) = 30.3$, $p = 0.003$]. There was not a significant difference in CO response for the two kinds of breathing gas [$F(1,6) = 6.4$, $p = 0.053$], the two levels of PPB [$F(1,6) = 1.4$, $p = 0.298$], and the two levels of G-suit pressure [$F(1,6) = 0.1$, $p = 0.774$]. There was a significant PPB time × breathing gas interaction [$F(6,6) = 2.9$, $p = 0.023$] (**Fig. 3**).

S_pO_2 was continuously 100% during PPB with pure oxygen. S_pO_2 changes were a linear function of time [$F(1,6) = 15.2$, $p = 0.011$] during PPB with low oxygen. There was a significant difference in S_pO_2 response for the two levels of PPB [$F(1,6) = 17.1$, $p = 0.009$]. There was a significant PPB time × PPB level interaction [$F(6,6) = 6.7$, $p < 0.0001$] (**Fig. 4**). The average decrease in S_pO_2 during 69-mmHg PPB with low oxygen was 5% below the baseline, and the lowest was 86%, occurring at a G-suit pressure of three times breathing pressure. The average decrease in S_pO_2 during 59-mmHg PPB with low oxygen was 9% below the baseline, and the lowest was 78%, occurring at G-suit pressure of four times breathing pressure.

There was a significant difference in SFT scores for the two kinds of breathing gas [$F(1,6) = 17.7$, $p = 0.008$] (**Fig. 5**). The average SFT score during PPB with pure oxygen was 3970.5 ± 1050.4 and 2708.0 ± 702.7 during PPB with low oxygen. There was not a significant difference in SFT score for the two levels of PPB [$F(1,6) = 0.03$, $p = 0.867$] and the two levels of G-suit pressure [$F(1,6) = 0.8$, $p = 0.414$]. Compared with the baseline, SFT scores in all eight experimental conditions decreased significantly by 1737.7∼3418.0 ($t = 5.528$∼14.666, $p \leq 0.003$).

DISCUSSION

The alveolar partial pressure of oxygen (P_AO_2) falls precipitously upon human rapid decompression to high altitude.[9] In an operational setting, 70-mmHg PPB would normally be used to provide get-me-down protection from an altitude of 60,000 ft (18,288 m).[8,12,18] However, Fraser`s study[12] indicated that 60-mmHg PPB with the Combined Advanced Technology Enhanced Design "G" Ensemble (COMBAT EDGE or CE) and the Tactical Life Support System (TLSS)[14] could provide 3 min protection against the development of syncope at 60,000 ft (18,288 m). Therefore, we supposed that 59-mmHg PPB and 69-mmHg PPB with our garment would provide sufficient P_AO_2 and adequate perfusion of the central nervous system with oxygenated blood during rapid decompression at 59,055 ft (18,000 m) when using 100% oxygen emergency breathing gas.

The physiologically equivalent altitudes[17] in aviation medicine may be stated in terms of equality of alveolar oxygen tension and a strict interpretation of the alveolar equivalence would require steady state conditions, the determination of the carbon dioxide tensions in both cases, and knowledge of the value of the respiratory exchange ratio. However, it is satisfactory to determine equivalence on the basis of equality of inspired (tracheal) oxygen tension for most

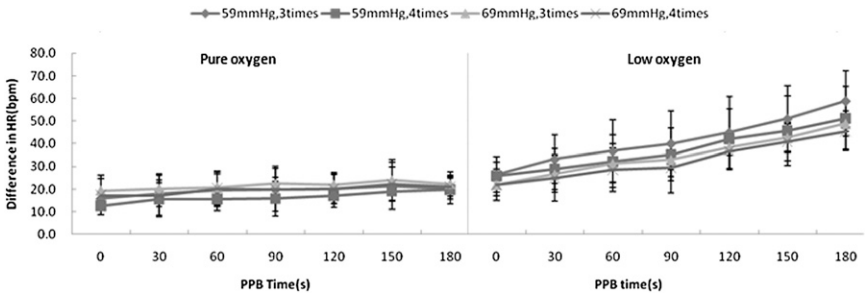

Fig. 1. Absolute changes in heart rate (HR) from the average of the 3-min control period over 3 min of PPB and four PPB conditions for pure oxygen vs. low oxygen mixture. Data represent the average of the final 10 s of each 30 s, and are expressed as mean ± SD.

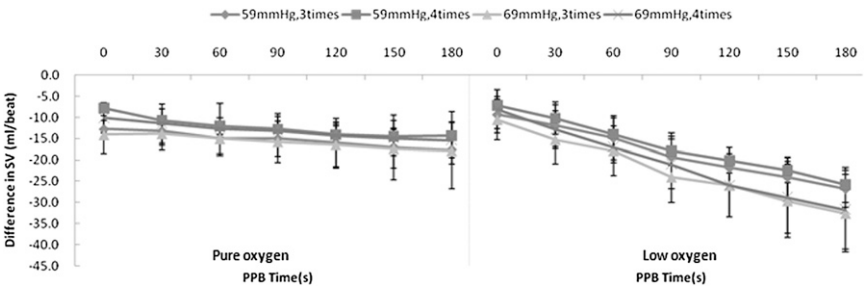

Fig. 2. Absolute changes in stroke volume (SV) from the average of the 3-min control period over 3 min of PPB and four PPB conditions for pure oxygen vs. low oxygen mixture. Data represent the average of the final 10 s of each 30 s, and are expressed as mean ± SD.

practical purposes.[17,24] P_IO_2 is the partial pressure of inspired oxygen, which is calculated as: $P_IO_2 = (P_B - PH_2O)\ F_IO_2$, where P_B is breathing gas pressure [the sum of ambient barometric pressure (760 mmHg) and PPB pressure], F_IO_2 is the fraction of inspired oxygen concentration, and PH_2O is water vapor pressure [47 mmHg at body temperature and pressure, saturated with water vapor (BTPS)].[21] According to the above formula, the P_IO_2 was 68 mmHg during 59 mmHg PPB with 8.8% oxygen with a balance of nitrogen at ground level (P_B = 760 mmHg), and the P_IO_2 was also 68 mmHg during 59 mmHg PPB with 100% oxygen at 59,055 ft (18,000 m). Therefore, it would be reasonable to believe that 59 mmHg PPB with 8.8% oxygen at ground level results in the hypoxia equivalent (in terms of P_IO_2) of 59 mmHg PPB with 100% oxygen at an altitude of 59,055 ft (18,000 m). Likewise, 69 mmHg PPB with 10.0% oxygen approximately simulated 69 mmHg PPB with 100% oxygen at 59,055 ft (18,000 m) in hypoxia, for the P_IO_2 was 78 mmHg in both conditions.

HR was a sensitive physiological index of physiological changes in response to hypoxia[17] and PPB. There was a slight increase of HR at steady state (the average increase each 3 min was 19 bpm) at all levels of PPB with pure oxygen (Fig. 1). Similar HR increases during 69-mmHg PPB with pure oxygen were reported in the study of Goodman et al., in which 70-mmHg PPB breathing air with a G-suit pressure of four times breathing pressure was adopted when using CE,[14] and also in the study of Ackles et al., in which 70-mmHg PPB breathing air with a G-suit pressure of three times breathing pressure was adopted when using the Swedish jerkin and G-suit.[1] The highest HR occurred at 69 mmHg with a G-suit pressure of three times breathing pressure when breathing pure oxygen. This indicated that the protection from the garment was weakest under this condition. However, with low oxygen, there were progressive elevations (the average each 3 min was 37 bpm) in HR at all PPB levels, with the greatest elevation occurring at 59 mmHg with a G-suit pressure of three times breathing pressure (Fig. 1). These results suggested that the protection by a G-suit pressure of three times breathing pressure was weakest during 59-mmHg PPB. HR increases during PPB with low oxygen were consistent with the changes in HR during rapid decompression reported by Fraser et al.[12] The HR increase caused by PPB may be regulated by receptors in the atria and great veins detecting a sharp reduction in venous return and right atria filling during PPB[16]. Hypoxia stimulates the carotid body and leads to further increases in HR during PPB with low oxygen. Therefore, HR increase during PPB with low oxygen was obviously greater than with pure oxygen.

PPB causes an immediate transfer of breathing pressure to the vascular structures, which leads to the progressive pooling of blood in dependent regions. The pooling of blood, which is the effect of loss of effective blood volume plus tissue filtration, results in poor venous return and a decreased SV.[14] The changes in SV during PPB in this study agreed with previous work studying cardiovascular responses to PPB. The SV changes during PPB with pure oxygen were similar to Balldin and Wranne`s study[3] and Ackles' study[1] with air. The declines in SV during 59-mmHg PPB with an 8.8% gas mixture were similar to that of 60-mmHg pure oxygen PPB with TLSS during rapid decompression at 60,000 ft (18,288 m) by Fraser et al.[12] In our study, the average reduction in SV during 3-min PPB with low oxygen was 20 ml/beat, which was significantly greater than the 14 ml/beat reduction during PPB with pure oxygen. Thus, it would appear that hypoxia is the factor responsible for the greater reduction of SV. Hypoxia further increased HR, which had already increased during PPB. HR was too fast to maintain enough left ventricular filling (preload), which lead to a synergistic decrease in SV.

The reduction in SV due to PPB was appropriately compensated for by increases in HR, which resulted in maintained CO at PPB with pure oxygen and increased CO at PPB with low oxygen. When breathing pure oxygen, there was no significant difference of CO between baseline and PPB ($p > 0.05$). HR increased to a greater extent with this garment, which was sufficient to maintain CO despite the fall in SV. These changes in CO were similar to Goodman's study,[13] which did not find significant CO changes from the control values during PPB with TLSS breathing air. However, Balldin and

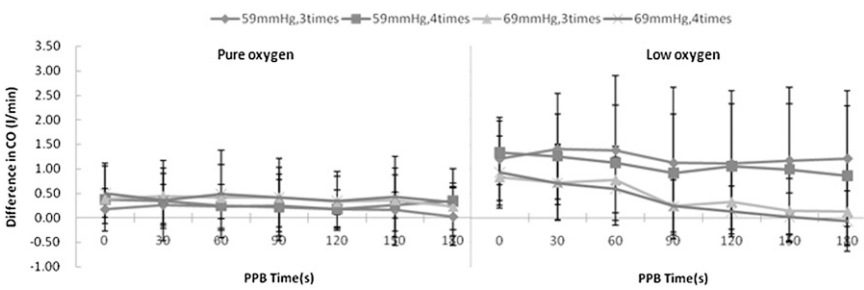

Fig. 3. Absolute changes in cardiac output (CO) from the average of the 3-min control period over 3 min of PPB and four PPB conditions for pure oxygen vs. low oxygen mixture. Data represent the average of the final 10 s of each 30 s, and are expressed as mean ± SD.

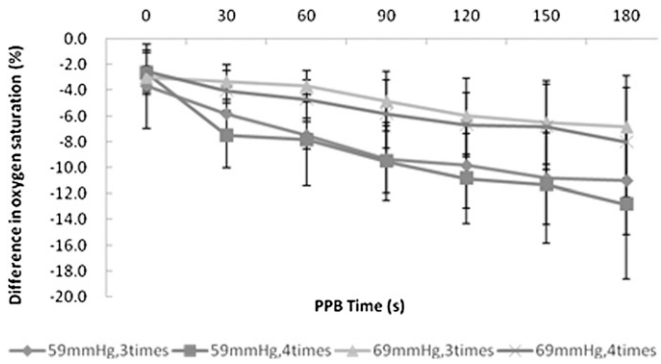

Fig. 4. Absolute changes in peripheral oxygen saturation (S_pO_2) from the average of the 3-min control period over 3 min of PPB and four PPB conditions for the low oxygen mixture. Data represent the average of the final 10 s of each 30 s, and are expressed as mean ± SD.

Wranne`s study[3] and Ackles' study[1] with a British RAF ensemble, Swedish ensemble, and Canadian forces ensemble found a decrease in CO during PPB of 70 mmHg breathing air.

The different garments and different methods of measuring CO used in this experiment may have contributed to the discrepancy in results. Firstly, the garments in this study and Goodman's study might provide better protection against PPB than the garments in Balldin's study and the British RAF ensemble, Swedish ensemble, and Canadian forces ensemble in Ackles' study. Secondly, the electrical bio-impedance CO measurements had different bioimpedance algorithms,[10] which might have led to different results. Additionally, the accuracy of CO measurement using bioimpedance cardiography was less than that of magnetic resonance imaging,[23] direct Fick measurement,[22] and Doppler echocardiography,[5,11] which could result in the discrepancies between studies. Even so, this noninvasive CO measurement could still be employed when studying change in CO for the same volunteers under different experimental conditions.

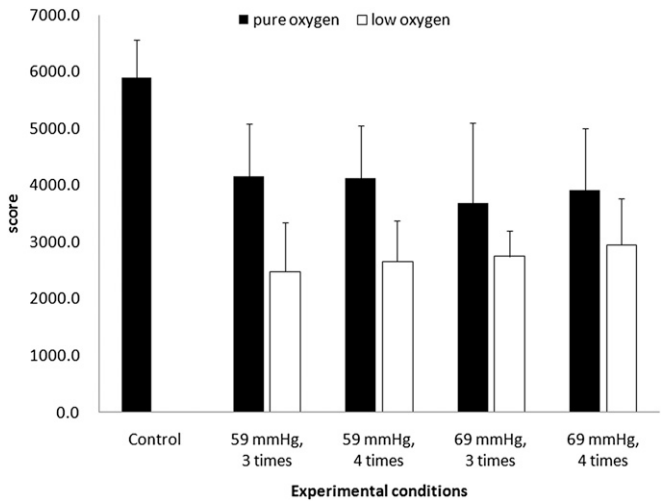

Fig. 5. Average task scores for the control, two levels of PPB, and two levels of pressure ratio during PPB with pure oxygen and a low oxygen mixture. $N = 6$. Variance bars represent standard deviation.

A surprising finding of this study was the actual increase in CO ($P < 0.001$) during PPB with low oxygen. We supposed that the combined effects of hypoxia and garment protection lead to the increase in CO, which was calculated by multiplying SV and HR. Garments provided protection from pooling of blood in the abdomen and lower limbs and increased venous return, which minimized the reduction of effective blood volume. At the same time, hypoxic exposure increased HR by 45 to 60 bpm above baseline at the third minute during PPB. When the extent of HR rising was greater than the extent of SV falling, CO appeared to increase. This result should be treated with caution in view of the fact that PPB continued only for 3 min. If the duration of PPB had been prolonged, the sharp increase in HR would not continue and the increase in CO would not be maintained.

There were no changes in S_pO_2 across time or all levels of PPB when breathing pure oxygen, which was in accordance with S_pO_2 when breathing air in a previous study.[13] The tendency of S_pO_2 to fall over 3 min of PPB with low oxygen was similar to previous rapid decompression studies conducted at 60,000 ft (18,288 m),[8,12,19] but the systematic oxygen state was better. In this study, the oxygen concentration in the gas mixture was calculated on the basis of equality of P_IO_2 instead of P_AO_2, which may cause hypoxic stress when breathing low oxygen at ground level to be a little lower than breathing pure oxygen at 59,055 ft (18,000 m). Secondly, it would take several seconds for pressurized pure oxygen to be delivered to the oxygen mask after the start of rapid decompression in experiments and the delay in delivery of pressurized pure oxygen at high altitude causes the intensity of hypoxia to be greater. Additionally, the protective effects against PPB provided by different garments (jerkin and G-suit) in these studies were different and affected subjects' systematic oxygen state, which is displayed in the different S_pO_2 measurements.

PPB had a negative effect on SFT performance in our study. SFT scores in all eight experimental conditions were lower than the baseline by 1737.7～3418.0, which may be attributed to distraction,[19] physical discomfort[16] (e.g., respiratory difficulty, limb and abdominal tenderness), and vision impairment[16] associated with PPB. The wide range of decrease in SFT scores during PPB with different experimental conditions might be caused by the experimental conditions applied and hypoxia may have a synergistic effect with PPB on SFT. Lindeis' experiment[19] argued that hypoxia was a major source of the slowing of reaction time during PPB. In this study, the average SFT scores during PPB with pure oxygen was 3970.5, much higher than the scores of 2708.0 during PPB with low oxygen. Our study reinforced that hypoxia induced by breathing 10.0% and 8.8% oxygen gas mixture is a major cause of the decrease in performance during PPB.

To our knowledge, there is no study comparing the physiological responses during PPB with pure oxygen and low oxygen as our study did. The results of this study suggested that hypoxia exacerbates PPB's negative effect on both the cardiovascular system and SFT performance. During 3-min PPB at ground level, HR, SV, and S_pO_2 were sensitive indexes

reflecting the responses of the cardiovascular system to PPB, and the CO was a direct measurable total response of the cardiovascular system to PPB and different oxygen levels. The changes in HR, SV, and S_pO_2 during PPB with pure oxygen were smaller than that during PPB with low oxygen. Therefore, evaluation of the protective performance of garments against PPB at ground level by investigating physiological responses to PPB should take into account hypoxia as an important contributor.

In this study, the concentration of low oxygen gas mixture was calculated on the basis of equality of inspired (tracheal) oxygen tension rather than equality of alveolar oxygen tension. Therefore, we could not confirm whether 69-mmHg PPB with 10.0% oxygen at ground level could simulate 69-mmHg PPB with pure oxygen at 59,055 ft (18,000 m) and 59-mmHg PPB with 8.8% oxygen at ground level could simulate 59-mmHg PPB with pure oxygen at 59,055 ft (18,000 m); rapid decompression experiments are necessary in the future.

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