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■原著

Effect of normal air pressure low oxygen concentration environments on resting metabolism

常圧低酸素濃度環境が安静時代謝に与える影響

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Abstract : In order to examine whether normal pressure and low oxygen environments are effective as exercise loads, we used respiratory gas analysis to look into the impact of 30 minutes of exposure to normal pressure low oxygen concentration conditions on energy metabolism. Subjects were 7 healthy adult males. Method: A low oxygen concentration environment at normal pressure was set up using membrane separation at a normal oxygen concentration. Subjects rested for 30 minutes in a seated position in each of the test conditions, and readings of their energy expenditure rate (kcal/min), lipid oxidation rate (mg/min), and glucose oxidation rate (mg/min) were obtained using respiratory gas analysis, and a comparative investigation was carried out on these. Results: The EER in the low oxygen concentration environment at normal pressure was the same as that in a normal oxygen environment, however, the lipid oxidation rate in the low oxygen concentration environment at normal pressure was significantly lower than that in the normal oxygen environment, and the GOR in the low oxygen concentration environment at normal pressure was significantly higher than that in the normal oxygen environment. Conclusion: These results suggested that unlike in high altitude environments, glucose usage may be accelerated in low oxygen concentration environments at normal pressure, in which only oxygen concentration is decreased.

Key words : normal air pressure, low oxygen environment, resting metabolism, indirect calorimetry

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I Introduction

There have been an increasing number of cases of life style related diseases in Japan. Male 50% older than 30 years old and female 50% older than 50 years old are the hyperlipemia patients in Japan[1]. The 22.1 million adults in Japan, over 20% of the adult population, either have or are suspected of having diabetes[2]. The increasing medical cost of lifestyle diseases is an extremely important issue for Japan, and various measures are been taken, such as the "Healthy Japan 21" program.

Moreover, it is known that the incidence rate of conditions such as coronary heart disease and hypertension is low among people living at high altitudes, namely 1,000～3,000 m above sea level, and it is also known that many such people have long life expectancies.

Also, it has been pointed out that training at high altitude is effective in improving lipid and glucose metabolism[3]. Terrados et al.[4] reported that four weeks of intermittent endurance training in a low oxygen concentration environment (60～70% $\dot{V}O_{2MAX}$) and at low pressure, at an altitude of 2,300 m, is effective in increasing lipid oxidation and reducing glycolysis.

Kikuchi et al.[5] pointed out that endurance exercise for athletes in an artificial low oxygen concentration environment at low pressure, at an altitude of 2,000 m, may improve lipid metabolism, and it may be effective in weight loss compared to that in a normal environment. However, it is very difficult to actually carry out training at high altitude or in a low-oxygen environment at low pressure from physical and financial points of view. Moreover, in recent years it has become possible to create low oxygen concentration environments at normal pressure using relatively simple devices. High altitude environments have the feature that oxygen concentration and pressure are both low. If it is low concentration environments that have a positive impact on energy metabolism, it may be easy to realize effective training environments.

The purpose of this study was to examine whether normal pressure low oxygen concentration environments can be combined with other conditions in applying an exercise load, and whether such environments are effective.

In the present study, respiratory gas data was used to look into the impact of low oxygen concentration environments at normal pressure on energy metabolism.

In addition, this study took approval of an ethic committee of Kochi rehabilitation Institute.

II Subjects and method

1. Subjects

Subjects were seven healthy adult males. Their mean age was 21.5 (the age range was 21～22 years old). Their mean height, weight and body surface area were 167.6±3.3 cm, 62.3±5.8 kg and 1.71±0.09 m^2. We explained the study aims, details, and points to note to the subjects, and started the experiment after obtaining written informed consent.

2. Method

The experiment was carried out in a room with a temperature of 27～28℃ and humidity of 40～50%. A vinyl chloride tent (volume of 4.0 m^3) the Fujiwara et al.[6] patent were used, and a high/ low oxygen air generator using a membrane separation method as reported by Ookura[7] (separation membrane: UBEN2, made by Ube Kosan; compressor : SLP-22C, made by Anest Iwata) were used to prepare a low oxygen concentration environment (oxygen concentration of 14.5%, 0.7 atm, equivalent to an altitude of 3,000 m; hereinafter referred to as the "low oxygen environment"), and also a normal oxygen concentration environment was prepared (oxygen concentration of 20.9%, 1.0 atm ; hereinafter referred to as the "normal oxygen environment") (**Fig. 1**).

In the present study, an experiment was firstly carried out in the normal oxygen concentration environment, and a subsequent experiment was car-

ried out in a low oxygen concentration environment a week thereafter.

In each environment, subjects sat in a resting position for 30 minutes, and the their energy expenditure rate (EER, kcal/min), and lipid oxidation rate (LOR, mg/min) and glucose oxidation rate (GOR, mg/min) were obtained using respiratory gas analysis, and a comparative analysis was carried out. EER, LOR and GOR were calculated using the following formulae[8].

$EER = (3.581 \times VO_2\ (L) + 1.448 \times VCO_2\ (L))/1{,}000 - 1.773 \times NU$; $LOR = 1.689 \times (VO_2\ (L) - VCO_2\ (L)) - 1.943 \times NU$; $GOR = 4.571 \times VCO_2\ (L) - 3.231 \times VO_2\ (L) - 2.826 \times NU$. NU (mass of urea nitrogen excreted per minute) was set at 0.008 g/ min. Additionally, EER, GOR, and LOR were adjusted for body surface area. Also, subjects did not eat dinner and fasted until measurements were carried out the following morning.

During the experiment, an ECG monitor was used to monitor the heart rate (HR, bpm), and subjects were monitored for arrhythmia. The percutaneous arterial oxygen saturation rate (SpO_2) was measured using a pulse oximeter (NBP-400, NELLOR PUPITANBENNETT). A respiratory gas analyzer (Aero-Monitor AE-300S, Minato Medical Science) was used to continuously measure respiratory gas data using the breath-by-breath method. Measurements were taken every minute from the start until the end of the experiment, the average of each 5 minute interval was named Stage 1 to Stage 6, and a comparative investigation was carried out on these Stages (**Fig. 2**).

The Wilcoxon signed-ranks test was used for the statistical method in comparing data between the low and normal oxygen concentration environments. A one-way analysis of variance and multiple comparison tests were used in comparing the stages in a given oxygen concentration environment. The significance level for each Stage was set at $p < 5\%$. SPSS Ver.18 was used to carry out statistical analyses.

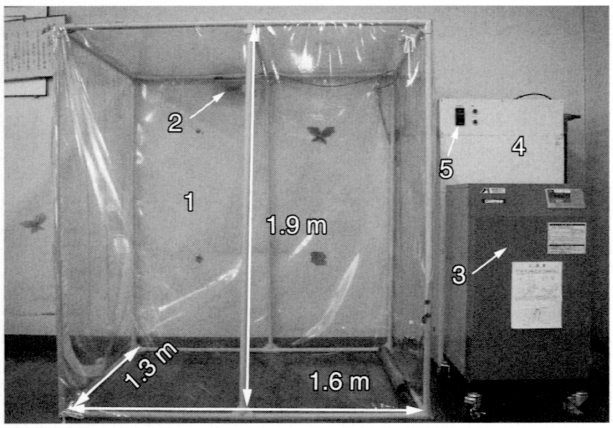

Fig. 1 High/low oxygen air generator
Vinyl chloride tent (Volume : 4.0 m^3)
1 : Oxygen room, 2 : Oxygen sensor, 3 : High/Low oxygen air generator, 4 : Oxygen concentration controller, 5 : Oxygen monitor

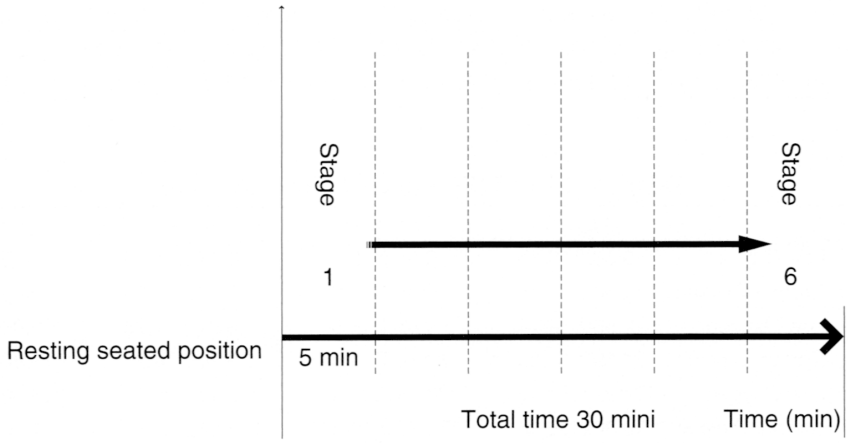

Fig. 2 Illustration of experiment plan

III Results

Their mean SpO_2 were 93.4±1.2% at Stage 1, 92.4±1.3% at Stage 2, 91.3±1.8% at Stage 3, 90.9±2.4%at Stage 4, 91.1±2.6% at Stage 5 and 91.2±2.5% at Stage 6 in low oxygen concentration environments respectively. Their mean SpO_2 were 97.5±0.4% at Stage 1, 97.3±0.6% at Stage 2, 97.2±0.6% at Stage 3, 97.3±0.4% at Stage 4, 97.4±0.2% at Stage 5, 97.6±0.4% at Stage 6 in normal oxygen concentration environments respectively. There were significant differences in all stages between low oxygen concentration environments and normal oxygen concentration environments (**Table 1**, $p<0.05$). Also, in the low oxygen concentration environment, there was a small difference found from Stage 3 onwards.

It was considered that the amount of oxygen supplied to the body reached a stable level in Stage 3 and onwards, and EER, LOR, and GOR were compared in these Stages (**Table 2**). There were no significant differences in LOR between the low and normal oxygen concentration environments. There was a significant difference in LOR at Stage 3 and onwards between the low and normal oxygen concentration environments, and the values were lower in the low oxygen concentration environment ($p<0.05$). There was a significant difference in GOR between the low and normal oxygen concentration environments, and the values were high in the low oxygen concentration environment ($p<0.05$).

IV Discussion

We analyzed the effect on resting energy metabolism of the exposure to normal pressure low oxygen environment.

Oxygen taken into the body is affected by the aspiratory oxygen concentration. In air at 1 atm (760Torr), alveolar O_2 partial pressure (P_AO_2) is approximately 100Torr at an oxygen concentration of 20.9%, and it is approximately 56.4Torr at an oxygen concentration of 14.5%. Thereafter, oxygen moves to the alveoli through pulmonary capillary blood via a diffusion mechanism, it is taken into the body, and arterial O_2 partial pressure (P_aO_2) becomes equivalent to P_AO_2. In the low oxygen condition in the present study, since P_AO_2 was equal to P_aO_2, it was estimated at approximately 56.4Torr. Normally, arterial O_2 partial pressure is 60% at a P_aO_2 of 60torr, and therefore it was considered that it becomes almost stable at 90～91% at Stage 3 and later, and that the oxygen supply at low oxygen concentrations stabilizes.

Based on this, EER, LOR, and GOR were compared at Stage 3, at which it was considered that the volume of oxygen supplied to the body stabiliz-

Table 1 SPO_2 (%) at each Stage

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6
Low Oxygen	93.4 ± 1.2	92.4 ± 1.3	91.3 ± 1.8	90.9 ± 2.4	91.1 ± 2.6	91.2 ± 2.5
Normal Oxygen	97.5 ± 0.4	97.3 ± 0.6	97.2 ± 0.6	97.3 ± 0.5	97.4 ± 0.2	97.6 ± 0.4

* : $p<0.05$

Table 2 EER, LOR and GOR for each Stage

		Stage 3	Stage 4	Stage 5	Stage 6
EER ($kcal/min/m^2$)	Low Oxygen	0.66± 0.15	0.68± 0.14	0.67± 0.18	0.75± 0.16
	Normal Oxygen	0.69± 0.05	0.68± 0.04	0.70± 0.06	0.71± 0.06
LOR ($mg/min/m^2$)	Low Oxygen	2.58± 4.14	4.41± 8.80	4.91± 7.75	2.05± 2.75
	Normal Oxygen	23.19±15.86	20.10±15.44	23.20±14.21	17.80± 19.86
GOR ($mg/min/m^2$)	Low Oxygen	227.20±89.22	239.14±94.97	219.43±90.50	268.36±101.69
	Normal Oxygen	150.36±36.06	155.76±49.39	156.27±51.65	177.85± 52.00

* : $p<0.05$

es, and at subsequent Stages.

GOR values were significantly higher in the low compared to the normal oxygen concentration environment. Since glycolysis inside mitochondria is inhibited in patients with hypoxemia in high altitude environments (low oxygen concentration environments at low pressure), a mitochondrial decoupling protein is used in place of glucose. Further, it has been reported that as a result of making up for the lack of ATP by increasing the efficiency of ATP binding with anaerobic glycolysis, the use of glucose increases, blood sugar decreases, and insulin secretion also decreases, and consequently, insulin sensitivity improves[9]. In the present study, it was considered that subjects had hypoxemia in the low oxygen concentration environment, based on their SPO_2 results, and it was also considered that a large amount of glucose was used due to a similar effect. Therefore, the results suggested that glucose utilization may increase even in low concentration environments at normal pressures, where only oxygen concentration is decreased, unlike in a high-altitude environment. It is necessary to further look into the benefits of such environments for use in treating diabetes, the incidence of which has been continually increasing.

LOR values were significantly lower in the low oxygen concentration environment than in the normal one. It has been reported that staying and training in high-altitude environments increases sympathetic nerve hormone secretion due to a decreased oxygen saturation level in low oxygen concentration environments[9]. Free fatty acids are released by adipocytes, mediated by β 3AR, increasing lipid metabolism[10]. In these preliminary studies, subjects had to climb up a mountain before being exposed to a low oxygen concentration environment, and measurements were taken during a stay on a mountain for four days to several weeks. The exposure time to the low-concentration environment in the present study was only 30 minutes, and it was considered that this difference affected the results. It is necessary to change the conditions by extending the continual exposure time in a low oxygen concentration environment and increasing the number of times of repeated exposure, and it is also necessary to look into the impact of changing such conditions.

There were no significant differences in EER in each Stage of normal and low oxygen concentration environments. Therefore, it was considered that exposure to the low oxygen environment for a short period of time does not affect the energy consumption in a resting seated position; however, the results of a preliminary study[11] showed that heart rates at rest increased after subjects were exposed to low oxygen concentration environments for short periods of time, and there was also a tendency for air ventilation volume to increase, although this increase was not significant.

Naturally, such changes should increase energy consumption; therefore it was considered that it is necessary to review these points by extending the exposure time. It is necessary to look into glucose and lipid metabolism during the post-exercise recovery period in a low oxygen concentration environment going forwards.

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要　旨：（目的）常圧低酸素環境が運動負荷として有効であるかを検討する為に，常圧低酸素条件へ30分暴露させた場合のエネルギー代謝に与える影響について呼気ガス分析から検討した。（対象）健常成人男性7名。（方法）通常酸素濃度と膜分離方式により常圧低酸素環境を設定した。各条件下で30分間の安静座位を行い，呼気ガス分析からエネルギー消費率（energy expenditure rate，kcal/分），脂肪酸化率（lipid oxidation rate，mg/分）およびブドウ糖酸化率（glucose oxidation rate，mg/分）を求め比較検討した。（結果）常圧低酸素環境は，通常酸素環境に比べEERは同量であるが，脂肪酸化率は有意に少なく，ブドウ糖酸化率は有意に多かった。（結語）高地環境とは異なり酸素濃度のみを低下させた常圧低酸素環境で，糖質利用が促進される可能性が示唆された。

キーワード：通常気圧，低酸素環境，安静時代謝，間接熱量測定法

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