Effect of head-down human body position on chemoreflex control of breathing

Eugene S. Ermolaev[1,4], Alexander I. Dyachenko[1, 2, 3, 4], Yury A. Shulagin[1], Alexander O. Goncharov[3], Artem V. Demin[1]

[1]State Scientific Center of the Russian Federation – Institute of Biomedical Problems of the Russian Academy of Sciences, IMBP RAS, Moscow, Russia.
[2]General Physics Institute named by A.M. Prokhorov of the Russian Academy of Sciences, GPI RAS, Moscow, Russia.
[3]Department of Molecular and Biology Physics, Moscow Institute of Physics and Technology (State University), MIPT, Moscow, Russia
[4]Department of Biomedical Techniques, Bauman Moscow State Technical University, BMSTU, Moscow, Russia

Abstract— **Modified methods aimed for future studies of chemoreflex control of breathing during long space missions are presented. A study of the control in sitting and head-down supine subjects was performed by these methods. Tidal volume and ventilatory hypercapnic responses were analyzed in $P_{ET}CO_2$ range between 45 mmHg and 65 mmHg. Progressive hypercapnic – hypoxic rebreathing revealed posture changes in chemoreflex control, so it is reasonable to use this method in space studies as well as the methods of hyperoxic rebreathing and of isocapnic rebreathing. Chemoreflex control of tidal volume response, i.e. V_TR, has a greater sensitivity to posture than ventilation response, i.e. VR, so it is recommended to include tidal volume in the parameters of study in space flights.**

Keywords— **chemoreflex control of breathing, tidal volume response, ventilatory response, sitting upright position, supine head-down position.**

I. INTRODUCTION

Chemoreflex control of breathing plays a major role in adjustment of ventilation to metabolic demand and changes of CO_2 and O_2 contents in the inspired air. Studies in space revealed changes of human breathing control.

During 6-months of space missions the voluntary breath holding time (BHT) increased: BHT after inspiration increased from 69±4 s to 90±8 s ($p<0.05$) and BHT after expiration increased from 34±6 s to 42±9 s (nonsignificant), i.e. 31% and 25% higher than preflight values respectively [1]. After landing BHT were similar to preflight values.

The hypoxic ventilatory response (VR) was reduced, but hypercapnic VR was steepened somewhat in both short spaceflights and supine subjects [2].

There was no any study of VR during long space missions. To further understand effect of microgravity on control of breathing it is necessary to perform measurements of both hypoxic and hypercapnic VR in long space flights. Various modifications of experimental techniques could be used for studies of VR. Standard ground-based equipment and methods are not well suitable for this purpose because usually used balloons with oxygen are dangerous in space. Another limitation is a demand for minimal dimensions of equipment. All these means that a special apparatus and methods should be developed for the study of chemoreflex control of breathing in space. This small apparatus could be useful for clinical evaluation of chemoreflex control of breathing.

The purpose of this work was a development of modified methods aimed for future studies of VR during long space missions and a study of VR in sitting and supine subjects by these methods.

II. MATERIAL AND METHODS

An experimental setup included bag in box for rebreathing with a set of tubes and valves. The maximal volume of the bag was 7 l and the volume of box with tubes was 20 l. Gas flow was measured by an ultrasound gas flow meter (Moscow State Mining University, measured flow ranges 0-20 l/s). End-tidal CO_2 and O_2 were registered respectively by custom-made CO_2-meter (Triton, Russia) and O_2-meter (Beckman OM-11, USA). Lung volumes were measured by helium dilution technique (VIASIS Master Screen, Germany).

Eight normal subjects in this study were volunteers with age from 20 to 25 years, who had no history of lung diseases. Before the study an informed consent was obtained from every subject.

The experimental protocol of respiration via rebreathing apparatus included: 5 min of a normal breathing with room air, maximal BH after maximal inspiration, 2 min of a normal breathing with room air, 1 min of hyperventilation to obtain P_{ET} CO_2 about 20-25 mmHg, rebreathing in the bag during 10-12 min or up to obtaining $P_{ET}CO_2$ about 60 mmHg, breathing with room air.

Each subject performed 4 different runs:

- Run 1 – hypercapnic ventilatory response starting breathing room air in the upright seated position (VR1), VR1 was obtained in $P_{ET}CO_2$ range from 45.3±0.5 mmHg to 60.2 ± 1.4 mmHg, while $P_{ET}O_2$ decreased from 89.1±9.2 mmHg to 60.3±7.0 mmHg.

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- Run 2 – hypercapnic ventilatory response starting breathing room air in the supine head-down position -12,5° (VR2), VR2 was obtained in $P_{ET}CO_2$ range from 45.7±0.3 mmHg to 60.2 ± 0.8 mmHg, while $P_{ET}O_2$ decreased from 88.2±3.7 mmHg to 57.8±3.6 mmHg.
- Run 3 – hypercapnic ventilatory response starting breathing hyperoxic gas mixture in the upright seated position (VR3), VR3 was obtained in $P_{ET}CO_2$ range from 45.3±0.4 mmHg to 60.2±0.6 mmHg, while $P_{ET}O_2$ decreased from 381.3±7.8 mmHg to 335.1±13.6 mmHg.
- Run 4 – hypercapnic ventilatory response starting breathing hyperoxic gas mixture in the supine head-down position -12,5° (VR4), VR4 was obtained in $P_{ET}CO_2$ range from 45.6±0.2 mmHg to 60.1 ± 0.6 mmHg, while $P_{ET}O_2$ decreased from 382.5±24.1 mmHg to 325.6±35.7 mmHg.

Ventilatory responses were analyzed in terms of a linear line of best fit of ventilation against $P_{ET}CO_2$.. Tidal volume responses V_TR1, V_TR2, V_TR3, V_TR were also obtained and analyzed respectively in the same runs 1-4 in terms of a linear line of best fit of tidal volume (V_T) against $P_{ET}CO_2$. All responses were analyzed in $P_{ET}CO_2$ range between 45 mmHg and 65 mmHg.

Statistical comparisons of runs were by paired t-test.

III. Results

A representative example of VR and a linear line of best fit of ventilation against $P_{ET}CO_2$ obtained in the range between 45 mmHg and 65 mmHg is presented on Fig. 1. Group mean results of VR and V_TR in terms of parameters of the linear line of best fit of ventilation $\dot{V}$ and tidal volume V_T against $P_{ET}CO_2$ are presented in table 1 and Figs 2 a,b. The parameters under consideration are slopes $S_V = \Delta\dot{V} / \Delta P_{ET}CO_2$ and $S_{VT} = \Delta V_T / \Delta P_{ET}CO_2$; P_{V0} and P_{VT0} are $P_{ET}CO_2$ at a calculated $\dot{V}$ and V_T of zero respectively. The parameters are defined in according to the following equations (1):

$$\dot{V} = S_V \cdot (P_{ET}CO_2 - P_{V0})$$
$$V_T = S_{VT} \cdot (P_{ET}CO_2 - P_{VT0}) \qquad (1)$$

Significance of differences between parameters obtained in runs was estimated by Student's paired t-test (table 2).

Student's paired t-test revealed that VR1 was significantly (P<0.02) more than VR3 and VR2 was significantly (P<0.05) more than VR4. In the upright seated position $P_{ET}CO_2$ at a ventilation and a tidal volume of zero was by 2.20 ±1.58 mmHg more in hypoxia than in hyperoxia (P<0.05). Differences in breathing frequency between runs were not significant.

Transition from the sitting upright to the supine head down position reduced functional residual capacity reduction by 1.15 ± 0.24 l.

Table 1 Parameters of the linear line of best fit

Run	S_V, l/min/mmHg	P_{V0}, mmHg	S_{VT}, l/min/mmHg	P_{VT0}, mmHg
1	2.22±0.75	33.98±3.34	0.067±0.006	23.30±5.62
2	2.47±0.79	37.24±2.69	0.093±0.007	31.70±4.99
3	1.56±0.43	32.16±3.05	0.044±0.014	21.83±11.57
4	1.86±0.50	34.07±2.87	0.055±0.013	31.72±10.47

Table 1 Significance of differences between parameters

	$S_V \setminus S_{VT}$				$P_{V0} \setminus P_{VT0}$			
Run	1	2	3	4	1	2	3	4
1	-	0.99	0.99	0.95	-	0.98	NS	NS
2	0.8	-	0.998	0.995	0.95	-	0.8	NS
3	0.98	0.95	-	0.9	0.95	0.999	-	NS
4	0.9	0.95	0.9	-	0.9	0.95	NS	-

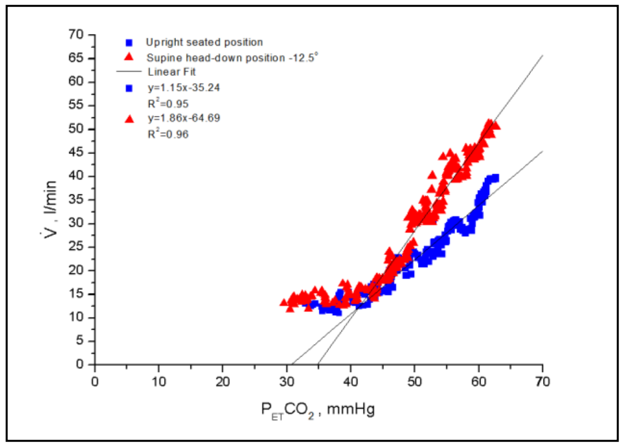

Figure 1 A representative example of VR in upright seated position and supine head-down position with linear lines of best fit

IV. Discussion

One of the purposes of this work was a development of modified methods aimed for future studies of chemoreflex sensitivities during long space missions. Rebreathing method is better suitable than steady-state method because rebreathing could be performed without a high pressure balloon with CO_2. Besides that in a modified rebreathing method which included a prior hyperventilation proved provided the best estimate of central-chemoreflex sensitivity of the three compared methods [3] including steady-state Read's rebreathing technique [4, 5]. Usually rebreathing starts from breathing a gas mixture containing 7% CO_2 [3, 4, 5]. In our experiments a rebreathing started from the room air . After the beginning of rebreathing $P_{ET}CO_2$ increased up to 45 mmHg, i.e. reached normal venous blood value, between 5 min and 6 min. After that reached about 60 mmHg between 5 min and 7 min In total our modified rebreathing method takes up to 13 min. There is no any need of any high pressure balloon in this method.

Two types of respiratory chemoreflex control parameters were considered in this paper: ventilation and tidal volume. Considering VR, we obtained significant differences between VR1 and VR3, VR2 and VR4 that is between ventilatory responses to CO_2 in hypoxy and hyperoxy. But the differences between VR1 and VR2, VR3 and VR4 were not significant, i.e. there was no any effect of human body position on chemoreflex control of breathing in terms of VR.

Paired Student's t-test revealed an increase 0.025±0.015 l/mmHg of slope of in hypoxy in the head down supine posture in comparison with upright sitting posture (in V_TR4 vs V_TR3, $p<0.01$). $P_{ET}CO_2$ at a tidal volume of zero increased by 7.8±5.1 mmHg ($p<0.02$). In our technique VR and V_TR to CO_2 in hypoxy include predominantly response

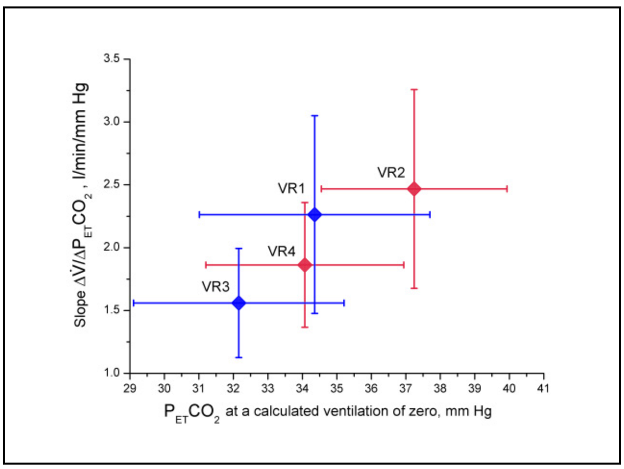

Figure 2a Group mean results of VR in runs 1, 2, 3, 4

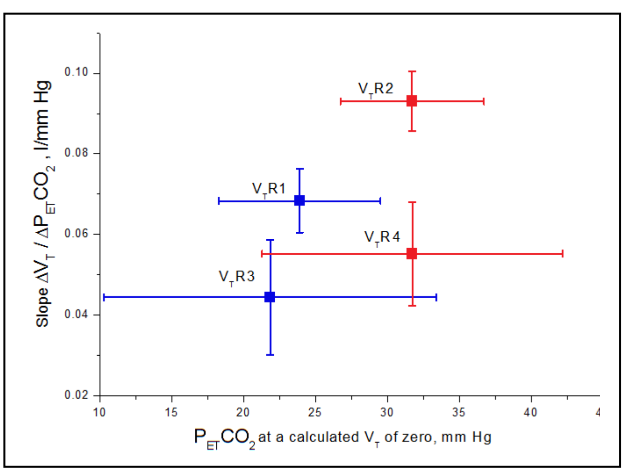

Figure 2b Group mean results of V_TR in runs 1, 2, 3, 4

to rising CO_2 and a negligible response to decreasing O_2 because arterial blood saturation by O_2 in our study was not lower than 90%. We should emphasize that the slope of the tidal volume response to progressive isocapnic hypoxia was significantly lower supine than upright [6]. Probably head down posture decreases the slope of the tidal volume response to progressive isocapnic hypoxia as well. So in runs 1 and 2 the obtained increase of the slope of the tidal volume responses to CO_2 cannot be induced by response to decreasing O_2.

Paired Student's t-test demonstrated that an increase of slope of V_TR in hyperoxy in the head down supine posture was not significant with comparison with upright sitting posture ($p<0.2$). Study of V_TR [6] obtained the same: the slope of the tidal volume responses to CO_2 was not significantly different supine compared to upright (0,156±0,027 L*mmHg^{-1} versus 0.165±0.007 L*mmHg^{-1}, respectively). But we obtained much lower slopes. This is because in [6] arterial blood saturation by O_2 and $P_{ET}O_2$ were lower than in our study. We believe that in our study a higher range of saturation and $P_{ET}O_2$ better suites normal physiological conditions and is preferable for space studies. Our study as well as the study [2] did not obtain any effect of posture on $P_{ET}CO_2$ at a ventilation of zero. But we obtained that $P_{ET}CO_2$ at a tidal volume of zero increased by 9.9±7.9 mmHg in supine head down posture in comparison with upright sitting position. This means that chemoreflex control of tidal volume, i.e. V_TR has a greater sensitivity to posture than VR.

Comparing runs 1 and 2 one can see from table 1 that a transition from sitting to supine head down position induced a greater relative increase in a slope of V_TR than in a slope of VR. This means that in the supine head down in comparison with sitting position a rise in V_T is greater. This could be partly induced by an increased respiratory resistance in supine head down position due to decrease functional respiratory capacity. A decreased functional respiratory capacity and increased resistance to breathing was obtained in supine position [7] and water immersion [8]. With increased resistance a rise in ventilation due to rise in tidal volume rather than in frequency is preferable because of lower rise in mechanical work of breathing.

V. CONCLUSIONS

1. Progressive hypercapnic – hypoxic rebreathing revealed posture changes in chemoreflex control, so it is reasonable to use this method in space studies as well as the methods of hyperoxic rebreathing and of isocapnic rebreathing.

2. Chemoreflex control of tidal volume response, i.e. V_TR has a greater sensitivity to posture than ventilation response, i.e. VR, so it is recommended to include V_T in parameters of study in long space flights.

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Author: Eugene S. Ermolaev
Institute: State Scientific Center of the Russian Federation – Institute of Biomedical Problems of the Russian Academy of Sciences, IMBP RAS
City: Moscow
Country: Russia
Tel: +79851861894
Email: 1861894@mail.ru