UDC: 616.152.21; 612.271:611.36
DOI: 10.31651/2076-5835-2018-1-2025-2-23-30

M. O. Zavhorodnii
Bogomoletz Institute of Physiology NAS of Ukraine, Kyiv
Centre of Astronomical, Medical and Ecological Researches NAS of Ukraine, Kyiv
ORCID ID: https://orcid.org/0000-0003-1719-9864
V. I. Nosar
Bogomoletz Institute of Physiology NAS of Ukraine, Kyiv
ORCID ID: https://orcid.org/0009-0000-6268-2711
P. K. Tsapenko
Bogomoletz Institute of Physiology NAS of Ukraine, Kyiv
Centre of Astronomical, Medical and Ecological Researches NAS of Ukraine, Kyiv
ORCID ID: https://orcid.org/0000-0002-1196-015X
V. I. Portnichenko
Bogomoletz Institute of Physiology NAS of Ukraine, Kyiv
Centre of Astronomical, Medical and Ecological Researches NAS of Ukraine, Kyiv
dr.v.portnichenko@gmail.com
ORCID ID: https://orcid.org/0000-0003-1473-2408

OXIDATIVE FUNCTION OF RAT LIVER MITOCHONDRIA DURING ACUTE HYPEROXIA AND RECOVERY

Energy metabolism in the liver, a key organ regulating both substance and energy metabolism in the body, depends critically on oxygen consumption. The primary organelles responsible for oxidative energy metabolism are mitochondria. Hyperoxia and oxygen therapy are widely used as therapeutic interventions in hepatic diseases and metabolic disorders. However, the specific effects of hyperoxia on energy metabolism and the oxidative function of liver mitochondria remain insufficiently understood.

***Purpose**. The aim of this study was to investigate the oxidative function of rat liver mitochondria under different types of hyperoxic exposure.*

***Methods.** The oxidative function of mitochondria was examined in 35 male Wistar rats. The polarographic method described by Chance and Williams was used. Mitochondrial respiration was assessed in liver homogenates using an open platinum electrode and a thermostabilized chamber containing the incubation medium and oxidation substrates. The oxygen consumption rate was measured under conditions of resting respiration ($V4^S$), active respiration (V3), and controlled respiration ($V4^{ATP}$) immediately after exposure to hyperoxia, as well as on days 1, 3, 5, 7, and 14 post-exposure. Respiration was stimulated by the addition of 200 μmol/L ADP. The respiratory control ratio ($V3/V4^{ATP}$) and the phosphorylation efficiency (ADP/O ratio) were calculated.*

***Results.** Under hyperoxic conditions, the rate of active respiration (V3) significantly increased during the oxidation of FAD-dependent succinate, but not during the oxidation of the NAD-dependent glutamate + malate mixture. The efficiency of oxidation and phosphorylation was restored by day 7 after hyperoxic exposure when electron transport chain Complex II was involved, whereas with Complex I substrates, it remained below baseline for 14 days. A significant increase in mitochondrial energization was observed from day 5 onward during the oxidation of NAD-dependent substrates compared to the immediate post-exposure level.*

***Originality.** This study demonstrates for the first time that hyperoxia-induced alterations in liver mitochondrial oxidative function occur in a phase-dependent manner.*

***Conclusions.** During hyperoxia, mitochondrial respiration is activated through electron transport chain Complex II, while the activity of Complex I is suppressed. It is proposed that Complex II contributes to the adaptive response of mitochondrial respiration to hyperoxic exposure.*

***Keywords:** mitochondria, liver, polarography, Chance method, hyperoxia, oxygen.*

Introduction

At present, there is no clear consensus regarding the effects of hyperoxia (HO) during oxygen therapy on energy metabolism under either normal or pathological conditions. While several studies have shown that hyperoxia and hyperoxemia may exert detrimental effects in critically ill patients [1], oxygen therapy remains an established and effective approach in the treatment of hepatic and metabolic disorders [2]. Furthermore, the administration of hyperoxic gas mixtures containing more than 30% O_2 during surgical procedures is routinely used to maintain adequate and stable blood oxygen saturation or to provide a pulmonary oxygen reserve in cases of airway dysfunction [3].

It is well known that tissue hypoxia develops in injured areas during the healing process. Numerous studies have demonstrated that normobaric hyperoxic exposure promotes wound healing and attenuates inflammation in both somatic and visceral organs [4–6]. Despite the promising therapeutic potential of normobaric hyperoxia, the mechanisms underlying its beneficial effects remain a matter of debate and require further elucidation. The wide variability in hyperoxic exposure protocols, coupled with a lack of standardized analytical approaches, further complicates the interpretation and comparison of experimental data.

Mitochondria are the principal consumers of oxygen in the body and play a central role in cellular energy metabolism. These organelles are responsible for the active oxidation of energy substrates and the synthesis of adenosine triphosphate (ATP) through oxidative phosphorylation. At the same time, mitochondria are also the main source of reactive oxygen species (ROS) [7]. The regulation of energy metabolism and carbohydrate transformation within the body is largely dependent on the functional state of liver mitochondria [8].

Exposure to hyperoxic conditions has been shown to influence mitochondrial energy metabolism, potentially leading to oxidative stress and tissue injury as a result of excessive ROS generation. However, the specific features of mitochondrial oxidative function and oxygen metabolism in the liver under hyperoxic conditions remain poorly understood.

Therefore, the present study aimed to characterize the changes in the oxidative function of liver mitochondria following exposure to hyperoxia.

Materials and methods

The experiments were conducted on 35 male Wistar rats, which were divided into two groups: 1) "control" (n = 5), and 2) "hyperoxia" (n = 30). The control group consisted of intact rats that were kept under standard vivarium conditions with free access to water and food. These rats were in a chamber without a hyperoxic mixture throughout the hyperoxic session. Animals from the "hyperoxia" group were exposed to an acute single exposure to a normobaric hyperoxic mixture (35% oxygen) for a period of three hours. Subsequently, to study the effect on oxidative metabolism of liver mitochondria during the recovery period after acute hyperoxia, studies were conducted for fourteen days at periods 1, 3, 5, 7 and 14 days.

In order to study the oxidative function of liver mitochondria, a homogenate was prepared. Liver fragments obtained from rats that had been anesthetized with ether (1.5 g/kg) were promptly placed on ice and subsequently homogenized using a mechanical homogenizer, with the addition of a 0.9% cold KCl solution (4°C). The mitochondrial isolation medium contained (mmol/L): KCl – 120, HEPES – 10, K_2CO_3 – 2, EGTA-1 (pH 7.2), and the incubation medium – KCl – 120, HEPES – 10, K_2CO_3 – 2, KH_2PO_4 – 2 (pH 7.2) [9, 10]. The processes of respiration and oxidative phosphorylation in mitochondria were studied by the polarographic method according to Chance and Williams [11]. For the purpose of conducting polarographic studies called "Polarograph LP 7" (Czech Republic, 1974) with an open platinum electrode was utilized. The device underwent calibration using a 0.9% sodium chloride (NaCl) solution saturated with oxygen for a duration of 24 hours (maximum oxygen pressure) against a 0.9% NaCl solution with the incorporation of sodium sulfate dihydrate (Na_2SO_3) at a concentration of 1 mg/ml (minimum oxygen pressure). A volume of 1 ml of homogenate was introduced into a polarographic cell. Subsequently, 1 ml of incubation medium and the requisite dose of oxidation substrate were added. Thereafter, alterations in O_2 partial pressure over time were

documented. The recording was carried out using a paper recorder called "Polarograph LP 7" (Czech Republic, 1974). The following oxidation substrates were used (mmol/l):

1) succinate (Sc) – 0.35

(oxidized by the II complex of the electron transport chain);

2) glutamate – 3 and malate – 2.5

(oxidized mainly by the I complex of the electron transport chain) [11]. Respiration was stimulated by the introduction of 200 μmol/l ADP (Sigma Aldrich, USA). The rate of mitochondrial respiration during the oxidation of substrates in the resting state ($V4^S$), the rate of phosphorylation or ADP-stimulated (V3) and controlled ($V4^{ATP}$) respiration were determined, and the respiratory control according to Chance and Williams ($V3/V4^{ATP}$) and the ADP/O ratio, which reflects the efficiency of phosphorylation, were calculated [10, 11]. For the purpose of statistical analysis of the obtained data, generally accepted methods of variational statistics were utilized, employing the GraphPad Prism 8 software program (GraphPad Software, Inc., USA). The data were examined for normality using a Kolmogorov-Smirnov test to ensure the distribution was appropriate for the analysis. The samples were then subjected to a one-way analysis of variance (ANOVA) test, with the Bonferroni criterion employed as a post hoc test. The level of statistical significance was established as $P \leq 0.05$. The results were presented as mean ± standard error of mean (M±m).

Results and Discussion

The level of oxygen consumption in the $V4^S$ state during the oxidation of FAD-dependent succinate significantly increased ($P<0.05$) immediately after exposure to hyperoxia and 1 day after exposure to hyperoxia. Beginning on the third day following exposure to HO, the level of oxygen consumption by liver mitochondria in the $V4^S$ state reverted to the basal level. This level remained relatively stable until day 14, as illustrated in Table 1. The oxygen consumption during stimulation of mitochondrial respiration with adenosine diphosphate exhibited a significant increase ($P < 0.05$) compared to the baseline level immediately following hyperoxic exposure, persisting up to and including day 3. On the fifth day, a "breakthrough" in mitochondrial energization was observed, during which the level of oxygen consumption significantly differed from that immediately after exposure to HO. Starting from the fifth day, a further decrease in oxygen consumption was observed, and it did not differ from the basal level. (Fig. 1A) The level of controlled breathing under the influence of HO increased significantly relative to the basal level immediately after the hyperoxic session and was significantly higher after 1 day ($P<0.05$), while after 5 days it approached the basal level (Table 1).

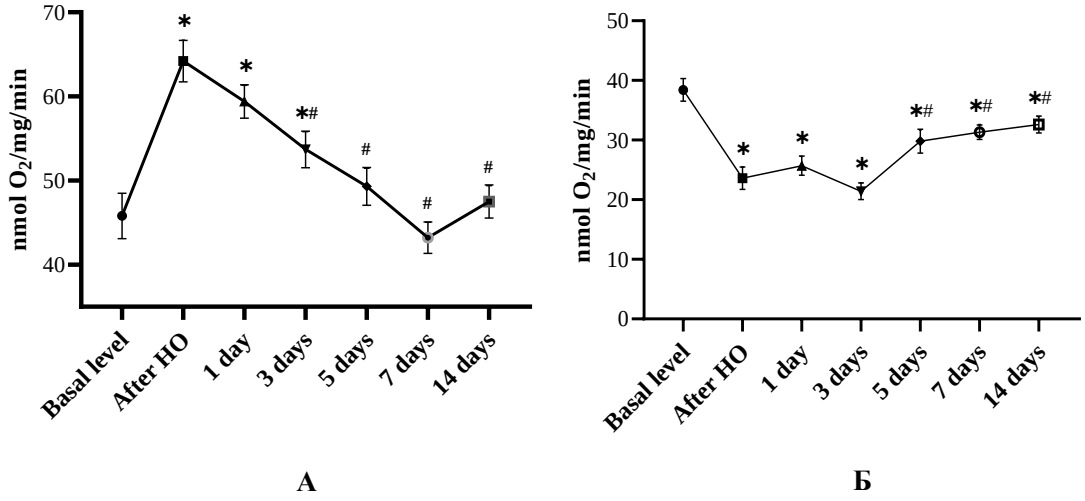

Fig. 1. The rate of ADP-stimulated respiration (V3) in rat liver mitochondria was measured under conditions of hyperoxia (HO) exposure during the oxidation of A) FAD-dependent succinate; B) NAD-dependent substrates.

Notes: ***** – P<0,05 compared to basal level; # – P<0,05 compared to point "after HO".

The efficiency of mitochondrial respiration ($V3/V4^{ATP}$) exhibited a significant decrease ($P<0.05$) immediately after exposure to HO and after 1 day, and on the 5th day after exposure to hyperoxia – did not differ from the basal level. Conversely, starting from the 7th day, an enhancement in the efficiency of mitochondrial respiration was observed relative to the basal level (see Table 1). This phenomenon can be attributed, primarily, to an increase in the level of controlled respiration immediately after exposure to HO and after one day. Concurrently, the ADP/O indicator, which reflects the degree of conjugation of oxidation and phosphorylation and the efficiency of phosphorylation of ADP to ATP [12], did not demonstrate a significant decrease ($P<0.05$) only immediately after exposure to HO, and on the first day did not differ significantly from the basal level. The restoration of phosphorylation efficiency was observed from the 7th day after exposure to hyperoxia (see Table 1).

Table 1

Indicators of mitochondrial respiration under the influence of acute HO under the conditions of using the substrate sodium succinate (M±m).

Substrate	Sodium succinate, 5 mmol			
	$V4^S$	$V4^{ATP}$	$V3/ V4^{ATP}$	ADP/O
	mmol $O_2/min^{-1}/mg^{-1}$		c.u.	
Basal level	10,2±0,90	10,8±1,2	4,24±0,09	1,57±0,04
After hyperoxia	16,7±1,1*	17,7±1,4*	3,62±0,07*	1,42±0,06*
1 day	14,2±1,2*	15,0±1,3*	3,94±0,11*	1,48±0,04
3 days	12,8±0,87	13,2±0,98	4,04±0,19	1,52±0,07
5 days	10,8±0,92	12,0±1,4	4,11±0,15	1,53±0,10
7 days	9,1±1,0	10,0±0,94	4,32±0,87*	1,58±0,11
14 days	12,6±1,7	11,1±1,1	4,28±0,10*	1,60±0,15

Note: ***** – P<0,05 compared to basal level.

Thus, the impact of acute HO resulted in an augmentation of mitochondrial oxygen consumption, with the involvement of FAD-dependent succinate. This phenomenon returned to its basal level after a period of 3-5 days. The efficiency of respiration and phosphorylation decreased only with the direct effect of acute HO, and by day 3, these indicators returned to their initial values. This is consistent with the literature data, since, as is known [13], succinate is actively used as an oxidation substrate in hyperoxia therapy in intensive care. In turn, the utilization of succinate, which is oxidized in the mitochondria with the participation of the complex II of the electron transport chain, contributes to a decrease in the production of reactive oxygen species by the mitochondria in case of impaired oxygen homeostasis [14].

In the context of mitochondrial oxidation of NAD-dependent substrates (glutamate + malate mixture), disparate reactions of liver tissue to acute hyperoxia were observed. Consequently, the level of mitochondrial respiration at rest exhibited a tendency to decrease immediately after exposure to HO, and a significant decrease was observed ($P < 0.05$) three days after exposure to HO (see Table 2). The level of mitochondrial energization under conditions of ADP-stimulated respiration demonstrated a significant decrease immediately after hyperoxic exposure ($P < 0.05$). Additionally, it was observed to be lower in comparison to the basal level after 3, 5, 7, and 14 days, although a tendency towards recovery emerged, as it was higher after 5, 7 and 14 days in comparison to the level of energization after hyperoxia (Fig. 1B). Under controlled breathing conditions ($V4^{ATP}$), a significant decrease ($P<0.05$) in the rate of oxygen consumption was observed only immediately after hyperoxia, and after 5 days this indicator returned to the basal level (see Table 2).

Table 2

Indicators of mitochondrial respiration under the influence of acute HO under the conditions of using the substrate glutamate+malate mixture (M±m).

Substrate	Sodium glutamate 5 mmol + malate 2,5 mmol			
	$V4^S$	$V4^{ATP}$	$V3/ V4^{ATP}$	ADP/O
	mmol $O_2/min^{-1}/mg^{-1}$		c.u.	
Basal level	7,3±1,0	7,9±0,70	4,86±0,05	2,59±0,06
After hyperoxia	5,6±0,9	5,7±0,95*	4,14±0,04*	2,32±0,04*
1 day	5,9±0,87	6,1±1,2	4,21±0,09*	2,38±0,08*
3 days	5,1±1,0*	5,7±1,1*	3,74±0,03*	2,27±0,03*
5 days	8,2±1,2	7,7±1,3	3,87±0,05*	2,42±0,04*
7 days	8,0±1,4	7,7±1,2	4,06±0,07*	2,34±0,03*
14 days	7,2±0,77	7,8±0,94	4,18±0,05*	2,46±0,05

Note: ***** – P<0,05 compared to basal level.

As a result, the level of respiratory control in the context of acute HO exhibited a significant decrease (P<0.05) throughout the experimental period. Parallel significant changes (P<0.05) were observed in the level of ADP/O (Table 2). Accordingly, the level of ADP-stimulated respiration during the oxidation of NAD-dependent substrates under HO conditions was significantly lower throughout the duration of the experiment. This finding is also evident in the efficiency of oxidation and phosphorylation ($V3/V4^{ATP}$ and ADP/O).Thus, the mitochondria of rat liver tissues respond to acute hyperoxia through the I and II complexes of the electron transport chain in distinct ways: the I complex of the electron transport chain appears to be more sensitive to the effects of hyperoxia, presumably due to its role in oxidizing NAD-dependent substrates. Consequently, the levels of oxygen consumption by mitochondria decrease, and with them the efficiency of respiration and phosphorylation. Complex II of ETC (oxidation of FAD-dependent substrates) demonstrates reduced vulnerability to the influx of HO.

In numerous studies of oxygen metabolism, it has been demonstrated that relative changes in oxygen availability, as opposed to constant hyperoxia or hypoxia, exert a more substantial influence on the expression of the transcription factor HIF [15–17]. Consequently, cells interpret the return to normoxia after hyperoxic exposure or the transition from normoxia to hypoxia as oxygen deficiency, leading to the induction of the synthesis of genes regulated by HIF-1 [15–17]. Accordingly, the observed manifestations of mitochondrial dysfunction in liver cells, as evidenced by an increase in O2 consumption under conditions of FAD-dependent substrate oxidation and a decrease in NAD-dependent substrate oxidation, bear a strong resemblance to the changes that have been documented under conditions of hypoxia [19, 20]. These effects can be explained by the development of the hyperoxic-hypoxic paradox [18], in which there is a shift of the hemoglobin dissociation curve to the left, resulting in disrupted oxygen diffusion into the tissue and subsequent tissue hypoxia. This, in turn, is accompanied by spasms of small vessels, which further complicates oxygen delivery to the tissue and leads to the activation of lipid peroxidation and the development of oxidative stress. It is noteworthy that the oxidative function of mitochondria undergoes changes under the influence of hyperoxia, which can be considered a phase-dependent phenomenon. Subsequent to the hyperoxic state, a restructuring of energy metabolism is observed, accompanied by the inhibition of complex I and the activation of complex II of the electron transport chain. This phenomenon has been previously demonstrated in works devoted to the influence of hypoxia [19, 20]. As ETC complex I exhibits higher sensitivity to stress factors [10, 21], we observed a

consistent decline in oxygen consumption, oxidation efficiency, and phosphorylation within the liver's mitochondria in response to hyperoxia. It is hypothesized that hyperoxia induced by this regimen altered the function of the first complex, such that restoration of its function was not observed on the third day after the hyperoxic session. Beginning on the fifth day and continuing until the conclusion of the experiment, a significant increase in oxygen consumption may indicate the involvement of compensatory mechanisms for the optimal level of mitochondrial energization, particularly oxidation with the participation of ETC complex II. The rate of FAD-dependent succinate oxidation through ETC complex II, which literature data indicate compensates for the insufficiency of ETC complex I [14, 21-22], returned to the basal level after the 5th day of hyperoxic exposure, which supports our assumption.

The results obtained can be used for further studies of the role of mitochondria in adaptation to HO. The involvement of mitochondrial genes in the functional reorganization of the electron transport chain remains unclear. This is a key question regarding the protective effect of HO on liver mitochondria.

Conclusions

- Changes in the energization of liver mitochondria under hyperoxia conditions are phase-dependent.
- The I complex of ETC of liver mitochondria exhibits higher sensitivity to the effects of hyperoxia, which impacts the efficiency of oxidation and phosphorylation. The complex II undergoes only minor changes up to three days following exposure to hyperoxia.
- The oxidation of FAD-dependent substrates by liver mitochondria has been shown to compensate for the energy deficiency that results from impaired functioning of the ETC complex I.

References

1. Damiani, E., Donati, A., & Girardis, M. (2018). Oxygen in the critically ill. Current Opinion in Anaesthesiology, 31(2), 129–135. https://doi.org/10.1097/aco.0000000000000559
2. Sun Y, Wen Y, Shen C, Zhu Y, You W, Meng Y, Chen L, Feng Y, Yang X, Chen ZB. Sun, Y., Wen, Y., Shen, C., Zhu, Y., You, W., Meng, Y., Chen, L., Feng, Y., Yang, X., & Chen, Z.-B. (2018). Hyperbaric Oxygen Therapy in Liver Diseases. International Journal of Medical Sciences, 15(8), 782–787. https://doi.org/10.7150/ijms.24755
3. Müller-Wirtz, L. M., Kiefer, D., Knauf, J., Floss, M. A., Doneit, J., Wolf, B., Maurer, F., Sessler, D. I., Volk, T., Sascha Kreuer, & Fink, T. (2021). Differential Response of Pentanal and Hexanal Exhalation to Supplemental Oxygen and Mechanical Ventilation in Rats. Molecules, 26(9), 2752–2752. https://doi.org/10.3390/molecules26092752
4. Choi, M., Tamrakar, P., Schuck, P. F., Proctor, J. L., Moore, A., Asbury, K., Fiskum, G., Coksaygan, T., & Cross, A. S. (2018). Effect of hypobaria and hyperoxia during sepsis on survival and energy metabolism. Journal of Trauma and Acute Care Surgery, 85, S68–S76. https://doi.org/10.1097/ta.0000000000001909
5. Sukhotnik I, Brod, V., Lurie, M., Rahat, M. A., Sergei Shnizer, Nitza Lahat, Mogilner, J. G., & Bitterman, H. (2009). The effect of 100% oxygen on intestinal preservation and recovery following ischemia-reperfusion injury in rats. Critical Care Medicine, 37(3), 1054–1061. https://doi.org/10.1097/ccm.0b013e31819d0f5c
6. Kemal Uslu, Hasan Deniz Tansuker, Alper Tabaru, Selim Engin Egeren, Kemal Kutay Kulahci, Pınar Bulut, Funda Emre, & Oktay, M. F. (2020). Investigation of the effects of thrombocyte-rich plasma, systemic ozone and hyperbaric oxygen treatment on intraoral wound healing in rats: experimental study. European Archives of Oto-Rhino-Laryngology, 277(6), 1771–1777. https://doi.org/10.1007/s00405-020-05872-5
7. Divakaruni, A. S., & Jastroch, M. (2022). A practical guide for the analysis, standardization and interpretation of oxygen consumption measurements. Nature Metabolism, 4(8), 978–994. https://doi.org/10.1038/s42255-022-00619-4
8. Han, H.-S., Kang, G., Kim, J. S., Choi, B. H., & Koo, S.-H. (2016). Regulation of Glucose Metabolism from a liver-centric Perspective. Experimental & Molecular Medicine, 48(3), e218–e218. https://doi.org/10.1038/emm.2015.122
9. Kondrashova, M. N., Fedotcheva, N. I., Saakyan, I. R., Sirota, T. V., Lyamzaev, K. G., Kulikova, M. V., & Temnov, A. V. (2001). Preservation of native properties of mitochondria in rat liver homogenate. Mitochondrion, 1(3), 249–267. https://doi.org/10.1016/s1567-7249(01)00025-3
10. Kurhaluk, N., Lukash, O., Nosar, V., Portnychenko, A., Volodymyr Portnichenko, Wszedybyl-Winklewska, M., & Winklewski, P. J. (2019). Liver mitochondrial respiratory plasticity and oxygen uptake evoked by cobalt chloride in rats with low and high resistance to extreme hypobaric hypoxia. Canadian Journal of Physiology and Pharmacology, 97(5), 392–399. https://doi.org/10.1139/cjpp-2018-0642

11. Chance, B., Williams, G.R. (1955). Respiratory enzymes in oxidative phosphorylation. Kinetics of oxygen utilization. Ibid. 217,383–393. PMID: 13271402.
12. Estabrook, R. W. (1967). Mitochondrial respiratory control and the polarographic measurement of ADP: O ratios. Methods in Enzymology, 41–47. https://doi.org/10.1016/0076-6879(67)10010-4.
13. Orlov, Y.P., Afanasyev, V.V. (2018). Hypoxia and hyperoxia in the practice of anesthesiology and reanimatology. The role of succinates in critical conditions. Reports of Surgery, 26(2), 226-237. https://doi.org/10.1016/0076-6879(67)10010-4.
14. Hadrava Vanova, K., Kraus, M., Neuzil, J., & Rohlena, J. (2020). Mitochondrial complex II and reactive oxygen species in disease and therapy. Redox Report : Communications in Free Radical Research, 25(1), 26–32. https://doi.org/10.1080/13510002.2020.1752002 .
15. Cimino, F., Balestra, C., Germonpré, P., De Bels, D., Tillmans, F., Saija, A., Virgili, F. (2012). Pulsed high oxygen induces a hypoxic-like response in human umbilical endothelial cells and in humans. Journal of Applied Physiology, 113(11), 1684–1689. https://doi.org/10.1152/japplphysiol.00922.2012
16. Balestra, C., & Kot, J. (2021). Oxygen: A Stimulus, Not "Only" a Drug. Medicina, 57(11), 1161. https://doi.org/10.3390/medicina57111161
17. Hadanny, A, & Efrati, S. (2020). The Hyperoxic-Hypoxic Paradox. Biomolecules, 10(6), 958. https://doi.org/10.3390/biom10060958
18. Lukyanova LD. (2013) Mithochondria signaling in adaptation to hypoxia. Fiziol. Zh. 59(6), 141–154. https://doi.org/10.15407/fz59.06.141
19. Portnichenko VI, Nosar VI, Portnichenko AG, Drevitska TI, Sidorenko AM, Man`kovska IM. (2012). Phase changes in energy metabolism during periodic hypoxia. Fiziol. Zh. 58(4), 3–12. https://doi.org/10.15407/fz58.04.003
20. Tretter, L., Patocs, A., & Chinopoulos, C. (2016). Succinate, an intermediate in metabolism, signal transduction, ROS, hypoxia, and tumorigenesis. Biochimica et Biophysica Acta (BBA) - Bioenergetics, 1857(8), 1086–1101. https://doi.org/10.1016/j.bbabio.2016.03.012.
21. Zhao, H. W., Ali, S. S., & Haddad, G. G. (2012). Does Hyperoxia Selection Cause Adaptive Alterations of Mitochondrial Electron Transport Chain Activity Leading to a Reduction of Superoxide Production? Antioxidants & Redox Signaling, 16(10), 1071–1076. https://doi.org/10.1089/ars.2011.4504

Завгородній М. О., Цапенко П. К., Носар В. І., Портніченко В. І.

ОКИСЛЮВАЛЬНА ФУНКЦІЯ МІТОХОНДРІЙ ПЕЧІНКИ ЩУРІВ ПІД ЧАС ГОСТРОЇ ГІПЕРОКСІЇ ТА ВІДНОВЛЕННЯ

Енергетичний обмін у печінці, ключовому органі, що регулює як речовинний, так і енергетичний обмін в організмі, критично залежить від споживання кисню. Основними органелами, відповідальними за окислювальний енергетичний обмін, є мітохондрії. Гіпероксія та киснева терапія широко використовуються як терапевтичні втручання при захворюваннях печінки та метаболічних порушеннях. Однак специфічний вплив гіпероксії на енергетичний обмін та окислювальну функцію мітохондрій печінки залишається недостатньо вивченим.

Мета. *Метою цього дослідження було дослідити окислювальну функцію мітохондрій печінки щурів за різних типів гіпероксичного впливу.*

Методи. *Окислювальну функцію мітохондрій досліджували у 35 самців щурів Вістар. Використовували полярографічний метод, описаний Чансом та Вільямсом. Мітохондріальне дихання оцінювали в гомогенатах печінки за допомогою відкритого платинового електрода та термостабілізованої камери, що містить інкубаційне середовище та субстрати окислення. Швидкість споживання кисню вимірювали в умовах дихання у стані спокою (V4S), активного дихання (V3) та контрольованого дихання (V4ATP) одразу після впливу гіпероксії, а також на 1, 3, 5, 7 та 14 дні після впливу. Дихання стимулювали додаванням 200 мкмоль/л АДФ. Були розраховані коефіцієнт контролю дихання (V3/V4ATP) та ефективність фосфорилювання (співвідношення ADP/O).*

Результати. *В умовах гіпероксії швидкість активного дихання (V3) значно зростала під час окислення FAD-залежного сукцинату, але не під час окислення суміші NAD-залежного глутамату та малату. Ефективність окислення та фосфорилювання відновлювалася до 7-го дня після гіпероксичного впливу, коли був задіяний комплекс II ланцюга електронного транспорту, тоді як з субстратами комплексу I вона залишалася*

нижчою за базовий рівень протягом 14 днів. Значне збільшення енергетизації мітохондрій спостерігалося з 5-го дня під час окислення NAD-залежних субстратів порівняно з рівнем безпосередньо після впливу.

Оригінальність. *Це дослідження вперше демонструє, що індуковані гіпероксією зміни окислювальної функції мітохондрій печінки відбуваються фазозалежним чином.*

Висновки. *Під час гіпероксії мітохондріальне дихання активується через комплекс II ланцюга електронного транспорту, тоді як активність комплексу I пригнічується. Припускається, що Комплекс II сприяє адаптивній реакції мітохондріального дихання на гіпероксичний вплив.*

Ключові слова: *мітохондрії, печінка, полярографія, метод Чанса, гіпероксія, кисень.*

Надійшла до редакції / Received: 08.10.2025
Схвалено до друку / Accepted: 16.12.2025