OXYGEN TRANSPORT DURING ELECTRICAL STIMULATION OF EMOTIOGENIC HYPOTHALAMIC STRUCTURES

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UDC 612.26-06: 612.826.4.014.424

Hypertensive structures of the hypothalamus were subjected to periodic electrical stimulation in unanesthetized, immobilized rabbits. After each period of stimulation, lasting 5 min and repeated at intervals of 5 min, the state of the mechanisms of oxygen transport (hemodynamics, affinity of hemoglobin for oxygen, oxygen capacity of the blood) was investigated. During the first two or three periods the oxygen consumption of the animals was increased, but later it fell because the function of the energy-dependent mechanisms of oxygen transport no longer corresponded to the requirements of the body. A decrease in the affinity of hemoglobin for oxygen under these conditions contributes to better deoxygenation of the blood in the tissues.

KEY WORDS: hypothalamus; emotional stress; oxygen consumption; oxygen transport; circulation; oxygen capacity of the blood; affinity of hemoglobin for oxygen.

The character of the somatic and autonomic changes developing in response to electrical stimulation of the hypothalamus necessitates increased energy expenditure and corresponding changes in the oxygen transport system. The arterial blood pressure (BP) rises [2, 4, 7-9], the blood flow is reduced in the intestine [13] and increased in the muscles [12, 15], and the arteriovenous difference (AVD) in oxyhemoglobin concentration is modified [10]. Activation of the circulation is an important and rapidly realized mechanism in the general oxygen transport system, but it is not the only mechanism; the functional characteristics of the system are also determined by the state of affinity of hemoglobin for oxygen and by the oxygen capacity of the blood (OCB) [6].

Considering the role of hypothalamic structures in the formation of the functional system of emotions, hypothalamic stimulation is widely used in order to reproduce their somatic and autonomic effects [1, 2, 4, 8]. For that reason the determination of the state of the various functional components of the oxygen transport system during hypothalamic stimulation may make an important contribution to the understanding of the mechanisms of development of adaptive responses in various forms of emotional stress and their sequelae.

EXPERIMENTAL METHODS

Experiments were carried out on 26 rabbits in which a hypertensive response was obtained to stimulation after insertion of a bipolar nichrome electrode into the middle or posterior group of hypothalamic nuclei. The electrode was inserted after preliminary catheterization and cannulation of the external jugular vein and the common carotid and femoral arteries under general anesthesia.

Electrical stimulation by square pulses (1 msec, 80-100 Hz, initial voltage 2-2.5 V) was applied to the unanesthetized animals fixed in a frame. The pulse voltage was increased by 0.5-1 V in each successive period. Stimulation continued for 5 min and was repeated at intervals also of 5 min. The strength of the current varied in different experiments from 30 to 210 μA.

The central venous pressure (CVP) and BP were measured by the direct method and the cardiac output (CO) was determined by the thermodilution method [5]. The ECG was recorded in three standard leads. The OCB was calculated after determination of the hemoglobin concentration. The oxyhemoglobin concentration in arterial and mixed venous blood was determined with the 057 oxyhemometer, calibrated against samples of rabbit's blood with different concentrations of oxyhemoglobin, made up by mixing completely deoxygenated and oxygenated blood. The cuvette and the solution for diluting the blood were kept at a constant temperature. To

Department of Normal Physiology, Grodno Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Debov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 8, pp. 136-139, August, 1979. Original article submitted February 22, 1978.

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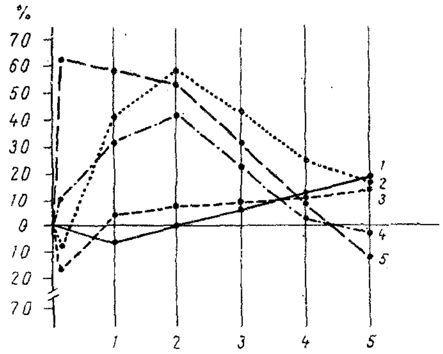

Fig. 1. Changes in AVD for oxygen concentration (1), CO (2), $\dot{V}O_2$ (3), BP (4), and R (5), in % of initial data during 5 min of stimulation of hypothalamic emotiogenic structures. Ordinate, change in indices studied (in % of initial values); abscissa, time (in min).

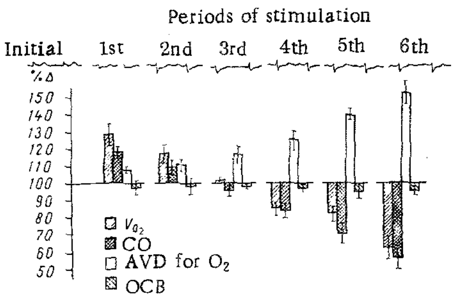

Fig. 2. Changes in $\dot{V}_{O_2}$, CO, and AVD for oxygen concentration, and ECG after each period of stimulation of hypothalamic emotiogenic structures. Ordinate, change in indices studied (% of initial data).

estimate the affinity of hemoglobin for oxygen a sample of mixed venous blood in a saturator was brought to equilibrium with a gas mixture containing 3.4% O_2, 5% CO_2, and 91.6% N_2, after which the oxyhemoglobin concentration was determined. The values of pO_2 corresponding to atmospheric pressure and the composition of the gas mixture, and the oxyhemoglobin concentration in the blood sample were used to calculate p_{50} and the oxyhemoglobin dissociation curve [11]. The resistance to the blood flow (R), the work of the heart (A), the oxygen consumption ($\dot{V}O_2$), and AVD for oxygen were calculated from the results.

EXPERIMENTAL RESULTS

Changes in the indices of oxygen transport and, in particular, in the hemodynamics, during the first period of electrical stimulation were the result of the increased oxygen consumption of the animal (Fig. 1). During the first 3-10 sec of increase of BP transient disturbances of cardiac rhythm were observed on the ECG or BP kymogram. A sharp increase evidently led to an increase in BP, when the heart was unprepared for the additional work. This was shown by the increase in CVP to 7.2 ± 1.2 cm water. Very small increases in the volume load (injection of 0.3-0.5 ml physiological saline into the region of the orifices of the venae cavae during determination of CO) were often accompanied by omission of the next cardiac contraction and a fall in BP. These findings suggest that the decrease in CO during the first few seconds of stimulation must be regarded not only as reflex in origin, but also, evidently, as unprovided for energetically. Immediately after this first response to electrical stimulation of the hypothalamus, the oxygen transport system became established at a new level of function, characterized by an increase in CO, A, and AVD and by a relative decrease in R. Changes in BP in each successive period of electrical stimulation were indistinguishable from

TABLE 1. Indices of Oxygen Transport System During Electrical Stimulation of Hypothalamus

Index	Initial data	After each period of electrical stimulation					
		1st	2nd	3rd	4th	5th	6th
BP, mm Hg	89 ± 5,6	86 ± 6,0	81 ± 4,1	80 ± 2,1	78 ± 3,0	77 ± 4,0	71 ± 7,0
CVP, cm water	2 ± 0,4	1 ± 0,1	2 ± 1,1	1,3 ± 0,7	2,4 ± 0,9	4,1 ± 0,1	5,5 ± 1,6
CO, ml/min	294 ± 4,2	332 ± 5,4	343 ± 10,1	264 ± 9,2	220 ± 12,3	190 ± 14,9	176 ± 9,1
R, dynes · sec · cm^{-5}	25 232 ± 1,096	22 198 ± 1 347	19 742 ± 962	25 312 ± 1 402	27 608 ± 2 612	32 388 ± 1 623	32 240 ± 2 742
A, J	3,59 ± 0,159	3,88 ± 0,172	3,794 ± 0,20	2,92 ± 0,09	2,24 ± 0,90	2,04 ± 0,50	1,58 ± 0,10
Hb, g %	9,3 ± 0,1	9,3 ± 0,07	9,3 ± 0,8	9,25 ± 0,4	9,16 ± 0,06	8,09 ± 0,61	7,92 ± 0,12
OBC, ml	12,6 ± 1,2	12,6 ± 0,4	12,5 ± 0,6	12,5 ± 0,8	12,5 ± 1,1	11,0 ± 1,2	10,77 ± 0,8
SaO_2, %	92 ± 0,4	93 ± 1,3	91 ± 0,8	91 ± 0,2	90 ± 1,7	91 ± 0,4	89 ± 1,9
SvO_2, %	52 ± 0,7	49 ± 1,8	48 ± 1,6	45 ± 0,4	39 ± 1,7	36 ± 0,8	28 ± 1,4
AVD, %	41 ± 1,2	43 ± 2,1	43 ± 1,8	48 ± 0,2	52 ± 1,3	58 ± 1,7	62 ± 2,3
V_{O_2}, ml	15,6 ± 0,6	19,42 ± 1,1	17,74 ± 1,4	14,49 ± 0,8	13,01 ± 0,9	12,1 ± 0,7	11,56 ± 1,6
p_{50}, mm Hg	25 ± 0,3	24 ± 0,8	24 ± 0,1	—	27 ± 0,5	—	28 ± 0,9

SaO_2, SvO_2 denote oxyhemoglobin concentration in arterial and venous blood respectively.

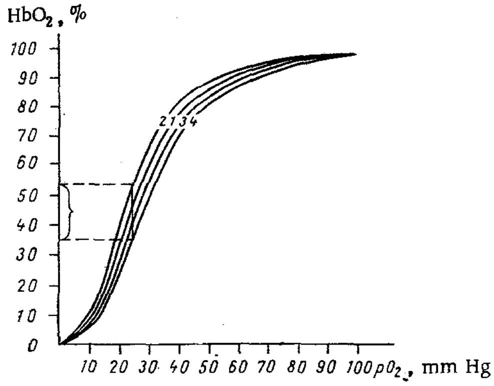

Fig. 3. Oxyhemoglobin dissociation curves before experiment (1; p_{50} = 26 mm Hg, pH = 7.43) and after second (2; p_{50} = 24.2 mm Hg, pH = 7.34), fourth (3; p_{50} = 28.2 mm Hg, pH = 7.32), and sixth (4; p_{50} = 30 mm Hg, pH = 7.30) periods of electrical stimulation. Bracket denotes increase in AVD for oxyhemoglobin concentration at end of experiment on account of a decrease in affinity of hemoglobin for oxygen. At initial values of CO = 264 ml/min, OBC = 16.7 ml, and AVD = 39%, $\dot{V}_{O_2}$ was 16.8 ml/min; after sixth period of electrical stimulation CO = 120 ml/min, OBC = 15.6 ml, AVD = 62%, and $\dot{V}_{O_2}$ fell to 11.7 ml/min.

those described in the literature [2, 8, 9]. The hypertensive response increased until the 3rd-4th period of electrical stimulation, after which, despite an increase in the strength of stimulation, it fell slowly. After three or four periods of stimulation signs of myocardial hypoxia appeared on the ECG: a negative T wave, the S-T interval below the isoelectric line, and a decrease in the R/S ratio. These changes in the ECG subsequently increased progressively (Fig. 2). Whereas CVP in the initial periods increased only during stimulation, later it remained higher than initially even after the end of stimulation, further evidence of depression of cardiac function (Table 1).

The oxygen consumption of the animals was increased during the first two or three periods of electrical stimulation, but later it decreased, not because of a decrease in the oxygen demand, and not because of adaptation of the mechanisms utilizing oxygen, but because the functioning of the oxygen transport system could not satisfy the needs of the animal. The constancy of the oxygen saturation of the arterial blood indicates that the external respiratory system was not the limiting link in the chain of oxygen consumption. Changes in the oxygen consumption and the functional indices of oxygen transport that were found (Fig. 2) indicate that during the first periods of electrical stimulation the oxygen demand was satisfied mainly through an increase in the work of the heart. Later, CO and OBC fell and AVD increased.

Besides other factors determining AVD, the state of the affinity of hemoglobin for oxygen is also of the greatest importance [6, 14]. Dynamic investigations of the affinity of hemoglobin for oxygen after two periods of electrical stimulation showed a shift of the dissociation curve in mixed venous blood to the right, due mainly to a decrease in the pH of the blood (the Bohr effect). Recalculation of p_{50} for a standard value of pH showed the following relationship. After the first two periods of electrical stimulation the affinity of hemoglobin for oxygen increased: p_{50} fell from 25 ± 0.3 to 24 ± 0.1 mm Hg ($P < 0.01$). Later p_{50} increased to 28 ± 1.2 mm Hg, thus promoting further deoxygenation of the blood.

The very small increase in the affinity of hemoglobin for oxygen at the beginning of the experiment could be explained by activation of the sympathicoadrenal system and, possibly, by an increase in the blood level of cyclic 3',5'-AMP, which in high concentrations can increase the affinity of hemoglobin for oxygen [3]. Whereas in healthy animals such a shift of the dissociation curve is compensated by the work of the heart, it can be tentatively suggested that when the heart is damaged in stress states signs of hypoxia can develop much sooner and give rise to more serious aftereffects. The subsequent decrease in the affinity of hemoglobin for oxygen was evidently the result of developing hypoxia, during which the dissociation curve is always shifted to the right [6, 14].

When the level of deoxygenation of the blood is monitored in vivo, affinity of hemoglobin for oxygen is one of the most important mechanisms responsible for physiological stability in the oxygen transport system, especially when the functioning of the energy-dependent mechanisms of oxygen transport is depressed. The importance of the decrease in the affinity of hemoglobin for oxygen in the development of adaptive responses in the oxygen transport system is clearly demonstrated by the following example (Fig. 3). If the capillary–tissue pO_2 gradient was the same at the beginning and at the end of the experiment, under those conditions the quantity of oxygen supplied to the tissues as a result of the decrease in affinity was increased by 4 ml, which is one-third of the total oxygen utilized (11.67 ml).

Autonomic changes during electrical stimulation of the hypotensive structures of the hypothalamus in immobilized, unanesthetized animals thus take place against the background of increased oxygen consumption, the result of activation of the systems of the body and also, evidently, of a decrease in the efficiency of oxygen utilization. During repetitive stimulation of the hypothalamus the energy-dependent mechanisms of oxygen transport suffer, with a consequent disparity between the quantity of oxygen supplied and the quantity needed by the body.

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