LOCAL CEREBRAL BLOOD FLOW VELOCITY IN NEWBORN RATS IN NORMOCAPNIA AND HYPERCAPNIA

V. R. Purin and E. V. Syutkina

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The local cerebral blood flow (LCBF) in the caudate nucleus was investigated in experiments on unanesthetized newborn rats by determining the rate of hydrogen saturation of the brain tissue and the cerebral blood volume was studied by plethysmography. LCBF in newborn animals was found to be considerably lower than in adults. Inhalation of CO_2 by newborn, unlike by adult rats, did not cause an increase in LCBF and the cerebral blood volume also remained unchanged.

KEY WORDS: cerebral blood flow; hypercapnia; newborn animals.

The velocity of the blood flow in the brain of newborn rabbits has been found (by the microglobule method) to be 25 ml/100 g/min [8]. In newborn puppies (autoradiography with [^{14}C]antipyrin) the blood flow was found to be 40 ml/100 g/min in the tissue of the thalamus and 60 ml/100 g/min in the cerebral cortex. The corresponding values for adult animals were 1.5-2 times higher [9]. During nitrous oxide anesthesia no difference in the velocity of the cerebral blood flow was found by the Kety–Schmidt method in children aged from 11 days to 12 months; it was 69 ± 8.0 ml/100 g/min, i.e., higher than in adults [13]. Data on the effect of hypercapnia on the cerebral blood flow also are contradictory: In sheep fetuses between the 105th and 145th days of gestation an increase in pCO_2 of the arterial blood by 1 mm Hg led to an increase in the blood flow through the carotid artery by 5.1 ± 1.4 ml/100 g/min [10], whereas in newborn pigs under the same conditions the carotid blood flow decreased by 20% [11]. In newborn monkeys inhalation of CO_2 caused an increase in the cerebral blood flow, although it was much smaller than the increase in adult animals [12].

The effect of hypercapnia on the cerebral blood flow was investigated in newborn rats.

EXPERIMENTAL METHOD

Experiments were carried out on 22 rats aged 1-3 days and on 38 adult Wistar rats. The following parameters were recorded: the local cerebral blood flow (LCBF), as the rate of saturation of the brain tissue with hydrogen, changes in the cerebral blood volume (CBV), by photoplethysmography, the ECG, and respiration. The newborn animals were fixed by gentle bandaging on a constant-temperature stage at 36-37°C, which allowed investigation without general anesthesia. Under local anesthesia with 0.5% procaine solution an incision was made in the skin on the head and a glazed platinum electrode 0.1 mm in diameter was introduced through the coronal suture so that its free end, 0.9 mm long, was in the caudate nucleus. The head wound was covered with polyethylene film. Adult animals were anesthetized with pentobarbital in a dose of 40 mg/kg, secured to a constant-temperature platform, and the electrode was inserted in the same way. The silver chloride reference electrode was introduced under the skin. The potential difference between the electrodes was balanced by the power source of the LP-7 polarograph [2, 6]. The high-resistance zero indicator was a pH-340 millivoltmeter. Photoplethysmography was carried out with a KS-18 filter [3]. The results were read on the scale of a M-95 microammeter. A Pul's-10 attachment served as the respiration transducer, and respiration and the ECG were recorded on an Alvar encephalograph. The platform with the animal was covered by a glass bell jar with a capacity of 12 liters. To create a hypercapnic gas mixture CO_2 was introduced into the chamber. After an interval of 5 min 450 ml H_2 was injected into the chamber, keeping the O_2 concentration at the 20% level (this

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TABLE 1. LCBF During Inhalation of Air

Rats	Statistical index	$LCBF_S$	$LCBF_E$	Difference between values of two consecutive measurements: $\frac{LCBF_E - LCBF_S}{LCBF_S}$, %	$\frac{LCBF_{E1} - LCBF_{E2}}{LCBF_{E1}}$, %	$\frac{LCBF_{S1} - LCBF_{S2}}{LCBF_{S1}}$, %
Adult	n	71	75	71	7	15
	$M \pm m$	63,0±2,75	58,3±2,53	—1,66±2,65	15,86±6,22	11,40±5,27
Newborn	n	40	40	40	7	18
	$M \pm m$	19,0±0,69	17,9±0,64	—2,90±4,18	7,86±2,87	—1±4.48

Legend. $LCBF_S$) Calculated from saturation; $LCBF_E$) calculated from elimination.

TABLE 2. LCBF During Inhalation of Hypercapnic Mixtures (in % of initial level of LCBF during inhalation of air)

% of CO_2 in chamber	Rats			
	adult		newborn	
	n	$M \pm m$	n	$M \pm m$
3—6	15	146,21±9,59		
8—10	15	190,93±20,34		
11—15	15	238,13±28,36	22	107,22±3,34

was continuously monitored by a Narco oxymeter). The gases were rapidly mixed by means of a fan. If the experiment was carried out while air was breathed, recording the saturation curve was followed by recording the curve of elimination of hydrogen from the brain tissue. In both newborn and adult animals basically monoexponential curves were obtained so that LCBF could be calculated by the equation $LCBF = 69.3/T_{1/2}$, where $T_{1/2}$ is the time of half-saturation with or half-elimination of H_2 from the brain tissue. In the case of biexponential curves, the method of splitting into components [7] was used.

EXPERIMENTAL RESULTS

The results of measurement of LCBF during breathing the ordinary air of the room are given in Table 1. The mean values of LCBF calculated from the rate of saturation were indistinguishable from those calculated from the rate of elimination ($P > 0.1$). LCBF in the caudate nucleus of newborn rats was found to be significantly lower than in adults, even if anesthetized. This cannot be regarded as an error due to the slow gas exchange in the lungs. In an additional series of experiments on nine newborn animals anesthetized with ether, the electrode was introduced into the left atrium. During both saturation of the arterial blood with H_2 and its elimination by 90% about 35 sec was needed. In three experiments in which the electrode was introduced into the iliac artery of adult animals this time was 18 sec.

In adult animals the inhalation of a hypercapnic gas mixture led in most cases to an increase in the frequency and amplitude of respiration, but this was not observed in the newborn rats. As reported previously [3], inhalation of CO_2 by newborn rats does not lead to dilatation of the cerebral vessels. The same result was observed in this series of the present experiments.

In adult animals during inhalation of a hypercapnic gas mixture (Table 2) LCBF increased regularly, to reach 238% of its initial level when the CO_2 concentration in the chamber was 11-15%; in newborn animals under the same conditions no response of LCBF could be observed. This applies not only to mean values: The differences between individual data recorded during normocapnia and hypercapnia were within the limits of ordinary variations of two consecutive tests carried out at the same interval of time during inhalation of the ordinary air of the room ($P > 0.1$).

In adult animals barbiturates, in anesthetic doses, reduce the blood flow in the caudate nucleus by 33-60% [4, 5]. It can accordingly be concluded that the normal LCBF in this part of the brain in newborn rats is 20-25% of its value in adults. The low blood flow at this age period is perhaps compensated by the more complete extraction of O_2 from the blood because of the relatively smaller size of the bodies of the nerve cells [1]. This argument is supported by the surprisingly low pO_2 of the blood of the longitudinal sinus and the high arteriovenous oxygen difference in the brain of newborn infants [14].

The partial pressure of carbon dioxide is the main factor controlling the velocity of the cerebral flow in adults. A reactivity to carbon dioxide correspondingly must be regarded as one of the fundamental distinguishing features of the newborn. However, this feature is found only in animals blind at birth. Sheep, on whose fetuses similar investigations were carried out at the end of the period of gestation, can see at birth, and the level of visual function of Macaca rhesus at birth is also relatively high. In a species unable to see at birth the response to pCO_2 develops later as an adaptation to conditions of extrauterine existence, calling for a sharp change in the levels of brain activity.

LITERATURE CITED

1. Yu. Ya. Kislyakov, Mathematical Models of the Circulation and Gas Exchange in the Brain [in Russian], Leningrad (1975), p. 109.
2. Yu. E. Moskalenko et al., Intracranial Hemodynamics [in Russian], Leningrad (1975), p. 44.
3. V. R. Purin and E. V. Syutkina, Byull. Éksp. Biol. Med., No. 1, 9 (1975).
4. J. M. Fein, J. Willis, J. Hamilton, et al., Stroke, 6, 42 (1975).
5. C. Fieschi, L. Bozzao, A. Agnoli, et al., Exp. Brain Res., 7, 111 (1969).
6. J. L. Haining, M. D. Turner, and R. M. Pantall, Circulat. Res., 23, 313 (1968).
7. D. H. Ingvar and N. A. Lassen, Acta Physiol. Scand., 54, 325 (1962).
8. I. Jarai, J. Physiol. (London), 202, 559 (1969).
9. C. Kennedy, G. D. Grave, J. W. Jehle, et al., J. Neurochem., 19, 2423 (1972).
10. L. J. Mann, Exp. Neurol., 26, 136 (1970).
11. G. D. Reddy, N. Gootman, N. M. Buckley, et al., Biol. Neonat., 25, 249 (1974).
12. M. Reivich, A. W. Brann, H. Shapiro, et al., Panminerva Med., 13, 169 (1971).
13. G. Settergren, B. S. Lindblad, and B. Persson, Acta Paediatr. Scand., 65, 343 (1976).
14. J. Wenner, in: Perinatale Medizin, Vol. 3, Stuttgart (1972), pp. 322-323.