PHYSIOLOGY

THE BLOOD SUPPLY OF THE BRAIN DURING REFLEX REACTIONS

Second Report

THE BLOOD SUPPLY OF THE BRAIN DURING INTEROCEPTIVE IRRITATION OF THE SMALL INTESTINE IN THE PRESENCE OF HYPERCAPNIA

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In the preceding report it was shown that with irritation of the interoceptors of the small intestine in some cases there occurs an increase, and in others a decrease, in the blood supply of the brain. On the basis of an analysis of synchronous changes in the volumetric rate of blood flow and in arterial pressure, the supposition was advanced that the nature of the reaction of the vessels of the brain during interoceptive irritation on the whole depends on the initial tonus of these vessels prior to irritation. For the purpose of verifying experimentally this hypothesis in the present work research was done on the blood supply of the brain during interoceptive irritation in the presence of hypercapnia.

As the data in the literature affirm, the pressure of CO_2 in the blood exerts a considerable influence on the state of tonus of the brain vessels. In a single experiment the pressure of CO_2 in the blood of different animals may vary considerably, depending upon the extent of narcosis, operative procedures and the character of respiration.

It has been established by a series of examinations (for a survey of the literature see the article by Bouckaert and Jordan [5]) that, when the pressure of CO_2 in the blood is increased, as a result of the direct, peripheral effect of CO_2 on the vessel walls there occurs dilation of the vessels and an increase in the supply of blood to the brain, while, when the pressure of CO_2 in the blood falls off, there occurs a constriction of the vessels and a decrease in the brain's blood supply. In contrast to other vascular regions a central vasoconstricting effect of CO_2 is not manifested on the vessels of the brain.

The threshold of the dilating effect of CO_2 for the vessels of the brain proved to be very low. These vessels are dilated at that level of CO_2 in the inspirated air at which neither the respiratory nor the vasomotor center reacts [6, 9, 10 et al].

Some research was devoted to a study of arterial pressure reactions during interoceptive irritation in the presence of short-term hypercapnia. E. Sh. Airapetyants [1], V. N. Zvorykin [2] and T. V. Popova [4] observed during weak hypercapnia(5-7% CO_2 in the mixture) an intensification of the reaction only in those cases in which there was a distinct reaction of respiration and blood pressure in response to inspiration of mixtures containing CO_2. Strong hypercapnia (10% and higher) is accompanied by a two-phase change in the arterial pressure reaction during irritation of the interoceptors: in the initial stages an increase was observed and in the subsequent stages a depression or distortion of the reaction. There is no data in the literature on the change in the blood

supply of the brain during interoceptive irritation in the presence of hypercapnia.

EXPERIMENTAL METHODS

Experiments were conducted on 19 adult dogs under morphine-urethane narcosis.

In accordance with our project we employed low concentrations of CO_2 in the inspirated air, under the influence of which there appeared a distinct increase in the blood supply of the brain and negligible changes in respiration and arterial pressure. For inspiration of the mixtures Douglas bags were used with respiratory valves in a T-pipe inserted in the trachea. Inhalation of the mixture continued for 10-15 minutes.

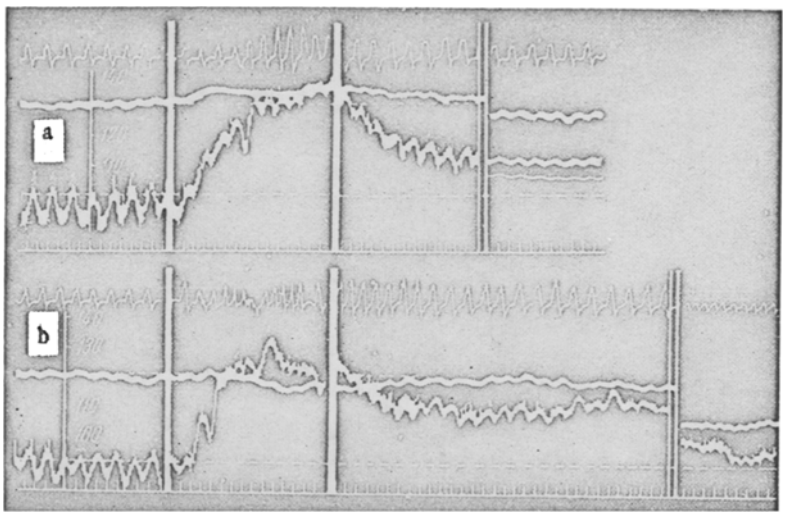

Fig. 1. Photokymogram of the experiment of September 17, 1954. a) Reaction to irritation of the interoceptors during breathing of the air of the room; b) reaction to irritation of the interoceptors 14 minutes after cessation of inhalation of a mixture containing 7.1% CO_2. From above down: respiratory movements, volumetric rate of blood flow in the meninges, arterial pressure, time scale. Vertical lines: the beginning and end of irritation. Double vertical lines: interruption of recording. Broken lines: level of the characteristics being recorded prior to the beginning of irritation.

Irritation of the interoceptors was effected by inflating a section of the small intestine with air under a pressure of 80 mm of mercury. This stimulation was performed 2-3 times until a stable reaction was obtained while the animal breathed the air of the room, once during inhalation of the CO_2 mixture and several times in the course of 1-2 hours after the animal reverted back to breathing the air of the room. The intervals between irritations amounted to not less than 15 minutes. In order to judge the blood supply of the brain we recorded the volumetric rate of blood flow in the meninges by the thermoelectric method using a flat thermoelectrode.

The arterial pressure in the femoral artery was recorded with a mercury manometer and respiratory movements with a pneumograph. All the indicated characteristics were recorded synchronously on a photokymograph.

EXPERIMENTAL RESULTS

During inhalation of the mixtures of air containing 4.5-7.5% CO_2 there was observed a small increase in the amplitude, an alternating increase and decrease in the frequency of respiratory movements and negligible changes in the level of the arterial pressure, which increased as well as decreased within the limits of 5 to 8 mm on a mercury column. At the same time the blood supply of the brain increased after 4-8 seconds and

remained at the higher level throughout the entire period the mixture was inhaled. The significant increase in the volumetric rate of blood flow while arterial pressure was practically unchanged shows that, at the concentrations of CO_2 which we employed, a lowering of tonus occurred, which was manifested by the dilation of the vessels of the brain.

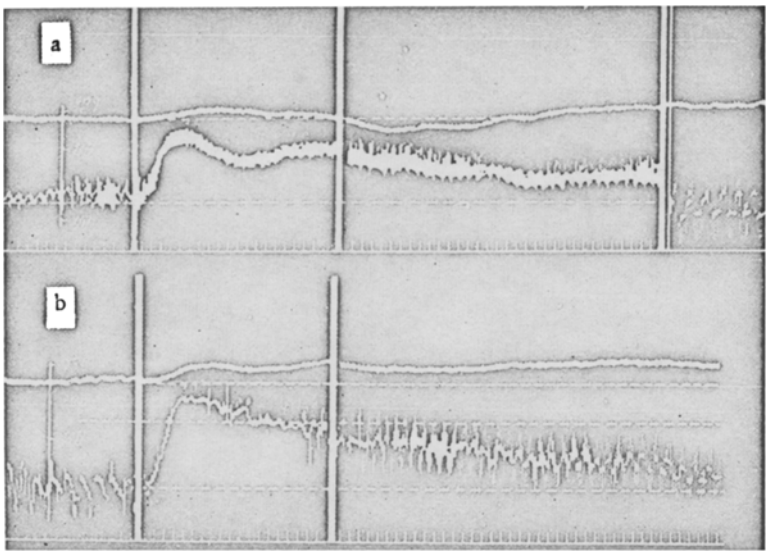

Fig. 2. Photokymogram of the experiment of November 20, 1954. a) Reaction to irritation of the interoceptors during breathing of the air of the room; b) reaction to irritation of the interoceptors during inhalation of a mixture containing 6.9% CO_2. From above down: volumetric rate of blood flow in the meninges, arterial pressure, time scale.

After an animal reverted to breathing the air of the room, within 30-90 seconds the amplitude and frequency of respiratory movements were restored. Arterial pressure, after falling below the initial level for 20-30 seconds, gradually returned to the starting level after 2-3 minutes. Within 10-20 seconds the blood supply of the brain began to decrease, often falling below the starting level, and was restored after 3-8 minutes.

When the room air was breathed, there occurred in all of the experiments in response to irritation of the interoceptors an increase in arterial pressure, in 14 experiments the blood supply of the brain increased (Fig. 1,a), and in 5 experiments a two-phase reaction was observed: an initial increase and a subsequent decrease in blood flow, especially marked in the first few seconds at the conclusion of stimulation (Fig. 2,a). The decrease in blood flow during an increase in arterial pressure indicates constriction of the vessels of the brain.

Irritation of the interoceptors during inhalation of the mixtures containing CO_2 against a background of increased blood supply to the brain led in all of the experiments, regardless of the nature of the original reaction, to an increase in the blood supply of the brain (Fig. 2,b). The blood supply level attained during irritation in the majority of cases was not reduced at the conclusion of stimulation until termination of inhalation of the mixture, although the arterial pressure was restored (Fig. 2,b). In not a single case during inhalation of the CO_2 mixture were phases of reduction of blood flow observed. The reaction with respect to arterial pressure during this time changed negligibly in comparison with the reaction prior to hypercapnia: at times the increase in arterial pressure during irritation of the interoceptors was somewhat greater than, at times somewhat less ($\pm$ 5-10 mm), and at times the same as in the reaction prior to hypercapnia.

The greater increase and the absence of a reduction phase in the blood supply of the brain during interoceptive irritation in the presence of hypercapnia may be the result of changes in the functional state of the vasomotor center and corresponding impulsation to the vessels of the brain, as well as of changes in the functional state of the vascular wall. Under the conditions of those of our experiments in which small concentrations of

CO_2 were used in the mixtures inhaled, it was hardly possible to assume a decrease in vasoconstricting impulsation from the vasomotor center, inasmuch as the rise in arterial pressure during irritation of the interoceptors was practically the same as the rise prior to hypercapnia. At the same time the decrease in tonus of the vessels of the brain which accompanies hypercapnia, the weakening of the muscular layers of the vascular wall, is linked with the change in functional state of the vessels. On the one hand the weakened wall, under the influence of increased intravascular pressure during irritation of the interoceptors, is stretched more vigorously, and the vascular lumen is passively increased. According to the data of Forbes and his co-workers [6], when normal muscle tonus exists in the vessels of the pia mater, passive dilation of these vessels is negligible or absent even with a very sharp and sudden rise in arterial pressure. When the tonus of these vessels is lowered, their passive dilation is considerable even with a small increase in arterial pressure.

On the other hand, when the vascular wall is weakened, the reactivity of the vessels may change with respect to vasoconstricting influences. Thus H. Rein [10] and H. Rein and U. Otto [11] observed in the inert muscles of the extremities at the normal body temperature of an animal a constriction of the vessels in response to squeezing of the carotid arteries, inhalation of mixtures containing CO_2 and injection of epinephrine. Constriction of the vessels in the presence of these same influences did not occur, however, or was considerably weaker against a background of dilated vessels of the muscles in connection with active hyperemia and when the animal was chilled. The same effect prevailed in response to injection of vasodilating substances. B. Folkow [7] observed during dilation of the vessels of the extremities with adenosinetriphosphate a sharp decrease in the vasoconstricting effect in response to irritation of the sympathetic chain. N. Lüdwigs and M. Schneider [8] did not observe during hypercapnia a decrease in the blood supply of the brain in connection with irritation of the cervical sympathetic nerve, a decrease which was clearly marked prior to hypercapnia.

Proceeding from these data, one must consider that the cause of the change in the reaction of the vessels of the brain resulting from interoceptive irritation during hypercapnia is the lowering of the tonus of the brain vessels in consequence of the peripheral effect on them of the CO_2 in the blood.

The functional state of the vessels of the brain after the animal reverts to breathing the air of the room is restored only gradually, and considerably later than the blood supply of the brain, respiration and arterial pressure. During the first few minutes (from 5 to 10 minutes) after the animal reverted, there was observed during irritation of the interoceptors in all of the experiments an increase in the blood supply of the brain, but it was less marked than before and during hypercapnia, while at the conclusion of the stimulation a prolonged after-effect was not observed: restoration of the original level takes place within the first few seconds.

Subsequently, 20-40 minutes after inhalation of the CO_2 mixture was stopped, in the experiments with an initial two-phase reaction during irritation of the interoceptors, a phase of reduction in blood flow was observed, as it also was prior to hypercapnia. In the majority of experiments with an initial (prior to hypercapnia) single-phase reaction during irritation of the interoceptors there occurred in this period, instead of an increase, a decrease in blood flow (Fig. 2,b), and the initial single-phase reaction was restored only after 60-90 minutes.

Consequently, when the excess carbon dioxide is removed from the blood, the irritability of the vessel walls of the brain to vasoconstricting influences during interoceptive stimulation, before it returns to its original state prior to hypercapnia, passes through a phase of elevation, in consequence of which are created the conditions for lowering the blood flow of the brain in the presence of reflex influences. The data which we obtained show that one of the factors which determine the unequal reaction of the brain vessels during interoceptive irritation is the level of CO_2 pressure in the blood.

SUMMARY

Dynamics of the changes in the blood supply of the brain under the excitation of the interoceptors of the small intestine under usual conditions and under short-term hypercapnia were studied in dogs anesthetized with morphine – urethane. Volumetric velocity of the blood flow in the brain membranes was registered using the thermoelectrical method, as well as the arterial pressure and respiratory movements.

It was noted that during hypercapnia, against a background of the increased blood supply of the brain (owing to the drop of the tonus of the brain vessels), the excitation of the interoceptors brought about a significant increase in the blood supply of the brain in all the cases regardless of the nature of the original reaction before hypercapnia. 60-90 seconds after the termination of the hypercapnia an inversion of the usual reaction was observed; instead of an increase, a decrease of the blood supply of the brain took place. The observed changes of the responses of the brain vessels under the interoceptive excitation during and after hypercapnia are due to the changes in the functional condition of the wall of the blood vessels brought about due to the effect of the increased pressure of CO_2 in the blood.

observed: instead of the increase, a decrease of the blood supply of the brain takes place. The observed changes of the responses of the brain vessels under the interoceptive excitation during and after hypercapnia are due to the changes in the functional condition of the wall of the blood vessels brought about under the effect of the increased pressure of CO_2 in blood.

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