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AUTOREGULATION OF CEREBRAL BLOOD CIRCULATION UNDER ORTHOSTATIC TESTS

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16. Abstract

Autoregulation of cerebral blood flow (ACBF) under orthostatic tests (OT) was estimated in acute experiments on rabbits and cats under local anesthesia according to changes of perfusion pressure (PP) in carotid arteries, cerebral blood flow, pressure in the venous system of the brain and resistance of cerebral vessels. OT was modeled by turning a special table with the animal fastened to it from a horizontal to a vertical (head up or head down) position at 40-80°. In most experiments ACBF correlated with the changes of PP. Different variations of ACBF and its possible mechanisms are discussed.

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AUTOREGULATION OF CEREBRAL BLOOD CIRCULATION UNDER ORTHOSTATIC TESTS

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We know that rapid changes from the horizontal to the vertical position (head /263* up or down) is accompanied by characteristic changes in the dynamics of cerebral blood perfusion [5, 6, 14]. In such situations for the normal functioning of the CNS what is needed is maintenance of adequate blood supply to the brain and this is controlled by complex autoregulatory mechanisms. The latter, however, have not been sufficiently investigated and in many respects are still debatable [7-9, 13]. The purpose of the present research was an attempt to investigate the character and dynamics of cerebrovascular autoregulatory reactions in the case of rapid changes in body position in a vertical plane.

Method

Acute experiments were conducted with 25 rabbits weighing 2.5-3.5 kg and with 8 cats weighing 2.5-3.5 kg. The nonanesthetized animals (for the cats an ether stupefacient was used) were fastened to a special table so that their position could be changed around a horizontal axis at the level of the external auditory passages. Changes in table position provided the possibility of modeling the orientation of the gravitational field corresponding to the body position of the animal head down or head up. Continuous recording of cerebral blood flow (CBF) was done with a flowmeter of our own construction [1] connected with both common carotid arteries. The extracranial branches of the carotid arteries which supply the soft tissues of the head were ligatured in accord with generally accepted methodological recommendations. Thus, the recorded blood flow reflected the blood supply to the brain in the carotid reservoir. BP was recorded in a common carotid artery. Pressure in the venous cerebral vessels was measured with an aqueous manometer connected with the cranial extremity of the external jugular vein or with the sagittal sinus. The level of venous pressure was determined visually and recorded on a kymograph tape and this proved

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* Numbers in the margin indicate pagination in the foreign text.

CHANGES (IN % OF INITIAL VALUES) OF CEREBRAL BLOOD FLOW (ΔCBF) AND CEREBRAL VASCULAR RESISTANCE (ΔCVR) WITH HIGHER OR LOWER PERFUSION PRESSURE (PP) IN ORTHOSTATIC TESTS

Objects	Type of PP change (mm Hg)	CBF	CVR
Rabbits	PP rise in the 40-160 range	-0.1 ± 1.4 $p > 0.05$	$+20.1 \pm 2.4$ $p < 0.001$
	PP drop in the 150-40 range	-1.36 ± 1.9 $p > 0.05$	-17.8 ± 1.6 $p < 0.001$
Cats	PP rise in the 80-190 range	$+3.2 \pm 2.3$ $p > 0.05$	$+18.0 \pm 2.5$ $p < 0.001$
	PP drop in the 190-80 range	-6.6 ± 2.3 $p < 0.05$	-13.6 ± 2.0 $p < 0.001$

Note: Plus sign = rise, minus sign = drop.

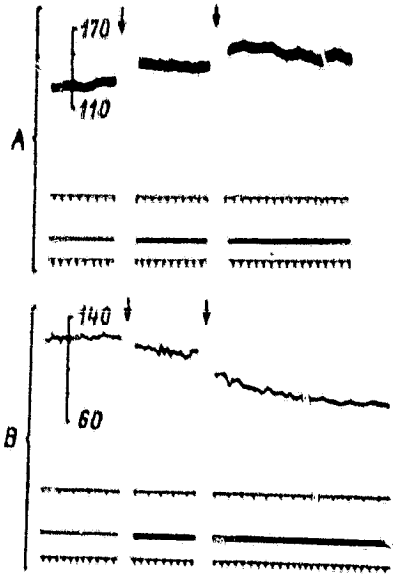

Fig. 1. CBF in rabbits in OT. A - head down, B - head up. From top: BP, CBF (space between dots in A is 2 ml, in B is 2.5 ml), OT, time in 5 sec intervals. Arrows show 1 min pause.

suitable for subsequent comparison of cerebral hemodynamic indices. Heparin was used as anticoagulant.

All operations connected with the preparation of vessels, ligature and cannulation were done under local novocain anesthesia. In the cat experiments local anesthesia was accompanied by the use of myorelaxants (diplacin or lystenone administered IV). Stable pulmonary ventilation was maintained with an artificial respirator. /264

The type of cerebrovascular autoregulatory reaction was judged according to the indices of CBF and of measured resistance of cerebral vessels at various levels of PP (perfusion pressure) during OT (orthostatic tests). PP in the carotids was calculated by subtracting the venous pressure in the cerebral vessels from that in the carotid artery. OT lasting 3-5 min was modeled by turning the table and the animal (head up or down) at an angle of 40-80° from the horizontal. In each experiment 4-10 OT were conducted. total results of 83 tests with rabbits and 45 tests with cats are given in the Table.

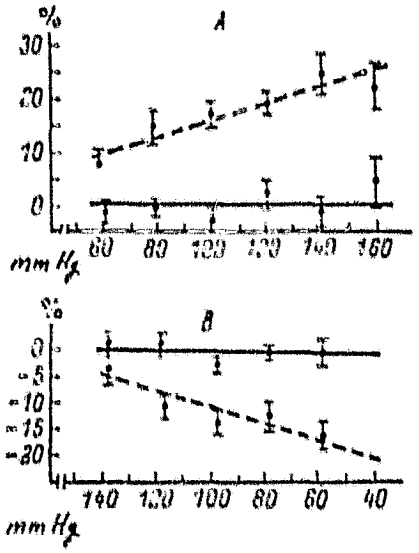

Fig. 2. CBF changes (solid line) and CVR (broken line) in rabbits in OT. A - head down, B - head up.

Research Results

In the horizontal rabbit experiments the initial level of arterial pressure was on the average 97.5±3.9 mm Hg, venous pressure 83.6±5.0 mm H_2O, CBF was 22.5±1.3 ml/min, CVR (cerebral vascular resistance) 1.08±0.06 mm Hg/100 g/min/ml.

In the OT head up the PP fell by 30-60 (average 34.0±4.1) mm Hg; the pressure in the venous vessels of the brain went down by 15-60 (average 38.8±8.3) mm H_2O. When the animals were returned to the horizontal position the initial indices were restored. During OT in the opposite direction (head down) we noted a rise in PP by 20-60 (average 41.7±3.6) mm Hg and in the venous pressure by 30-100 (average 48.6±6.9) mm H_2O. Some rabbits (5 out of 25) presented PP changes in OT that were weak and fleeting or else there were no signs of autoregulation. Such experiments were excluded from the research materials.

Thus, in most of the experiments it was possible to determine CBF changes and CVR under different conditions of PP in a range from 40 to 160 mm Hg (see Table). This table shows that the increase in PP was accompanied by an increase in CVR which in 30% of the OT appeared completely adequate for maintaining stable blood flow (Fig. 1 A). In 30% of the tests CBF was reduced, despite the increase in PP, which is evidence that vascular autoregulatory reactions went into spasm. In 40% of the tests autoregulation appeared inadequate and the increase in vascular resistance was accompanied by an increase in cerebral blood flow (CBF). When PP dropped to various levels in the range of 150-40 mm Hg, in the majority of OT we noted a reduction in cerebrovascular resistance. In 25-30% CBF remained constant /265 (Fig. 1 B). In approximately the same percentage of tests CBF increased. In the other cases (about 40% of the tests) CBF decreased despite the decrease in vascular resistance. CBF was considerably reduced when PP was lower than 60-50 mm Hg. Apparently this level of PP is the lower limit for autoregulation and beyond it

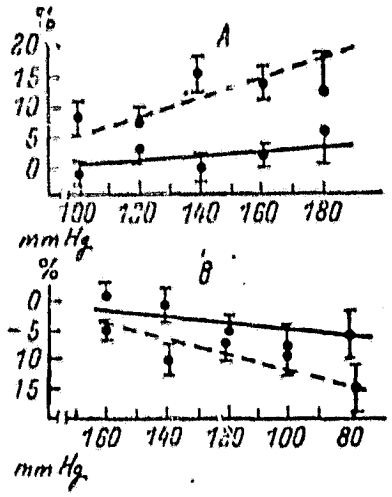

Fig. 3. CBF changes (solid line) and CVR (broken line) in cats. A - head down, B - head up.

there occurs passive deceleration of blood flow (interruption of autoregulation) corresponding to the drop in PP. We had no success in establishing the upper limits for the interruption of autoregulation, since in the rabbits PP would habitually rise to 140 mm Hg and in rare cases even a level of 150-160 mm Hg.

In the horizontal cat experiments the initial level of BP was on the average 136.2±8.8 mm Hg, the venous 96.0±8.4 mm H_2O, CBF 30.1±1.5 ml/min, CVR 1.52±0.09 mm Hg/100 g/min/ml.

In OT head down the PP in most experiments rose by 10-60 (average 33.8±5.7) mm Hg and the venous pressure by 40-100 mm H_2O. When the OT was in the opposite direction (head up) the PP went down by 20-50 (average 37.7±4.8) mm Hg, the venous by 35-70 mm H_2O and in some cases down to zero. Thus, the changes (rise or fall) in the levels of PP for the cats were in the range of 80-190 mm Hg. Gradual changes of PP were accompanied in most cases by a characteristic autoregulatory reaction aimed at preserving a relatively stable flow of blood to the brain. It should be noted that in some experiments (3 out of 8) there was no autoregulation or there were no substantial changes in PP. The Table shows the results only of those experiments in which most of the OT were accompanied by steady changes in BP and autoregulatory reaction.

As we see from the Table, the rise in PP from 80 to 190 mm Hg was accompanied in most cases by a significant increase in vascular resistance due to which cerebral blood flow in 25% of the OT did not change appreciably. However, in a number of cases CBF nevertheless increased despite heightened vascular resistance. During some observations CBF went down, which is evidence of an immoderate increase in vascular resistance.

When the PP went down from 190 to 80 mm Hg CVR went down to a different degree. In approximately 20% of the OT the reduction in vascular pressure was completely adequate for maintaining stable blood flow and in some cases CBF even went up despite the drop in PP. However, in a number of OT the reduction in vascular resist- /266

tance was clearly inadequate and blood flow went down passively to correspond with the drop in PP. In the cat experiments there was no determination of exact limits for PP beyond which there is a regular interruption of autoregulation. Apparently these limits are beyond the range of the PP changes observed.

Evaluation of Results

The results of our investigation have shown that an orthostatic load is accompanied in most experiments by real changes in PP and completely satisfactory autoregulation of cerebral vascular reactions (Figures 2, 3). However, in cats this reaction was visible to a lesser degree than in rabbits. There was particular impairment of autoregulatory reactions in cats when PP went down and this induced a reliable reduction in CBF. Apparently some weakening of the autoregulatory reaction in cats may be explained by partial ether anesthesia during the time the animals were rendered immobile. We know that anesthesia inhibits the autoregulatory reactions of cerebral vessels.

Data exist [2, 10] to show that when the OT is used arterial pressure is quickly restored due to presoreceptor sinocarotid reflexes. Apparently the novocain anesthesia in our experiments blocked the neuroreflex control of the carotid sinuses, thus favoring more pronounced changes in BP during OT. On analysis of the type of cerebrovascular reactions in response to OT we may note several of their variants. In most cases changes in PP (up or down) induced adequate autoregulatory reactions in the cerebral vessels and CBF remained stable. However, in some experiments the rise of PP was accompanied by an immoderate increase of resistance to blood flow and this produced a negative effect, i. e. a diminution of CBF. This may have occurred especially as the result of spasms of the resistive cerebral vessels. The increase in venous pressure during orthostatic load (head down) apparently did not result in any real resistance to blood flow, since in a number of cases the CBF increased when there was a similar increase of venous pressure. When the PP went down, cerebral blood flow sometimes went up, apparently as the result of excessive diminution of CVR. /267

Thus, along with adequate autoregulation of vascular reactions that maintain CBF at a relatively stable level, there occurred a superautoregulation which, if the PP rises, may create a danger in the form of development of spasm in the cerebral

vessels. There is a certain danger likewise present in those not infrequent cases where CBF showed a tendency toward passive changes corresponding to PP, an indication of inadequate autoregulatory mechanisms.

In some experiments we noted an increase in vascular resistance as a response to the rapid fall in PP and here CBF sharply decelerated. Such a paradoxical phenomenon is reminiscent of that described by G. I. Mchedlishvili [7] comprising essentially a spasm of the main cerebral arteries under terminal conditions.

In the light of contemporary concepts about the effect of the autonomic nervous system on the tonus of cerebral vessels, it may be suggested that there is a neuroreflex genesis behind the observed autoregulatory cerebrovascular reactions. We do not exclude the participation of the metabolic and myogenic components (Ostroumov-Beyliss phenomenon). The data gathered in the last few years [3, 11, 12, 15] favor the neurogenic mechanism, data on real changes in the autoregulatory reaction of cerebral vessels following adrenergic block. However, we do not know where the receptive fields of these reflexes are located. There is still no agreement on the question of the role of the carotid pressoreceptors in the regulation of the tonus of the cerebral vessels. A very interesting question is that of the receptor apparatus in the walls of the venous cerebral sinuses, particularly of the sinus cavernosus [4]. It has been established that a rise of pressure in the venous sinuses of the brain induces a reflex contraction of the internal carotid and spinal arteries [7]. In our experiments in OT the pressure in the venous system of the brain changed within fairly broad limits and apparently played an important role in autoregulatory reactions.

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