CHANGES IN TONE OF THE CAT CAROTID ARTERY IN RESPONSE TO CHANGES IN RATE OF BLOOD FLOW

S. A. Balashov and A. M. Mel'kumyants

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KEY WORDS: carotid artery; velocity of blood flow; x-ray contrast substance.

The main arteries of skeletal muscle [4], the limb [2], heart [6], skin, intestine, and thyroid gland [8] are sensitive to the rate of blood flow along them: They dilate in response to an increase and constrict in response to a decrease in the velocity of blood flow. In acute experiments dilatation of arteries in dogs and cats begins 10-40 sec after the increase in blood flow due to opening of an arteriovenous shunt.

Meanwhile, in chronic experiments on dogs [7], the diameter of the carotid artery (CA), the blood flow in which was increased by means of an arteriovenous fistula, became significantly greater than the diameter of a control artery only when 1 week had elapsed after creation of the fistula. Measurements made 3 days after connection of CA with the external jugular vein revealed no change in diameter of the shunted artery compared with the control. This result could signify either that dilatation of CA in response to an increase in the rate of blood flow takes place after an incommensurately longer latent period than in all arteries studied previously, or that the techniques used in [7] can reveal changes in the vessel wall taking place only as a result of prolonged action of an increased blood flow.

The aims of the present investigation were as follows: to determine whether CA dilates immediately after the velocity of the blood flow in it is increased; in the case of a positive answer to this question, to study dependence of the magnitude of this response on the factor by which the velocity of the blood flow in the artery is increased and, finally, to discover how the use of the x-ray contrast substance in [7] affects arterial tone.

EXPERIMENTAL METHOD

Altogether 16 acute experiments were carried out on cats weighing from 1.9 to 5.0 kg, anesthetized with urethane and chloralose (0.6 and 0.04 g/kg, respectively). The scheme of the experiment is illustrated in Fig. 1. The right common CA was dissected from the point of its departure from the thorax as far as the carotid sinus. Branches given off from CA to muscles and the thyroid gland were ligated. After injection of heparin (1500 U/kg) the distal segment of CA was connected by rubber tubes with the right jugular vein, and the proximal segment was connected to the output of a PN-3 perfusion pump [5]. The inlet pipe of the perfusion pump was connected to the central segment of the left femoral artery. The pressure in CA was stabilized at 100 mm Hg by means of an automatic tracking system [1]. Blood from the left femoral artery was injected by the perfusion pump into the test CA. Blood passed along it into the left jugular vein, via the D2M flow detector of an RKE-1 electromagnetic flowmeter and an electrohydraulic throttle, the effector element of the pressure stabilization system. The external diameter of CA, dissected free from the tissues for a length of 4-5 mm, was measured with a contact capacitive displacement transducer [3].

Signals from the electromanometer, acting as detector of the pressure stabilization system, the flowmeter, and the diameter transducer were recorded on two-channel KSPP-4 potentiometers. The animal's condition was judged from the level of its arterial pressure, measured by an electromanometer in the femoral artery. The CA chosen for testing was immersed throughout the experiment in mineral oil, whose temperature was maintained at 34-35°C.

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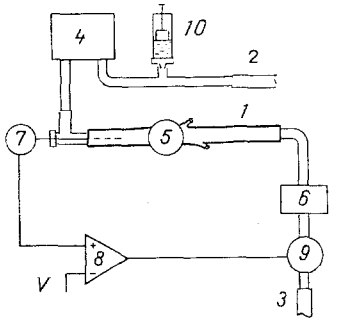

Fig. 1

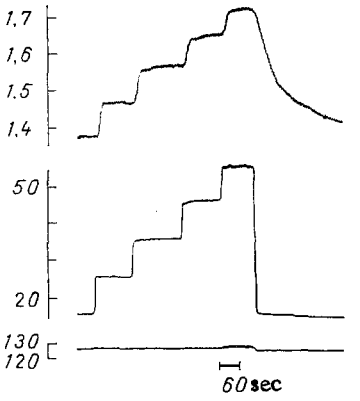

Fig. 2

Fig. 1. Scheme of experiments. 1) CA, 2) femoral artery, 3) jugular vein, 4) perfusion pump, 5) diameter transducer, 6) transducer of electromagnetic flowmeter. Pressure stabilization system: 7) electromanometer, 8) differential amplifier, 9) hydraulic throttle, 10) syringe for injecting Verografin rapidly into artery. V) Constant tension assigning level of pressure stabilization.

Fig. 2. Change in diameter of CA in response to increase in velocity of blood flow in it with step of 10 ml/min. From top to bottom: diameter (in mm), blood flow (in ml/min), stabilized pressure in CA (in mm Hg).

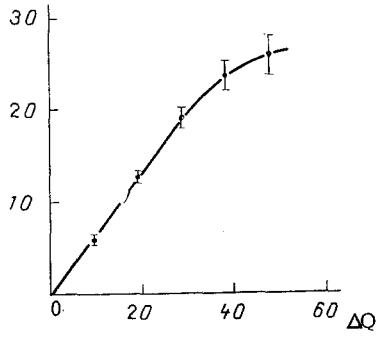

Fig. 3. Dependence of degree of dilatation of CA on increase in blood flow. Abscissa, increase in blood flow (ΔQ, ml/min); ordinate, degree of dilatation of artery (Δd/d, % of initial diameter).

After the end of the operation the blood flow through the artery was established at 10-15 ml/min. In each experiment measurements began with observation of the dilator response of CA to a rapid increase in the volume velocity of the blood. To do this, the output of the perfusion pump was increased in 2-3 min to 40-50 ml/min, after which it was returned to the previous level. Next, the blood flow in the artery was increased in steps of 10 or 5 ml/min and the character of dependence of the diameter of CA on the velocity of the blood flow in it and the latent period of the response for increases of blood of different magnitude was determined.

For comparison with the results obtained in [7], in which the diameter of CA was measured roentgenoangiographically, in the last period of the experiment 0.1-0.5 ml of Verografin (76%, from Spofa, Czechoslovakia) was injected rapidly into blood flowing into CA and changes in diameter of the artery due to the action of this x-ray contrast substance were recorded.

EXPERIMENTAL RESULTS

The trace of changes in diameter of CA (Fig. 2) caused by an increase in blood flow from 15 to 55 ml/min with a step of 10 ml/min shows that an increase in volume velocity of the blood flow leads to dilatation of CA; the latent period of this reaction did not exceed 25 sec. CA, like the femoral artery in cats [2] and many of the trunk arteries of dogs [4, 8],

thus responds to an increase in velocity of blood flow by dilatation with a latent period measured in seconds or several tens of seconds. Dilatation of CA induced by an increase in the blood flow along it was stable, i.e., it persisted throughout the time when the velocity of the blood flow in the artery was increased. During the first 40-120 sec after the increase in velocity of blood flow there was an increase in diameter of the artery, after which it stabilized at the new (above the initial) level, with no tendency to diminish.

Dependence of the increase in diameter of CA on the velocity of blood flowing along it is illustrated in Fig. 3. Just as with the femoral artery of cats [2] an increase in blood flow led to an increase in the diameter of CA; up to flow rates of 40-50 ml/min the increase in diameter was a linear function of the increase in volume velocity of the blood flow. A further increase in flow caused a smaller increase in diameter, and the curve flattened out on a saturation plateau. The maximal dilatation of CA averaged 25 ± 6% of the original diameter, but in some animals the diameter was increased by 40-45%.

Rapid injection of Verografin into CA caused dilatation of the artery, to such a degree that it could exceed the maximal value of the dilator response of CA to an increase in velocity of the blood flow. The greater the quantity of Verografin injected into the artery, the greater the degree of dilatation of CA induced by it. Maximal dilatation was observed after injection of 0.3-0.5 ml Verografin into the artery in the course of 2 sec when the blood flow was 15 ml/min.

The results of all investigations to study the sensitivity of the artery to the rate of blood flow were similar: An increase in the rate of blood flow after a latent period lasting several seconds or tens of seconds induced relaxation of the vascular smooth muscles, leading to dilatation of the artery. The greater the increase in blood flow, the more marked the dilatation. This dilatation lasted as long as the blood flow in the artery was increased, and the original diameter was not restored until after the blood flow had decreased to its initial level. The only result not in harmony with this general pattern was obtained in [7], and accordingly, it was decided to study whether CA in fact does not dilate immediately after the velocity of the blood flow in it increases, or whether the result obtained in [7] is due to attendant factors due to the technique of measurement of diameter.

The latent period of the dilatator response of the cat CA to an increase in the velocity of the blood flow in it did not exceed 25 sec, and CA thus did not differ in this respect from any of the arteries studied previously. It was also shown that Verografin, the x-ray contrast substance used in [7], causes marked dilatation of the artery. The results of angiography thus provide a measure of the properties of the vascular skeleton rather than of the tone of the smooth muscles. A similar shortcoming is characteristic also of another technique used in [7], namely estimation of the diameter of the artery from the volume of fluid contained in a segment of artery of known length, at a given transmural pressure. Five consecutive cycles of loading and unloading of the artery (as was done in [7]) considerably reduce the tone of its muscles, and the curve of dependence of volume on pressure in this state, moreover, reflects chiefly the properties of the vascular skeleton only. Since the two methods of determination of the diameter of the artery lead to a significant reduction in smooth muscle tone, it would not be surprising that when these methods were used good correlation was observed between the results [7].

Considering these particular features of these methods of determination of the diameter of arteries, we can evidently explain also the fact that in [7] no dilatation of the shunted artery was found compared with the control 3 days after creation of the fistula, and that dilatation of this kind was found 1 week or longer periods of time after the blood flow in the artery increased. Rodbard [9] suggested that morphological changes may take place in the wall of arteries subjected for a long time to the action of an increased shear stress (which is equivalent to an increase of blood flow in the artery).

Three days is evidently not long enough for the action of increased shear stress on the arterial wall to lead to a change in those mechanical properties of the vessel wall that are in fact revealed by the methods used in [7], i.e., methods leading to a considerable fall in smooth muscle tone. At the same time it is probable that 1 week is long enough for the commencing changes in the skeleton of the vessel to be determined by these methods.

By examining together the hypothesis stated in [9], the results of the investigation [7], and those of the present experiments, it is evidently possible to imagine the train of events taking place in response to an increase in blood flow in an artery. After a latent period

calculated in seconds or tens of seconds the artery dilates as a result of a decrease in tone of its smooth muscles and it maintains its increased diameter as long as the blood flow in it is increased. If this increase of blood flow is maintained for a short time only, when the velocity of the blood flow falls to its initial level the diameter returns to its initial value. If the blood flow cannot return to its initial level (the presence of a chronic shunt), structural changes aimed at a lasting increase in caliber of the vessel take place in the arterial wall.

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RESPONSES OF OXYTOCINERGIC AND VASOPRESSINERGIC CELLS OF THE SUPRAOPTIC AND PARAVENTRICULAR NUCLEI OF THE RAT HYPOTHALAMUS TO REPEATED INJECTIONS OF THYROTROPHIN RELEASING HORMONE

I. A. Krasnovskaya

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It has been conclusively demonstrated by immunohistochemistry that cells containing and, probably, producing thyrotrophin releasing hormone (TRH) are located in the region of the paraventricular nucleus (PVN) of the hypothalamus [10]. However, the location of these cells does not coincide with that of the main mass of Gomori-positive neurosecretory cells of PVN, whose participation in regulation of thyroid function is indicated by much, although indirect, experimental evidence [1-4]. There is also information on the direct influence of vasopressin and oxytocin on release of thyroid-stimulating hormone (TSH) by cells of the adenohypophysis [8, 11]. However, the source of the vasopressin and oxytocin in the brain may not necessarily be confined to PVN and the supraoptic nucleus (SON) of the hypothalamus [3, 5, 7]. The problem of the role of the oxytocinergic and vasopressinergic cells (OE and VE cells, respectively), of these nuclei in the regulation of thyroid gland function has not been resolved. The view is still held that OE and VE cells respond differently to the same influence, although this has not been verified experimentally. This view was confirmed by investigations which demonstrated the opposite neurotrophic effects of vasopressin and oxytocin [15]. Aside from experiments with disturbance of water metabolism [7], there have been few studies of the response of OE or VE cells [12, 14]. The writer is unaware of any investigations in which the state of the OE and VE cells was analyzed simultaneously under experimental conditions. No such investigations likewise have been undertaken when thyroid function was disturbed.

Laboratory of Neuroendocrinology, I. M. Sechenov Institute of Evolutionary Physiology and Biochemistry, Academy of Sciences of the USSR, Leningrad.

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