SYNCHRONIZED CHANGES OF BLOOD FLOW IN THE TWO COMMON CAROTID ARTERIES OF CATS DURING A SYSTEMIC PRESSOR RESPONSE TO CATECHOLAMINES

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In the extensive literature devoted to the study of the dynamic or structural features of the blood supply to the brain, almost until the present time there has been no attempt to differentiate between the two hemispheres, i.e., it has apparently been assumed that these vascular regions are the same or identical [1, 5]. However, we know that when the four main arteries of the brain are intact, their blood flows are not mixed in the circle of Willis, but each supplies definite zones of the ipsilateral hemisphere. Thus the vascular regions of the right and left hemispheres under normal conditions function as if they were separate, and belonging to the vascular territories of different arteries. In some recent experimental publications attention has been drawn to differences in the reactivity of vessels of symmetrical brain structures relative to various procedures associated with functional and neurochemical asymmetry of the brain, and with local regulatory influences on the vessels [11, 12, 14]. Meanwhile suggestions have been put forward regarding the possible causes of the "purely" hemodynamic asymmetry revealed in functionally inert vascular regions [13].

As one of the first stages in determination of the degree of vascular asymmetry of the brain and elucidation of its nature, it was considered important to compare the hemodynamic characteristics of symmetrical territories of distribution — of the right and left common carotid arteries, consisting largely of regions of the cerebral cortex. Great practical importance of data on regional differences in blood supply to the brain has been emphasized by clinical studies [10].

In the present investigation a method widely adopted for the study of the regional circulation was used, namely analysis of the hemodynamics at "entry," in the afferent arteries, with which, however, it is still rare to use parameters of the pulsatile flow in intact vessels. We used this method previously to study regional differences in the circulation of the heart and lungs [7, 8]. The condition of complete integrity of the vessels in the territory of distribution was of great important in the present investigation, for under those circumstances the biomechanical properties of the blood flows entering the circle of Willis are preserved. Synchronized recording ensured maximal comparability of the blood flow parameters in the two arteries. The systemic pressor response to injection of catecholamines (CCh) was used as the model of hemodynamic "disturbances."

The particular anatomical features of the cat (reduction of the internal carotid artery and often also of the anterior communicating branch of the circle of Willis [1], and the similarity to man in the topography zones supplied by the carotid arteries, absence of specific hemispheric dominance) determined the choice of the test object.

The aim of the investigation was to study synchronized changes in the blood flow in the two common carotid arteries of a cat during the systemic pressor response to injection of adrenalin or noradrenalin (NA).

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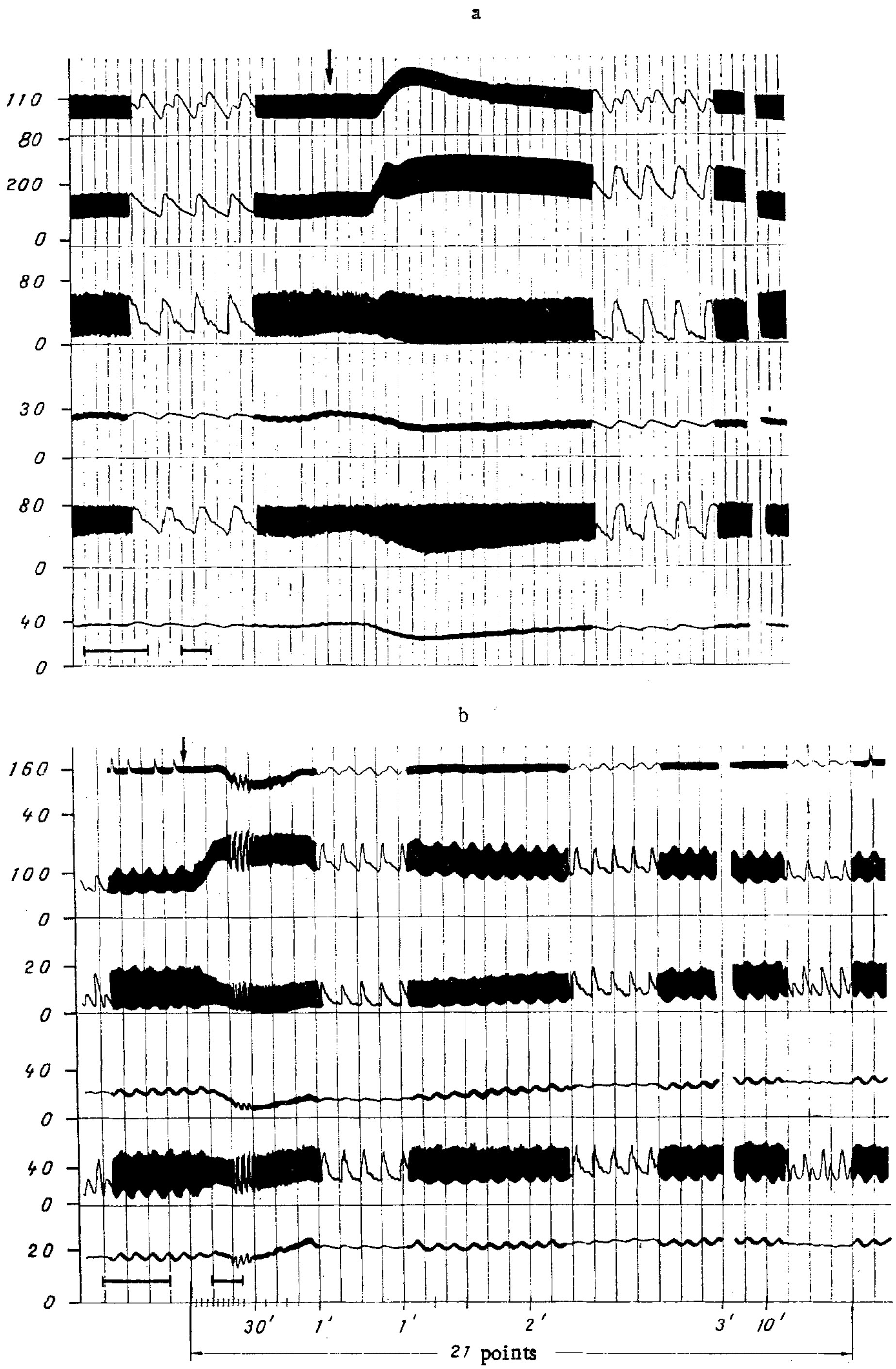
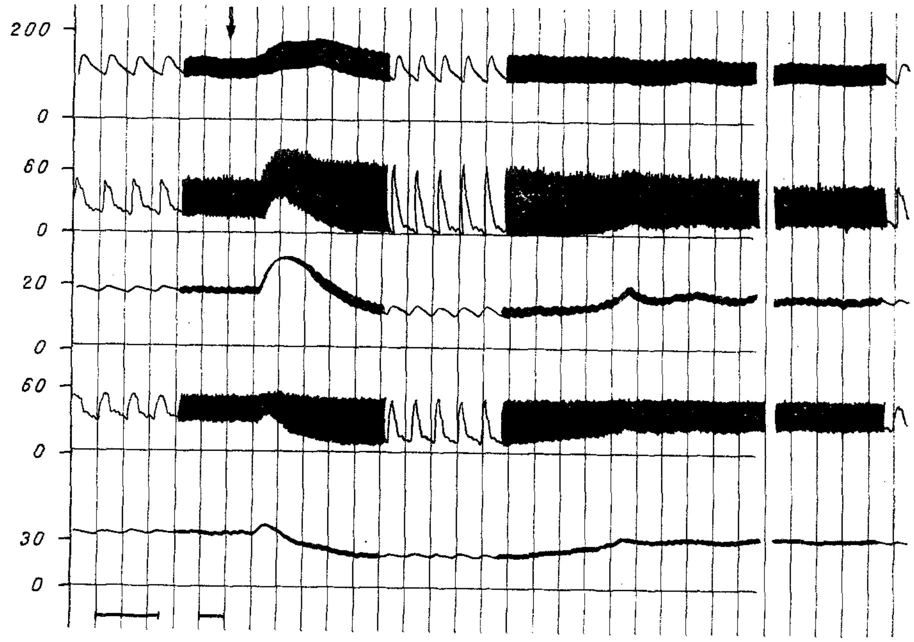


Fig. 1. Changes in blood flow in common carotid arteries after injection of NA. a) 2 μg/kg NA (animal No. 5), b) 4 μg/kg NA (animal No. 4). Traces from top to bottom: HR, beats/min, BP (in mm Hg), linear velocity of blood flow in right carotid artery (in cm/sec), mean VVR (in ml/min), linear velocity of blood flow in left carotid artery (in cm/sec), mean VVL (in ml/min), time marker 10 sec. Here and in Fig. 2 arrow indicates beginning of injection of drug.

EXPERIMENTAL METHOD

Experiments were carried out on 19 cats weighing about 3.5 kg, anesthetized with pentobarbital (40 mg/kg, intraperitoneally) 2-3 h before the beginning of the measurements. The blood flow was measured by the ultrasonic method with the aid of specially made transducers, calibrated in units of volume velocity of the blood flow, and a two-channel recorder [2].

a



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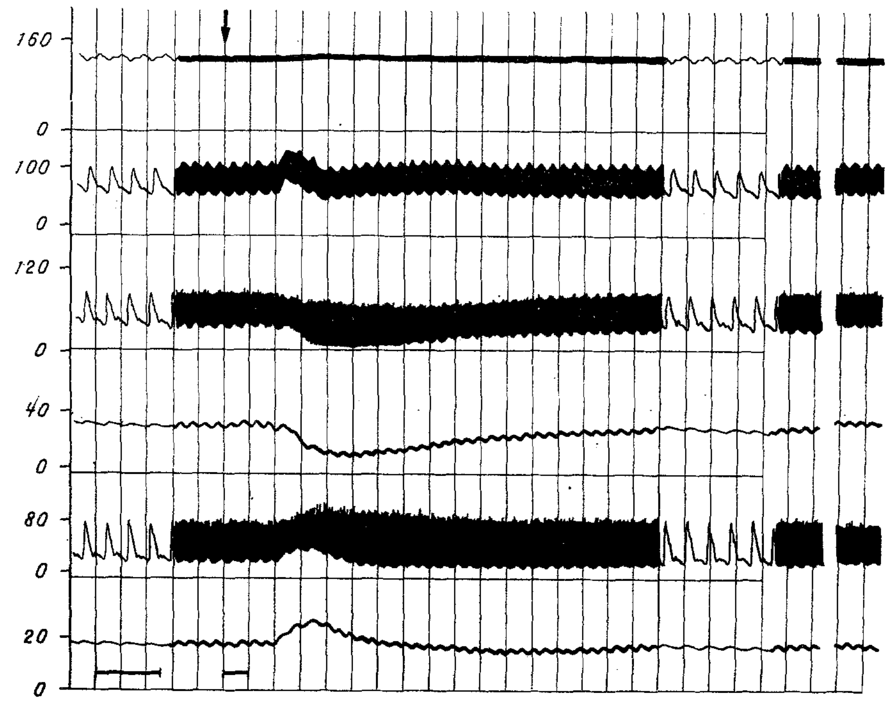

Fig. 2. Changes in blood flow in common carotid arteries in response to injection of adrenalin. a) 2 μg/kg adrenalin (primary response, animal No. 3). Traces from top to bottom the same as in Fig. 1 except HR; b) 4 μg/kg adrenalin (animal No. 9). Traces from top to bottom the same as in Fig. 1.

The heart rate (HR) was recorded by a cardiotachometer, triggered by the pulse blood flow signal [3]. The pressure in the femoral artery was measured by means of a micromanometer [4] and recorded on a type N 3031 recorder. In response to intravenous injection of adrenalin and NA, doses of between 2 and 10 μg/kg, which induce a general pressor response in anesthetized cats [9], were used. Within these limits, on repeated injection increasing

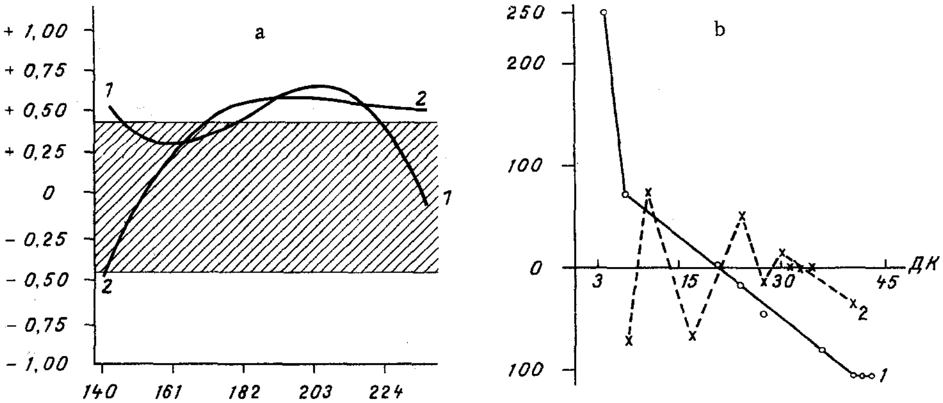

Fig. 3. Factors determining relationship between blood flows in common carotid arteries. a) Dependence of coefficient of correlation of VVR and VVL on maximal BP reached during responses to injection of CCh. Abscissa, BP (in mm Hg); ordinate, coefficient of correlation (r). 1) Injection of adrenalin, 2) injection of NA. In shaded area correlation is not significant; b) dependence of diastolic flow in arteries on its initial level during first responses to injection of adrenalin. Abscissa, initial value of DC (in cm/sec): ordinate, change in DC (in % of initial value). 1) In right carotid artery, 2) in left carotid artery.

doses of the drugs were used, in order to avoid "habituation" and transformation of the arterial pressure (BP) response. The results were subjected to statistical analysis by Student's test and by Wilcoxon's test for tied pairs. Multiple correlation and regression analysis of the parameters was carried out, using Fisher's test. The calculations were done and the regression graphs plotted by the Olivetti-6060 computer.

EXPERIMENTAL RESULTS

Initial values of BP in the group of animals studied varied from 110 to 160 mm Hg (mean 140 mm Hg), and HR varied from 112 to 260 beats/min (average 173 beats/min). Parameters of the systemic hemodynamics (SH) for each separate animal remained constant during 40-60 min of recording, as did the volume velocity of the blood flow in the right and left carotid arteries (VVR and VVL, respectively), and the diastolic (DC) and systolic (SC) components of the pulsating blood flow (PF) in the two arteries. Wider limits of variation of VVR than of VVL were observed for the group of animals (15-43 and 16-40 ml/min, respectively); among the values of VVL, moreover, there was a more distinct mode (31-35 ml/min). VVL was greater than VVR in 16 of the 19 animals. The average value of VVR was 24.11 ± 3.11 ml/min, and of VVL 32.63 ± 3.11 ml/min ($p < 0.01$). On statistical analysis the dispersion of the values of VVR was 1.5 times greater than that of VVL. DC in the right artery was lower but SC was higher than in the left, namely 23.4 and 32.5 cm/sec ($p = 0.05$) and 72.3 and 64.3 cm/sec ($p < 0.01$), respectively.

These data indicated greater variability in function of the territory of the right artery and a higher resistance of its bed in general and of the peripheral zones in particular [6, 7].

Nine animals in which the initial values of BP and HR were within the above-mentioned limits, and whose ratio between volume velocities (VV) included places in which VVR was higher than VVL also, received three to four injections of adrenalin followed by two or three injections of NA in increasing doses. The interval between injections was determined on the basis of stabilization of the parameters of SH and the blood flow in the arteries, and was 15-20 min. Altogether 34 responses to injection of adrenalin and 26 to injection of NA were observed. Virtually no completely identical changes in VV of the blood flow and in PF were observed in the responses to injection of CCh. The most characteristic responses were a decrease in VV accompanied by a marked increase in BP and HR (more especially to injection of NA), although they differed either in their time course or in the behavior of the component of PF (Fig. 1a). During a decrease in HR in the responses to injection of NA, the decrease in VVL was less marked or absent (Fig. 1b). In the responses to the first injection of adrenalin a considerable increase in VVR could be observed (Fig. 2a), whereas among the smaller changes in BP there were some opposite responses in the arteries (Fig. 2b). Thus dependence of the blood flow in the two arteries on the systemic hemodynamics, the initial level of VV, the components of PF, and the order of administration of the drugs could differ.

Dependence of the character of relations between VV in the arteries and systemic BP is shown in Fig. 3a. Regression graphs of dependence of the coefficient of correlation of VVR and VVL on the maximal level of BP reached during the response are shown.

To assess this and other dependences multiple correlation analysis (MCA) of all the recorded parameters of SH, VV, and PF in the arteries was undertaken in each separate response. The variables were values of the parameters at 21 points on the time scale, occupying the period from 2 sec to 10 min after injection of CCh. The time intervals were shorter during the period of development of the response (under 30 sec), and thereafter they gradually increased. By this method it was possible to characterize relations between the parameters in responses which followed a different time course. The time scale is illustrated in Fig. 1b. During plotting of the regression graph, approximation by a third degree polynomial was used.

It will be clear from Fig. 3a that VVR and VVL exhibited significant positive correlation only with BP levels of above 170-180 mm Hg. Positive correlation was stable only in responses to injection of NA. A marked response of BP to injection of adrenalin led to an increase in the number of opposite responses. The "scatter" of the values of the coefficients of correlation relative to the regression line 2 shown in Fig. 3a (in response to injection of NA) was an order of magnitude less than that relative to line 1 (in response to injection of adrenalin). Thus similarity in the character of the responses of VVR and VVL was exhibited only when BP was distinctly raised and it was found more regularly during the action of NA than of adrenalin.

Quantitative differences in responses of the blood flow in the arteries may be reflected in the following data. Minimal values recorded for VVR in response to injection of adrenalin amounted to 17% of the initial level, compared with 40% for VVL; the maximal values were 170 and 140%, respectively. Thus the range of changes in VV for the territory of the right artery was 253%, and 200% for the left. In response to injection of NA the range of changes in VVR was 200% (20-120%) and of VVL 210% (30-140%). The mean negative deviation for VVR was 44% and for VVL it was 35%. The trend of these differences is significant ($p = 0.05$). Thus responses to adrenalin exhibited the greater vasomotor possibilities of the territory supplied by the right artery, although NA or repetition of the injections reduced dilatation of the right vascular bed. Restriction (construction) during general pressor responses remained stronger in the territory of the right artery.

Differences in reactivity of the peripheral zones of the right and left vascular territories, estimated by the diastolic component of PF, were even more marked. For instance, in 29% of responses to adrenalin and in 36% of responses to injection of NA, DC in the right artery fell to zero (Figs. 1 and 2). Such changes in the left artery were observed in only 6 and 10% of response, respectively.

During the first injections, when minimal doses of adrenalin were given, differences were clearly observed in the dependence of response of the peripheral zones of the arterial bed on their initial state (Fig. 3b), With the minor degree of the changes in response to injection of the CCh taken as evidence of complete self-regulation of the vascular bed and of the optimal state of the region, it will be clear that in animals with initial constriction of the bed adrenalin induced marked dilatation in the territory of the right artery, increasing the value of DC by 250%. Conversely, with initial dilatation, the same doses of adrenalin induced construction, which lowered DC to zero. Dependence of the degree of initial dilatation on that of subsequent constriction and vice versa evidently is stronger in the territory of the right artery, for even with a small sample and with individual variations in the systemic response, it was manifested as a regular feature. Under identical conditions the territory of the left artery showed vasomotor response of an indefinite type of injection of adrenalin, when the initial resistance was increased, but when the resistance was low, the constrictor action of adrenalin was much weaker than in the right territory.

On the whole, the range of vasomotor possibilities of the peripheral zones of the left arterial bed was only one-third of that of the right artery, where it reached 350%.

Thus the range of changes in VVR was less than DC in the same artery, evidence of possible reciprocity of the proximal and distal zones of the vascular bed. Conversely, in the left carotid artery, the range of changes in VV was greater than DC, evidence of the unity of regulation of the whole vascular bed.

Comparison of synchronously recorded initial parameters of the state of VV and PF, and comparison of reactivity to injection of CCh and the relationship to parameters of SH in the general pressor response thus indicated functional differences between the territories of distribution of the right and left common carotid arteries. At the same time, it was found that marked "disturbances" of SH largely cancel out the initial functional differences. It seems evident that under these conditions active interaction between different "control circuits" and involvement of all the reserve mechanisms in the response contribute to the achievement of closely similar results in blood supply regulation. However, differences in the functional organization of the vascular regions may be of essential importance in the development of pathological changes.

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