PHOTOHEMOTACHOMETRIC INVESTIGATIONS OF THE FUNCTIONS OF THE NEUROMUSCULAR APPARATUS OF THE INTERNAL CAROTID ARTERIES. REPORT 1. EXPERIMENTAL METHOD AND THE EFFECTS OF CERTAIN PHYSIOLOGICALLY ACTIVE SUBSTANCES

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When investigating the regulation of the circulation of the blood within an organ it is essential to differentiate not only morphologically, but also functionally, between the various divisions of the vascular system of the organ. Recent researches have shed light on several fundamental problems concerning the functional organization of the vascular system of the brain [3]. In particular, they have demonstrated the important role of the regional arteries of the brain (internal carotid and vertebral arteries) in the regulation of the cerebral circulation during the compensation of various circulatory disorders in the brain [4].

Because the four regional arteries of the brain are joined together in the region of the circle of Willis by relatively short and wide anastomoses, from the point of view of the blood supply to the brain the system of the internal carotid and vertebral arteries is a single system, i.e., the cerebral circulation depends on the mean resistance of all four arteries of the brain. The physiological properties of this particular system of arteries may therefore be studied by measuring the mean resistance in them, by simultaneously recording the blood pressure at its beginning and end, i.e., in the aorta and the circle of Willis [1, 2]. Nevertheless, not all the problems arising in connection with the physiology of the regional arteries of the brain can be solved by the use of this technique.

In the present paper we describe the results of investigations of the function of the neuromuscular apparatus of the regional arteries of the brain by means of the method of photohemotachometry.

Method of photohemotachometry. The photohemotachometer can be used to make continuous recordings of the functional state of one of the internal carotid or vertebral arteries. The investigation of the regional arteries of the brain individually during the application of some factor or factors to the particular artery concerned has the advantage that the inflow of blood into the circle of Willis and the blood supply to the brain are practically undisturbed*. In these conditions the mechanisms of regulation of the cerebral circulation are readily revealed, for the compensatory mechanisms which usually prevent experimental results from being obtained are not functioning [4].

The principle of operation of the photohemotachometer was first described by Cybulski in 1885 [5]. From the 1920's onward, this apparatus has been used extensively in Klisiecki's laboratories, and this worker has improved its construction and also given a theoretical explanation of its operation [7, 8].

A special cannula, consisting of two branch tubes for a differential manometer, is tied into the divided blood vessel; between the two tubes is a hydraulic resistance in the form of two right-angled bends (Fig. 1). When blood flows through the cannula, part of its energy is expended in overcoming the resistance. This causes a fall in pressure, the magnitude of which is shown by the pressure difference in the differential manometer (R). The greater the velocity of the blood flow, the larger this difference, and vice versa. The readings of the differential manometer are re-

*Carlyle and Grayson [6] showed that the blood supply to the brain is not disturbed even if one of the internal carotid arteries of the rabbit is completely excluded.

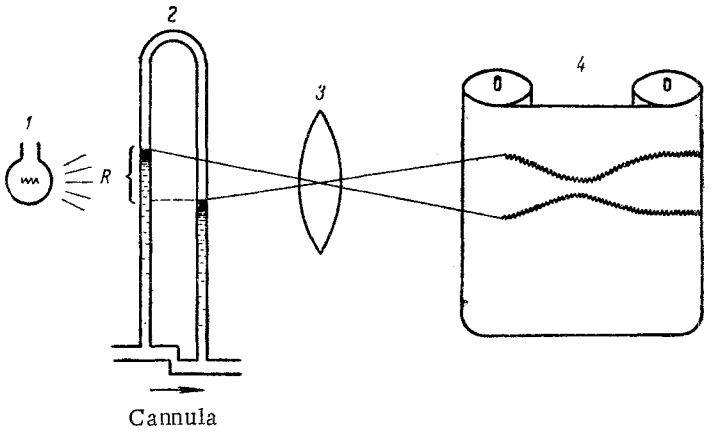

Fig. 1. Scheme of the photohemotachometer. 1) Light source; 2) differential manometer; 3) optical system; 4) photokymograph.

corded on a photokymograph. Each apparatus must be calibrated. By means of this apparatus it is possible to measure the absolute values of the linear and volume velocity of the blood flow in the blood vessel examined.

The advantages of this method over most others used to measure the blood flow in individual blood vessels are as follows: 1) The apparatus is simple and can be used in any physiological laboratory; 2) the simplicity of construction on the one hand, and the photographic recording, on the other, almost exclude the possibility of obtaining artefacts, which may always interfere with the use of complex electronic systems; 3) in contrast to most other methods of measuring the blood flow*, the photohemotachometer can be used to obtain quantitative data relating to the linear velocity of the blood flow in millimeters per second, and to the volume velocity in cubic millimeters per second.

We tied the cannula of the photohemotachometer into the common carotid artery in dogs and rabbits after careful ligation of all its branches except the internal carotid artery. Under these circumstances the readings of the photohemotachometer in fact related to the internal carotid artery.

Although the photohemotachometer records the velocity of the boood flow throughout the length of the common and internal carotid arteries, the roles of the individual segments of these essels in the creation of the vascular resistance differ. Firstly, the width of the common carotid artery in dogs and rabbits is many times greater than that of the internal, so that the resistance is mainly dependent on the state of the lumen of the latter vessel. Secondly, whereas the common carotid artery is elastic in type and almost incapable of dilating or constricting in response to various factors, the internal carotid artery can vary its lumen within wide limits[4]. Because of this feature the changes in the velocity of the blood flow recorded by the photohemotachometer are the result of changes in the width in the internal carotid artery on the same side.

Because the blood flow in both internal carotid arteries was recorded simultaneously, it was possible to judge the state of the cerebral vessels situated on the periphery of the circle of Willis. For instance, during the action of relatively small concentrations of physiologically active substances, the effect was observed only on the ipsilateral side and the general arterial pressure and the blood flow in the contralateral artery remained unchanged. This demonstrated that the general resistance of the cerebral arteries situated on the periphery of the circle of Willis was unchanged; otherwise, this must have been reflected in the blood flow in the internal carotid artery on the contralateral side.

Hence, the photohemotachometer can be used to record the intensity of the blood flow and the resistance in the various regional arteries of the brain individually, and in particular in the internal carotid arteries.

The effect of physiologically active substances on the neuromuscular apparatus of the internal carotid arteries. Many workers have investigated the action of physiologically active substances, such as adrenalin, acetylcholine, and histamine, on the cerebral vessels. Nevertheless, the results of their experiments have been found to disagree, mainly

*In view of the fact that when electrical recording is used the impulses from the pick-up may be amplifiedthousands of times, the criteria of "larger" or "smaller" cannot be used to judge whether in fact the recorded changes are significant so far as the organism is concerned or are too small to be of physiological importance.

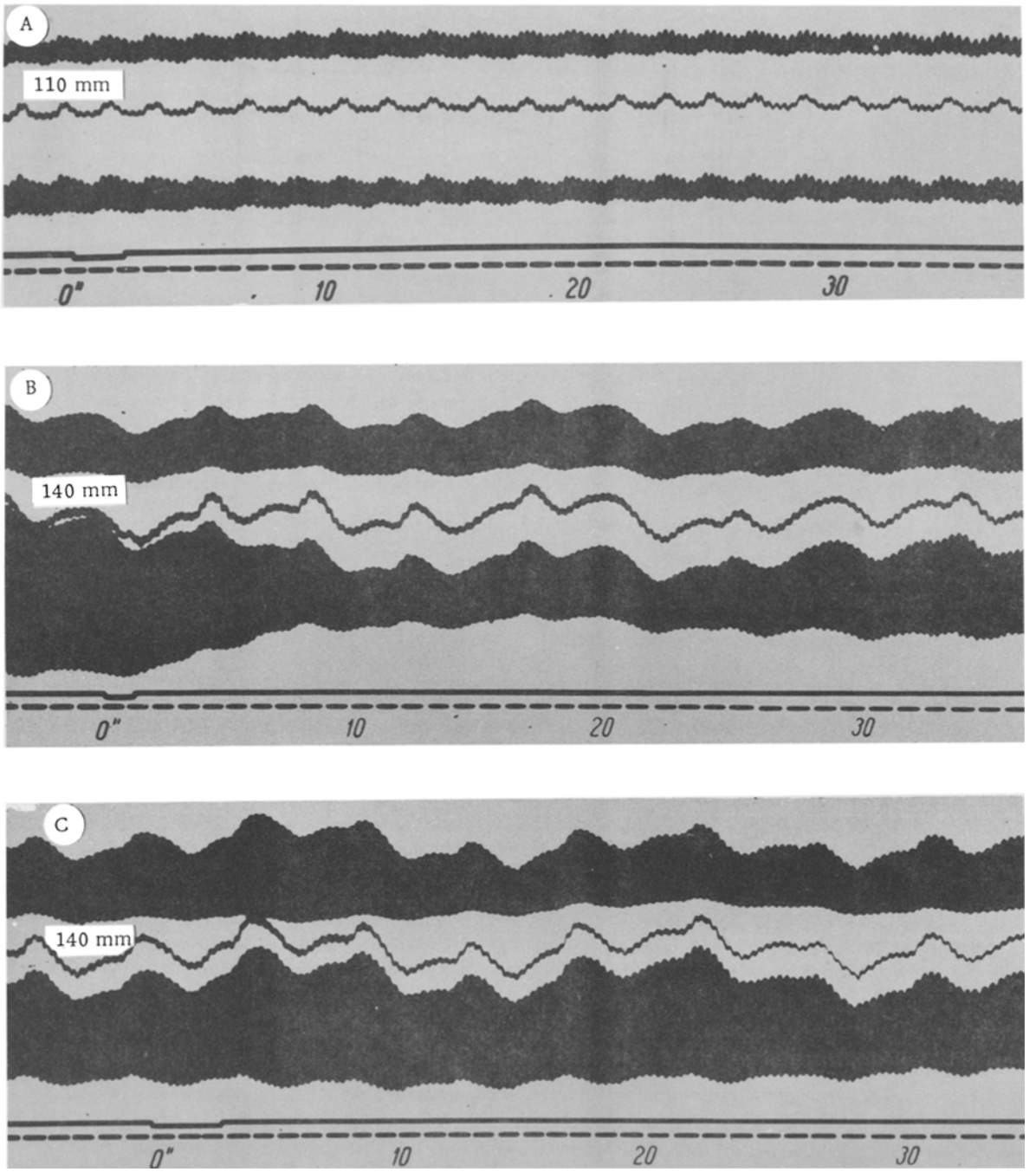

Fig. 2. Constriction of the internal carotid artery (ica) and external carotid artery (eca) after the local action of adrenalin. A) Dog weighing 16 kg. Significance of the curves (from above down): blood flow in the left (control) ica; arterial pressure in the femoral artery (compensator in operation); blood flow in the right ica: 0 sec – 0.98 ml/sec, 15 sec – 0.69 ml/sec, 35 sec – the same; marker of injection of 0.5 μg adrenalin into the right ica; time marker (1 sec). B) and C) Dog weighing 15 kg. Significance of curves (from above down): blood flow in the left ica; arterial pressure in the femoral artery (compensator not in operation); blood flow in the right eca; marker of intra-arterial injection of 0.5 μg adrenalin; time marker (1 sec). B) Injection of adrenalin into the right eca; volume velocity of blood flow: 0 sec – 3.16 ml/sec, 15 sec – 1.79 ml/sec, 35 sec – 2.17 ml/sec. C) Injection of adrenalin into the left ica; volume velocity of blood flow: 0 sec – 1.65 ml/sec, 15 sec – 1.46 ml/sec.

because the substances were administered in different doses and by different methods; moreover, in most cases the general arterial pressure level changed regularly, and this had a marked influence on the width of the lumen of the cerebral vessels. However, it may be concluded from analysis of the results in the literature that, as in other parts of the body, adrenalin has a constricting influence on the cerebral vessels, and acetylcholine and histamine a dilating effect, although this action, as a rule, is weak and inconstant [9].

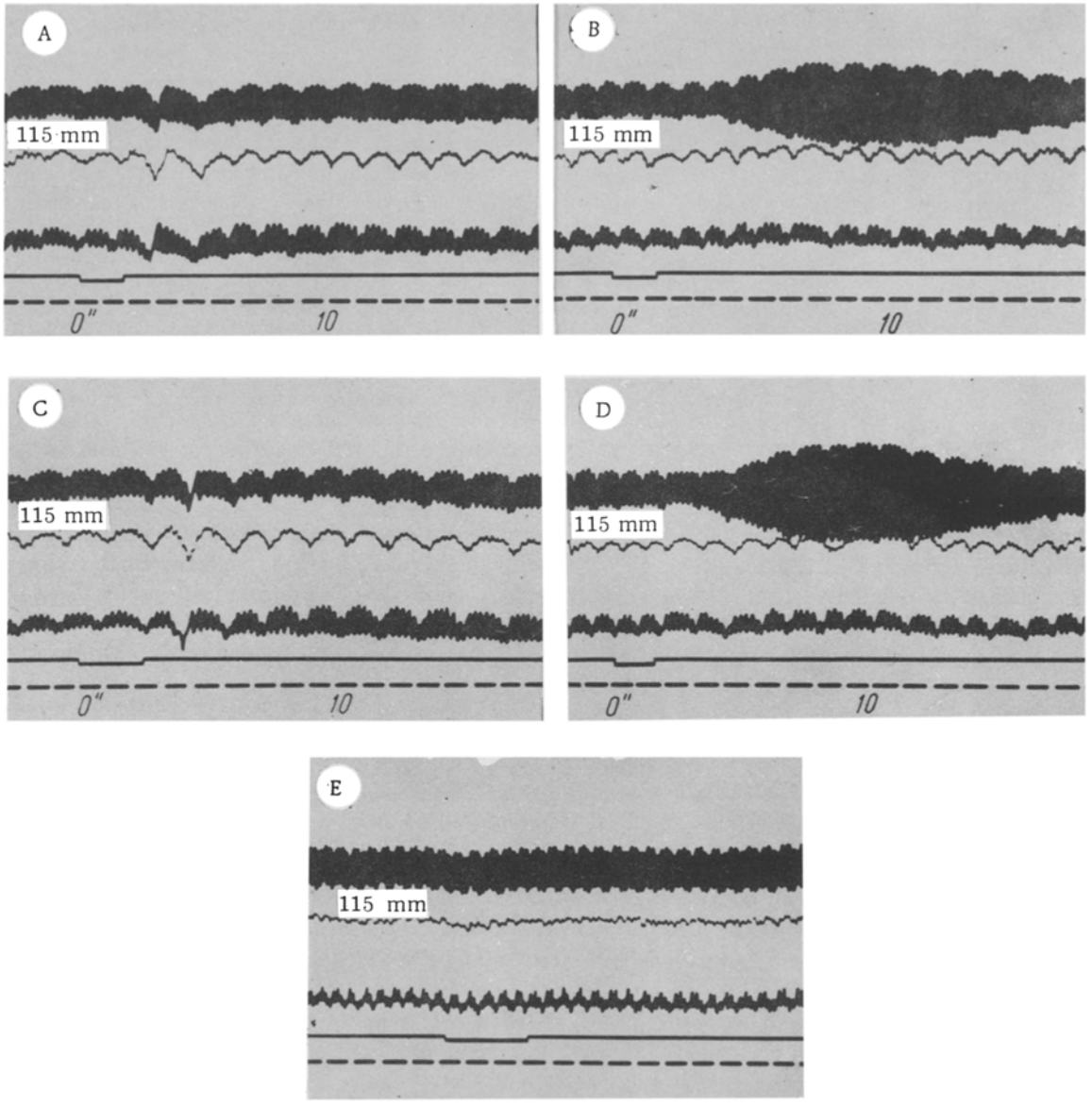

Fig. 3. Dilation of the internal carotid artery and external carotid artery after intra-arterial injection of acetylcholine and histamine (dog weighing 16.5 kg). Significance of the curves (from above down): blood flow in the left eca; arterial pressure in the femoral artery; blood flow in the right ica; marker of injection of drugs; time marker (1 sec). A) Injection of 1 μg acetylcholine into the ica; volume velocity of blood flow: 0 sec – 0.78 ml/sec, 10 sec – 1.27 ml/sec. B) Injection of 1 μg acetylcholine into the eca; volume velocity of blood flow: 0 sec – 2.21 ml/sec, 10 sec – 3.49 ml/sec. C) Injection of 1 μg histamine into the ica; volume velocity of blood flow: 0 sec – 0.64 ml/sec, 10 sec – 1.27 ml/sec. D) Injection of 1 μg histamine into the eca; volume velocity of blood flow: 0 sec – 2.21 ml/sec, 10 sec – 3.95 ml/sec. E) Control: simultaneous injection of the same volume (0.1 ml) of a 0.85% solution of NaCl as was injected in the case of acetylcholine and histamine into both arteries; volume velocity of the blood flow was unchanged.

The problem of the effect of physiologically active substances on the regional arteries of the brain (the internal carotid and vertebral arteries) has received very little study. G. I. Mchedlishvili [1] investigated the effect of adrenalin on the system of the regional arteries of the brain as a whole. It was necessary to use a relatively large dose and to administer the drug for a long period or repeatedly in order to obtain an appreciable constriction of the internal carotid and vertebral arteries, leading to a lowering of the blood pressure in the circle of Willis.

In the present paper we describe the results of investigations, using the photohemotachometer, of the action of adrenalin, acetylcholine, and histamine on one of the regional arteries of the brain (the internal carotid artery) in the dog. The drugs were injected intra-arterially in the region of the cannula of the photohemotachometer, which was tied into the common carotid artery. In some cases the external carotid artery was ligated and the action of these drugs on the internal carotid artery was studied. In other cases, for control purposes, only the internal carotid artery was ligated and the effect of the drug on the system of the branches of the external carotid artery was studied.

During the action of the physiologically active substances on one internal carotid artery alone we found that even very small doses produce an effect. In Fig. 2 we show the effect of 0.5 μg of adrenalin on the internal carotid artery, which was appreciably constricted, and the velocity of the blood flow in this vessel fell by 30%, whereas in the contralateral artery the blood flow was unchanged (Fig. 2, A). Another experiment showed that adrenalin has a weaker action (the velocity of the blood flow fell by 22%, Fig. 2, C) on the internal carotid artery than on the external (the velocity of the blood flow fell by 44%, Fig. 2, B).

In Fig. 3 we show the results of the action of acetylcholine and histamine on the internal carotid arteries; for control purposes we studied the effect of these drugs on the external carotid arteries. During the action of 1 μg of acetylcholine on the internal carotid artery (Fig. 3, A) the vessel was dilated, and the blood flow through it increased by approximately 64%; during the action of the same dose of the drug on the branches of the external carotid artery (Fig. 3, B) it also dilated, and the velocity of the blood flow increased by 53%. Histamine had roughly the same dilating action on the internal and external carotid arteries (Fig. 3, C and D). It is clear from Fig. 3, E that when the same volume of isotonic saline solution was injected for control purposes, the state of the internal carotid arteries was unchanged.

Hence, the internal carotid arteries, like the external, are subject to the powerful influences of the humoral agents of nervous origin, which cause significant changes in the lumen of these vessels even in low concentrations.

The method of photohemotachometry has great possibilities for the investigation of physiological and pharmacological agents and their effects on the individual regional arteries of the brain (internal carotid and vertebral arteries) without the need for isolating these arteries from the rest of the body.

SUMMARY

Photohemotachometry (after Cybulski-Klisiecki) is a simple and convenient method for quantitative recording on a photokymograph of the blood circulation volume velocity in large blood vessels. While measuring the circulation in the internal carotid artery of dogs it was revealed that the neuromuscular apparatus of this vessel is almost as sensitive to the physiologically active agents as that of the external carotid artery branches. Following local intravascular injection of 0.5 microgram of adrenalin the internal carotid arteries become constricted. One microgram of acetylcholine and the same dose of histamine cause dilation of these arteries.

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