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ON THE REFLEX REGULATION OF THE CEREBRAL BLOOD FLOW AND THE CEREBRAL VASO-MOTOR TONE.

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In previous papers [1932, 1933, 1934] we were able to show with several techniques (Stromuhr of Weese, Stromuhr of Rein, Hürthle's method) that, in dogs, the carotid sinus reflexes do not affect the cerebral vaso-motor tone in an active way; indeed, lowering the carotid sinus pressure produces a passive increase of the cerebral blood supply which is due to the reflex increase of the general blood-pressure, while conversely increasing the pressure in the carotid sinus produces a passive decrease of the cerebral blood flow due to the reflex decrease of the general arterial blood-pressure.

In the case of a fall of the carotid blood-pressure, the blood is diverted by means of the carotid sinus reflexes from the somatic and peripheral cephalic areas to the cerebral circulation, whose blood vessels do not participate actively in the carotid sinus reflexes. The blood flow to the central nervous system thus increases, while on the contrary the blood flow decreases, as a result of the reflex vaso-constriction, in the peripheral cephalic tissues (muscles and skin of the head) and in the somatic organs. The cerebral blood supply is thus passively dependent on the general arterial pressure, which is regulated by the carotid sinus and aorta reflexes. H. Rein [1929, 1931], on the other hand, contended that the cerebral vessels were collaborating actively in the changes of the cerebral blood flow induced by the carotid sinus reflexes. In his opinion, a decrease of pressure in the carotid sinus produces an increase of the cerebral blood flow not only in a passive way, by means of the increase of the general

blood-pressure, but also actively, by a simultaneous active vaso-dilatation in the cerebral area.

More recently M. Schneider and D. Schneider [1934] confirmed our experimental observations and conclusions concerning the influences of the carotid sinus reflexes on the cerebral circulation. These authors, however, concluded from another series of experiments that the blood-pressure also regulates actively the cerebral vaso-motor tone by means of a reflex mechanism, the origin of which should be localized, not in the carotid sinus but in the arteria meningea media. According to these authors, lowering or increasing the pressure in the arteria meningea media would put into action respectively a reflex vaso-dilatation and a reflex vaso-constriction in the cerebral circulation. Those conclusions of M. Schneider and D. Schneider were also supported by Kl. Gollwitzer-Meier and P. Eckardt [1934].

As the conclusions of some of our experiments performed with the technique of Hürthle (registration of the cerebral pressure in the internal carotid after ligature of the external carotid) or with the techniques of Weese and Rein (measurements of the blood flow in the internal carotid after occlusion of the external carotid) have been questioned by M. Schneider and D. Schneider on the basis of their so-called meningeal cerebral vaso-motor reflex, it has seemed to us necessary to submit our previous experimental conclusions to a new control.

I. Anatomical connections between the external and the internal carotid arteries in dogs.

In the experiments of M. Schneider and D. Schneider, clamping the external carotid artery in dogs produces both on the same side, and on the opposite side, an increase of blood flow in the internal carotid which the authors suppose to be of a reflex cerebral origin. Since the increase of internal carotid blood flow is also obtained by clamping the internal maxillary artery before the origin of the arteria meningea media, and not by clamping the internal maxillary artery beyond the origin of the arteria meningea media, these authors have concluded that this reflex has its origin in the arteria meningea media.

The main reason why the authors admitted a reflex and not a purely hydrodynamic origin for the explanation of their observations is, as they say, that they did not find in dogs any important vascular connections between the internal and external carotid or its branches. In order to examine whether the observations of M. Schneider and D. Schneider

were really due to a reflex mechanism and are not to be explained by the existence of vascular connections between the internal carotid and the external carotid or its branches, we first made a series of anatomical controls of the cephalic blood vessels.

For this purpose we injected, through the internal maxillary artery, at its origin, into the cephalic circulation of a series of dead dogs, heated paraffin coloured with methylene blue. After cooling off the preparation, the arteries which had been injected were easy to recognize, since they were distended by the paraffin and coloured by the methylene blue. First we wish to point out that after the injection of paraffin only into one of the internal maxillary arteries, all the vessels of the Circle of Willis, the cerebral vessels and the external and internal carotids on the opposite side were also completely filled up with paraffin (Fig. 1). Besides negligible branches going from the arteria meningea media to the internal carotid, it was possible to see, by dissecting the preparation as shown by Figs. 1 and 2, that an important branch (Fig. 1, *3*) connects the ophthalmic artery, and thus the internal maxillary artery (Fig. 1, *2*), to the internal carotid (Fig. 1, *1*). The origin of this anastomotic branch is somewhat difficult to find, since it is applied very intimately to the skull. After entering into the skull through the fissura orbitalis, this branch, which is called by the anatomists "arteria ophthalmica interna" (Bellarminow) or "ramus anastomoticus" (Fig. 1, *3*), goes directly to the internal carotid; this branch is as important as the internal carotid itself (Fig. 1, *1*) and as the branch of the internal carotid going to the circulus Willisii (Fig. 1, *5*). These series of anatomical preparations thus show definitely that the anastomosis between the external carotid and the internal carotid is a very important one and confirms the classical views about the existence of this branch in the dog [Ellenberger and Baum, 1891]; our findings, however, do not agree with the opinion of M. Schneider and D. Schneider, who consider this anastomosis as a very small and insignificant one, since they write: "Zwar bestehen zwischen dem Externa- und dem Internagebiet direkte Anastomosen, nämlich ein winziger Ast zwischen Meningea media und Interna und ein kleiner Ast zwischen Ophthalmica externa und interna. Sie sind aber ausserordentlich klein und in keinem Falle vergleichbar den Kollateralen im Circulus Willisii, wovon wir uns durch Injektionspräparate überzeugt haben."

Since a very important anastomosis connects the internal maxillary artery with the internal carotid, we may at once suggest a purely physical explanation for the phenomena observed by M. and D. Schneider: the

external carotid or the internal maxillary artery being clamped, the flow in the internal carotid must indeed increase for two reasons; the first reason being the suppression of the flow coming from the anastomotic

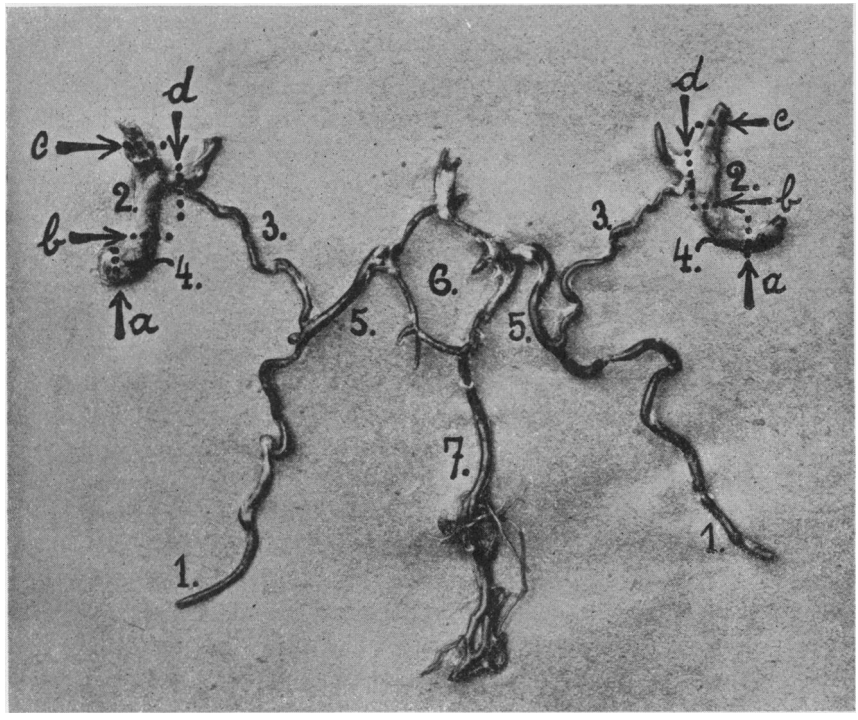

Fig. 1. Photograph of an original injected preparation in a dog. The injection has been made through the left internal maxillary artery. *1*, internal carotid; *2*, internal maxillary artery (prolongation of the external carotid); *3*, "ramus anastomoticus" or internal ophthalmic artery, going from the origin of the ophthalmic artery to the internal carotid; *4*, arteria meningea media; *5*, internal carotid, going to the circulus Willisii; *6*, circulus Willisii. Levels of occlusion: ↑ *a*, occlusion of the internal maxillary artery before the origin of the arteria meningea media and of the ophthalmic artery; *b*→, occlusion of the internal maxillary artery beyond the origin of the arteria meningea media and before the origin of the ophthalmic artery; *c*→, occlusion of the internal maxillary artery beyond the origin of the arteria meningea media and of the ophthalmic artery; *d* ↓, occlusion of the ophthalmic artery.

branch which normally opposes the flow coming from the internal carotid; the second reason being the absence of blood supply by the internal maxillary artery to its area after clamping the external carotid or the internal maxillary artery itself. Under such conditions, the internal

carotid has indeed to supply, through the anastomotic branch, the blood to the arteries which depend normally on the internal maxillary artery and the flow through the internal carotid must naturally increase under these conditions.

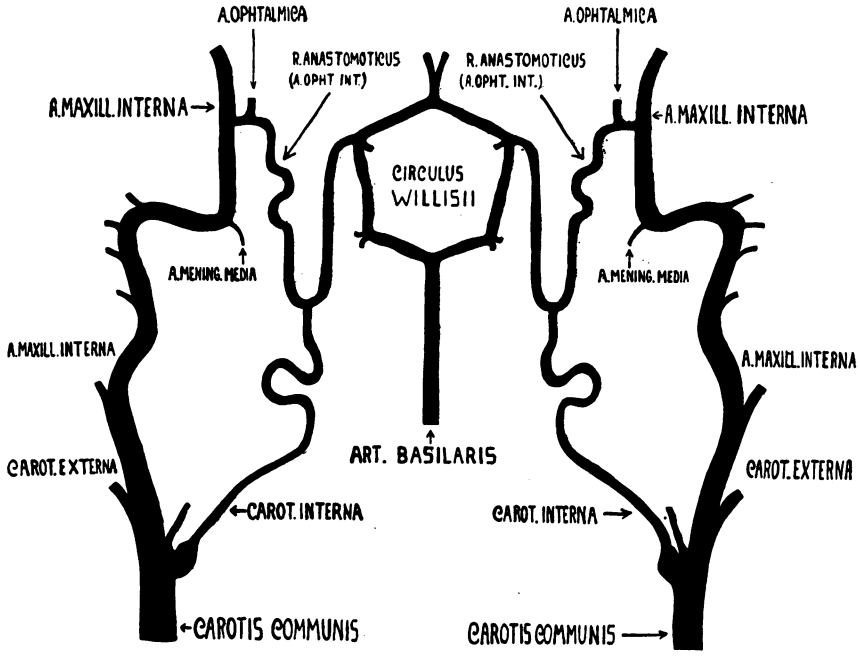

Fig. 2. Blood vessel supply to the circulus Willisii and the brain, taken from a series of original preparations in dogs.

II. Physiological evidence of important vascular connections between internal and external carotids.

Having given the anatomical demonstration of the connection between internal and external carotids, we will now consider the physiological evidence. For this purpose we have examined whether the central nervous system of a dog, the head of which is only supplied by the branches of the external carotid arteries, after exclusion of all the other arterial branches, could be kept alive and in good condition; if such an experiment is successful, the physiological demonstration would be given that very important arterial branches go from the external carotids to the cerebral circulation. To be sure that all the other branches excepting those coming from the external carotids were excluded, we perfused the isolated head of a dog *B* by a dog *A*, by connecting, with Payr's cannulæ,

the cephalic ends of the common carotids of head *B* with the cardiac ends of the carotids of *A* and the cephalic ends of the jugular veins of head *B* with the cardiac ends of the jugulars of *A*, the internal and occipital arteries of head *B* being ligated and a crusher being applied to separate completely the head *B* from its trunk; the vagi only were kept intact between head and trunk of dog *B*, in order to allow us to examine the reactions of the cardio-inhibitory centre of head *B*.

The following experiment can be given as an example of the results obtained:

Dog *A* 18 kg., dog *B* 16 kg. chloralosane anæsthesia. Perfusion of the head of dog *B* by dog *A*: all the tissues of the neck of dog *B* are separated by means of a crusher, excepting both vagi; the thyroid arteries, the occipital arteries and the tissues between the origin of internal and external carotids of head *B* are ligated. The heart rate of trunk *B* is recorded with a manometer of Gad.

17.05. Respiratory movements and palpebral reflexes of the perfused head are excellent. The internal carotid arteries of head *B* are then ligated: the perfusion of head *B* by the external carotids only is thus started. Heart rate of trunk *B*, 215.

17.20. Palpebral reflexes still excellent, respiratory movements of the head normal, head very active. Heart rate of trunk *B*, 205, thus practically no slowing of the heart rate since 17.05. Both external carotids are then clamped; after 1 min. one observes a disappearance of the palpebral reflexes, respiratory movements of head *B* and a slowing of the heart of trunk *B*, the rate dropping to 145; after 1½ min. the heart rate of trunk *B* drops to 100; this slowing of the heart is due to the stimulation of the cardio-inhibitory centre of head *B* by the central anæmia produced by clamping off both external carotids.

This experiment shows by means of a physiological test that very important arterial branches must go from the external carotid arteries to the cerebral circulation, since they are sufficient, after clamping off all the other blood supply, to keep the brain alive and in excellent condition; one must admit, since we have also given the anatomical evidence, that the important arterial branches of the external carotids, supplying the nervous centres, are the direct and large anastomotic branches between the ophthalmic arteries and the internal carotids.

III. Origin of the increase of cerebral blood flow in the internal carotid by clamping off the external carotid.

M. Schneider and D. Schneider claimed that they observed an increase of blood flow in the internal carotid by clamping off the external carotid or its prolongation, the internal maxillary artery. No reactions were obtained by the occlusion of the lingual or of the external maxillary artery; on the other hand, clamping off the internal maxillary artery beyond the processus pterygoideus and the origin of the arteria meningea media did not affect the blood flow in the internal carotid; the authors

therefore concluded that a cerebral vascular reflex exists, which is provoked by blood-pressure changes in the arteria meningea media. However, the authors do not mention the exact level of the occlusion beyond the arteria meningea media, so that it is impossible to know whether this clamping has been made in their experiments before or after the origin of the ophthalmic artery which gives off the anastomotic branch to the internal carotid. Therefore it seemed necessary to examine the changes occurring in the blood flow of the internal carotid after clamping the internal maxillary artery and its branches at different levels.

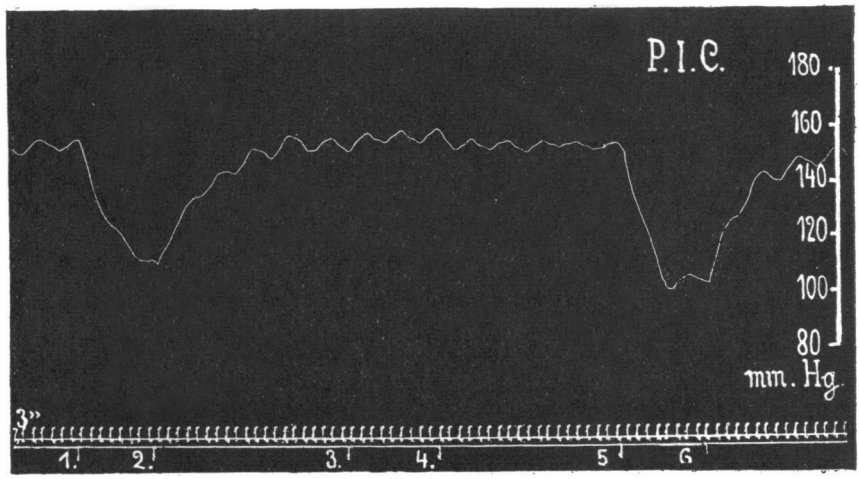

Fig. 3. Pressure (peripheral resistance and blood flow) in the cephalic end of the internal carotid of a chloralosanized dog. *1–2*, clamping and release of the internal maxillary artery (level ↑ *a*, Fig. 1); *3–4*, clamping and release of the internal maxillary artery (level *c*→, Fig. 1); *5–6*, clamping and release of the internal maxillary artery (level *b*→, Fig. 1).

To examine this question, we used Hürthle's method for recording the changes of the peripheral resistance in the vascular area of the internal carotid. A mercury manometer was connected with the cephalic end of the internal carotid; the internal maxillary artery and its branches were then clamped at several levels on the same side or on the opposite side. In all these experiments the carotid sinus was denervated on the side where the internal maxillary artery was clamped in order to avoid vaso-motor carotid sinus reflexes.

Fig. 3 shows the results obtained in one of these experiments. From *1* to *2*, the left maxillary artery is clamped before the origin of the arteria

meningea media and the anastomotic branch (level ↑ *a*, Fig. 1); this clamping produces, as expected, a marked fall of pressure in the cephalic end of the left internal carotid. From *3* to *4* the left internal maxillary artery is clamped off (level *c* →, Fig. 1) beyond the origin of the arteria meningea media and the anastomotic branch (going off from the ophthalmic artery); no change occurs in the pressure in the cephalic end of the internal carotid. From *5* to *6* the left internal maxillary artery is clamped (level *b* →, Fig. 1) beyond the origin of the arteria meningea media and before the origin of the ophthalmic artery (giving off the anastomotic branch to the internal carotid); in this case, although no decrease is produced in the pressure inside the arteria meningea media, still the same very marked fall occurs in the pressure of the cephalic end of the internal carotid.

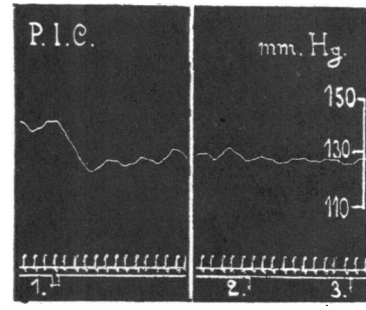

Fig. 4. Pressure (peripheral resistance and blood flow) in the cephalic end of the internal carotid of a chloralosanized dog. *1*, ligature of the ophthalmic artery (level *d* ↓, Fig. 1); *2–3*, clamping and release of the internal maxillary artery (level ↑ *a*, Fig. 1), the ophthalmic artery being ligated.

These experiments show that the decrease of flow through the anastomotic branch, even when it does not affect the pressure in the arteria meningea media, provokes the typical fall of pressure in the cephalic end of the internal carotid artery (which must correspond to an increase of flow in this artery).

The following example of the further results which we have obtained confirms completely this observation. Fig. 4 shows the record of the pressure in the cephalic end of the left internal carotid in a dog after isolation of the left internal maxillary artery and its branches and denervation of the left carotid sinus. Clamping off the ophthalmic artery (level *d* ↓, Fig. 1) produces an immediate fall of pressure in the cephalic end of the internal carotid. It is interesting, however, that in this case the occlusion of the ophthalmic artery produces a less marked decrease of the pressure in the cephalic end of the internal carotid than the occlusion of the internal maxillary artery before (level *b* →, Fig. 1) the origin of the ophthalmic artery. This can easily be explained: when clamping off the ophthalmic artery (level *d* ↓, Fig. 1) one suppresses the blood flow through the anastomosis between internal maxillary artery and internal carotid, and only a small part (ophthalmic artery) of the circulatory area of the internal maxillary artery is cut off, and so must be supplied by blood coming from the internal carotid. On the other hand, clamping off the

internal maxillary artery before the origin of the ophthalmic artery (level $b \rightarrow$, Fig. 1) not only suppresses the flow through the anastomosis between internal maxillary artery and internal carotid, but it also suppresses the connection of the internal maxillary artery with an important circulatory area normally supplied by it (all the branches coming from the internal maxillary artery beyond the ophthalmic artery) and which has now to be supplied by the internal carotid; in this case, the fall of pressure in the cephalic end of the internal carotid, and thus the increase of blood flow in this artery, must be of course much more marked than in the first case.

The ophthalmic artery being clamped, the subsequent occlusion of the internal maxillary artery before the origin of the arteria meningea media (level $\uparrow a$, Fig. 1) does not affect in the slightest way the pressure in the cephalic end of the internal carotid artery (Fig. 4, *2*).

These experiments show that the origin of the decreased peripheral resistance, and thus the increased blood flow, in the internal carotid after clamping off the internal maxillary artery or the external carotid is not located in the arteria meningea media but in the anastomotic branch which connects the internal maxillary artery and the external carotid, through the ophthalmic artery, with the internal carotid.

IV. Control of the reflex origin of the increased blood flow in the internal carotid after decreasing the pressure in the internal maxillary artery.

Considering that the experiments described above show that the increased blood flow in the internal carotid, as observed by M. Schneider and D. Schneider after clamping off the internal maxillary artery, has its origin, not in the arteria meningea media, but in the anastomotic branch connecting the external carotid with the internal carotid, it seemed likely that the phenomena observed by M. Schneider and D. Schneider were to be explained in a mechanical hydrodynamic way. However, in order further to determine whether the observed phenomena were purely mechanical and not at least partly of a cerebral reflex origin, we tried to provoke the phenomena successively in a normal and in a decerebrated animal.

Fig. 5 shows the record of the blood-pressure in the cephalic end of the right internal carotid in a anæsthetized dog. Clamping off the right external carotid produces a marked fall of the pressure in the central end

of the right internal carotid (Fig. 5, *1*). The dog is then completely decerebrated by removing the brain through an opening made in the skull. After decerebration, clamping off the right external carotid did produce, as before, a very intense fall of the cephalic pressure in the internal carotid, this decrease of peripheral resistance being even more marked than before the decerebration (Fig. 5, *2*). Since our experiments show

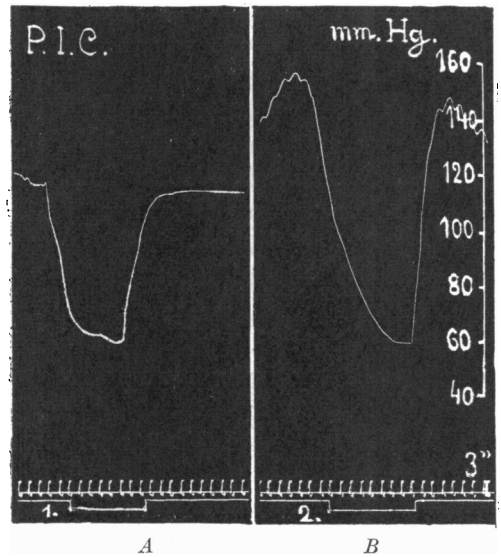

Fig. 5. Pressure (peripheral resistance and blood flow) in the cephalic end of the internal carotid of a chloralosanized dog. *A*, *1*, occlusion of the internal maxillary artery (level ↑ *a*, Fig. 1). Between *A* and *B* the dog is decerebrated. *B*, *2*, occlusion of the internal maxillary artery (level ↑ *a*, Fig. 1).

that the occlusion of the internal maxillary artery or the external carotid produces changes in the vascular area of the internal carotid which are just as marked after decerebration as before, we have to conclude that this phenomenon cannot be attributed to a meningeal-cerebral reflex.

These observations may also explain why M. and D. Schneider still observed the increase of flow in the internal carotid after clamping the external carotid even when the bulbar vaso-motor centres had been excluded.

V. EXPERIMENTS OF ARTIFICIAL PERFUSION OF A DEAD HEAD OF A DOG BY MEANS OF THE INTERNAL CAROTID, BEFORE AND DURING A SYNCHRONOUS PERFUSION BY THE EXTERNAL CAROTID.

In this series of experiments the head of a chloralosanized dog was completely separated from the trunk by means of a crusher. The nervous centres were killed by bleeding the animal, washing out its cephalic circulation by means of a cold Ringer solution and stopping the circulation in the centres during more than half an hour. The cephalic end of one internal carotid was then connected with a Dale-Schuster pump, the

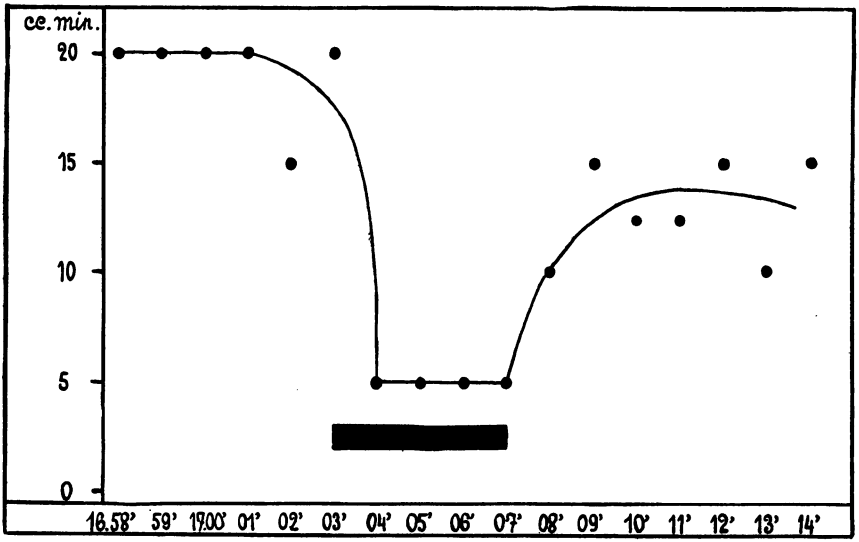

Fig. 6. Perfusion of an isolated head of a dead dog through one internal carotid and one internal maxillary artery, both arteries being connected with two different Dale-Schuster pumps. Ordinates: blood flow through the internal carotid. From 16.58 to 17.03 the head is perfused by the internal carotid only. From 17.03 to 17.07 the head is perfused at the same time through the internal carotid and the internal maxillary artery (▬), the perfusion pressure through both arteries being maintained at the same level. At 17.07 the perfusion through the internal maxillary artery is interrupted again, the perfusion being maintained through the internal carotid only.

cephalic end of the internal maxillary artery on the same side being connected to a second Dale-Schuster pump, in order to measure synchronously the inflow through both arteries. The perfusion fluid used was a mixture of two parts of Ringer solution with one part of defibrinated blood collected the day before from another dog. The perfusion liquid was

allowed to escape through the jugular veins, the common carotid on the side opposite to the perfused arteries being ligated.

Fig. 6 shows the results obtained in one of these experiments. The curve shows the inflow of the pump which was perfusing the left internal carotid: this inflow being nearly 20 c.c. per min. when perfusing only through the internal carotid; the perfusion pressure in the internal carotid having been stabilized at 12 cm. Hg. The perfusion is then started also through the internal maxillary artery, with the same perfusion pressure as in the internal carotid (Fig. 6, ▬), and at once the inflow through the internal carotid artery drops markedly, reaching the low point of 5 c.c. per min. When the perfusion through the internal maxillary artery is stopped again, the inflow to the internal carotid immediately rises again, reaching the mean value of 12·5 c.c. per min. This increase of blood flow in the internal carotid, when the perfusion through the internal maxillary artery is interrupted, is even higher in this experiment on a dead dog than the values obtained by M. Schneider and D. Schneider in a living animal; these authors observed indeed only an increase of about 90 p.c., whereas the increase of blood flow in the experiment described above reaches 150 p.c.

These experiments confirm the idea that the so-called "meningea reflex" must without any doubt be explained only by mechanical hydrodynamic factors and must be related to the direct connection between the internal and external carotids.

Discussion.

In the experiments described above, we have investigated the theory put forward by M. Schneider and D. Schneider and accepted by Kl. Gollwitzer-Meier and P. Eckardt. We were able to demonstrate that a very important branch connects directly the internal maxillary artery, the prolongation of the external carotid, with the internal carotid and the circulus Willisii; this branch is physiologically very important for the cerebral blood supply, since it is sufficient to keep the centres alive and in good condition when the brain is perfused only by the external carotids, all the other cerebral arteries being ligated. We were further able to demonstrate that the increased flow in the internal carotid after clamping the external carotid has its origin, not in the arteria meningea media, as propounded by M. Schneider and D. Schneider, but in the anastomosis itself which connects the internal carotid with the external carotid. Clamping off the internal maxillary artery beyond the arteria meningea media and before the origin of the anastomotic branch produces indeed

the typical change in the peripheral resistance (blood flow) in the internal carotid, which is also observed after clamping off the origin only of the ophthalmic artery giving off the anastomotic branch. On the other hand, clamping the internal maxillary artery before the origin of the arteria meningea media, after ligating the anastomotic branch, does not affect the circulation through the internal carotid artery. The phenomena described by M. Schneider and D. Schneider must be explained further by hydrodynamic factors, since they are just as marked in a decerebrate animal, or in a dead head, as in a normal animal.

As a consequence of the very important direct connections existing in the circulus Willisii between the arteries supplying the nervous centres (Fig. 2), a purely hydrodynamic mechanism must also be admitted for explaining the increase of blood flow in the internal carotid when the external carotid is clamped, not on the same side, but on the opposite side. The same purely hydrodynamic mechanism explains why in the experiments of Kl. Gollwitzer-Meier and P. Eckardt the occlusion of several arteries going to the bulbo-encephalic centres increases the flow in the other arteries going to the circulus Willisii.

Our experiments do not support the existence of vaso-motor reflexes which would control the vaso-motor tone of the brain in relation with blood-pressure changes in the meningeal or cerebral vascular areas. They support the conclusion of our previous publications concerning the passive changes of the cerebral blood flow by the modifications in the arterial blood-pressure, and also support our conclusions concerning the mechanism and the role of the carotid sinus reflexes in the regulation of the cerebral blood flow and the cerebral blood-pressure.

Summary.

1. In dogs a large direct anastomosis connects the external and internal carotids, going directly from the ophthalmic artery (a branch of the external carotid) to the internal carotid.

2. This anastomotic branch is physiologically very important in dogs, since the circulation through it is sufficient to keep the cephalic nervous centres alive in excellent condition when all the other arteries going to the centres have been excluded.

3. Experiments involving clamping the external carotid, or the internal maxillary artery at different levels, or the ophthalmic artery, show that the decrease of the peripheral resistance (increased flow) in the internal carotid is only observed when the ophthalmic artery (which is the

origin of the anastomotic branch) is clamped, and not when the clamping is limited to the arteria meningea media.

4. As the changes in the peripheral resistance and in the blood flow through the internal carotid by clamping the external carotid are obtained equally well after decerebration or during perfusion of a dead head as in normal conditions, such changes of blood flow cannot, of course, be related to meningeal reflexes or to cerebral vaso-motor reactions.

5. The changes in the blood flow through the internal carotid by clamping the external carotid are related to hydrodynamic factors, the mechanism of which is to be explained by the existence of the large direct vascular connection between the internal and the external carotids.

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