Anzahl	Mittleres Trockengewicht der Kostalknorpel von je zwei Tieren	cpm/g Trockengewicht Mittelwert	Statistische Sicherung
12 Normaltiere, Gewicht 280–300 g .	0,45 g	930 ± 148 cpm $n = 6$	Unterschied stark gesichert (t-Verteilung)
36 Skorbuttiere, Gewicht 180–200 g .	0,38 g	475 ± 34 cpm $n = 18$	

Normaltiere erhielten infolgedessen in unseren Versuchen, bezogen auf ihr Körpergewicht, rund ein Drittel weniger Schwefel als die leichteren Skorbuttiere. Dieser Umstand macht es erklärlich, dass die Differenz des aufgenommenen Schwefels zwischen Normal- und Skorbuttieren in unseren Versuchsreihen um rund ein Drittel kleiner war als jene der Tiere von REDDI und NÖRSTROM.

B. JASIŃSKI und R. LOTMAR

Rheumaklinik und Institut für Physikalische Therapie der Universität Zürich und Robapharm AG., Basel, 27. April 1959.

Summary

The utilization of sulphate labelled with S^{35} to the synthesis of chondroitin sulphate of the cartilage of normal and scorbutic guinea pigs has been examined. The average incorporation of S^{35} in the costal cartilage in the deficient animal was about one half that of the normal.

Changes in Cerebral Blood Supply Caused by Changes in the Pressure Drop along Arteries to the Brain of the Cat

The resistance of a vascular bed is usually estimated from simultaneous records of the blood flow and the arteriovenous pressure drop. Since the major part of this pressure decrement is usually believed to occur at the level of the terminal arteries and arterioles[1], the upstream pressure is regarded as being equal to the systemic blood pressure which is recorded in a large artery. However, when arteries are long and narrow, their resistances cannot be neglected. In such cases, there may also be a fall in pressure in the arteries themselves and this may vary in relation to changes in arterial blood flow and to changes in arterial calibre. As a consequence, when a number of vascular beds are coupled in parallel at the end of a narrow artery, a strong vasodilatation in one of them may cause a redistribution of the flow of blood at the expense of the others.

The object of the present investigation was to determine whether or not the resistance of the arteries to the cat's brain is large enough to influence the cerebral blood flow (SCHMIDT and HENDRIX[2]). The arterial anatomy of the head of the cat differs markedly from that of the human, for in the cat the internal carotids are usually small or absent whereas the external carotids have anastomotic branches to the circle of Willis through a *rete mirabile*[3]. The basilar artery is usually well developed. The relative proportion of carotid and vertebral arterial pressures determines the position of the 'dead point' of flow in the arteries below the base of the brain[4]. Under normal conditions, this point is situated in the rostral end of the basilar artery. We have tried to solve our problem by comparing cortical blood flow and pressure in the anterior part of the basilar artery during various experimental conditions. Since this pressure was sometimes found to be much lower than the systemic blood pressure, our next problem was to determine whether the pressure decreased all along the cranial arteries, or whether the fall was confined to the abovementioned *rete*. The physiological effect of the pressure drop in the cranial arteries was also studied by recording the electrocorticogram.

Methods.—All the cats were anaesthetized with 'Nembutal' (40 mg/kg intraperitoneally). A few of them were, in addition, immobilized with 'Flaxedil' and artificially ventilated. Blood pressures were recorded by strain gauge manometers which showed very little change in volume during large changes in pressure. The bones of the base of the skull were removed, and the basilar artery was exposed, ligated and cannulated with a fine nylon tube or glass pipette connected to the transducer with a wide-bore polyethene catheter. The systemic blood pressure was measured through a catheter in the femoral or iliac artery. Cortical blood flow was determined by the method of INGVAR and SÖDERBERG[5] in which the outflow from the cannulated superior sagittal sinus is recorded with an electronic drop counter. The bones of the skull were removed as far as was necessary to interrupt all important anastomoses to the diploic veins. The animal was completely heparinized and the sinus cannulated. The dura was covered with cellulose sponge and the bony defect repaired with dental acrylate cement, molded to form a watertight seal around the sinus cannula. The free end of the cannula was kept in a fixed position relative to the sinus. The blood was returned to the animal by intravenous infusion at a rate equal to the outflow. The electrocorticogram (EEG) was obtained with silver ball electrodes implanted epidurally and an Offner electroencephalograph, type A.

Results.–In animals judged to be in good condition, the basilar artery pressure was initially 70 to 90% of the systemic level. The pulse pressure recorded was usually very small even when the pressure was measured with a transducer that had a volume deflection as low as 0·1 mm³/100 mm Hg[6].

We have confirmed the observation of SCHMIDT and HENDRIX that extracranial vasoconstriction, e.g. elicited by weak sympathetic stimulation, favoured the flow of blood to the brain. This effect is due to a reduction in the pressure drop from the systemic circulation to the cerebral arteries, as a consequence of reduced blood flow through those extra-cranial tissues that are supplied by the external carotids. Conversely this pressure drop was exaggerated during a state of extracranial vasodilatation caused, for example, by section of the sympathetic nerves.

[1] E. M. LANDIS, Heart *15*, 209 (1929–1931).

[2] C. F. SCHMIDT and J. P. HENDRIX, Res. Publ. Ass. nerv. ment. Dis. *18*, 229 (1937).—C. F. SCHMIDT, *The Cerebral Circulation in Health and Disease* (Thomas, Springfield 1950).—U. SÖDERBERG and N. WECKMAN, Acta radiol. *50*, 317 (1958).

[3] P. M. DANIEL, J. D. K. DAWES, and M. M. L. PRICHARD, Philos. Trans. [B] *237*,173 (1953).

[4] D. A. McDONALD and J. M. POTTER, J. Physiol. *114*, 356 (1951).

[5] D. H. INGVAR and U. SÖDERBERG, Acta physiol. scand. *42*, 130 (1958).

[6] Statham transducer P23 g.

Strong sympathetic stimulation was required to produce intracranial vasoconstriction. This diminished cortical blood flow[7], but, as a rule, also reduced basilar pressure (Fig. 1 *a* and *b*). We have concluded from our records and from direct inspection of the blood vessels that this reduction in cerebral blood flow is mainly due to constriction of arteries.

On the other hand, vasodilatation of small cerebral vessels, elicited by acetylcholine (Fig. 1 *c*), ether and some other substances, was sometimes more pronounced than one would expect from comparing records of systemic pressure and of cortical blood flow, because there was generally an increase in the pressure gradient from the carotid to the basilar artery.

The basilar pressure was not a linear function of the systemic pressure when the latter was altered artificially. There seems to be increased arterial tone in response to very high pressures. In addition, very low pressures favoured the constriction that could be induced by sympathetic stimulation. However, the effects are difficult to evaluate because of the changes in blood flow that follow altered pressure.

Noradrenaline elicited the same effects as sympathetic stimulation but arterial constriction could only be induced by fairly unphysiological doses (Fig. 1 *d*, *e*, and *f*). There was a synergism between sympathetic activity and noradrenaline. The arterial constriction elicited by these procedures was also favoured by low systemic blood pressure and by mechanical stimulation of the arteries, e.g. during the dissection at the beginning of the experiment. Adrenaline had an effect similar to that of noradrenaline but weaker, and was also found to dilate small cerebral vessels.

The arterial spasm seen after strong sympathetic stimulation could lead to complete occlusion of the vessels. This occurred both at the carotid level and inside the skull, and was demonstrated by clamping the carotid artery. In those cases where the carotid was already occluded on one side, a clamp on the same side had no effect on the basilar pressure or on the cerebral blood flow. When arteries inside the skull were strongly constricted, a clamp on the carotid caused a further reduction of the basilar pressure. However, this experiment cannot be done in all animals since there is often a considerable asymmetry in the vascular supply of the cat's brain.

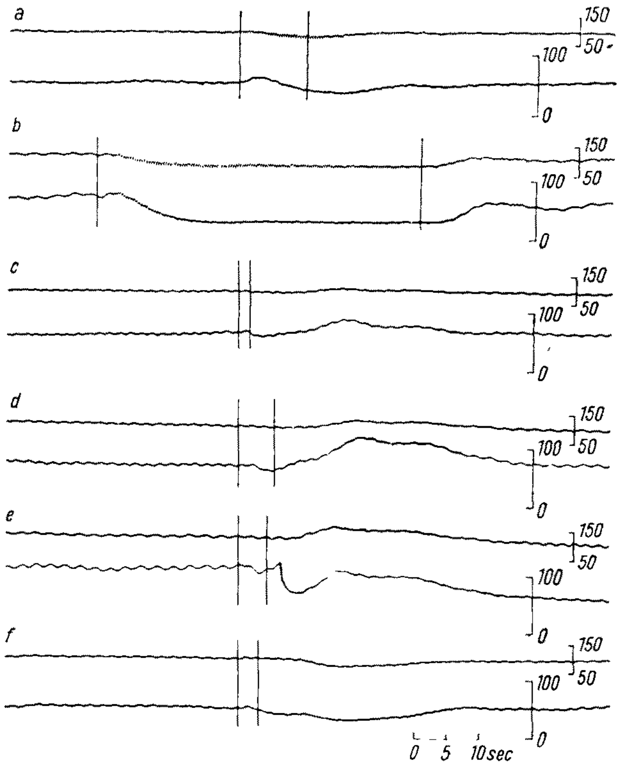

Fig. 1.—Cat 2·6 kg. Nembutal. Pairs of records of femoral (upper) and basilar (lower) pressures. Calibrations in mm Hg to the right. Signals from the femoral pressure transducer electronically damped. *a* and *b*: Between marks, electrical stimulation of the left cervical sympathetic trunk (2V in *a*, 4V in *b*) 33 pulses per sec. *c*, *d* and *e*: The effect of 1, 2 and 3 μg respectively of l-noradrenaline HCl injected into the left carotid artery through a cannula in the lingual artery. *f*: The effect of 1 μg acetylcholine injected by the same route.

A similar asymmetry was also found in the development of the carotid sinus. Thus, when clamping the common

7 B. Holmqvist, D. H. Ingvar, and B. Siesjö, Acta physiol. scand. *40*, 146 (1957).

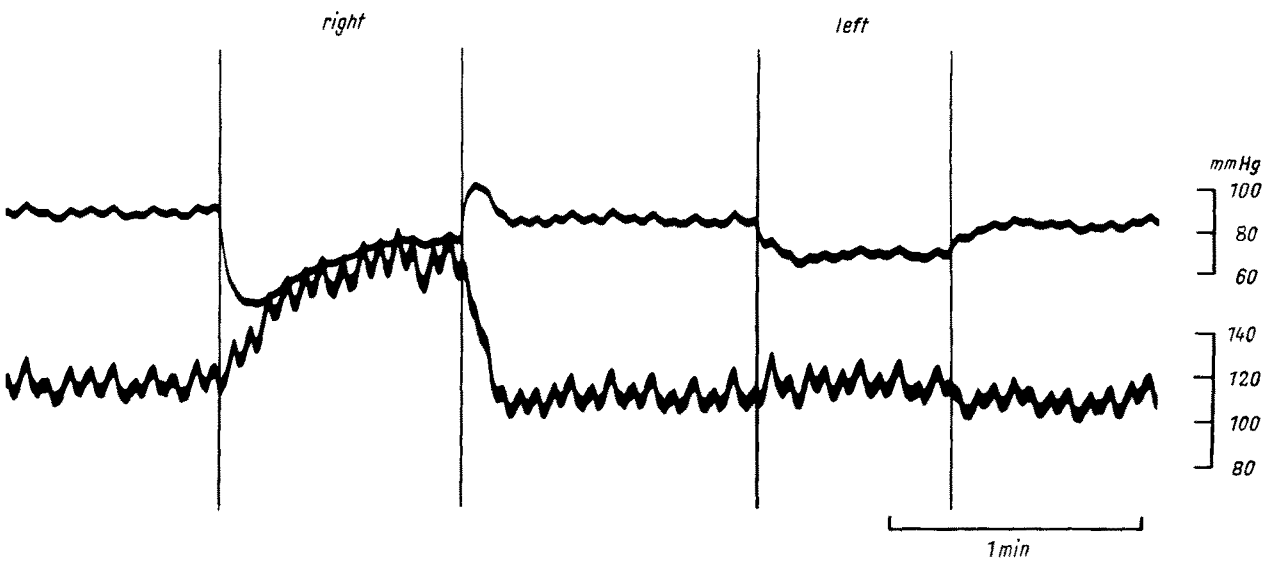

Fig. 2.—Cat 3·6 kg. Nembutal. Blood pressure of basilar (above) and femoral (below) arteries. Calibrations to the right. As indicated, right or left common carotid artery occluded. Note large pressure fall in the basilar artery coincides with strong carotid sinus reflex.

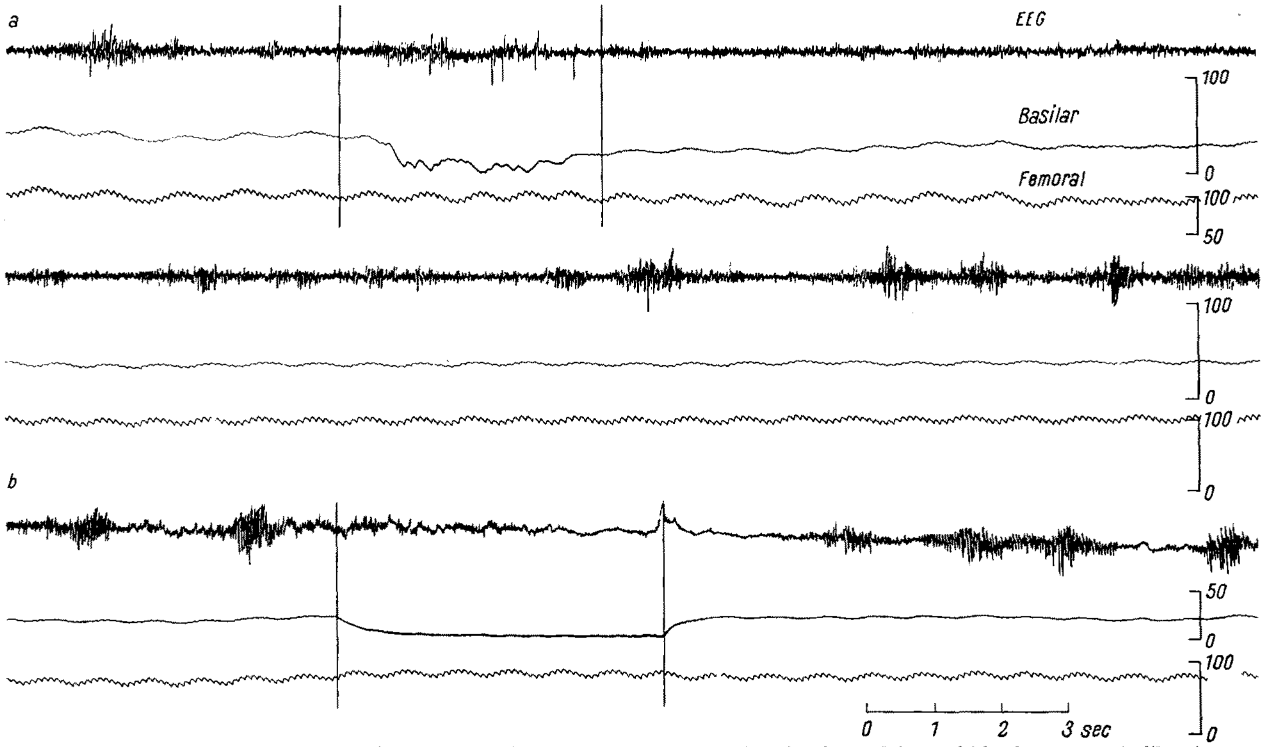

Fig. 3.—Cat 3·9 kg. Nembutal. Records from above: EEG from the cruciate region; basilar and femoral blood pressures (calibrations to the right). *a*: Two continuous records from the lightly anesthetized animal. Between vertical lines we tried to open the jaws and elicited a closing reflex and an 'arousal' reaction that is traced to the middle of the second record. Note irregular fall of basilar pressure. *b*: Cat now immobilized with 'Flaxedil'. Opening the jaws reduces basilar pressure to zero and EEG shows depressed cortical activity.

carotid artery was followed by decreased basilar pressure and reduced cortical blood flow, there was always a strong carotid sinus reflex raising the systemic blood pressure, whereas in those cases where the anastomoses were badly developed between the carotid artery on one side and the circle of Willis, the reflex from the sinus region on the same side was weak or absent (Fig. 2).

Arterial occlusion was also obtained after large doses of serotonin. In one experiment, this spasm was released by a serotonin antagonist[8].

Wide separation of the animal's jaws caused a mechanical occlusion of the blood vessels between the carotids and the circle of Willis. In the intact anesthetized animal, jaw opening to the critical angle of 30° to 40° or more caused reflex closure, but in the curarized preparation where this reflex is abolished, complete arrest of arterial flow could be obtained by passive separation of the jaws. Electrical stimulation of the lingual nerve could evoke mouth opening to such an angle that the cerebral blood flow was significantly lowered.

The vertebral and basilar arteries are not large enough to replace the carotids during a strong carotid constriction. Therefore, all procedures that seriously reduced the carotid blood flow also influenced brain function. Slow waves, or even flattening of the EEG records could thereby be induced (Fig. 3). Increased tone in skeletal muscle, similar to that seen after anemic decerebration according to POLLOCK and DAVIS[9], was also observed during constriction of the carotid arteries.

Conclusion.—The pressure drop in the extra- and intracranial portions of the arteries to the cat's brain is sometimes large enough significantly to influence the cerebral blood flow. The fall in blood pressure in the arteries varies with arterial vasomotor activity as well as with changes in blood flow both inside and outside the skull. No evidence for special vasomotor activity in the carotid *rete* has been found. In view of previous reports in the literature, the finding of a considerable pressure drop in narrow arteries is not unexpected. Nevertheless, one would believe that the anatomical arrangement consisting of a number of arteries running in parallel to the circle of Willis would always permit adequate supply of blood to the brain. However, the present results show that a reduction in blood flow through one or two of these arteries cannot always be satisfactorily compensated for by increased flow in the remaining vessels. As a consequence, signs of depressed cerebral activity appear when the carotid arteries are markedly constricted.

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U. SÖDERBERG and N. WECKMAN

Nobel Institute for Neurophysiology, Karolinska Institute, Stockholm (Sweden), May 6, 1959.

Zusammenfassung

Bei der Katze kann der Druckabfall in den extra- und intrakraniellen Anteilen der Hirnarterien unter gewissen Bedingungen genügend gross werden, um die Hirndurchblutung in eindeutiger Weise zu beeinflussen. Schwankungen des Druckgradienten in den Arterien werden durch die arterielle Vasomotorik und Veränderungen der Durchströmung derjenigen Gewebe bedingt, die von den Aa. carotidae externae versorgt werden.

[8] Methyl-lysergic acid diethylamide (MLD-41) and 5-hydroxytryptamine (serotonin) were kindly provided by Sandoz AG., Basel.

[9] L. J. POLLOCK and L. DAVIS, J. comp. Neurol. *50*, 377 (1930).