Acta Neurochirurgica 25, 19—36 (1971)

Department of Neuropathology (Chairman: Prof. Dr. J. Cervòs-Navarro),
Department of Nuclear Medicine (Chairman: Prof. Oeff),
Klinikum Steglitz der Freien Universität Berlin

Cerebral Blood Flow During Increased Subarachnoid Pressure

The Influence of Systemic Arterial Pressure

By

F. Matakas, M. Leipert, and **J. Franke**

With 9 Figures

Summary

In rhesus monkeys and cats cerebral intracranial pressure was increased by intracranial fluid injection. Increased liquor pressure was transferred to the superficial cerebral veins, which caused a reduction of cerebral perfusion pressure. An arterial pressure response occurred as soon as the perfusion pressure was less than 100 mm Hg. The pressure increase was dependent on the percent rate of perfusion pressure decrease in relation to the systemic arterial pressure. Carotid flow measured in monkeys showed a slight reduction as long as the perfusion pressure was higher than 50 mm Hg but was marked when it fell below that value. The systemic arterial pressure had a significant influence on cerebral vessel resistance independent from the perfusion pressure. During increased intracranial pressure the cerebral blood volume seemed to be moderately decreased.

Under normal conditions cerebral blood flow (CBF) is controlled by an autoregulation mechanism. This mechanism guarantees a sufficient and constant blood supply even when the arterial pressure is as low as 50 mm Hg, provided that no further disorders complicate the situation (Lassen 1959, Häggendal 1965, Harper 1965).

The main consequence of intracranial hypertension is a reduction of the cerebral perfusion pressure (pP) which may result in a decreased CBF. However, the organism is able to counteract this danger by various mechanisms. Because of the copious perfusion under normal conditions the brain can tolerate a considerable reduction of blood

flow. By reason of the dilatation of cerebral vessels the CBF may remain sufficient even when the pP is lower than 50 mm Hg. There is another mechanism which is usually regarded as a means by which the necessary blood flow may be restored, viz. the increase of systemic arterial pressure which always occurrs with intracranial hypertension. The role of the so-called Cushing response, however, is not clear so far.

The present study was undertaken to evaluate the influence of subarachnoid hypertension on CBF and cerebral function. We have attempted to answer the following questions: 1. In what way is CBF dependent on intracranial pressure? 2. Where does vascular obstruction take place? 3. At which pressure is cerebral function hindered? 4. How does systemic arterial pressure influence CBF?

Material and Methods

9 monkeys (macacca mulatta 3,000–4,000 gms) and 7 cats (2,270–4,150 gms) were used. For the experiment the animals were anaesthetized with 50 mg/kg pentobarbital sodium (Nembutal) and 0.3 mg Atropine injected intramuscularly. Tracheostomy was performed and after muscular relaxation with 2 ml/kg nortoxiferrinium chloride (Alloferin) the animals were artificially respirated with a Starling pump for the whole course of the experiments. Blood gases were controlled regularly and kept normal. In order to produce hypercapnia the monkeys were respired with a gas mixture of 30% O_2, 20% CO_2, 50% N_2. Flow measurements during hypercapnia were undertaken after the normal course of experiments.

A polyethylene catheter was inserted into the aorta through the femoral artery in order to record arterial pressure and for blood sampling. For recording the sinus blood pressure of 6 cats and 2 monkeys a polyethylene catheter was inserted into the sagittal sinus, in 3 cases in a frontal, in 5 cases in a dorsal direction.

For recording and increasing the subarachnoid pressure a small hole was made into the parietal skull and closed again with a small rubberbung fixed with Histacryl N. A cannula (20 G) was then inserted through the rubber into the subarachnoid space and was connected with a Statham transducer and an infusion pump. This method provided complete closure of the intracranial space. In order to achieve a constant difference between arterial and subarachnoid pressure the infusion pump was controlled by an electronic control system which made the pump inject an isotonic saline solution (Na^+ 322 mg; K^+ 15.6 mg; Ca^{++} 10 mg; Mg^{++} 2.4 mg; Cl^- 376 mg; lactate$^-$ 401 mg ad 100 ml aqua dest.) into the subarachnoid space in accordance with the systemic arterial pressure, the subarachnoid fluid absorption and the pP selected. This method guaranteed a constant pP for unlimited periods of time, no matter how much the arterial pressure changed.

CBF in monkeys was measured with a microflowmeter the probe of which measured 2 mm in diameter. It was applied to the common carotid artery after ligation of the external carotid artery and, if necessary, the superior thyroid artery.

When the preparation was finished the normal carotid flow was recorded for 30–60 minutes. The mean of the measured values was regarded as 100% carotid flow. Several times during the experiments the carotid

artery was completely occluded for periods of some seconds. The mean of the flow values thus obtained was regarded as the O-niveau.

For measuring cerebral blood volume erythrocytes of 8 ml blood were washed, incubated with 100 μCi chromium 51, and re-injected. Activity of the brain was recorded with a detector adjusted over the parietal region. For comparison, the activity of the frontal part of the head excluding cerebral activity was also measured.

All investigations were made under a constant pP beginning with an intracranial pressure of O. The pP was then lowered to 100, 80, 60, 40, 20, 10, 0, —10 mm Hg. Each level was maintained for about 20 minutes before changing to the next one. 100–150 ml isotonic salt solution were generally used for each animal so as to increase the intracranial pressure. At the beginning of the experiment the haematocrit was 35% on the average, at the end 25%.

During the experiments EEG, ECG, pressure in the aorta, in the subarachnoid space, and in 6 cases in the sagittal sinus were constantly recorded. Body temperature was controlled and kept constant by means of a heating blanket.

The whole experiment took 6 to 8 hours, of which 2 to 3 were needed for preparation.

Results

Venous Blood Pressure

In 2 monkeys and 6 cats sagittal sinus blood pressure was measured during various intracranial pressures. The technique of insertion was performed in such a way that only a small amount of blood could pass that part of the sinus where the catheter lay. Neither in monkeys nor

Table 1. *Sinus Blood Pressure in Correlation to Intracranial Pressure*

Animal No.	pP mm Hg	pArt. mm Hg	pIC mm Hg	pSin. mm Hg
monkey				
AM 2	155	155	0	7–10
	80	140	60	5
(catheter in	70	190	120	6–7
dorsal direction)	40	220	180	7–8
	50	100	50	4
	30	70	40	4
	20	190	170	4
cat				
KM 13	70	70	0	0.5
	80	100	20	10–15
(catheter in	80	140	60	45–50
frontal direction)	50	120	70	55
	50	120	70	60
	40	150	110	100
	20	140	120	90
	0	200	200	130

in cats did this manipulation lead to any disturbances of the EEG. In 4 of the animals where the catheter was directed backwards, the sinus pressure was not influenced by intracranial pressure. Its value oscillated between 0 and 10 mm Hg during the whole experiments (Table 1). In 2 cases the sinus pressure became slightly lower when the intracranial pressure rose.

In those 3 cases where the catheter had been inserted frontally and in 1 animal of the first group the sinus pressure was fully dependent on intracranial pressure. After rapid instillation of an isotonic solution into the sinus, the pressure rose abruptly and fell to its normal value within 1 minute. Thus it was ascertained that it was connected by venous anastomoses to the still intact drainage system. The sinus pressure in these cases showed an increase parallel to that of the intracranial pressure, but never exceeded the arterial blood pressure even when the intracranial pressure was as much as 50 mm Hg higher than the arterial blood pressure. This was tested in few cases after the regular experiments. However, the sinus pressure measured was always somewhat lower than the intracranial pressure, at low values less so than at high ones.

These results demonstrate that the intracranial venous blood pressure could be equated with the liquor pressure.

Arterial Blood Pressure

An increase of intracranial pressure regularly caused an immediate rise of systemic blood pressure. Only rarely was the response of the blood pressure delayed for some seconds. In some cases the blood pressure remained elevated throughout the period of increased intracranial pressure, in one case as long as about 5 hours. But in other cases the immediate rise of the blood pressure was followed by a slow fall so that the initial value was reached again within 5–10 minutes. The blood pressure reacted equally promptly to a decrease of the intracranial pressure. When the difference was marked, blood pressure fell below the initial level. Fig. 1 demonstrates the correlation between pP and systemic arterial pressure. The abscissa represents the percent rate of the pP in comparison with the initial systemic blood pressure. One of the monkeys showed a significantly greater sensitivity to changes of the pP though the curve of its reaction is identical in its form to that of the others.

Carotid Flow

Because of the fact that in cats the brain is supplied with blood by arteries which also give branches to the extracerebral tissues, CBF was measured only in the 9 monkeys. Therefore the following refers only

to them. The absolute amount of blood flow of the internal carotid artery was different in each animal. With the exception of 3 animals where it was 8, 10, 12, it did not differ much from 22 ml/min. There was no correlation between body weight and absolute blood flow measured.

A decrease of the pP to less than 100 mm Hg influenced the carotid flow in all animals. Except for one animal, the original arterial pressure was higher than 100 mm Hg so that a pP of 100 mm Hg or less

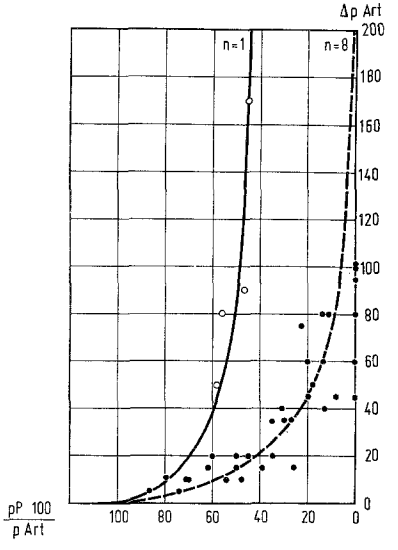

Fig. 1. Correlation between the percent rate of pP in relation to initial systemic arterial pressure and blood pressure increase. All pressure scales refer to mm Hg both here and in the following figures.

was achieved by intracranial hypertension. The change of blood flow occurred within a few minutes after alteration of the pP and remained constant within narrow limits for the whole period of a constant pP (Fig. 2). In Fig. 3 the correlation is shown between pP and carotid flow. As the absolute rate was different in the animals, the pP is plotted against the percent rate of carotid flow. The influence of a decreased pP was essentially the same in all experiments and for all animals, with only one exception, where a temporary hypoventilation caused hypercapnia. The resulting curve was quite independent from the original blood pressure which the animal had at the beginning of the experiment. At a pP of 50 mm Hg the blood flow was on the average reduced only to little more than ¼. From this point on the reduction was more marked. A further decrease of the pP to 20 mm Hg reduced the blood flow by half as much again to only a quarter of the original

level. When hypercapnia was produced the carotid flow sometimes changed at a pP of 50, 40, 30, and 20 mm Hg. But the results were not significant.

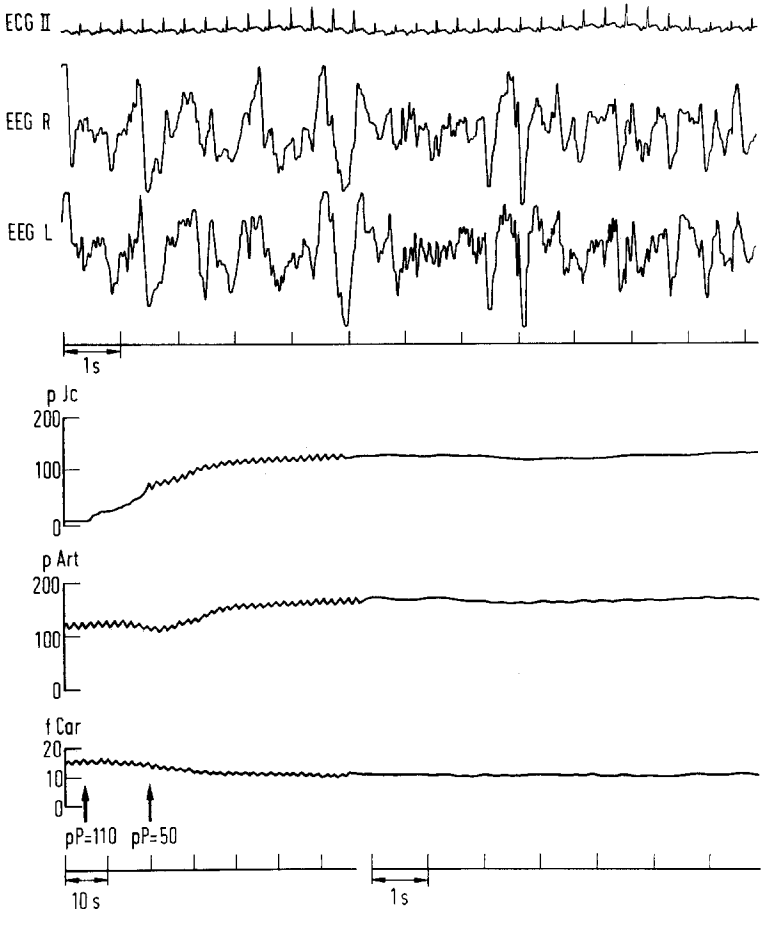

Fig. 2. A considerable reduction of pP only leads to a moderate decrease of carotid flow. The EEG does not change.

Peripheral vessel resistance of the brain calculated as $\frac{\text{pIC–pArt}}{\%\,\text{f Ca}}$ mm Hg min ml^{-1} is shown in Fig. 4. The dotted line shows the theoretically estimated curve presuming that until a pP of 50 mm Hg is reached, autoregulation compensates the decreasing pP by vasodilation which was assumed to be maximal at a pP of 50 mm Hg. The corresponding curve of the blood flow measured by us has its minimum at a pP of

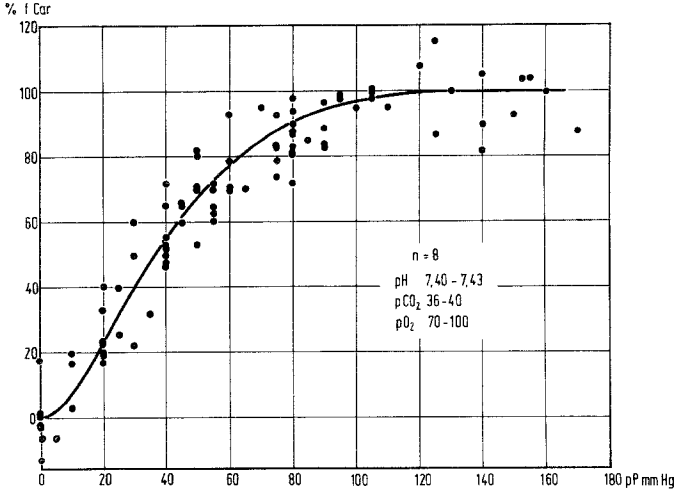

Fig. 3. Correlation between cerebral pP and carotid flow.

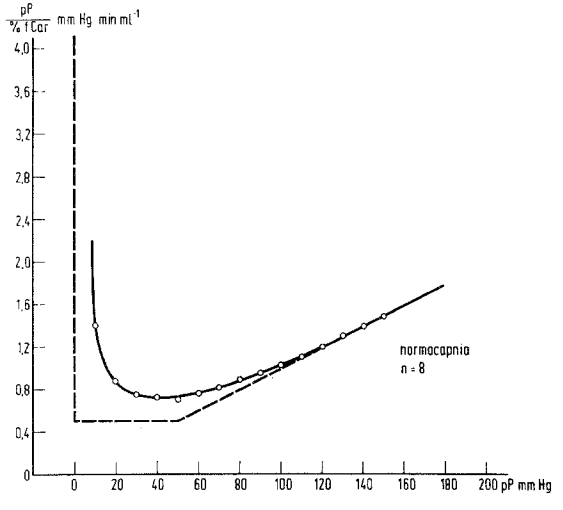

Fig. 4. Correlation between peripheral vessel resistance and pP (continuous curve). The curve represented in Fig. 3 was used as basis of calculation for this curve. The dotted line represents the theoretically calculated behaviour of cerebral vessel resistance.

50 but becomes not as low as the theoretically calculated curve. This corresponds well to the blood flow curve which had its greatest steepness from a pP of 50 mm Hg on downwards but began to fall already before.

When the pP was equal or lower than 50 mm Hg a change of the systemic arterial pressure had a significant influence on the carotid flow. As no artificial means were used to provoke this phenomenon, the level where it spontaneously occurred and the degree of arterial pressure alteration were different for the animals although it could

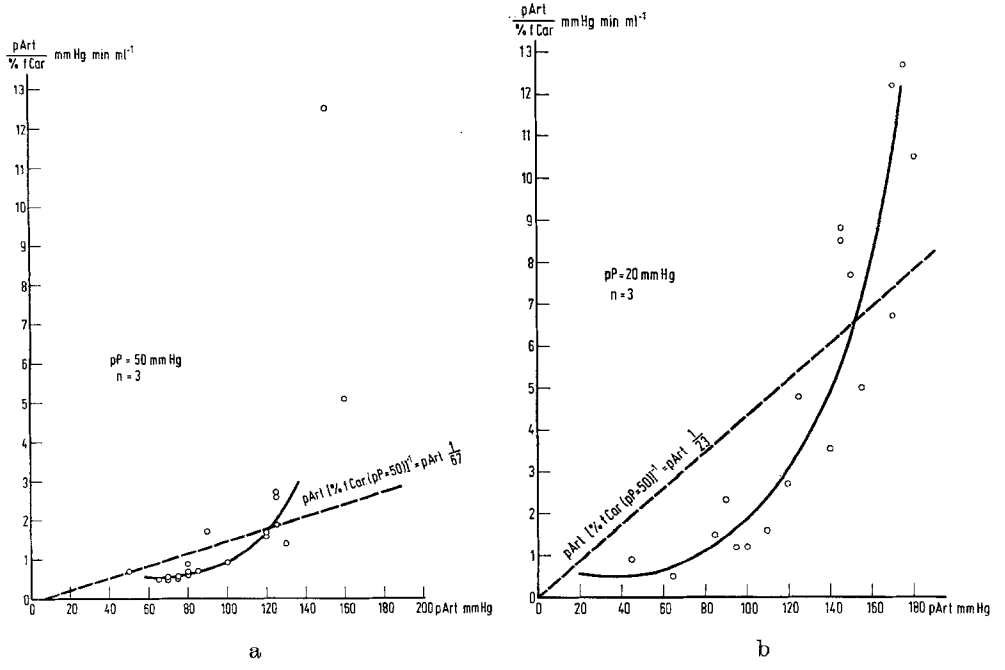

Fig. 5a, b. Correlation between vessel resistance of carotid or cerebral arteries and systemic arterial pressure. The dotted lines represent the theoretically calculated correlation provided that systemic arterial pressure has no influence on carotid flow. The values as shown by the curve of Fig. 3 were taken as presumed values of carotid flow which correspond to a pP of 50 (a) and 20 (b) mm Hg, they are 67% and 23%. The circles represent the empirically found values.

be observed in all animals. Fig. 5 demonstrates the effect of different arterial pressures on cerebral vessel resistance during a pP of 50 and of 20 mm Hg.

Blood Volume

Cerebral blood volume showed only little change during the experiments. The maximum change observed in one of the animals together with a marked decrease of the extracerebral cranial blood volume

was 29%. The minimum was 6.4%. Whenever during a constant pP a significant and sudden change of the blood volume occurred, it was accompanied by a sharp rise of arterial blood pressure (Fig. 6). In all animals the cerebral blood volume fell irreversibly under the initial value when the pP was lowered to 60 mm Hg ($p < 0.05$). In 4 animals the final reduction did not start before the pP was lowered to 40 mm Hg. The volume of the extracranial tissues changed quite differently. There was no significant correlation between cerebral pP and blood volume of extracranial tissue.

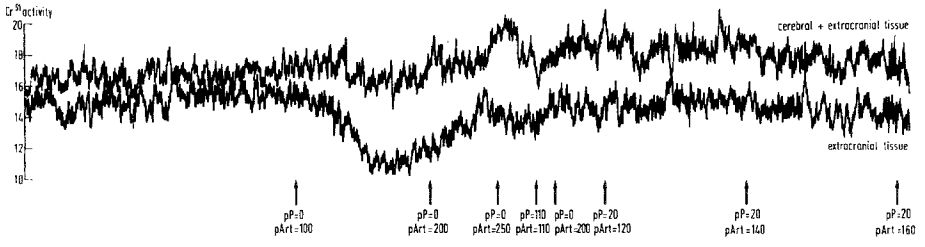

Fig. 6. Cr^{51} activity of cerebral and extracerebral tissues of the head. The scale indicates units of work. The increasing distance between the two curves indicates increasing cerebral blood volume, which is marked when the pP suddenly rises from zero to normal values. A fall in pP leads to a decrease of cerebral blood volume.

ECG

When the pP was lowered to 0 the ECG of 8 monkeys and 5 cats showed significant changes. Ventricular extrasystoles of the paroxysmal or bigeminial type were observed. A detailed description of this phenomenon will be published elsewhere.

EEG

At the beginning of the narcosis with Nembutal, isoelectric periods and a delta-rhythm were observed in 2 animals. In all other cases the EEG showed no anomalies. In general we observed an alpha-rhythm only occasionally changing to a somewhat faster rhythm of about 15–20. There were no lateralised differences but changes in amplitude were seen. In no case was the EEG altered before the pP had been lowered to 40 mm Hg. In the majority of cases a delta-rhythm appeared at a pP of 20–30 mm Hg (Table 2). An isoelectric EEG appeared at a pP between 30 and 0 mm Hg (Fig. 7). The deltafrequency caused by a lower perfusion usually disappeared completely after full restoration to normal pP and an alpha or at least a theta frequency was ob-

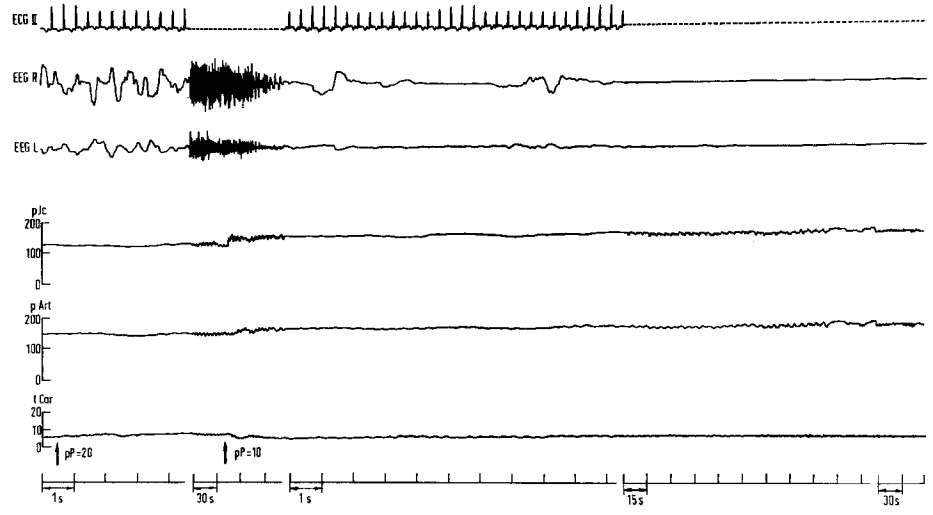

Fig. 7. Change of EEG when pP is lowered from 20 to 10 mm Hg.

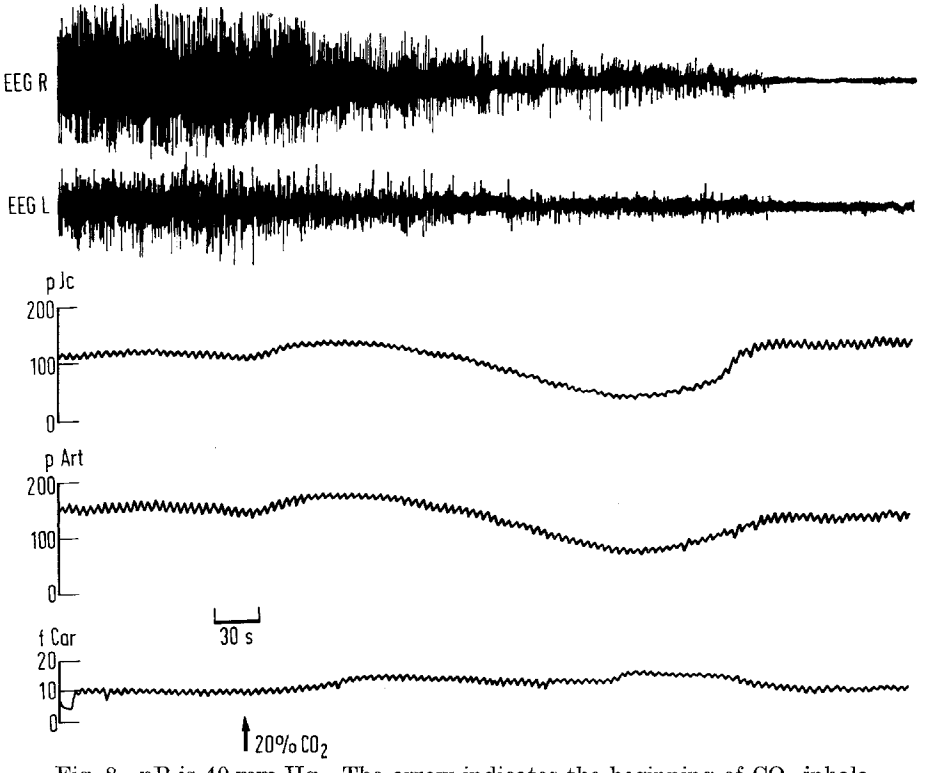

Fig. 8. pP is 40 mm Hg. The arrow indicates the beginning of CO_2 inhalation. There is a slight increase of carotid flow which is more pronounced when arterial pressure is lowered. — Immediately after CO_2 admixture to breathing air EEG amplitudes become smaller.

Table 2. *Changes of the EEG in Correlation to pP*

Animal No.	Appearance of δ-rhythm	Isoelectric EEG
monkeys	pP mm Hg	pP mm Hg
1	30	10–0
2	30	20
3*		20
4		30**
5	20	10–0
6	10	0
7	25	10–0
8	0–10	
9	20	10–0
cats		
10	30	10
11	40	20
12	?	20
13	20	10–0
14	20	10

* δ-rhythm after narcosis.
** EEG became isoelectric without appearance of a δ-rhythm.

served again following a pP of 0 maintained for a period not exceeding 10 minutes.

Where hypercapnia was produced, the EEG became extremely slow or completely flat when the pP was lower than 60 mm Hg (Fig. 8). These changes took place within 5–15 minutes. In no case was hypercapnia prolonged for more than 20 minutes. The EEG improved after normal or intensified ventilation.

Discussion

The amount of fluid flowing through a tube within a given time is determined by five parameters: the pressure gradient acting on the fluid, the diameter, length, elasticity of the tube, and the viscosity of the fluid. The same applies to the CBF. Apart from the length of vessels, all these factors are variable. The viscosity of the blood and elasticity of vessels and their importance for CBF has so far been little investigated (Finke 1965, Gottstein, Held 1969, Rosenblum 1970, Mead, Moody, Ruamsuke 1970) but cannot be considered here. Unless the viscosity of the blood is changed, the organism can regulate CBF either

by changing the pressure gradient or the total vessel diameter within the brain.

On condition that the systemic arterial pressure and the venous pressure are constant, the rate of blood flow can be varied only by change of vessel diameter of either the cerebral arterioles or capillaries. If on the other hand the systemic arterial pressure changes and CBF is to be kept constant by means of autoregulation, again only a change of vessel diameter is able to guarantee a constant perfusion rate. If we presume in addition that the diameter of cerebral capillaries remains constant, and that no cerebral arteriovenous shunt exists (Potchen, Holman, Evens, Agress, Hill 1971), it follows that a constancy of CBF is provided by a constant capillary blood pressure, independent from the systemic arterial blood pressure. As CBF remains constant unless the systemic arterial blood pressure diminishes below 50 mm Hg, we may conclude that cerebral arterioles are maximally dilated when arterial pressure is about 50 mm Hg, and that the pP of cerebral capillaries under normal conditions is below 40 mm Hg.

The situation is completely different in case of increased subarachnoid pressure. The subarachnoid veins are first susceptible to obstruction (Noell, Schneider 1948, Hedges, Weinstein, Kassell, Stein 1964, Hekmatpanah 1970). This was confirmed by our experiments. When the sinus catheter was directed frontally blood distal to the catheter could only just pass the point where the catheter had been inserted, being drained mostly by superficial cerebral anastomoses. Thus the pressure in the frontal part of the sinus was a measure of the pressure within the superficial veins of the brain. However, as the inserted catheter did not obstruct the sinus completely, the blood may partly have passed, especially when the pressure rose to higher levels. This explains the discrepancy between subarachnoid and sinus pressure with increasing arachnoid pressure. In the one case where the catheter was directed posteriorly and yet a rise of pressure was observed, the sinus although patent in its posterior part, must have been passively compressed by the subarachnoid fluid at certain points. This fact has been demonstrated by a number of authors (Langfitt, Weinstein, Kassell, Gagliardi, Shapiro 1966, Shapiro, Langfitt, Weinstein 1966, Sahar, Hochwald, Ransohoff 1970). It follows that the necessary CBF during increased subarachnoid pressure can only be provided if the driving pressure up-stream of the capillaries is increased. From a theoretical point of view this can be brought about either by dilatation of the arterioles or by an increase of the systemic arterial pressure.

Since Cushing (1902) it has been known that the organism reacts to intracranial hypertension with an increase of arterial blood pressure. Our investigations show that even a very slight rise in intracra-

nial pressure is sufficient to provoke this Cushing reflex. As the sensory centre is located inferior to the tentorium (Kramer, Tuynman 1967, Hoff, Reis 1969), it reacts only when the increased intracranial pressure acts upon the region of the medulla and upper cervical cord. In contrast to investigators who used an epidural balloon, our technique of artificial intracranial hypertension always guaranteed a uniform distribution of intracranial pressure as we could verify by own studies and as has been proved by detailed investigations (Langfitt, Weinstein, Kassell,

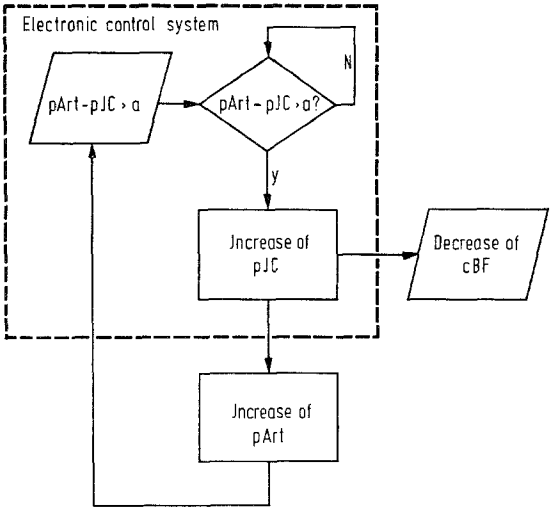

Fig. 9. The diagram represents the relation between Cushing response and intracranial pressure on the supposition that the latter is the input function for the former. For further explanation see text.

Simeone 1964, Langfitt, Weinstein, Kassell, Gagliardi 1964). However, the pressure response of the organism to cranial hypertension is not correlated with the absolute intracranial pressure, but to the ratio perfusion pressure/initial systemic arterial pressure. If it were dependent on intracranial pressure our experimental technique would have caused a maximum of pressure response following even a very slight increase of intracranial pressure as demonstrated in Fig. 9. Suppose that the initial arterial pressure is about 100 mm Hg and the intracranial pressure 10 mm Hg. By injecting fluid into the subarachnoid space the pP may be lowered to a = 50 mm Hg, so that the intracranial pressure is increased to 50 mm Hg. As a results of increased intracranial pressure the arterial pressure may rise to 120 mm Hg, thus inducing the extracorporeal control system to increase the intracranial

pressure again up to 70 mm Hg. The process would go on at least approaching asymptotically an upper limit equal for each pP, if the absolute intracranial pressure were the input function for the regulation of the Cushing reflex. Similar results have been obtained by Sagawa, Ross, and Guyton (1961) who found a logarithmic correlation between CBF and systemic arterial pressure, but only when the cerebral pP was lowered to less than 50 mm Hg. They assumed the CBF to be the stimulating factor for the pressure response.

As our investigations show that the Cushing response and its degree is dependent on the pP of the brain in relation to the systemic arterial pressure we may conclude that as the pP determines cerebral flow it is regulated by the CBF. The quantitative correlation between intracranial hypertension and Cushing response even suggests that the increase of systemic arterial pressure has some beneficial consequence for the brain (Jennett, Rowan, Harper, Johnstone, Miller, Deshmukh 1971). But the contrary seems to be the case. If the brain borders upon an incompressible mass—this is what happens in all cases of advanced brain oedema—a rise of arterial pressure induces a rise also of the intracranial pressure. If this resultant rise in intracranial pressure equals the rise in arterial pressure, as in our experiments, CBF is not improved but diminishes even more.

Several authors (Hedges, Weinstein, Kassell, Stein 1964, Langfitt, Kassell, Weinstein 1965, Risberg, Lundberg, Ingvar 1969, Hekmatpanah 1970) have concluded from their experiments that the correspondence of intracranial to arterial pressure in the state of intracranial hypertension is caused by a changing cerebral blood volume. There is, however, no agreement about where cerebral blood accumulation takes place. While most of the authors believed that it was the arterial part of the vascular system, the volume of which is increased, Hekmatpanah (1970) observed an engorgement of the venous channels in the subarachnoid space. Our investigations of cerebral blood volume have not provided support for either of these assumptions. This may be explained by the fact that we always referred to the pP. We even observed a decrease of cerebral blood volume during high values of intracranial pressure. A significant increase in blood volume should have manifested itself in a greater distance between the cerebral and extracerebral curve, no matter how great the rate of extracerebral activity was in either of the curves. Reactive hyperaemia following a large reduction in pP could be recognized in a significant increase of cerebral activity. Thus we may be allowed to conclude that any change in intracerebral blood volume could only have been minimal. We therefore consider the phenomenon of floating membranes, quite familiar to physiologists, the real cause of this parallelism. But whatever

the real explanation is, the Cushing reflex in a state of intracranial hypertension increases CBF only if the pP is also increased. But as long as the pP remains constant a reduced pP can be counteracted only by vessel dilatation. This dilatation reaches its maximum at a pP of about 50 mm Hg.

Our results differ in some respect from those of Häggendal, Löfgren, Nilsson, Zwetnow (1967), Zwetnow, Kjällquist, Siesjö (1968), Petersen, Zwetnow (1968), Jennett, Rowan, Harper, Johnston, Miller, Deshmukh (1971) who found a constant CBF as long as the pP was not lowered under 40 mm Hg. It is noteworthy, however, that according to Fig. 4 the vessel diameter in the animals with normocapnia and normoxia was largest at a pP of 50 mm Hg although carotid flow began to decrease much earlier. This means that the reduction of pP was not completely compensated by vessel dilatation.

The question now arises why CBF began also to decrease before the pP was lowered to 50 mm Hg in contrast to the observation of other authors. This question cannot be answered with certainty, but a suggestion may be put forward. The first is, that the above mentioned authors did not use a technique that guaranteed a constant pP. Our experiments indicate furthermore that CBF is not only regulated by metabolic agents. The change in carotid flow during a constant pP in dependence of the systemic arterial pressure proves that the carotid arteries or the larger arteries of the brain influence CBF by means of a myogenic reaction or by vasoconstriction caused by the release of catechol amines. Indication for a possible myogenic influence of the major arteries on CBF has been produced by Symon (1970), Harper, Deshmukh, Rowan, Jennett (1971). Ross Russel (1971) observed a significant vasoconstriction in surface arteries of the brain when he raised the blood pressure by adrenaline. On the other hand it is known that during a Cushing response noradrenaline is released (Kramer, Tuynman 1967, Kanzow, Dieckhoff, Holzgraefe 1970). The early fall of carotid flow in our experiments may therefore be caused by the Cushing response.

The rise of arterial pressure in the case of cerebral oedema does not necessarily produce an improved CBF. Until now there are no exact data concerning the quantitative influence of the systemic arterial pressure on the cerebral pP. Own studies revealed that the pP may be moderately increased by an arterial pressure rise even in the case of cerebral oedema. On the other hand arterial hypertension may increase capillary filtration pressure and therefore enforce the development of cerebral oedema in the case of damaged cerebral tissue (Klatzo 1967, Freeman 1969).

In our experiments the cerebral tissue was not injured and an ele-

vated capillary pressure was counteracted by an increased tissue pressure. Cerebral oedema developed only after ischaemia. It was a striking experience that the electroencephalographic activity of the animals was frequently depressed only at a very low pP, sometimes not more than 10 mm Hg. But we must assume that cerebral perfusion is better preserved when the pP is lowered by an increased venous rather than by a lowered arterial pressure. As the total diameter of cerebral capillaries is much larger than that of the arterioles, an extremely low arterial pressure does not guarantee the perfusion of all capillaries. The situation is different in the case of increased venous pressure when the increase is transferred undiminished to the capillaries which, if they are still patent and if there is still a positive pP, always have a higher blood pressure than the veins. Moreover, it must be recalled that the time of reduced pP was fairly short in our experiments. It is known that in man also a very high liquor pressure can occur for short periods (Schmidt 1963, Kjällquist, Lundberg, Ponten 1964, Greenfield, Tindall 1966), but certainly the brain is not able to stand a long lasting reduction of blood flow as must happen when the liquor pressure rises to values approaching the arterial pressure.

References

Cushing, H., Some experimental and clinical observations concerning states of increased intracranial tension. Amer. J. med. Sci. *124* (1902), 375—400.

Finke, J., Therapeutische Erfahrungen mit Rheomakrodex in Neurologie und Psychiatrie. Zbl. Neurol. Psych. *183* (1965), 232.

Freeman, J., Hypotension and cerebral ischemia. Int. Anesthesiol. Clin. *7* (1969), 841—859.

Gottstein, U., and K. Held, Effekt der Hämodilution nach intravenöser Infusion von niedermolekularen Dextranen auf die Hirnzirkulation des Menschen. Dtsch. med. Wschr. *94* (1969), 522—526.

Greenfield, J. C., and G. T. Tindall, Effect of acute increase in intracranial pressure on blood flow in the internal carotid artery of man. J. clin. Inv. *44* (1965), 1343—1351.

Häggendal, E., Blood flow autoregulation of the cerebral grey matter, with comments on its mechanism. Acta neurol. Scand. suppl. *14* (1965), 104—110.

— L. Löfgren, N. J. Nilsson, and N. Zwetnow, Die Gehirndurchblutung bei experimentellen Liquordruckänderungen. Acta neurochir. *16* (1967), 163.

Harper, A. M., The inter-relationship between $aPCO_2$ and blood pressure in the regulation of blood flow through the cerebral cortex. Acta neurol. Scand. suppl. *14* (1965), 94—103.

— V. D. Deshumkh, J. O. Rowan, and W. B. Jennett, Studies on possible neurogenic influences on the cerebral circulation. In: Brain and blood flow, pp. 182—186. Ed. R. W. Ross Russell. London: Pitman. 1971.

Hekmatpanah, J., Cerebral circulation and perfusion in experimental increased intracranial pressure. J. Neurosurg. *32* (1970), 21—29.

Hedges, T. R., J. D. Weinstein, N. Kassell, and S. Stein, Cerebrovascular responses to increased intracranial pressure. J. Neurosurg. *21* (1964), 292—297.

Hoff, J., and D. J. Reis, The Cushing reflex: Localization of pressure sensitive areas in brain stem and spinal cord of the cat. Neurologie *19* (1969), 308.

Jennett, W. B., J. O. Rowan, A. M. Harper, J. H. Johnston, I. H. Miller, and V. D. Deshmukh, Perfusion pressure and cerebral blood flow. In: Brain and blood flow, pp. 298—300. Ed. R. W. Ross Russell. London: Pitman. 1971.

Kanzow, E., and D. Dieckhoff, On the location of the vascular resistance in the cerebral circulation. In: Cerebral blood flow, pp. 96—97. Ed. M. Brock, C. Fieschi, D. H. Ingvar, N. A. Lassen, K. Schürmann. Berlin-Heidelberg-New York: Springer. 1969.

— — and H. Holzgraefe, Pressure drop in cerebral arteries at changes of the cerebrovascular resistance. In: Brain and blood flow, pp. 309—312. Ed. R. W. Ross Russell. London: Pitman. 1971.

Kjällquist, Å., N. Lundberg, and V. Ponten, Respiratory and cardiovascular changes during rapid spontaneous variations of ventricular fluid pressure in patients with intracranial hypertension. Acta neurol. Scand. *40* (1964), 291—317.

Klatzo, J., Neuropathological aspects of brain edema. J. Neuropath. exp. Neurol. *26* (1967), 1—14.

Kramer, W., and J. A. Tuynman, Acute intracranial hypertension—an experimental investigation. Brain Res. *6* (1967), 686—705.

Langfitt, T. W., J. D. Weinstein, N. F. Kassell, and F. A. Simeone, Transmission of increased intracranial pressure. I. Within the craniospinal axis. J. Neurosurg. *21* (1964), 989—997.

— — — and L. J. Gagliardi, Transmission of increased intracranial pressure. II. Within the supratentorial space. J. Neurosurg. *21* (1964), 998—1005.

— — — Cerebral blood flow with intracranial hypertension. Neurology (Minneap.) *15* (1965), 761—773.

— — — L. J. Gagliardi, and H. M. Shapiro, Compression of cerebral vessels by intracranial hypertension. I. Dural sinus pressure. Acta neurochir. *15* (1966), 213—222.

Lassen, N. A., Cerebral blood flow and oxygen consumption in man. Physiol. Rev. *39* (1959), 183—238.

Mead, C. O., R. A. Moody, S. Ruamsuke, and S. Mullan, Effect of isovolemic hemodilution on cerebral blood flow following experimental head injury. J. Neurosurg. *32* (1970), 40—50.

Noell, W., und M. Schneider, Zur Hämodynamik der Gehirndurchblutung bei Liquordrucksteigerung. Arch. Psych. Z. Neur. *180* (1948), 713—730.

Petersen, J., and N. Zwetnow, Effects of experimental intracranial hypertension on cerebral blood flow, EEG and blood brain barrier. Electroenceph. clin. Neurophysiol. *24* (1968), 88—89.

Potchen, E. J., B. L. Holman, R. G. Evens, H. Agress, and R. Hill, Some factors which limit the precision in the inert gas washout measurement of regional cerebral blood flow—the "shunt" spike and its significance. In: Brain and blood flow, pp. 94—97. Ed. R. W. Ross Russell. London: Pitman. 1971.

Risberg, J., N. Lundberg, and D. H. Ingvar, Regional cerebral blood volume during acute transient rises of the intracranial pressure (plateau waves). J. Neurosurg. *31* (1969), 303—310.

Rosenblum, W. J., Effects of blood pressure and blood viscosity on fluorescein transit time in the cerebral microcirculation in the mouse. Circ. Res. *27* (1970), 825—833.

Ross Russell, R. W., A micro-angiographic study of experimental cerebral ischaemia and of the effects of blood pressure changes. In: Brain and blood flow, pp. 215—217. Ed. R. W. Ross Russell. London: Pitman. 1971.

Sagawa, K., J. M. Ross, and A. C. Guyton, Quantitation of cerebral ischemic pressor response in dogs. Amer. J. Physiol. *200* (1961), 1164—1168.

Sahar, A., G. M. Hochwald, and J. Ransohoff, Cerebrospinal fluid and cranial sinus pressure. Relationship in normal and hydrocephalic cats. Arch. Neurol. *23* (1970), 413—418.

Schmidt, K., Das Verhalten des Liquordrucks bei der Barbiturat-Lachgas-Inkubationsnarkose und seine Bedeutung für die Narkoseführung bei Hirndruck und Hirnoedem. Der Anaesthesist *12* (1963), 76—81.

Shapiro, H. M., T. W. Langfitt, and J. D. Weinstein, Compression of cerebral vessels by intracranial hypertension. II. Morphological evidence for collapse of vessels. Acta neurochir. *15* (1966), 223—233.

Symon, L., Regional cerebrovascular responses to acute ischaemia in normocapnia and hypercapnia. J. Neurol. Neurosurg. Psychiat. *33* (1970), 756—762.

Zwetnow, N., Å. Kjällquist, and B. K. Siesjö, Cerebral blood flow during intracranial hypertension related to tissue hypoxia and to acidosis in cerebral extracellular fluids. Progr. Brain Res. *30* (1968), 87—92.

Authors' addresses: Dr. F. Matakas, Institut für Neuropathologie im Klinikum Steglitz der Freien Universität Berlin, Hindenburgdamm 30, D-1 Berlin 45, Germany; Dr. M. Leipert, Universitäts-Nervenklinik, Osianderstraße 22, D-74 Tübingen, Germany; J. Franke, Institut für Nuklearmedizin im Klinikum Steglitz der Freien Universität Berlin, Hindenburgdamm 30, D-1 Berlin 45, Germany.