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CEREBROVASCULAR IMPEDANCE MEASUREMENTS WITH US DOPPLER TECHNIQUE

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The Authors present different experimental models performed in the attempt to determine whether the alterations of brain circulation following an increase in the intracranial impedance can be estimated by systolic and diastolic common carotid artery (CCA) velocity Doppler signals recorded at 15-minute intervals until 60 minutes and 10 hours. In model 1 both jugular veins (JV) were ligated and Doppler signals were recorded at 15-minute intervals until 60 minutes. In model 2 ipsilateral external carotid artery (ECA) ligation was added to JV occlusion. In model 3 recording of Doppler signals was performed at 15-minute intervals until 60 minutes and 10 hours in the presence of ipsilateral ECA and bilateral JV occlusion. In model 4 Doppler signals were recorded in the presence of ipsilateral ECA occlusion alone.

Statistically significant results confirming the well-known theoretical relationship between increased encephalic impedance and flow velocity Doppler signals were obtained in model 3. The results demonstrated that a sudden increase in the encephalic impedance can affect both systolic and diastolic flow velocities in afferent vessels.

Later (from 60 minutes to 10 hours), systolic values tend to increase and at 10 hours are always higher than starting values. The diastolic values, however, remain inferior to the starting values, although showing a slight tendency to rise.

The Authors conclude that significative alterations of cerebrovascular impedance can be obtained by clamping both JV. However, these alterations can be recorded on the CCA only if the ipsilateral ECA is occluded, thus eliminating the risk of run-off across it, or if recordings are taken from the internal carotid artery.

1. Introduction

RISBERG and SMITH [12] demonstrated that Doppler carotid velocity determination is highly correlated to hemispheric blood flow measurements by the 133 Xenon inhalation method. A fairly accurate prediction of hemispheric blood flow from Doppler internal carotid and diastolic velocity values is possible in patients without abnormalities in these arterial systems.

For some time now, contributions have been published illustrating the possibility of measuring the variations of cerebrovascular impedance through a valuation in the form of Doppler sound waves which record the blood flow velocity in vascular sections above the cerebral circulation [1, 2, 4-11, 13-16]. There can be different causes for the alterations of impedance in the encephalic flow. Vascular constriction, intravasal obstructions, vasal wall compression with increasing transmural pressure, all contribute to the increase of impedance. This is diminished by arteriovenous malformations, arteriovenous fistula and by anastomosis and pathological shunts in tumoral tissues.

The first-mentioned condition is of great interest to the neurologist and neurosurgeon being more frequently encountered.

2. The purpose of this research

On examination of the available literature, it can be assumed that enough data have been collected to demonstrate the alterations of the blood flow in cerebroafferent vessels compared with cerebrovascular impedance. However, these data refer to two entirely unconnected situations. In fact, they lack mention of phenomena which appear after a sudden alteration of the impedance linked to the Pa02 and PaC02 of the brain and before the modifications of the flow velocity linked with the states of intracranial persistent hypertension reported on by the authors mentioned above.

We planned therefore an experimental model to check the alterations in the blood flow rate in cerebroafferent vessels during massive variations of the cerebrovascular impedance in order to follow their course covering a period of from 15 min. to 10 hours from the start of the increased cerebrovascular impedance.

The impedance increase in the rat is obtained by clamping both JV. The advantages of this model are:

1) an increase in the vasal resistance;

2) an harmonically-diffused increase in the intracranial pressure with no unilateral gradient pressure or different pressure between the various intracranial sectors.

The model thus obtained can be considered similar to the work of CUYPERS *et al.* [3], who blocked the cerebral blood flow by placing an obstacle in the

upper venus cava. They observed that increased venous pressure, which implies increased capillary pressure, causes an enormous swelling of the brain. When the venus cava was blocked the pressure at the Herophili torcular rose from 5.2 to 35.0 mm Hg and the brain tissue pressure rose from 3.8 to 17.6 mm Hg. After a few minutes Herophili torcular pressure began to fall and reached a steady state of 15.5 mm Hg after about 45 min., while the brain tissue pressure, which had risen initially after blocking the venus cava, fell to 4.0 mm Hg. The mean arterial blood pressure abruptly fell 25 ($\pm$20) mm Hg below its initial value, during a long lasting block, however, the mean arterial blood pressure returns to normal in all animals.

In our models, no change in the mean arterial blood pressure was observed. This technique which we created, i.e. clamping JV has been defined as model 1. The Doppler signals were recorded on the common carotid artery (CCA).

In model 2 in addition to the clamping of JV we associated the occlusion of the ipsilateral external carotid artery (ECA) to the CCA on which the recordings were made in order to eliminate the interferences created by the run-off through this vessel because of the technical impossibility of recording a signal at the internal carotid artery (ICA) level in the rat.

Model 4 with the ipsilateral ECA occlusion without JV clamping was planned to check if we are only measuring changes in CCA hemodynamics secondary to the removal of the ECA from the vascular system, rather than a change in the cerebral hemispheric flow due to JV ligation.

3. Materials and methods

The experimental series consisted of 80 white Wistar rats weighing 300 to 400 g, divided in four groups.

Model 1 (20 rats)

The animals were anesthetized with pentobarbital i.p. (30 mg/kg). The left CCA and both JV were exposed through a midline cervical incision. Then, CCA flow velocity signals were recorded by using a 8 MHz directional Doppler CW flowmeter (Angiodop 481, DMS). The distance between the tip of the ultrasonic transducer and the vessel (about 5 mm) was filled by a contact medium for ultrasonic transmission (Aquasonic 100, Parker Laboratories Inc.).

Fast Fourier Transform (FFT) real-time sound spectral analysis (Angioscan, Unigon Industries, Mt Vernon, NY) was also performed. Systolic and diastolic frequency values were obtained by recording sound spectral display in which switching of the cursor up or down allowed the frequency position of the cursor line to be read in Hz at the bottom of the screen.

Immediately after recording Doppler signals, both JV were ligated. Subsequently, CCA Doppler signals recording with spectrum analysis was performed at 15, 30, 45, and 60 min. from the time of initial occlusion.

Model 2 (40 rats)

In this group left ECA ligation was added to bilateral JV occlusion.

Model 3 (10 rats)

In this model the same circulation modifications were provoked as in model 2, but the recording of the systolic and diastolic Doppler signals was made not only at 15, 30, 45, 60 min., but also at 10 hours after the occlusion of the vessels.

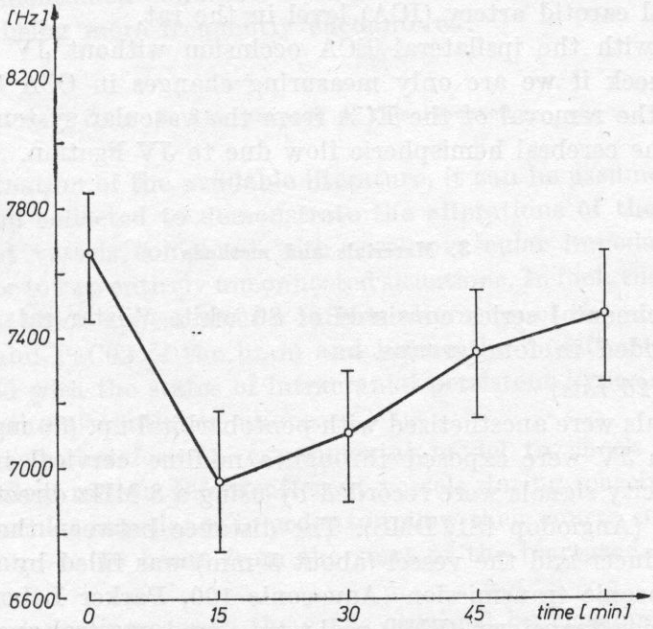
Model 4 (10 rats)

In this group only ECA was clamped and the systolic and diastolic values measured every 15 min. up to 60 min.

4. Results

Model 1 (20 rats)

The mean systolic peak values and the mean diastolic peak values show an inconsistent response to clamping both JV. In fact, 50 % of rats show a sig-



M:	7654.5	6969.5	7104.0	7353.0	7481.0
SD:	1279.7	1396.3	1270.6	1246.1	1262.5
SE:	204.9	223.6	203.5	199.5	204.8
SD/M:	0.1672	0.2003	0.1789	0.1695	0.1688

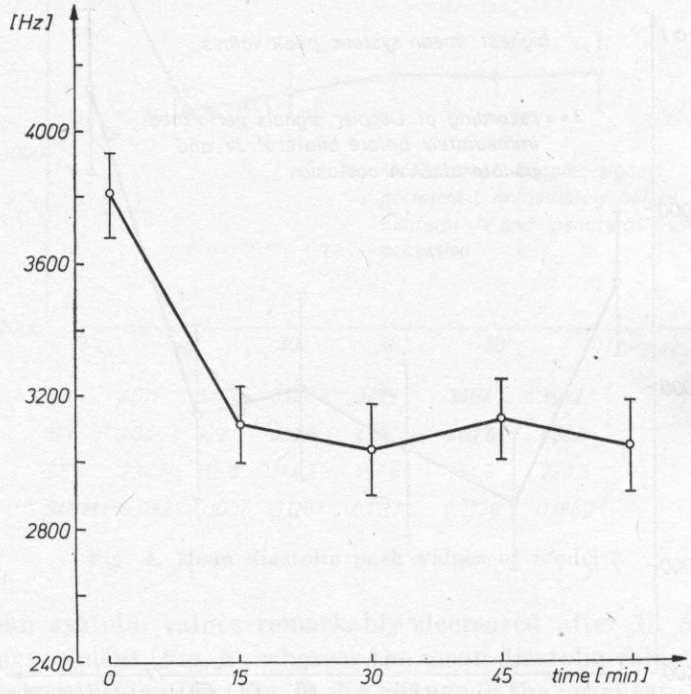
Fig. 1. Mean systolic peak values of model 2. In all figures: Ordinate-values of frequencies [Hz], abscissae-time of the experiment [minutes], *M* — mean values, *SD* — standard deviation, *SE* — standard error

nificant decrease of the mean systolic peak values 15 min. after JV occlusion; the other 50 % of rats show a significant increase in the mean systolic peak values 15 min. after JV occlusion. At 60 min. peak values were always higher than the starting ones. The diastolic flow pattern parallels the systolic one.

In this model statistical analysis gave significant results (at 0.05 level). Then, we cannot reject the "null hypothesis" and we concluded that there is no significant difference between the series of data.

Model 2 (40 rats)

The mean systolic peak values and the mean diastolic peak values allowed us to appreciate a difference in behaviour following the occlusion of JV and ECA. 74 % of the mean systolic peak values show a significant decrease 15 min.



M:	3812	3120	3045	3136	3048.42
SD:	540.26	518.46	558.79	583.04	603.33
SE:	123.95	118.94	128.19	133.76	142.21
SD/M:	0.1417	0.1662	0.1835	0.1859	0.1979

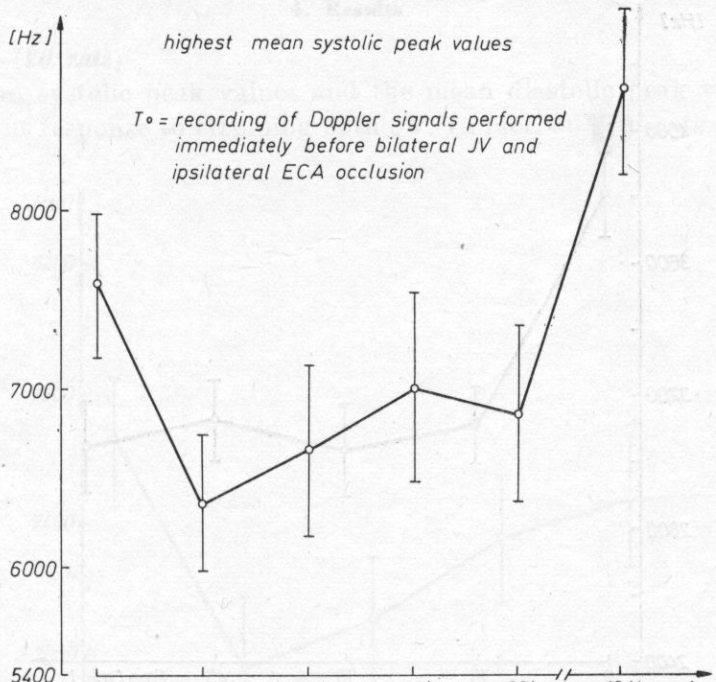
Fig. 2. Mean diastolic peak values of model 2

after JV and ECA clamping. The diastolic mean peak values also decrease at 15 min. in 89 % of cases. At 60 min. the mean systolic peak values were lower than the starting ones in 59 % and the diastolic mean peak values in 89 % (Figs. 1-2).

In this model the sign test was significant ($p < 0.01$) after 15 min. Then, we can reject the "null hypothesis" and may conclude that it is unlikely that the results are purely fortuitous.

The correlation coefficient r used to compare the data of the mean systolic peak values after 15 min. and 60 min. was computed to be 0.60 and differs significantly from zero at 0.001 level. Therefore, the two series of data seem to be positively correlated.

The sign test of the diastolic mean peak values is also significant after 15 min. and 60 min. for $p < 0.001$. The correlation coefficient $r = 0.82$ computed between the data after 15 min. and 60 min. differs significantly from zero at 0.001 level. This situation denotes a systematic stabilisation in the effects.



M:	7591	6362	6675	7022	6888	8720
SD:	1192.9	1096.5	1487.6	1650.5	1493.6	1406.2
SE:	397.6	387.6	495.8	550.2	497.9	468.7
SD/M:	0.0523	0.1723	0.0742	0.2350	0.2168	0.1612

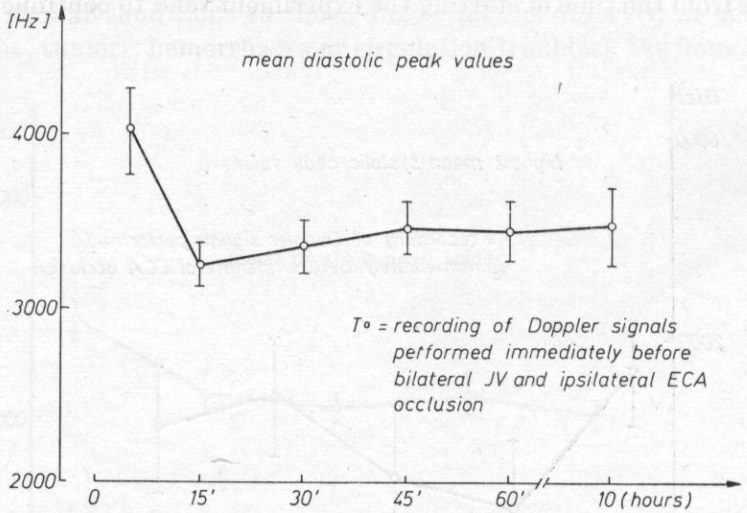
Fig. 3. Mean systolic peak values of model 3

Model 3 (10 rats)

In this group the alterations of systolic values observed in the experiment (JV and ECA occlusion = model 2) were similar to those observed in the group of 40 rats treated in the same way. It is interesting to note that at the 10th

hour of ECA and JV occlusion the systolic values were remarkably higher (Fig. 3) compared with the starting values and with those recorded after one hour from the beginning of the experiment. The diastolic values, however, remain inferior to the starting values, although showing a slight tendency to rise (Fig. 4).

Model 4 (10 rats)



M:	4017	3247	3360	3475	3457	3502
SD:	704	327	432.6	458	462.6	661.8
SE:	234.6	115.6	144.2	152.6	154.2	220.6
SD/M:	0.1752	0.1007	0.1287	0.1317	0.1338	0.1889

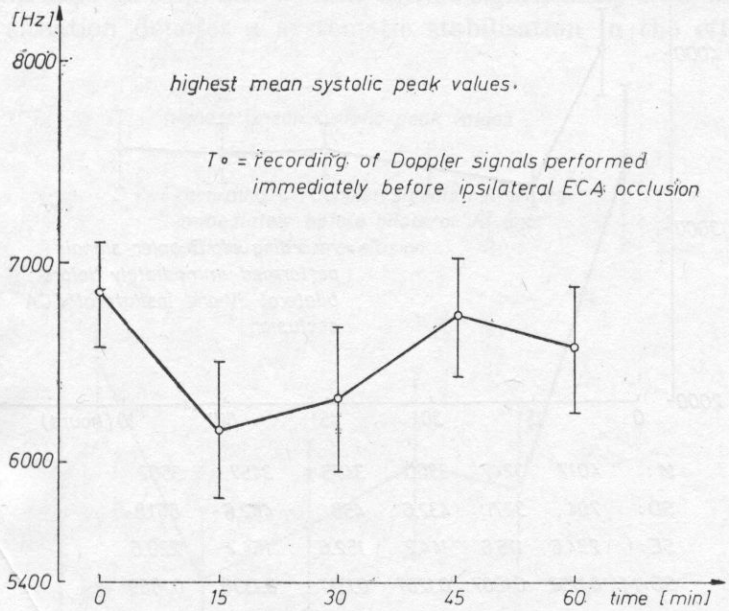
Fig. 4. Mean diastolic peak values of model 3

The mean systolic values remarkably decreased after 15 min. from the start of the experiment (Fig. 5), whereas the mean diastolic values after 15 min. did not decrease considerably (Fig. 6). No change in the heart rate was observed. The mean arterial blood pressure did not change. The intracranial pressure was not recorded to avoid trauma to the experimental model. However, brain swelling was constantly observed at the end of the experiments with JV ligation.

5. Discussion

Our experiments have pointed out an alteration of the association rate/cerebrovascular impedance linked to the time in which the examination is made with respect to the beginning of the increased cerebrovascular impedance condition.

A clear alteration is noted 15 min. after the beginning of the experiment, when the occlusion of JV and ipsilateral ECA of the CCA, from which the Doppler signals are taken, suddenly and in great measure abolish most of the draining vessels of the CCA (venous through JV and arterial through the ECA). At this moment both the systolic and diastolic values alter. They decrease considerably. Following this first phenomenon, a progressive increase in the systolic values is registered, which at 60 min. regain their original values and at 10 hours from the time of starting the experiment tend to continue increasing.



M:	6854	6160	6336	6744	6496
SD:	808.3	1075.9	1134.3	968.8	1038.1
SE:	255.6	340.2	358.7	306.3	328.2
SD/M:	0.1179	0.1746	0.1790	0.1436	0.1598

Fig. 5. Mean systolic peak values of model 4

The diastolic values, instead, behave differently at 60 min. Their values never reach the initial ones even after 10 hours.

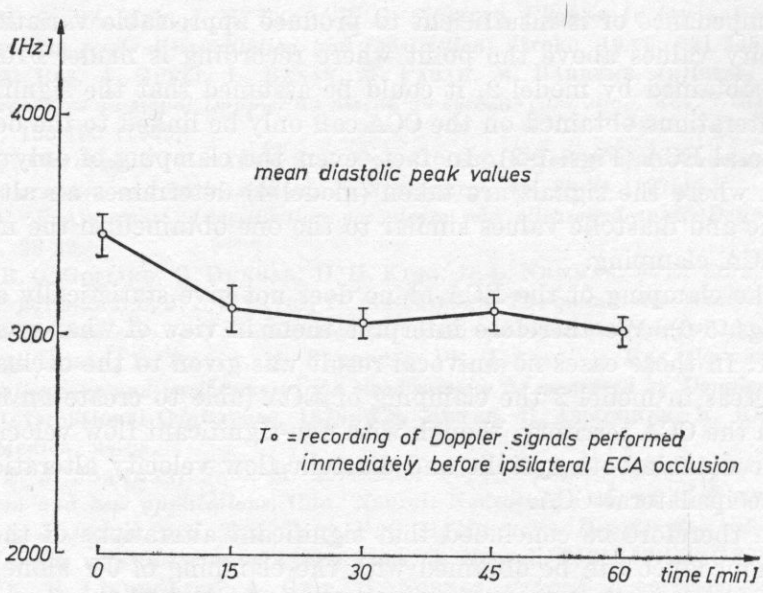
It can therefore be confirmed that in cerebroafferent vessels, when the cerebrovascular impedance increases rapidly, there are immediate alterations in both the systolic and diastolic values, but the reciprocal behaviour is very different.

Our findings, therefore, answer the problem facing us when we planned our experiment. From an examination of the flow velocity values, we can

complete the pattern of the behaviour of the blood flow rate in cerebroafferent vessels compared with the cerebrovascular impedance alterations.

From BEASLEY *et al.* [1] we learn that arterial constriction due to an increase of Pa02 causes a decrease in the systolic and diastolic values of the Doppler signals.

From this acute and transitory alteration of the cerebrovascular impedance, as our model illustrates, we pass on to an equally acute but lasting alteration that creates similar conditions to those due to lesions observed in human pathology (edema, tumors, hemorrhages or circulation troubles). We have been able



M:	3456	3112	3072	3136	3048
SD:	266.1	316.5	220.5	303.5	214.8
SE:	84.1	100.1	69.7	96	67.9
SD/M:	0.0769	0.1017	0.0717	0.0967	0.0704

Fig. 6. Mean diastolic peak values of model 4

to follow the evolution of the alterations of the blood rate in the cerebroafferent vessels during the period immediately following the start of the increase of cerebrovascular impedance. From this acute period typical alterations of the blood flow are created which precede and rapidly become similar within 10 hours to those observed by JONKMAN *et al.* [8] and STEIGER [14]: an increase in the systolic values and a decrease in the diastolic ones in cases of expansive intracranial lesions which are the cause of stable increased intracranial pressure. The results observed by LINDEGAARD *et al.* [9] (very high systolic values and reverse flow) in cases of the brain tamponade complete the range of the blood

flow velocity alterations of cerebroafferent vessels in time and for different grades of increase in the cerebrovascular impedance. We wish also to discuss the problem of where the Doppler signal reading should be taken from. We believe that the most reliable signals are those taken from the ICA. However, because of lack of space, it is impossible to record signals from the ICA of the rat. They were all therefore taken from the CCA. With regard to this, we should discuss the role the ECA and its clamping play in the development of the phenomena we reported and on the measures we effected.

According to the results obtained in model 1, it could be presumed that the clamping of the JV alone is unable to create an alteration of the cerebrovascular impedance or is insufficient to produce appreciable variations in the flow velocity values above the point where recording is made. From the information obtained by model 2, it could be assumed that the significant flow velocity alterations obtained on the CCA can only be linked to the occlusion of the ipsilateral ECA (Figs. 1-2). In fact, even the clamping of only the ipsilateral ECA where the signals are taken (model 4) determines an alteration in the systolic and diastolic values similar to the one obtained in the model with JV and ECA clamping.

But the clamping of the ECA alone does not give statistically significant results (Figs. 5-6). We therefore interpret them in view of what was observed in model 1. In those cases no univocal result was given to the occlusion of JV alone, whereas in model 2 the clamping of ECA (able to create an impedance increase in the CCA territory, though with non-significant flow velocity values) made more notable both systolic and diastolic flow velocity alterations observed on the ipsilateral CCA.

It can therefore be concluded that significant alterations of the cerebrovascular impedance can be obtained with the clamping of JV alone, but that these alterations can be recorded on the CCA only, if ECA territory is closed, whereby eliminating the risk of run-off across it or if, as pointed out by other authors [1-2, 12, 16], readings are taken from the ICA.

6. Conclusions

From our experiment we have been able to obtain the following information about the reliability of ultrasound Doppler examination in cases of increased cerebrovascular impedance:

1) With the Doppler examination of the cerebroafferent blood flow rate carried out on the ICA or on the CCA with the exclusion of the ipsilateral ECA, significant systolic and diastolic alteration values can be recorded.

2) The diastolic values are highly significant, due to their notably persistent decrease observed from the moment the impedance alteration started and up to 10 hours.

3) The systolic values only decreased notably during the first 15-30 min.

from the impedance increase start. During the interval between 1 hour and 10 hours from the beginning of the experiment the values rose significantly.

4) Remarkable evidence of altered impedance can be obtained within the first hour only if the basic or normal data are known. Only the progressive separating of the systolic values from the diastolic ones during the following hours could let us know without doubt, possibly by employing pulsation indexes, of the existence of an abnormal increase in the impedance.

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