MORPHOLOGY OF THE VASCULAR PRESSURE RECEPTORS IN DOGS AFTER CLINICAL DEATH

E. B. Khaisman and T. N. Grozdova

B. I. Lavrent'ev Laboratory of Neurohistology (Head – Dr. Biol. Sci. E. K. Plechkova), Institute of Normal and Pathological Physiology (Dir. – Active Member AMN SSSR V. V. Parin), AMN SSSR, and Laboratory of Experimental Physiology of Resuscitation (Head – Prof. V. A. Negovskii), AMN SSSR, Moscow
(Presented by Active Member AMN SSSR V. V. Parin)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 51, No. 3, pp. 110-116, March, 1961
Original article submitted June 11, 1960

During the restoration of the functions of the cardiovascular system at the time of clinical death by means of the centripetal infusion of blood into an artery under pressure, besides the restoration of the coronary circulation, an important role belongs to the reactions of the pressure receptors developing in response to excitation of the vascular reflexogenic zones [4, 7, 8, 12]. It has been shown by special investigations [10] that stimulation of the angioreceptors by a reflex mechanism increases the vascular tone and creates in the heart a state of "preparedness" for contraction. Depression of these angioreceptors by injection of novocain into the arterial blood stream during clinical death prevents the effective restoration of the activity of the heart by the subsequent intraarterial injection of blood.

In view of the importance of the vascular reflexogenic zones in the restoration of the functions of the cardiovascular system during the treatment of terminal states, it appeared to be of great theoretical and practical interest to investigate the structure of the nervous apparatus of these zones in dogs after clinical death.

EXPERIMENTAL METHOD

Experiments were carried out on 19 healthy adult dogs of both sexes. In the period of preparation for the experiment the animals received a subcutaneous injection of pantopon in a dose of 8 mg/kg body weight, and 40-50 minutes later the femoral vessels were dissected under local infiltrational anesthesia (20 ml of a 0.5% solution of novocain). A state of clinical death was then induced in the animals by allowing blood to flow freely from the femoral artery. Restoration of the vital functions of the animal was undertaken five minutes after clinical death by means of a comprehensive method: artificial respiration by means of an apparatus to pump air into the lungs, and the centripetal intraarterial infusion of blood with adrenalin. Should fibrillation of the cardiac muscle develop, condenser discharges were applied by L. N. Gurvich's method to overcome this condition.

Before bleeding was carried out, the dogs received an intravenous injection of heparin as blood stabilizer. During the experiments the arterial pressure and respiration were recorded on the kymograph. Observations on the animal's behavior and general condition were made throughout the experiment. At various periods of the recovery period (from a few hours to a few weeks) the animals were sacrificed by electrocution.

The material for neurohistological investigation was: a) the depressor zone of the arch of the aorta (aortis sinus); b) the carotid sinus; c) the areas near the orifice of the pulmonary veins and vena cava.

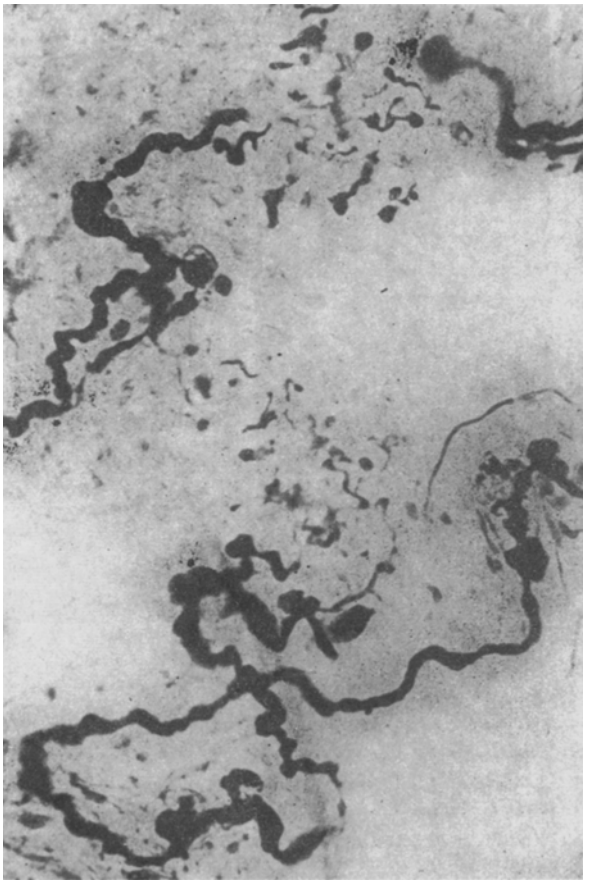

Fig. 1. Afferent nerve fibers and receptors from the depressor zone of the arch of the aorta. Experiment No. 5. Impregnation by Campos's method. Magnification 400×.

The staining methods used in the work were Campos's silver impregnation method for nerve cells and Spielmeyer's method for myelin.

We consider it necessary to preface the account of the results of this investigation with a few details regarding the morphology of the sensory apparatus of the vascular reflexogenic zones in normal physiological conditions. We have devoted a special investigation [13] to this problem, conducted on 70 healthy, sexually mature animals including 25 dogs. In all the animals studied it was found that in the homonymous reflexogenic zones the overwhelming majority of afferent nervous structures, consisting of thick myelinated nerve fibers and their endings in the form of compact tufts, show signs of reactive changes and degeneration. Hyperargentophilia and spiral convolution of the nerve fibers, foci of demyelination and massive flowing of neuroplasm, excessive collateral growth of axis cylinders and destruction of their neurofibrillary framework, "mummification" of nerve fibers and disintegration into fragments, hypertrophy or atrophy of the terminal arborizations – all these to some degree are characteristic features of this category of vascular pressure receptors.

Thus in ordinary conditions of existence these sensory nerve formations are distinguished by exceptionally wide morphological variability, beginning with the phenomenon of irritation and ending with far advanced stages of dystrophy.

EXPERIMENTAL RESULTS

In evaluating the severity of the anoxia in the investigation of terminal states consideration must be paid not only to the duration of clinical death, but also to the duration of the actual process of dying from blood loss, for the fact must not be ignored that the electrical activity of the brain is extinguished much sooner than the

Experiments on the Resuscitation of Dogs After Clinical

recovery of functions from onset of resuscitation			Time of sacrifice after onset of resuscitation
of respiration	of corneal reflex	of central nervous system	
7 min 22 sec	18 min 10 sec	Not investigated	1 hr
11 min	19 " 40 "	" "	2 hr
4 min 17 sec	13 " 5 "	" "	3 "
3 " 18 "	12 "	Subcortical functions	1 day
5 min 35 "	20 "	To the level of the midbrain	1 "
3 min 17 "	9 " 55 sec	Complete after 2 days	2 days
5 min 37 "	19 "	The same	2 "
4 min 5 "	14 " 35 sec		3 "
3 " 52 sec	17 " 30 "	" "	3 "
2 " 40 sec	16 " 45 "	" "	3 "
4 " 25 "	18 " 15 "	Subcortical functions	3 "
7 min 25 "	11 " 5 "	Complete after 2 days	5 "
4 min 33 sec	10 " 45 "	" " 2 "	5 "
5 min 50 sec	14 "	Incomplete after 5 days	6 "
4 min 30 "	12 " 13 sec	Complete after 2 days	7 "
3 " 28 "	13 "	" " 1/2 "	7 "
3 " 35 "	14 " 10 sec	" " 1/2 "	7 "
2 " 15 "	14 " 50 "	Subcortical function after 5 days	11 "
5 min 40 "	15 " 35 "	Complete after 24 hours	1 month

onset of agony. In the experiments to be described the duration of the process of dying varied in the animals from 8.5 to 20 minutes, and in 13 of the 19 animals it was greater than 12.5 minutes, i.e., it was above the mean duration. It must be remembered in this connection that from 30 to 40% of the time of dying was accounted for by agony.

Five minutes after the onset of clinical death and in the process of resuscitation the cardiac activity was restored in 16 of 19 experiments after 25-50 seconds, and in three animals, as a result of the development of fibrillation, considerably later – after 1.25-2 minutes (see table). Spontaneous respiration was restored relatively early (2-3.5 minutes after the beginning of resuscitation) in only six experiments. In ten experiments the periods of restoration of respiration varied from four to six minutes. In three experiments the times were later (7-11 minutes). The corneal reflexes appeared at the 10th-20th minute of the recovery period. The relatively complete restoration of the function of the central nervous system took place within the first 48 hours in 11 of the 19 dogs. In three dogs the recovery of the central nervous system was limited to subcortical, in two to purely brainstem functions. In the remaining three dogs no recovery of the central nervous system was studied, for in accordance with the conditions of the experiment they were sacrificed during the first few hours after resuscitation.

Thus depending on the general severity of the anoxia, on its duration and, evidently, on the individual characteristics of the experimental animals, the times of restoration of the vital functions varied within very considerable limits.

Moving on to the morphological character of the vascular pressure receptors, it must be pointed out that in all the experimental dogs the results of the neurohistological investigation were similar. We can therefore describe all the results together without consideration of individual groups.

In both the aortic and carotid sinuses and in the region of the orifices of the pulmonary veins and venae cavae of the experimental dogs we observed the same signs of reactive changes and destruction of the medul-

Death from Blood Loss for a Period of Five Minutes

Dog No.	Weight (in kg) and sex	Duration of process of dying	Duration of clinical death	Recovery time of cardiac reflex
1	10,1♀	13 min 30 sec	5 min	32 sec
2	10,8 ♂	9 " 30 "	5 " 5 sec	2 min 7 sec of respiration
3	12♂	7 " 47 "	5 " 3 sec	40 sec
4	15,2 ♂	12 " 47 "	4 min 58 sec	27 "
5	10,5 ♀	13 " 33 sec	5 min 2 sec	29 "
6	15♂	8 " 29 sec	5 " 1 sec	45 "
7	11♂	8 " 45 "	4 min 55 sec	25 "
8	15♂	8 " 23 sec	5 min 2 "	45 "
9	19♂	12 " 55 sec	5 " 10 sec	40 "
10	25,5♂	12 " 55 "	5 " 5 "	45 "
11	20♀	15 "	5 " 5 sec	30 "
12	11,7 ♀	13 " 40 sec	5 "	30 "
13	11,5 ♀	10 " 50 »	4 min 55 sec	24 sec
14	11 ♂	14 " 3 sec	5 min 2 sec	1 min 34 sec or respiration
15	12 ♂	12 " 55 sec	5 " 5 sec	30 sec
16	11,2 ♂	20 " 50 "	5 "	45 "
17	13,8 ♂	15 " 25 "	5 " 5 sec	1 min 15 sec of respiration
18	20,2 ♂	12 " 49 "	5 " 2 sec	30 sec
19	9,5 ♂	16 " 45 "	5 "	50 "

lated nerve fibers of large caliber and of their receptor apparatuses as characterize these sensory nerve structures in healthy (control) animals. We invariably encountered this same phenomenon of increased affinity for silver salts, the deformation of nerve fibers, the floods of neuroplasm, foci of demyelination, and the partial or complete fragmentation of axis cylinders during microscopic examination of preparations from the various pressure receptor zones of the experimental dogs. As also in the normal animals, all these phenomena were most conspicuous in the preterminal divisions of the nerve conductors, which in most cases were grossly thickened and hypertrophied.

In the receptor apparatuses we could now observe the phenomena of hyperplasia and homogenization of the terminal loops, end-plates and reticula, destruction of the neurofibrillary framework of the receptor with disintegration of the termianl components, and so on, with which we were already familiar from the study of the normal material (Figs. 1 and 2). We could find no other morphological signs which might have supplemented the general picture of the afferent innervation of the vascular reflexogenic zones in normal conditions, nor were there any quantitative changes. We were also unable to establish any relationship between the character and amplitude of the structural modifications of the vascular pressure receptors on the one hand, and the severity of the recovery period and the duration of survival of the animal after resuscitation in each individual case on the other hand.

It may be concluded from the foregoing account that the vascular pressure receptors are either insensitive or highly resistant to the action of such extraordinary factors as clinical death and the anoxia which inevitably accompanies it, and that they maintain their typical structure.

The results described, and also the conclusions derived from them, in our view are adequately confirmed by the physiological researches of Negovskii and his co-workers [4, 5, 6]. These investigations show that in a state of clinical death lasting 5-8 minutes in ordinary temperature conditions, or up to one hour in hypothermia, the vascular receptors maintain their excitability. It is this fact which makes it possible to restore the cardiac activitv and the vascular tone permanently and effectively.

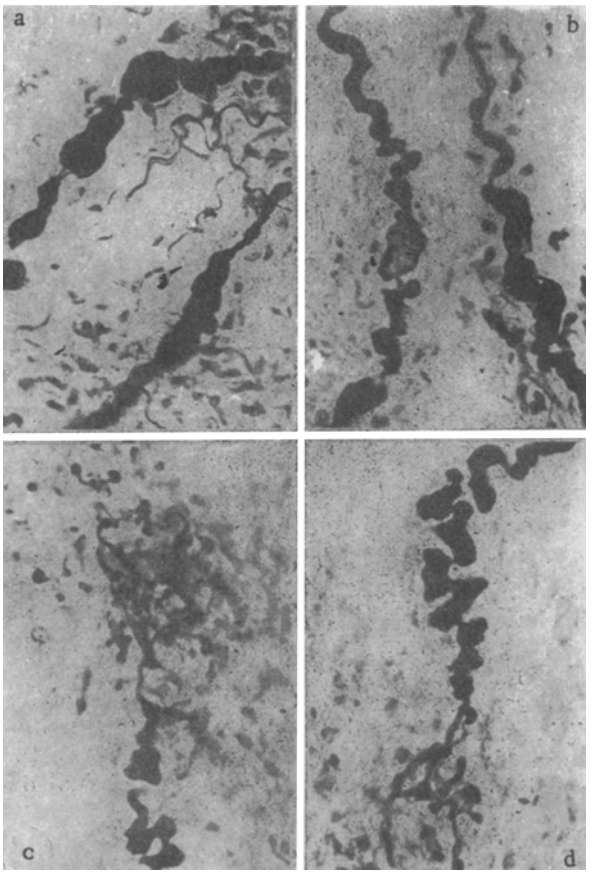

Fig. 2. Preterminal and terminal divisions of afferent nerve conductors from the carotid sinus (a), the depressor zone of the arch of the aorta (b) and the region near the orifice of the posterior vena cava (c) and the pulmonary vein (d). Experiment No. 9. Impregnation by Campos's method. Magnification 400×.

At the same time it must be pointed out that the results of our investigation are in disagreement with reports in the literature [1, 2 and others], according to which the afferent nervous apparatuses of the vascular reflexogenic zones and, in particular, the receptors of the regions near the orifices of the pulmonary veins and the venae cavae are very sensitive to the action of anoxia, and rapidly become involved in the pathological process when the body is in oxygen debt. Analysis of the relevant literature, however, shows that this disagreement may be explained not by differences in the actual results obtained, but by their interpretation, which in turn may be due to different notions of the criteria of "normal and "pathological" conditions for the vascular pressure receptors. When assessing their structural changes many neuromorphologists take as their starting point what Plechkova [9] calls their "hypothetical mean norm." In accordance with this"norm," the nerve conductors and receptors must have no significant signs of irritation, and still less of destruction and degeneration. The appearance of such signs is usually regarded as the result of interaction between the body and an extraordinary (pathogenic) stimulus. Such an interpretation of the structure of the vascular pressure receptors cannot be regarded as sound, for in normal physiological conditions these sensory nervous apparatuses characteristically show different forms of reactive and degenerative changes. This is shown not merely by our factual material, but also by the observations of other workers [3, 11, 14]. The significance of the problem of the criteria of "normal" and "pathological" for the vascular pressure receptors is not confined to the limits of the present investigations. On its solution depends not only the correct assessment of anoxia as a factor in the stimulation of the pressure receptors, but also the understanding of the role and the place of the various peripheral afferent apparatuses in the reactions of the body to a variety of adequate and inadequate influences.

SUMMARY

The author studied the morphology of the pressure receptors in the arch of aorta sinus, the orifices of the pulomonary veins, venae cavae in 19 dogs at various intervals (from several hours to 1 month) after a 5-minute clinical death. Silver impregnation of the nerve elements according to Campos and myelin staining after Spielmeier was used in this work. Neurohistological examination yielded the following results. The signs of reactive condition and destruction in the large myelinated nerve fibers and their receptor apparatus noted in the experimental animals in the mentioned vascular reflexogenic zones were the same as in the healthy (control) animals. There were no other morphological signs (or changes) in addition to the general picture of afferent innervation of the vascular reflexogenic zones under normal conditions. The data obtained lead to the conclusion that vascular pressure receptors are either insensitive or very resistant (preserving their structure) to the action of such extreme factors as clinical death and concomitant hypoxia.

LITERATURE CITED

1. B. A. Dolgo-Saburov, Innervation of the Veins [in Russian] (Leningrad, 1958).
2. V. V. Kupriyanov, The Experimental Morphology of the Vascular Receptors [in Russian] (Leningrad, 1955).
3. V. P. Kurkovskii, Doklady Akad. Nauk SSSR 113, 5, 1147 (1957).
4. V. A. Negovskii, The Pathophysiology and Therapy of Agony and Clinical Death [in Russian] (Moscow, 1954).
5. V. A. Negovskii and V. I. Soboleva, Arkh. Patol. 6, 58 (1956).
6. V. A. Negovskii et al., Byull. Éksp. Biol., i Med. 48, 11, 30 (1959).
7. L. S. Persianinov, Intraarterial Blood Transfusion in the Practice of Obstetrics and Gynecology [in Russian] (Minsk, 1955).
8. I. R. Petrov, in: Current Problems of Blood Transfusion [in Russian] (Leningrad, 1952) p. 22.
9. E. K. Plechkova, Vestnik Akad. Med. Nauk SSSR 4, 52 (1959).
10. E. M. Smirenskaya, Transactions of a Conference on the Pathophysiology and Therapy of Terminal States [in Russian] (Moscow, 1954) p. 38.
11. N. G. Smirnova, in: Morphology of the Sensory Innervation of the Internal Organs [in Russian] (Moscow, 1948) p. 106.
12. I. I. Fedorov, in: Intraarterial Transfusion of Blood and Drugs [in Russian] (Kiev, 1954) p. 7.
13. E. B. Khaisman, Abstracts of Proceedings of the Sixth All-Union Congress of Morphologists [in Russian] (Khar'kov, 1958) p. 432.
14. A. Abraham, Acta Biol. (Szeged, 1955) Nos. 1-4.

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
