The Acute Phase of Neurogenic Hypertension in the Rat

In the dog and rabbit, the onset of neurogenic hypertension is always preceeded by a latent period[1] that was not evident in our previous study in the rat[2]. In the present experiments, special attention was given to the initial changes in arterial pressure after sino-aortic denervation in this species. Furthermore, the possibility that denervation of the aortic area produces a different effect from the sinus area was also studied because such difference has been observed in chronic experiments[2].

Acute neurogenic hypertension. In rats under ether anesthesia, bilateral sino-aortic denervation was performed in a one-stage operation lasting 15–30 min, with a technique described in detail elsewhere[2]. The direct blood pressure in the aorta was recorded in the conscious unrestrained animals with the technique of chronically implanted cannulae described by WEEKS and JONES[3]. Immediately following recuperation from anesthesia, the blood pressure attained its maximum values, with no latent period for the development of the neurogenic hypertension. This is illustrated in Figure 1, which shows that 30 min after the denervation the rat was hypertensive and that its heart rate had dropped from the control value of 485 beats/min to 395 beats/min. The opposite pressure and heart rate changes are another indication that tachycardia and increased cardiac output are not the major determinants of neurogenic hypertension in the rat, as we have previously observed in chronic experiments[4]. The hypertensive levels exhibited by the rats in the first few hours remained quite constant in daily observations performed for up to 6 days, as is shown in Figure 2. Hence, we have set the 5th hour as the standard time for evaluating the severity of the hypertension induced by sino-aortic denervation.

Isolated denervation of aortic and sinus areas. 2 groups of 11 rats each were subjected to bilateral denervation, either of the aortic or the carotid baroreceptors. In our laboratory, the average value of the direct mean arterial pressure in the unanesthetized rat is 117 ± 11 mm Hg with 139 mm Hg ($\bar{x}$ + 2 S.D.) as the upper limit of normality[2]. As is shown in the Table, only 3 out of the 11 rats with denervated carotid baroreceptors presented pressures higher than 139 mm Hg, whereas all the 11 animals submitted to aortic denervation became hypertensive. The mean heart rate of these animals was 457 ± 5 ($x \pm$ S.E.) beats/min while for those with sinus denervation it was 499 ± 6 beats/min; this difference is statistically significant using the test of Wilcoxon. These results show that isolated denervation of the aortic areas produces a greater increase in pressure, notwithstanding the lowered heart rate. This again emphasizes the role played by the peripheral resistance as the most important single cause of neurogenic hypertension. It should be remembered that in the technique used for radical denervation of the aortic baroreceptors the cervical sympathetic trunk was cut. This could contribute to lowering the heart rate of these rats, because heart rate in these species markedly depends on a higher sympathetic tonus[5]. It is generally accepted that in the dog the sinus and aortic areas are equally important for the reflex regulation of blood pressure[1]. However, in experiments in which pressure changes were produced in the isolated aortic arch of the dog, LEVY et al.[6] observed that considerably higher pressure levels were necessary to obtain maximum cardiac and respiratory responses than when the carotid sinus was perfused. More recently, GLICK and COVELL[7] have shown that the effects on the heart rate were the same or, sometimes, the baro-

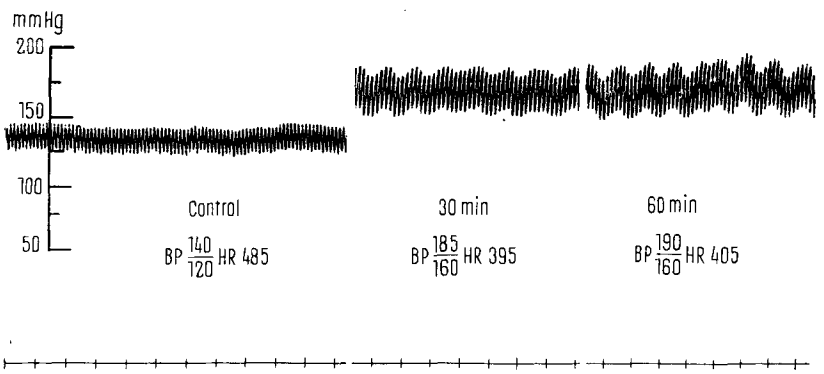

Fig. 1. Early phase of acute neurogenic hypertension. Blood pressure (BP) and heart rate (HR, beats/min) of a 250 g conscious male rat with a cannula chronically implanted in the aorta; effects of bilateral sino-aortic denervation measured at 30 and 60 min. Time markings: 1 sec intervals.

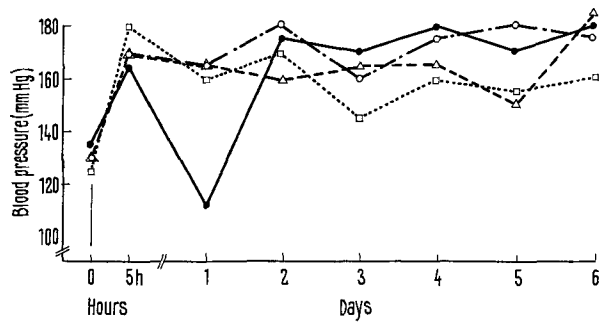

Fig. 2. Subsequent progression of neurogenic hypertension. Individual values of mean blood pressure measured in unanesthetized rats with implanted aortic cannulae in a 6-day period following bilateral sino-aortic denervation.

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receptors of the aortic areas predominated. The results herein presented indicate that in the rat the inhibitory effect on the sympathetic tonus exerted by the aortic baroreceptors is much more important than that of the carotid baroreceptors[8,9].

Individual values of the direct mean arterial blood pressure and heart rate 5 h after isolated denervation of the carotid or the aortic baroreceptors

	Carotid baroreceptors		Aortic baroreceptors	
	Blood pressure (mm Hg)	Heart rate (beats/min)	Blood pressure (mm Hg)	Heart rate (beats/min)
	112	530	147	430
	115	520	150	460
	118	500	150	480
	129	470	150	410
	131	480	153	450
	132	490	155	430
	135	510	160	490
	137	480	160	510
	142	490	162	460
	143	500	167	510
	154	520	177	400
(Means ± S.E.)	(132 ± 4)	(499 ± 6)	(157 ± 6)	(457 ± 5)

Resumen. Los resultados presentados demuestran que en la rata no existe período latente para el desarrollo de hipertensión neurogénica, ya que inmediatamente después de la sección bilateral de los nervios depresores aórticos y carotídeos la hipertensión arterial alcanza sus valores máximos. Por otra parte, se observó que, aún en esa fase aguda, la destrucción aislada de los presoreceptores aórticos o carotídeos tiene efecto diferente, siendo la denervación aórtica más efectiva em provacar hipertensión. Esos resultados sugieren que en la expecie rata los presoreceptores aórticos son normalmente más importantes para mantener una inhibición tónica sobre el sistema simpático.

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[9] The work was performed with the technical assistance of Mr. E. D. MOREIRA.

Fine Structural Alterations of Presynaptic Endings in the Superior Cervical Ganglion of the Cat after Exhausting Preganglionic Stimulation

For the understanding of the synaptic transmission, it seems necessary to clear up the functional role of the main structural elements of the pre- and post-synaptic terminals. DE ROBERTIS et al.[1,2], HUBBARD and KWANBUNBUMPEN[3] and DYACHKOWA[4] observed morphological changes at interneuronal synapses and neuromuscular junction, respectively, which could be taken in parallel with physiological changes in transmission.

These results support the hypothesis that synaptic vesicles play a certain role in the transmission; however, in most parts of the experiments quoted above no measures were taken to have a direct control over the actual state of the transmission, i.e. no parallel physiological recording was undertaken.

In this respect the superior cervical ganglion of the cat seemed to be more promising because it allows a direct physiological control of the actual level of transmission. Now we publish the first results of such a complex approach trying to correlate the submicroscopic morphology of the synapse with the physiological findings.

Cats of both sexes, weighing 1.5–2 kg, were anaesthetized with Nembutal i.p. (40 mg/kg). The superior cervical ganglia were exposed on both sides with the vessels supplying them. Perfusion experiments were performed using the method of KIBJAKOV[5] as modified by PERRY and PATON[6]. In other experiments the natural blood supply was preserved. Preganglionic stimulation was made with rectangular pulses of the following parameters: frequency 10–20/sec; duration 1 msec; amplitude 6–8 V. The contractions of the nictitating membrane and action potentials were recorded. The duration of stimulation ranged from 15 min to 2 h. After the stimulation period, the ganglia were subjected to routine electron-microscopic examinations.

In the ganglia with natural blood supply, after 90 min of stimulation no sign of fatigue occurred. The action potential shows maximum transmission and the ultrastructure of ganglionic synapses are similar to those in resting state[7], there is no change in number of synaptic vesicles, although more irregular form can be seen (Figure 1).

Perfusion of 60 min with Locke solution did not alter the picture appreciably. The excitability of the ganglion also remained normal. Preganglionic stimulation with the parameters mentioned above, however, led to a rapid exhaustion and after 15 min of stimulation a complete failure of transmission ensued. The electron-microscopic picture of such ganglia (Figure 2) revealed very marked changes: the presynaptic endings proved to be almost completely empty. A few vesicles seem to assemble around the site of the synaptic contact. The mitochondria in the presynaptic endings are heavily damaged: they are swollen and the well-known fine structure is apparently destroyed. The mitochondria of the postsynaptic elements are at the same time quite normal in appearance.

If we added to the perfusion fluid of the ganglion 10 mg/l choline chloride and stimulated them preganglionically with the above parameters, the transmission remained almost intact and we did not observe the above-mentioned

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