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EFFECTS OF CAROTID CHEMORECEPTOR AND BARORECEPTOR STIMULATION UPON THE SYMPATHETIC PREGANGLIONIC AND POSTGANGLIONIC CARDIAC NERVE AND SINGLE FIBER ACTIVITY IN CATS

P. SZULCZYK and A. TRZEBSKI

Department of Physiology, Institute of Physiological Sciences, School of Medicine
Warsaw, Poland

Abstract. The stimulation of arterial baroreceptors (blind sack technique) inhibited the preganglionic and postganglionic cardiac sympathetic activity. There were found three populations of single sympathetic preganglionic fibers (Th_3) responding in a different way to the stimulation of arterial baroreceptors and arterial chemoreceptors (infusion of the small volume of saline bubbled with CO_2 into the carotid sinus): (i) inhibited by carotid baroreceptors and excited by carotid chemoreceptors stimulation, (ii) inhibited by carotid baroreceptors and by carotid chemoreceptors stimulation, (iii) some fibers inhibited by baroreceptors did not change activity during stimulation of chemoreceptors. A functional role of each particular group of preganglionic sympathetic fibers is discussed.

INTRODUCTION

The activity of cardiovascular sympathetic nerves is continously modulated by afferent input from the arterial baro- and chemoreceptors (7, 10, 11, 22, 25). Recently it has been shown that neurons in the nucleus tractus solitarii, which respond with short latency to electrical stimulation of the sinus nerve, are excited by physiological stimulation of the carotid baro- and chemoreceptors (12). Therefore the interaction of baro- and chemoreflex appears in the medulla oblongata on the first neurons of these reflexes. On the other hand Miura and Reis (16) identified in the medulla oblongata two types of neurons excited separately either by carotid chemoreceptors or by baroreceptors stimulation only. These medullary neurons presumably represent a relay station transmitting input from arterial baro- and chemoreceptors to preganglionic neurons in the spinal cord.

The sympathetic neurons in the spinal cord are influenced by excitatory input from arterial chemoreceptors (3, 20, 24) and are inhibited by arterial baroreceptors (8, 22). The site of the last effect is, at least in part, at the spinal cord level (2, 4, 13). The question arises if the interaction of baro- and chemoreceptors' reflexes takes place, besides the medulla oblongata, also in the spinal cord on the preganglionic sympathetic neurons.

It was the aim of the present study to determine whether the same sympathetic preganglionic units are affected by the stimulation of baro- and chemoreceptors. The cardiac sympathetic nerve and the corresponding preganglionic white ramus Th_3, which provides preganglionic fibers to the stellate ganglion were selected for the study. We have shown recently (25, 26) that cardiac sympathetic activity is increased primarilly by chemoreceptor stimulation, being at the same time particularly responsive to a baroreceptor induced inhibition, which easily masks a chemoreceptor excitatory effect. Also the postganglionic sympathetic vertebral nerve, leaving the stellate ganglion, is excited or inhibited respectively by the chemoreceptor or baroreceptor stimulation (25, 26).

METHODS

The experiments were carried out on 16 cats. After preliminary ether anesthesia α-glucochloralose (40 mg/kg) and urethane (400 mg/kg) were administered intravenously. The femoral artery and vein were cannulated. The tracheostomy was performed. The animals were paralyzed by gallaminum triethiodidum in doses of 5–8 mg/kg. The arterial pCO_2, pO_2 and pH were measured on the femoral artery blood samples with Radiometer electrodes. The pH was maintained at the level of 7.39, pCO_2 at 30 mmHg and pO_2 at about 100 mm Hg. The acid–base balance was regulated by administration of bicarbonates and changing of respiratory parameters.

A thin polyethylene catheter was introduced into the lingual artery and was placed about 0.5 cm below the carotid sinus. Another catheter was introduced into the external carotid artery above the origin of the lingual artery and its end was placed at the level of carotid sinus.

For the stimulation of chemoreceptors 0.02 ml of physiological saline bubbled with 100% CO_2 were administered at a temperature of 37°C via thin catheter. The clamp on the common carotid artery remained open. To see whether the administered fluid had any effect on the central nervous system when reaching it through the pharyngeal or occipital arteries, the effect of chemoreceptor stimulation was checked in three cases before and after the sinus nerve section. After the cutting of the sinus nerve, the CO_2 saturated saline injected into the carotid sinus failed to produce a rise of the arterial blood pressure, or an increase of activity of the cardiac, vertebral or phrenic nerves.

Prior to baroreceptor stimulation the common carotid artery was clamped. The pressure in the sinus dropped to 30–50 mm Hg. Then the pressure in the sinus was suddenly raised to about 200 mm Hg by a very rapid injection of about 0.5 ml of saline or arterial blood into the sinus through a thin catheter.

The right stellate ganglion, the inferior cardiac nerve and the Th_3 white ramus were exposed by a removal of the three upper ribs heads. The phrenic nerve was reached dorsally. All nerves after the removal of sheaths were placed on bipolar platinum electrodes and were covered with liquid paraffin at 37°C. Single fiber preparations were made under binocular from the split filaments of the Th_3 white ramus.

The sympathetic nerve and single fiber activity was recorded after the capacity-coupled preamplification (low and high half amplitude responses at 1 and 5,000 Hz).

RESULTS

The influence of baroreceptors on the sympathetic preganglionic and postganglionic cardiac nerve activity. The experiments were performed on cats with intact buffer nerves. The spontaneous activity of the inferior cardiac nerve had a distinct cardiac and respiratory modulation. The modulations were less marked in the white ramus.

The stimulation of baroreceptors, induced by an increase of the systemic blood pressure following intraveous infusion of 2γ noradrenaline, inhibited the activity of the inferior cardiac nerve and only slightly affected the activity of the preganglionic white ramus Th_3 (Fig. 1). The stimulation of baroreceptors by a sudden increase of pressure in carotid blind sack up to 200 mm Hg inhibited both the activity of the inferior cardiac nerve and the white ramus Th_3. However, the inhibition of the cardiac nerve lasted longer than that of the preganglionic white ramus (Fig. 2).

The influence of baroreceptor stimulation on single Th_3 white ramus preganglionic units. The average rate of spontaneous activity of the single preganglionic units was within Th_3 white ramus 2.1/s. The spontaneous activity of 14 units had a respiratory modulation. Thirteen units were inhibited during excitation of baroreceptors by increase of the pressure in blind sack. Two units did not change the activity during baroreceptor stimulation (Table I).

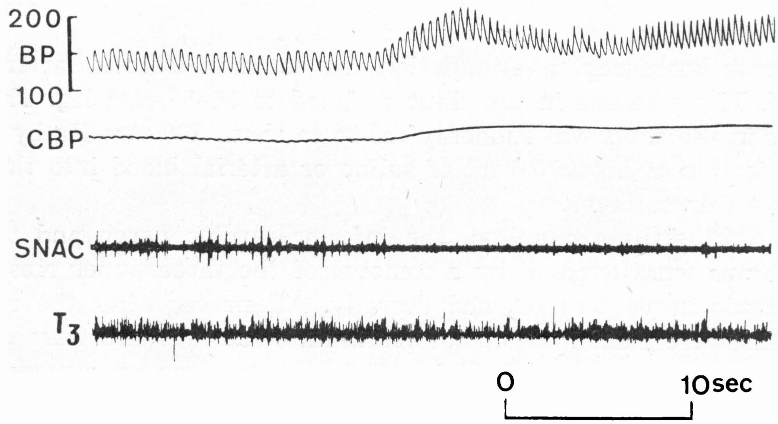

Fig. 1. The effect of blood pressure increase, evoked by intravenous infusion of 2γNa, upon the activity of inferior cardiac nerve and white ramus Th_3. Blood pressure calibration in mmHg. BP, blood pressure measured in the aorta; CBP, averaged blood pressure measured in the carotid sinus; SNAC, inferior cardiac nerve activity; T_3, Th_3 white ramus activity.

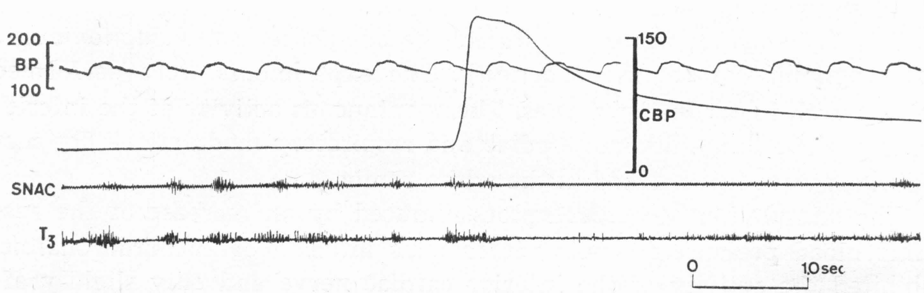

Fig. 2. The effect of blood pressure increase in partly isolated carotid sinus upon the activity of inferior cardiac nerve and Th_3 white ramus. Designations as in Fig. 1.

The influence of chemoreceptor stimulation on the sympathetic preganglionic and postganglionic cardiac nerve activity. In cats with buffer nerves intact the arterial chemoreceptor stimulation by local intrasinus injection of physiological saline bubbled with CO_2 caused a small rise of the arterial blood pressure (Fig. 3). The period between administration of

TABLE I

Properties of 16 preganglionic fibers from the white ramus Th_3. ↓, inhibition of activity; ↑, increase of activity; x, not checked; —, without change, lack of modulation; +, present.

Fiber	Response to baroreceptor stimulation	Response to chemoreceptor stimulation	Respiratory modulation	Heart rate/min	Spontaneous activity/s
1	↓	—	+	150	6.0
2	—	x	+	150	1.3
3	↓	x	+	165	1.8
4	↓	↓	+	165	5.1
5	↓	↑	+ —	150	1.6
6	↓	—	—	150	1.9
7	↓	—	—	150	2.3
8	↓	x	+	225	1.5
9	↓	—	+	210	0.8
10	↓	—	+	210	3.0
11	↓	—	+	210	0.6
12	↓	—	+	210	0.9
13	↓	x	+	210	0.6
14	x	x	+	210	0.9
15	↓	↓	—	165	3.0
16	—	—	—	165	1.8

the CO_2 saturated saline, and the beginning of arterial pressure rise may be regarded as corresponding to the arterial chemoreceptor stimulation. At that time no evident changes were observed in the activity of the cardiac nerve and the Th_3 white ramus. Later, due to a secondary rise of

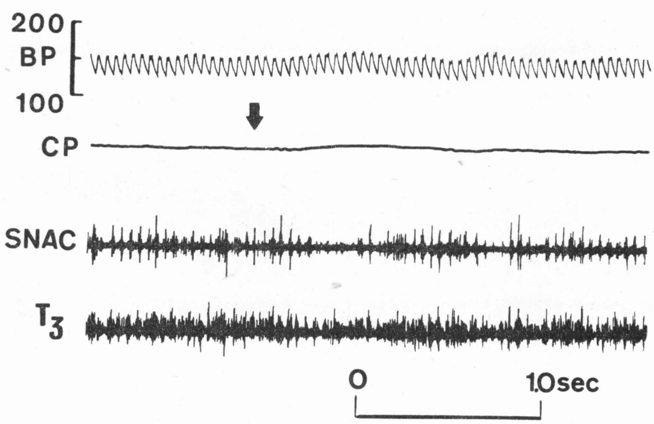

Fig. 3. The effect of arterial chemoreceptor stimulation upon the cardiac nerve activity and arterial blood pressure. Arrow indicates start of infusion of 0.05 ml acid saline into carotid sinus. Designations as in Fig. 1.

the blood pressure and of the arterial baroreceptor stimulation an evident inhibition of the cardiac nerve activity appeared with a slight inhibition of the Th_3 white ramus activity (Fig. 3). After a partial denervation of the arterial baroreceptors, the stimulation of the arterial chemoreceptors evoked an increase of the sympathetic cardiac nerve activity (25).

The influence of the arterial chemoreceptor stimulation on single Th_3 white ramus preganglionic units. Eight units did not change activity during the stimulation of arterial chemoreceptors. The activity of two units was inhibited. The inhibition of activity preceded the reflex increase of the blood pressure induced by chemoreceptor stimulation. These two units were inhibited also by baroreceptor stimulation and had a high spontaneous activity of 5.1/s and 3.0/s. One of these units was also respiratory modulated (Table I).

In a separate series of experiments both aortic nerves, both vagus nerves and one sinus nerve were cut. The remaining sinus nerve, which innervated the carotid area where the chemoreceptors were stimulated, was left intact. In such debuffered cats, contrary to the intact ones, the stimulation of carotid chemoreceptors evoked an increase of spontaneous activity in the preganglionic Th_3 white ramus fibers. The same fibers showed a clear inhibition following the carotid baroreceptor stimulation (Fig. 4).

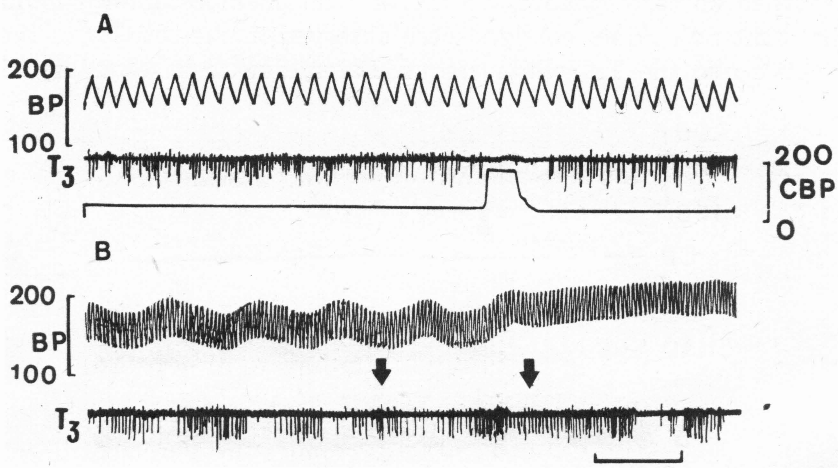

Fig. 4. The effect of carotid baro- and chemoreceptor excitation upon the same few fiber preparation from Th_3 white ramus. *A*: The excitation of carotid baroreceptors by the increase of blood pressure in the carotid sinus. *B*: The excitation of carotid chemoreceptors by infusion of acid saline into the carotid sinus. Time of infusion marked by arrows. T_3, activity of the few fiber preparation from Th_3 white ramus. Time calibration 1 s for *A* and 5 s for *B*.

DISCUSSION

It is generally accepted that sensitivity to the baroreceptor induced inhibition and cardiac modulation of a spontaneous activity are the characteristics of nerves supplying the heart and vascular bed (8, 17, 18, 22, 23, 25). However, there is some evidence that non-cardiovascular sympathetic nerves and fibers are also inhibited by baroreceptors. Kazdi and Geller (8) have shown that the splanchnic nerve activity is inhibited during the stimulation of baroreceptors. The splanchnic nerve, as other preganglionic nerves, probably contains also non-vascular sympathetic fibers. A different point of view is represented by Ninomiya et al. (17) and Nisimaru (18), who demonstrated that activity of the sympathetic nerves supplying the stomach and the skin is not inhibited by baroreceptors. It is possible that the inhibition of the sympathetic nerve activity depends on the strength of baroreceptor stimulation. Probably the inhibition of non-cardiovascular fibers of the sympathetic system is caused by increasing the strength of baroreceptor stimulation. To clarify this possibility, the activity of preganglionic and cardiac postganglionic sympathetic nerves was recorded. The activity of the cardiac postganglionic nerve can be used as an indicator of a degree of baroreceptor reflex operation because that nerve innervates only the heart and is sensitive to baroreceptor stimulation. The preganglionic Th_3 white ramus contains also cardiac fibers, because an electrical stimulation of the ramus evokes an excitatory response in the inferior cardiac nerve (21). However, a cardiac modulation of Th_3 white ramus spontaneous activity is not so marked as that of the postganglionic inferior cardiac nerve. The Th_3 white ramus single preganglionic fibers seldom showed a cardiac rythm of activity (22). It may be concluded that the Th_3 white ramus has both a cardiac baroreceptor modulated and a non-cardiovascular activity. An increase of the blood pressure by an intravenous infusion of norepinephrine (2γ/kg) and a subsequent baroreceptor stimulation inhibits the inferior cardiac nerve activity and only slightly affects the preganglionic white ramus activity. Such a stimulation of baroreceptors can be considered as rather static and weak. However, the stimulus was strong enough to inhibit the whole cardiac postganglionic activity. It therefore appears that the fibers in the white ramus which are not affected by the baroreceptor stimulation are non-cardiovascular. On the contrary, the stimulation of baroreceptors by a sudden increase of intrasinus pressure was followed by a complete inhibition of both the white ramus preganglionic and the inferior cardiac nerve postganglionic activity. That type of baroreceptor stimulus can be considered as dynamic and strong. Our results indicate that during a strong stimulation of baroreceptors, the preganglionic, probably non-cardiovascular activity, could be inhibited as well as the postganglionic activity. The stimulation of chemoreceptors by infusion of a small volume of saline bubbled with CO_2 into the carotid sinus failed to produce any excitation of sympathetic nerves to the heart in animals with all buffer nerves intact. These results are in agreement with our previous observations (25, 26). Presumably a reflex rise of the blood pressure caused by a chemoreceptor stimulation excites baroreceptors and a subsequent inhibition dominates over the chemoreceptor excitatory reflex. Our hypothesis is strenghtened by the fact, that the baroreceptor reflex effectively operates during a chemoreceptor stimulation and attenuates its effect upon the sympathetic and vascular system (6, 15, 19, 28). On the other hand, under particular conditions of a very strong and prolonged chemoreceptor stimulation a chemoreceptor induced excitation of the sympathetic cardiac and renal nerves may predominate over a baroreceptor induced inhibition (1, 26). When the influence of baroreceptors by cutting two aortic and one carotid sinus nerve was partly abolished the same population of sympathetic preganglionic neurons which was excited by a chemoreceptor stimulation was inhibited by a baroreceptor stimulation. Neurons, which had independent input from the arterial baro- and chemoreceptors (12, 16) were described in the medulla oblongata. It is possible that these cells transmit activity to spinal sympathetic preganglionic neurons through independent excitatory and inhibitory spinal pathways. Those independent influences could converge on common final preganglionic units excited by chemoreceptors and inhibited by baroreceptors. Seller (22) showed that a small part of the population of white ramus Th_3 preganglionic fibers could be excited by an adrenaline induced increase of the systemic blood pressure. He suggested that an increase of blood pressure evoked a cardio-cardiac reflex described by Malliani (14). Our results are not in disagreement with that idea, because under conditions of isolated baroreceptor stimulation by an increase of pressure in the carotid blind sack we were not able to excite preganglionic fibers, whereas it could be achieved during the systemic blood pressure rise.

The two preganglionic sympathetic fibers inhibited by chemoreceptor stimulation seem to deserve a particular interest. The inhibition was demonstrated in animals with buffer nerves intact. It was not due to an increase of the systemic blood pressure, and nor to a secondary stimulation of baroreceptors, because it took place before the increase of blood pressure appeared. Nevertheless, the units were inhibited also by the carotid baroreceptor stimulation. It has been shown recently (12) that in the nucleus tractus solitarii there are single neurons which are excited by both baro- and chemoreceptor convergent input (12). It is therefore possible that these particular neurons in the medulla oblongata are a relay station transmitting information from baro- and chemoreceptors to preganglionic sympathetic neurons, inhibited — according to our findings — by both baro- and chemoreceptor stimulation. The spinal or supraspinal localization of inhibitory synapse in this reflex is not known. Iriki et al. (9) and Grosse and Jänig (5) have shown that postganglionic fibers to the vascular bed of the rabbit and cat skin are inhibited by the stimulation with hypoxia or asphyxia. If those postganglionic fibers were inhibited by baroreceptors, it is possible that the chemoreceptor inhibitory effect on the particular sympathetic fiber activity accounts for the increased blood flow through the skin during hypoxia and arterial chemoreceptor stimulation. Such a possibility does not correspond however to the findings of Wallin et al. (27), who demonstrated that the activity of the sympathetic nerves supplying the skin in humans is not affected by arterial baroreceptor stimulation. It may be concluded that the preganglionic sympathetic nerve activity (Th_3) is inhibited under conditions of a strong arterial baroreceptor stimulation.

We have found the following types of preganglionic units: (i) inhibited by carotid baroreceptor and excited by carotid chemoreceptor stimulation; (ii) inhibited by carotid baroreceptor as well as by carotid chemoreceptor stimulation; (iii) some preganglionic neurons were inhibited by baroreceptors and they did not change activity during the stimulation of chemoreceptors. It is possible that either they had no input from arterial chemoreceptors, or that the stimulation of chemoreceptors was to weak to excite them.

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Paweł SZULCZYK and Andrzej TRZEBSKI, Institute of Physiological Sciences, School of Medicine, Krakowskie Przedmieście 26/28, 00-927 Warsaw, Poland.