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High Threshold Aortic Baroreceptor Afferents in the Sympathetic Nerve

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Abstract In anaesthetized cats, 40 sympathetic sensory units in the bracheocephalic artery (30 units) and the descending aorta (10 units) were recorded by means of single-unit preparation. Direct evidence is available for the mechanosensitive nature of the receptors in the sympathetic afferents at the level of T_3 and T_4. Two distinct types of receptors were found (Type I and Type II). Type I receptors, which were fast adapting, gave a spike discharge at each systolic height of pressure (70–110 mmHg). However, they sometimes failed to appear even at such systolic pressure. When the systemic pressure was increased by occluding the descending aorta or by infusing adrenaline solution intravenously, the frequency of discharge of Type I receptors increased and they behaved much the same as the typical sinoaortic baroreceptors. Type II receptors were activated by mechanical probing and at high systemic pressure, though they did not fire always synchronously with heart beat. On the basis of the study it may be suggested that Type I receptors are high threshold baroreceptors and like other systemic baroreceptors, play a role in homeostatic control presumably in a state of high blood pressure, but on the other hand Type II receptors do not play such a role.

Key words: sympathetic afferents, descending aorta occlusion, Type I receptor, Type II receptor, high threshold baroreceptors.

The existence of aortic sympathetic afferent fibers has already been reported using anatomical (MURATORI, 1934), clinical (WHITE *et al.*, 1952), and electrophysiological (UEDA *et al.*, 1969; COLERIDGE *et al.*, 1975; UCHIDA, 1975; PAGANI, 1975; MALLIANI and PAGANI, 1976) studies. It has been shown that information about various haemodynamic events is conveyed continuously to the spinal cord through sympathetic afferents with sensory endings lying in the cardiovascular system. Furthermore, in anaesthetized and vagotomized spinal cats, stretching of the wall of the thoracic aorta was found to induce reflex changes in the activity of sympathetic efferents in the left third thoracic ramus communicans (PAGANI *et al.*, 1974). The same stimulus simulating the effects of increased arterial blood pres-

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sure on the aortic wall, induced reflex increase in heart rate, myocardial contractility, and arterial blood pressure (LIOY *et al.*, 1974) by way of a reflex excitation of sympathetic activity. These experimental findings suggest the existence of positive feed back mechanisms in the neural control of circulation (MALLIANI *et al.*, 1975). Using electrophysiological studies MALLIANI and PAGANI (1976) have suggested that the afferent sympathetic fibers with aortic endings in cats are likely to mediate these reflexes. In the present study an attempt has been made to elucidate the properties of the sympathetic afferent with aortic receptors, which are likely to be involved in homeostatic control of blood pressure at the state of highly increased blood pressure.

METHODS AND MATERIALS

Investigations were carried out on 25 adult cats (2.5 to 3.5 kg body weight) of either sex anaesthetized with sodium pentobarbitone (Nembutal, Abbott Laboratories, India) using an initial intraperitoneal dose of 35–40 mg/kg body weight and maintaining anaesthesia with intravenous doses of 10 mg/kg as and when required. The trachea, femoral vein, femoral artery, and carotid artery were routinely cannulated. Blood pressure was recorded through a pressure transducer (Type-4-327-0129, Bell and Howell, CBC Division, USA) from either the carotid or femoral artery. The polythene cannula was inserted down the carotid artery keeping its tip at the aorta near its junction with the bracheocephalic trunk. In the case of the femoral artery, the cannula was kept at the same site. The site of the tip was always verified in open chested animals. The chest was opened by removing the upper seven ribs on the left side of the chest and the animal was kept under artificial respiration with Starling Ideal Respiratory Pump (INCO Ambala, India). Glucose saline (5%) was administered by drip into the femoral vein to maintain the normal body fluid and electrolyte balance. The body temperature was also monitored by recording rectal temperature which was maintained at 37–38°C by a heating blanket.

The membranous covering of the inner body wall around the region of the stellate ganglion and 1st–5th sympathetic rami was separated out carefully and extended medially without causing any rupture so that the liquid paraffin pool for nerve dissection can be prepared. The left stellate ganglion and its branches were exposed carefully. Suitable lengths of the thoracic sympathetic rami were separated from the surrounding connective tissue under a stereoscopic dissecting microscope.

The nerve was placed on a black ebonite dissecting plate and kept immersed in a warm paraffin pool. A small length of afferent thoracic rami at the level of T_2 to T_4 was desheathed and split into fine filaments under a stereoscopic dissecting microscope (Vickers Instruments, England). A fine filament of the peripheral cut end was placed on a pair of silver-silver chloride recording electrodes for studying single unit activity. The single unit activity was displayed on a dual

beam oscilloscope 5112, Tektronix Inc., Beaverton, Ore., USA) after amplification through a differential preamplifier (AM 502, Tektronix Inc.). Parallel connections were made to an audio-amplifier for monitoring the sound and to a thermionic 4FM tape recorder (Racal-Thermionic Ltd., Southampton, England) for recording the activity when necessary and played back to a storage Oscilloscope (5113, Tektronix Inc.) for further analysis and photography. After obtaining the single unit activity, localization of the receptor site was made precisely with a fine round tipped glass probe in the beating heart. The conduction velocity of these fibers was measured by peripheral stimulation technique (IGGO, 1958). The receptor site was stimulated by a square wave monophasic pulse (7–10 V, lms, 0.2–1 HZ) delivered from a stimulator (Grass S48, Grass Instrument Co., Quincy, Mass., U.S.A.) via an isolation unit (SIU 5). To study the reactivities of the aortic receptors in hypertensive condition, the descending aorta was occluded. Occlusion of the descending aorta was done by putting a fine snare around the aorta and occluding it whenever necessary. Care was taken to see that snare was very light and did not cause any mechanical irritation. Hypertensive agents like adrenaline were injected intravenously.

Drugs used: PGE_2 and $PGF_{2\alpha}$ (Upjohn Co., Kalamazoo, Mich. U.S.A.). Angiotensin II., succinylcholine (Sigma, U.S.A.), P.D.G. (Aldrich Co., U.S.A.) adrenaline (Burroughs Wellcome, India).

RESULTS

Aortic receptors of cats

A total of 40 units were recorded from the cardiac sympathetic afferents of the cat. Out of these, 27 were spontaneous and the remaining 13 were nonspontaneous. The units were situated (a) at the juction of bracheocephalic artery and the aortic arch (30 units) and (b) on the descending aorta (10 units). The average resting discharge rate of the spontaneous units was 2–4 impulses/sec at a pressure head of 90–120 mmHg. On mechanical probing this discharge rate increased to 18–25 impulses/sec (Fig. 1).

Receptors in the aortic arch which were located at the base of the bracheocephalic trunk exhibited synchronous spike discharge with each systolic height of blood pressure and behaved like baroreceptors (Figs. 2, 3). There was no discharge at diastolic phase of cardiac cycle. Figure 7a represents the average number of spikes synchronous with the systolic height of pressure during 20 cardiac cycles. The discharge rate increased with the rise of systolic pressure either with occlusion of descending aorta (Fig. 2) or with the intravenous administration of 10–15 μg/kg adrenaline (Fig. 3). Threshold blood pressure for activating receptors ranged from 70–110 mmHg, and number of observation against threshold blood pressure is presented in Fig. 4. The threshold pressure for activating a receptor was determined by noting the pressure at which the unit just started to discharge

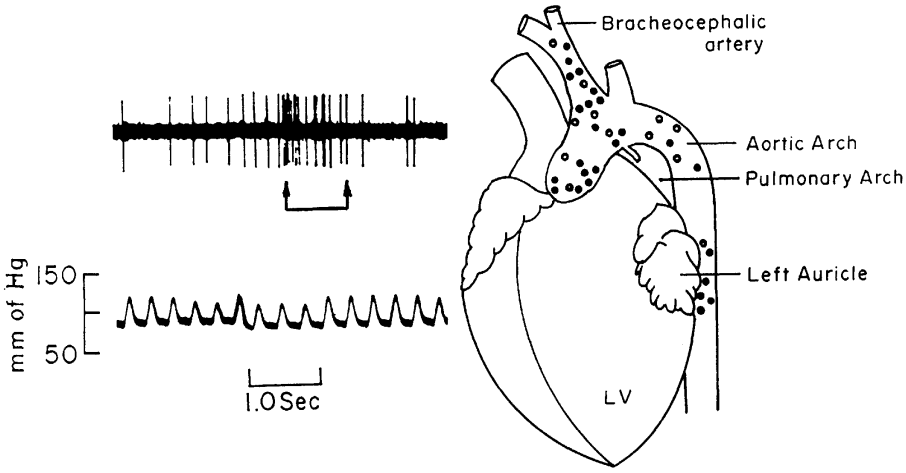

Fig. 1. Schematic diagram showing the distribution of sympathetic aortic receptors of cat over the surface of aortic arch, bracheocephalic artery, and discending aorta. The filled circles are spontaneous and the open circles are nonspontaneous receptors. Tracing at left shows the response pattern of one spontaneous aortic Type II receptor to mechanical probing. The arrows indicate the duration of stimulation. LV: left ventricle.

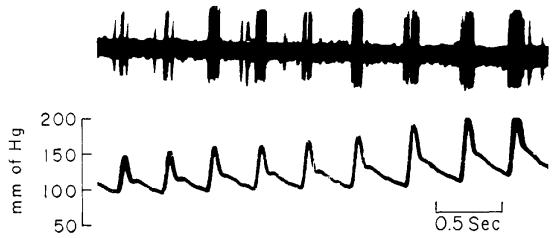

Fig. 2. Showing the response pattern of a Type I aortic receptor of cat after occlusion of descending aorta. Irregular discharge in diastolic phase is instrumental noise.

and completely disappeared with a slight drop of this pressure level. These aortic baroreceptors with sympathetic afferents normally gave occasional single spike at systolic phase (70–110 mmHg), but there were bursts of impulses at systolic phase only when the pressure was raised from 110–230 mmHg either by occluding the descending aorta or by administration of adrenaline. From the graphical representation (Fig. 5), it can be seen that the initial single spike discharge of such aortic receptors increased gradually from single to multiple spikes at systolic height of pressure during increase of blood pressure. After administration of adrenaline (10–15 μg/kg), the pressure normally increased up to 180–230 mmHg and the discharge rate from 0.5 ± 0.09 to 8.5 ± 0.21 impulses/sec.

The spontaneous discharge activity was in systolic peak phase with the aortic

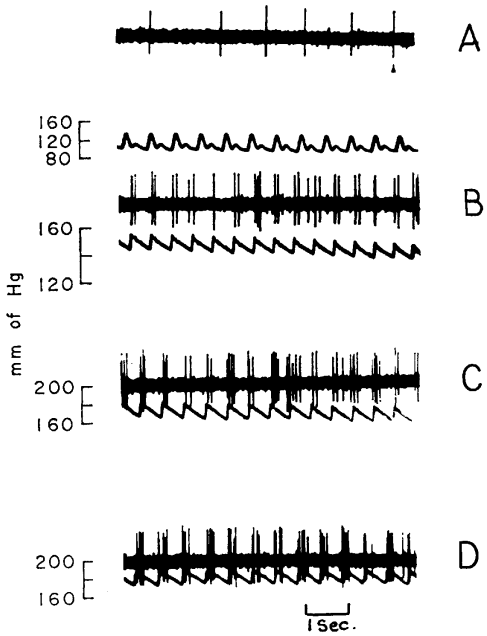

Fig. 3. Showing typical sympathetic baroreceptor discharge pattern to gradual rise of systemic pressure induced by infusing adrenaline (5 μg/kg, i.v.). Tracing "A" shows the normal resting discharge of one single unit and tracing "B," "C," and "D" show the increased frequency of discharge during the rise of pressure after adrenaline infusion.

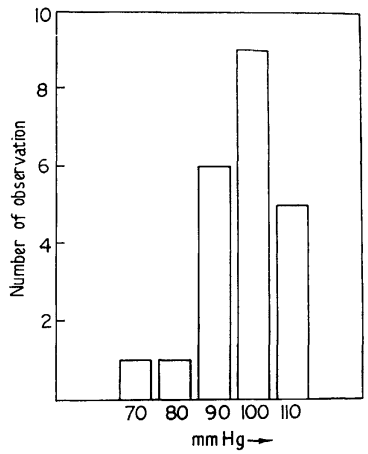

Fig. 4. Histogram showing the number of observations against threshold pressure (at which the spikes start to appear) for 22 single units of Type I receptor.

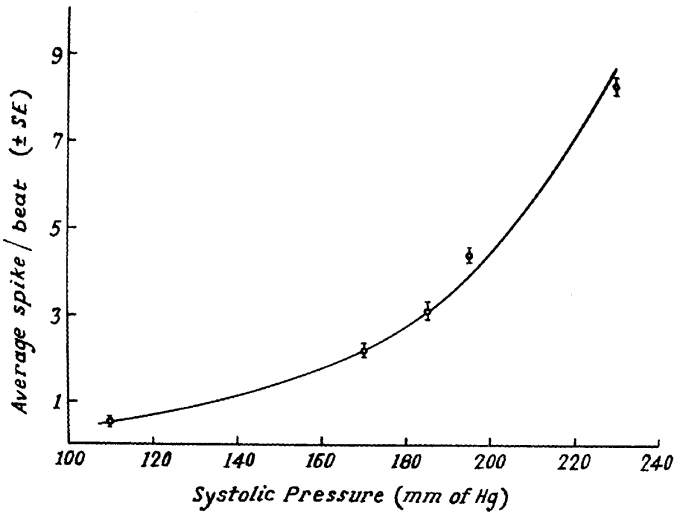

Fig. 5. Average (±S.E.) discharge pattern of ten Type I aortic receptors in cat against systolic height of blood pressure.

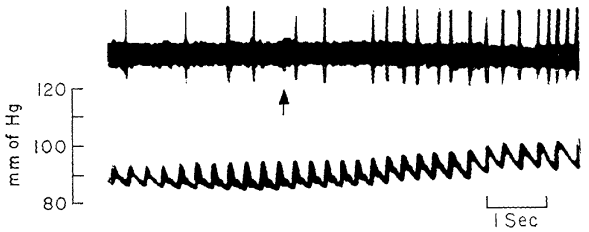

Fig. 6. Showing response pattern of a spontaneous Type II receptor of cat which fired asynchronously with each systolic height of pressure. Tracing before the arrow shows the resting discharge and that after the arrow shows the continuous firing of the unit during the application of adrenaline (5 μg/kg, i.v.). Arrow indicates the point of application of the adrenaline.

pressure pulse and consisted of not more than one discharge per pressure phase. It was increased during increases in aortic presssure and conversely, decreased during decrease in aortic pressure. On occlusion of the descending aorta or administration of adrenaline, both systolic and diastolic pressures were increased, but the firings were observed during systolic phase only. This phenomenon shows the typical rapidly adapting dynamic behavior of the baroreceptors.

The present observations indicate that the impulse traffic from aortic baroreceptors are also carried through the sympathetic afferents (T_3 and T_4) and that they get activated only at high pressure level and not so activated at normal resting pressure level (70–110 mmHg). On this basis these receptors may be described as high threshold baroreceptor afferents and may be designated as Type I receptors.

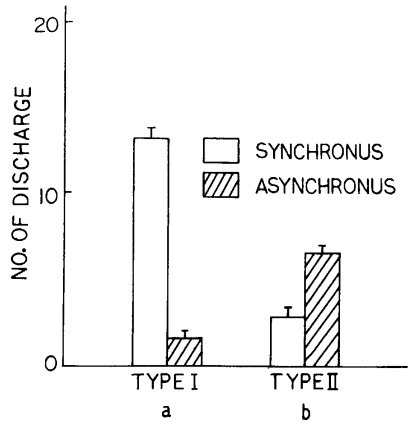

Fig. 7. The average number of discharges (±S.E.) synchronous and asynchronous with the systolic height of pressure during 20 and 10 cardiac cycles for Type I ($p<0.001$) and Type II ($p<0.01$) receptors respectively.

The pressor receptors were not excited following intravenous administration of different chemicals like PGE_2 and $PGF_{2\alpha}$ (2.5 μg/kg), succinylcholine (25 μg/kg), and PDG (100 μg/kg). But these receptors were excited mechanically by occluding the descending aorta (Fig. 2). Intravenous administration of angiotensin II (5 μg/kg) and adrenaline (5–10 μg/kg) could also excite these units (Fig. 3). This could be due to a rise of pressure level above normal. The conduction velocity of these sympathetic afferents was found to be in the range of 3.64–10.33 m/sec.

Another type of receptor was observed distributed over the wall of the arch of aorta and the descending aorta. These receptors fired irregularly, and single spike occasionally coincided with the systolic height of pressure. The discharge rate increased continuously during rise of pressure, but unlike Type I receptors described earlier, there was no such marked interruption of firings during the diastolic phase. These receptors fired irregularly and were mostly asynchronous with heart beat. Figure 7b represents the average number of asynchronous firing with systolic height of pressure during 10 cardiac cycles. The recoptors were excited by mechanical probing, on occlusion of the descending aorta and by increasing systemic pressure with adrenaline infusion (Fig. 6). But these receptors did not behave like baroreceptors and hence they have been designated as Type II receptors.

Most of the discharges of the Type I receptors synchronize ($p<0.001$) with the systolic height of pressure (Fig. 7a), while in Type II receptors most of the discharges do not synchronize ($p<0.01$) with the systolic height of pressure (Fig. 7b).

Therefore, Type II receptors which were not always excited at each heart beat and fired irregularly at high pressure seem to play no role in homeostatic function. On the other hand, Type I receptors which were excited occasionally or regularly at each heart beat and showed burst responses with heart beat at high pressure seem

to have a role in homeostatic control of blood pressure in a state of high blood pressure.

DISCUSSION

In the present investigation the sympathetic endings in the base of the brachiocephalic trunk that have been designated as Type I receptors were found to possess the same behavioral pattern as that of a baroreceptor with sinus afferents or aortic afferents (HEYMANS and NEIL, 1958) except for the difference in threshold pressure which is very high. But Type II receptors, located over the wall of arch of aorta and descending aorta, were not excited regularly with cardiac cycle. The threshold pressure for activating the Type I receptors ranged from 70–110 mmHg (Fig. 4) which is much higher compared to that of sinus and aortic baroreceptors with sinus and aortic afferents, respectively (HEYMANS *et al.*, 1931). WHITTERIDGE (1948) has shown that in aortic arch baroreceptors with aortic nerve afferents, there were bursts of impulses with 2–5 spikes at 60–80 mmHg pressure and at 125 mmHg pressure there were 10–15 spikes at systolic peak of each cardiac cycle with complete absence of discharge at diastolic phase. In the present study the Type I receptors bear a similar direct relationship between discharge and pressure (Fig. 5). Unlike aortic or sinus baroreceptors, these Type I receptors fired only once or sometimes no times per cardiac cycles at systolic pressure of 70–110 mmHg. But when the pressure was increased to 180–230 mmHg, the frequency of discharges per cardiac cycle increased to 4–8 spikes. On occlusion of descending aorta or administration of adrenaline, both systolic and diastolic pressure increased; the firings were observed during systolic phase only even when the diastolic pressure attained a much higher level shan the control systolic peak pressure. Thus these receptors show the typical rapidly adapting dynamic behavior of the baroreceptors. In this connection it may be mentioned that the sinus or aortic baroreceptors give a sustained discharge with such increased level of pressure (KOCH, 1931; HEYMANS *et al.*, 1931). Hence, these receptors can be described as high threshold baroreceptor afferents. Our results of Type I receptors corroborate with the findings of MALLIANI and PAGANI (1976) who reported the same type of discharge. In normal physiological conditions these receptors are normally not so active. But in high blood pressure conditions, these aortic Type I baroreceptors presumably take part in combating such change of pressure. Thus the peripheral haemodynamic information, even in the absence of reflexogenic depressor action of blood pressure by sino-aortic baroreceptor nerves, is transmitted to the higher center through the thoracic sympathetic afferents and spinal cord for returning the pressure to the lower level.

By raising the sinus pressure in steps and noting the change in systemic pressure, KOCH (1929, 1931) was able to plot the change of the systemic pressure in response to change in sinus pressure in animals. KOCH (1929, 1931) showed that

the maximum sensitivity of the reflex was in the region of 120 mmHg. However, below 55–60 mmHg and above 210 mmHg there was no reflex response to a fall or rise of pressure. HEYMANS *et al.*, (1931) repeated Koch's experiments and found that the maximum sensitivity of the reflex mechanism was between 85–110 mmHg.

From the observation of KOCH (1929, 1931) and HEYMANS *et al.*, (1931) it is clear that the threshold pressure for the baroreceptor endings with sinus or vago-aortic afferents is comparatively very low as regards the threshold pressure for such endings with sympathetic afferents of the aorta (Type I). In the present study the threshold pressure for Type I receptors was found to be higher than 60 mmHg. The Type I receptors started firing with one impulse per systemic height of pressure when the pressure was raised to 130–140 mmHg. The frequency of discharge further increased when the pressure was elevated more to 180–230 mmHg. As most of the Type I receptors are excited at high pressure only, they have been designated as high threshold sympathetic baroreceptor endings. These receptors are possibly involved in the control of cardiovascular homeostatis by signalling the sensation of systemic high pressure to the central nervous system during the state of high blood pressure.

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