Acta Pharmacologica Sinica 1987 Jan; **8** (1) : 35-40

Afferent pathways of aortic baroreceptor fibers in guinea pigs[1]

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ABSTRACT In guinea pigs, afferent fibers from aortic baroreceptors emerge from the aortic arch, and travel centrally as separate aortic depressor nerves (distinct from the vagus, the cervical sympathetic trunks and the recurrent laryngeal nerves) that merge into the superior laryngeal nerves. In guinea pigs anesthetized with urethane, orthodromic electrical stimulation of afferents in the aortic depressor and superior laryngeal nerves resulted in reflex hypotension. Bipolar electrical recording of afferent activity from the aortic depressor nerves revealed bursts of activity that were synchronous with cardiac

Received 1986 Jul 3 Revised 1986 Aug 10
[1] Supported in part by a grant from the Alberta Heart Foundation.
[2] Dr Sun is a Research Fellow of the Alberta Heritage Foundation for Medical Research.

systole. Activity of the nerves increased when arterial blood pressure was raised by phenylephrine, and it decreased when the pressure was lowered by sodium nitroprusside. Pulse-synchronous activity was recorded from the superior laryngeal nerve; severing the ipsilateral aotic depressor nerve eliminated this activity.

KEY WORDS guinea pigs; thoracic aorta; nerve fibers; pressoreceptors; electric stimulation; phenylephrine; neural transmission; nitroprusside

Arterial baroreceptors mediate cardiovascular reflexes that induce acute changes in the circulation[1]. Most of these baroreceptors are in the walls of the aortic arch and carotid sinus. Aortic baroreceptors are located at the origin of the left common carotid artery and left subclavian artery, and in the brachiocephalic artery at its bifurcation into the right subclavian and right common carotid artery[2].

In most species (including rabbit, cat, dog and human), afferents from aortic baroreceptors travel centrally in the main trunk of the vagus nerve or in separate aortic depressor nerves (ADN) adjacent to the vagi[3,4]. In rats, however, the pathways of aortic afferents can follow four routes: 1) via the vagus nerve; 2) via the cervical sympathetic trunk to the nodose ganglion, and thence centrally via the vagus; 3) via a separate aortic depressor nerve; and 4) via the recurrent laryngeal nerve (RLN) to the superior laryngeal nerve (SLN) through the communicating branch, and then centrally via the vagus[4-8]. These pathways may differ from rat to rat and in the two sides in the same animal.

During a preliminary investigation of upper airway reflexes in guinea pigs, we observed that central stimulation of one or both SLN induced reflex hypotension. Recordings of afferent activity from the SLN revealed bursts of firing that were synchronous with cardiac systole. We now report experiments in which we traced the afferent pathways of aortic baroreceptor fibers in guinea pigs by three approaches: dissection, electrical stimulation and electrophysiologic studies.

METHODS

Guinea pigs of either sex, weighing 440±SD 32 g, were anesthetized with urethane (1.25-1.75 g/kg, ip). The trachea was cannulated; the animals breathed room air spontaneously. Arterial blood pressure was monitored from a femoral artery via a tapered PE90 catheter, Statham P23Dd pressure transducer, and Hewlett-Packard 7454 A physiograph. The heart rate and electrocardiogram (ECG) were monitored with the same physiograph; the ECG triggered the heart-rate counter. Drugs were injected via a PE 50 catheter inserted into a jugular vein.

Drugs used were atropine sulfate (Fluka AG, Buchs SG, Switzerland), cimetidine (Smith Kline and French Canada, Mississauga, Ont.), clonidine (gift from Boehringer Ingelheim, Burlington, Ont.), hexamethonium (K & K Laboratories, Plainview NY, USA), mepyramine (Rhone-Poulenc Pharma Inc, Montreal, PQ.), phenylephrine (USP), propranolol (Ayerst Laboratories, Montreal, PQ.), and sodium nitroprusside (Hoffman-La Roche, Vaudreuil, PQ.),

Preparation of guinea pigs We used a dissecting microscope to isolate the following nerves: both SLN, adjacent to the larynx; both ADN, at the point where they joined the SLN; and the RLN, on both sides of the trachea. The nerves were cut; bipolar platinum electrodes were applied to the central ends, and connected via an isolation unit to a Grass S 44 stimulator. Stimulation was applied at 10 V, 10 Hz, for 1 ms repeatedly for 30 s. Peripheral-nerve activity was recorded from the distal ends of the cut nerves with a bio-electroamplification system built in our laboratory; this system comprises bipolar platinum electrodes, a high-impedance differential pre-amplifier, an instrumentation amplifier, a bandpass

filter, a 60-Hz notch filter, a rectifier and an integrator. The amplified and integrated signals were displayed on a Tektronix 5113 dual-beam oscilloscope, and photographs were taken for permanent record. The regions around the electrodes were flooded with mineral oil, to insulate the electrodes and prevent drying of the tissues.

Experimental design A minimum of 4 replicates was obtained in each series of experiments. All values are expressed as the $\bar{x} \pm SD$. Differences were examined with *t* test and were assumed significant at the 5% level.

The guinea pigs were divided into 6 groups and subjected to the following experiments. When drugs were given, no further procedures were attempted for at least 30 min (until recordings had returned to their former [control] patterns). *Group 1* (n = 4): central electrical stimulation of the RLN then SLN; then, bilateral vagotomy was performed. *Group 2* (n = 4): central stimulation of the SLN; then, atropine, mepyramine, cimetidine and propranolol were administered, in that order. *Group 3* (n = 4): central stimulation of the SLN; hexamethonium was administered, followed by clonidine; then the nodose ganglia were extirpated. *Group 4* (n = 5): central stimulation of the ADN, followed by administration of hexamethonium. *Group 5* (n = 4): electrical recording from the RLN and SLN. *Group 6* (n = 12): afferent activity from the ADN was recorded, and then phenylephrine was administered followed by sodium nitroprusside. At the end of each of these experiments, necropsy was performed and the course of the ADN to the region of the aortic arch was delineated.

RESULTS AND DISCUSSION

After preparing the animals for the experiments, we allowed 30 min to elapse for stabilization of their condition. At 30 min, mean arterial blood pressure was 46 ± 10 mm Hg and heart rate was 240 ± 39 beats /min (n = 33).

Central electrical stimulation of both SLN (n = 12 guinea pigs) induced reflex hypotension without altering heart rate significantly. It reduced mean arterial pressure from 39 ± 6 mm Hg (control) to 28 ± 7 mm Hg ($p < 0.01$) and caused the heart rate to fall from 228 ± 30 beats/min (control) to 218 ± 28 beats/min ($p > 0.05$). The hypotensive responses were abolished by hexamethonium (1 mg/kg) or clonidine (0.2 mg/kg), and eliminated by extirpating the nodose ganglia, indicating that they were mediated via vagal afferents and that autonomic ganglia and α-adrenoceptors were involved in responses. However, they were unaffected by atropine (0.1 mg/kg), mepyramine (0.5 mg/kg), cimetidine (1 mg/kg), and propranolol (1 mg/kg) or by bilateral cervical vagotomy. Thus, muscarinic receptors, H_1 or H_2 histaminergic receptors, and β-adrenoceptors are not involved in the responses. Also, the latter are not mediated via vagal efferents.

Results of central stimulation of the ADN (n = 5 guinea pigs) were similar to those produced by SLN stimulation. Mean arterial blood pressure was reduced from 53 ± 5 mm Hg (control) to 38 ± 8 mm Hg ($p < 0.01$) and the heart rate fell from 274 ± 42 beats/min (control) to 266 ± 39 beats/min ($p > 0.05$). Stimulation of the RLN had no effect on blood pressure or heart rate.

Recordings from the SLN revealed bursts of activity in synchrony with cardiac systole. This activity was unaltered after the internal and external SLN branches to the larynx had been cut, but was absent after the ipsilateral ADN had been severed. Similar bursts of baroreceptor activity were recorded from the ADN (Fig 1 and 2). Phenylephrine (50-100 μg/kg) increased arterial blood pressure and ADN activity (Fig 3), and induced reflex bradycardia. Sodium nitroprusside 100 μg/(kg·min)

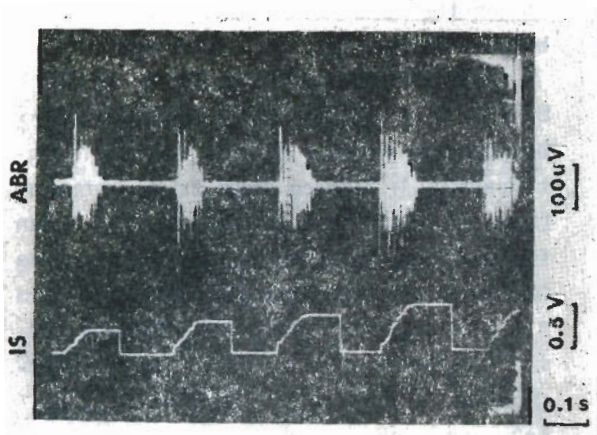

Fig 1. Bursts of aortic baroreceptor activity (upper trace–ABR) and the integrated signal (lower trace–IS) recorded from the aortic depressor nerve. Mean arterial blood pressure = 50 mmHg.

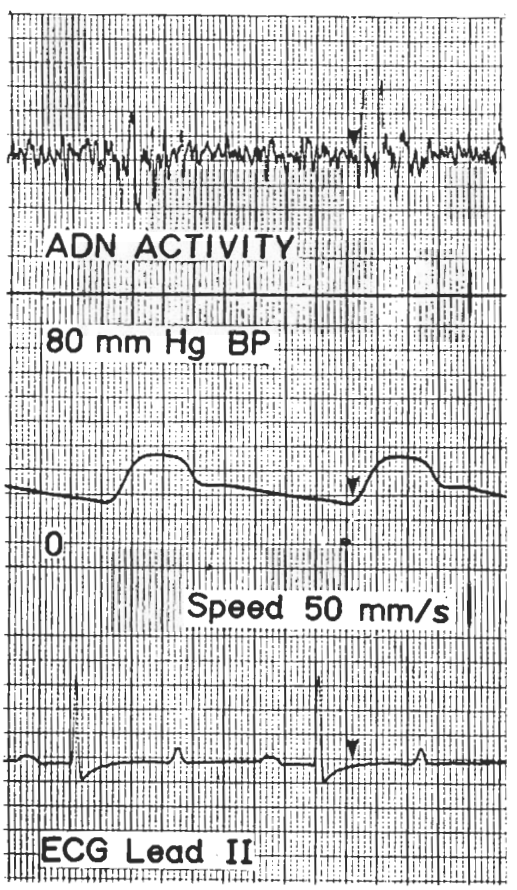

Fig 2. Signals show synchrony of the ADN activity (upper trace) with arterial blood pressure (middle trace) and lead II of the electrocardiogram (lower trace).

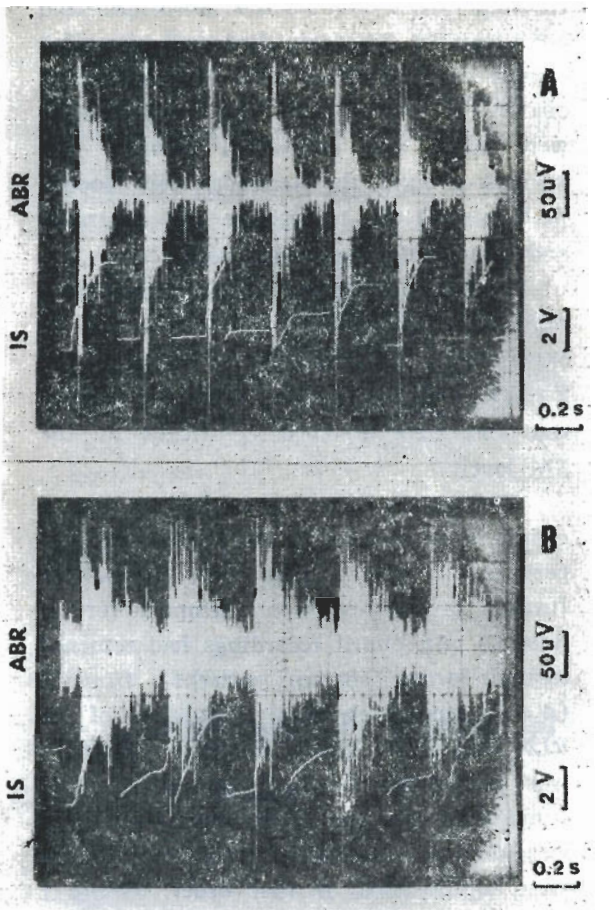

Fig 3. Increases in aortic baroreceptor activity (ABR) after raising the mean arterial pressure (MABP) with phenylephrine (100 μg/kg). IS = integrated signal. A: Control; MABP = 60 mm Hg. B: After phenylephrine; MABP = 85 mm Hg.

decreased arterial blood pressure and ADN activity (Fig 4). Recordings from the RLN did not show phasic activity.

All of the above findings are characteristic of arterial baroreceptor activity.

On tracing the ADN at necropsy, we found that they exited from the SLN and ran caudally toward the heart as separate nerves adjacent to, but distinct from, the cervical sympathetic trunks and the vagus nerves. They reached the aortic arch at the origin of the left common carotid artery on the left side, and at the bifurcation of the brachiocephalic artery into the right

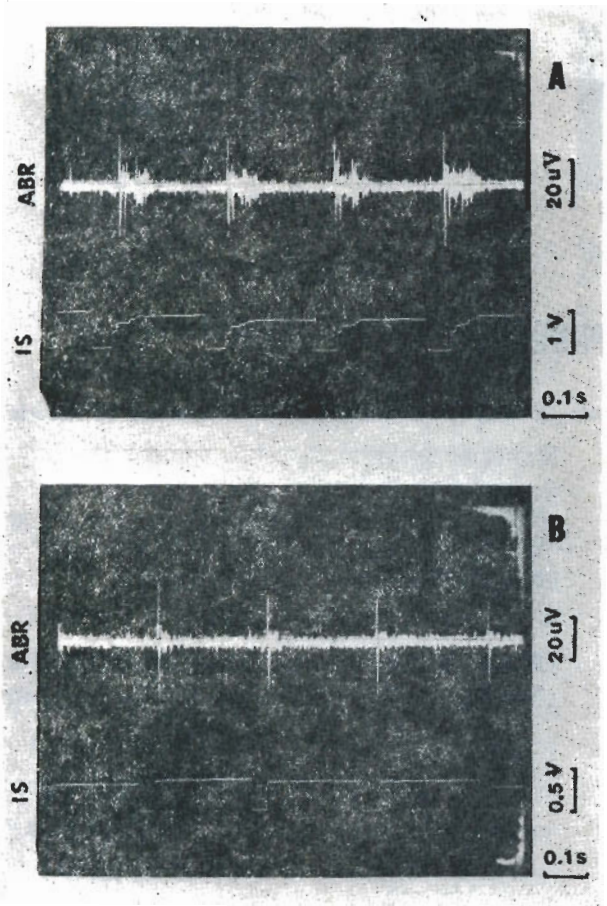

Fig 4. Decreases in ABR after lowering MABP with sodium nitroprusside 100 μg/(kg·min). A: Control; MABP = 60 mm Hg. B: After sodium nitroprusside; MABP = 30 mm Hg.

subclavian and common carotid arteries on the right (Fig 5).

Our results clearly show that, in guinea pigs, aortic-baroreceptor afferents form physiologically and anatomically separate aortic depressor nerves. In the mid-cervical region, the ADN are readily distinguishable from the RLN, the vagi, and the sympathetic trunks, as separate fine nerves running cephalad to join the ipsilateral SLN. This pattern of innervation was consistent in 11 of the 12 guinea pigs examined-unlike findings in rats, in which the aortic baroreceptor fibers can form part of the vagi, the RLN, and the sympathetic trunks, or appear as separate ADN. (In the 12th

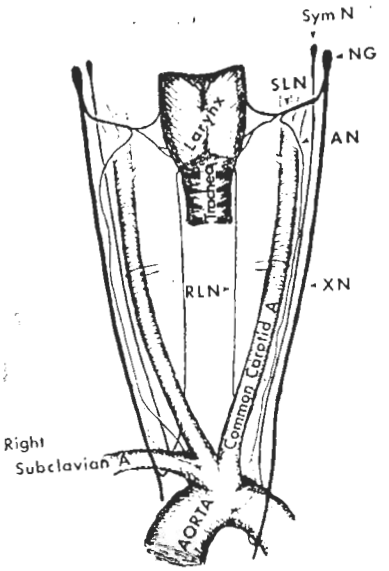

Fig 5. Drawing of nerves in cervical region of the guinea pig: AN, aortic depressor nerve; NG, nodose ganglion; RLN, recurrent laryngeal nerve; SLN, superior laryngeal nerve; Sym N, sympathetic nerve; and XN, vagus nerve. Scale approximately 2 × normal.

guinea pig, we were unable to demonstrate ADN).

We conclude that the aortic depressor nerves in guinea pigs are readily accessible and that this species shows promise as an animal model for investigating the electrophysiology of aortic baroreceptors *in vivo* and *in vitro*.

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中国药理学报 1987 年 1 月; **8** (1) : 35-40

豚鼠主动脉压力感受器的传入神经通路

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提要 豚鼠主动脉压力感受器神经纤维发自主动脉弓，形成独立的主动脉降压神经，继而汇入喉上神经传入中枢。这区别于大鼠主动脉压力感受器传入通路。电刺激豚鼠主动脉降压神经或喉上神经均引起反射性降血压作用。主动脉降压神经记录显示其传入神经冲动与心搏收缩期同步。此神经活动在苯福林升高血压时增强，在硝普钠降压后减弱。喉上神经记录显示类似的神经活动；但该活动在同侧主动脉降压神经横切后消失。此发现提示豚鼠可作为体内或体外研究主动脉压力感受器电生理特性的合适动物模型。

关键词 豚鼠；胸主动脉；神经纤维；压力感受器；电刺激；去氧肾上腺素；神经传递；硝普钠

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