Influence of cervical sympathetic nerve stimulation on carotid sinus baroreceptor afferents

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Summary. In rabbits and dogs, the response of low-threshold carotid sinus baroreceptor afferent fibres to cervical sympathetic nerve stimulation at various non-pulsatile steady pressures was examined. Fibres which possessed a rhythmic bursting discharge at low pressures increased this activity during sympathetic stimulation; all other low-threshold afferents were unaffected.

Post-ganglionic sympathetic nerves from the superior cervical ganglion innervate the region of the carotid bifurcation[3]. Specifically both the wall of the carotid sinus and the carotid body are sympathetically innervated. There is evidence that adrenergic mechanisms can alter the chemoreceptor sensitivity of the carotid body through modulation of carotid body blood flow[4]. Similarly it has been proposed that carotid sinus baroreflex behaviour can be modified by the effects of sympathetic nerve stimulation on mechanical properties of the sinus wall[5].

While several studies have shown baro-reflex modification after sympathetic activation[6,7], attempts at showing changes in receptor behaviour have not all been successful[8–10]. Baroreceptors in the carotid sinus give rise to both myelinated, (A-fibre), and unmyelinated, (C-fibre), afferents[11]. The former have low thresholds and are active at normal arterial blood pressures, while C-fibre afferents often have quite high thresholds and operate at hypertensive pressure levels[11–13]. In several early studies catecholamines applied to the wall of the carotid sinus were found to induce profound decreases in arterial blood pressure[14]. Recordings from few fibre filaments of the carotid sinus nerve showed that large increases in fibre activity followed catecholamine administration, but that increases in activity were limited to small fibres[15].

These observations are consistent with reports that cervical sympathetic stimulation somewhat reduces dynamic and static sinus wall strain[5], presumably reducing baroreceptor stimulation, while catecholamines appear to be able to directly stimulate unmyelinated C-fibre afferents arising from aortic arch baroreceptor endings[16].

Material and methods. We have recorded the behaviour of carotid sinus baroreceptor afferents during cervical sympathetic nerve stimulation. In 8 dogs and 6 rabbits, anaesthetized with chloralose (100 mg/kg b.wt, i.v.) the carotid bifurcation was isolated and perfused as described previously[7]. The carotid sinus nerve was identified and traced to its junction with the glossopharyngeal nerve, where it was sectioned.

Filaments possessing single active fibres were dissected and action potentials were amplified for recording on magnetic tape and paper. Only fibres demonstrating low threshold pressures (threshold pressure < 100 mg Hg) were examined.

Results. These afferents fell into 2 classes. A) Those fibres which were silent at subthreshold pressures and which, upon reaching threshold pressure responded with a continuous steady discharge (S-type) (25 dog; 12 rabbit). B) Fibres which behaved similarly to those described above except that at subthreshold pressures they exhibited a semiregular bursting discharge (B-type) (9 dog; 7 rabbit). This discharge was converted to a continuous steady discharge when pressure was raised to threshold. A similar classification of rabbit aortic nerve baroreceptors has been described[17].

S-type afferent fibres were unaffected by cervical sympathetic nerve stimulation at any intrasinus pressure. While this result was consistently obtained, it is possible that our somewhat limited sample included only afferent fibres which, for some undetermined reason, were unaffected by sympathetically-generated changes in sinus wall strain. We also made recordings from nerve filaments which contained several active baroreceptor afferents. When the sinus was animal-perfused all fibres in these filaments fired in pulse synchrony. Sympathetic stimulation reduced the total activity of these afferent filaments when intrasinus pressure was maintained at a steady value between 150 and 200 mm Hg (figure 1). In figure 2 the total activity reported represents that of large amplitude action potentials; smaller amplitude action potentials were eliminated from the count by appropriate level discrimination.

Afferents demonstrating B-type behavior were affected by sympathetic stimulation at subthreshold pressure. At low intrasinus pressures, where bursting activity was evident, sympathetic activity increased burst length and, in some

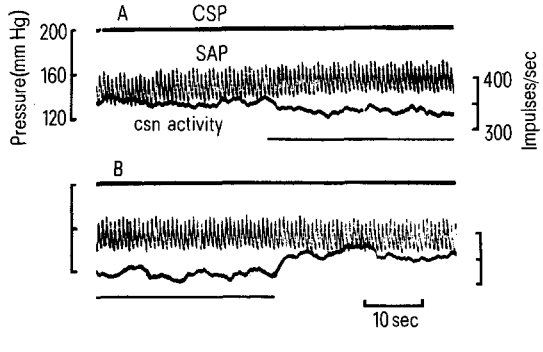

Fig. 1. A and B. Continuous record of a response to cervical sympathetic nerve (csn) stimulation in the dog. CSP, carotid sinus pressure; SAP, systemic arterial pressure. Baroreceptor activity was recorded from a small filament dissected from the carotid sinus nerve. Only large amplitude action potentials were counted.

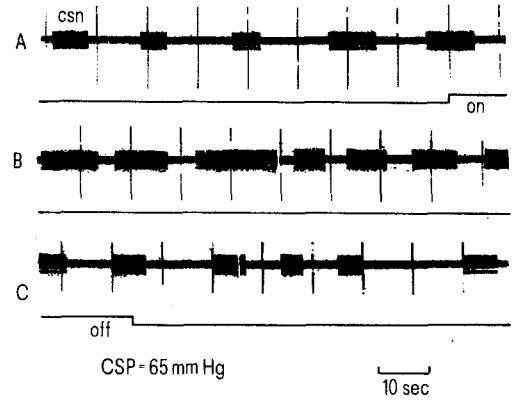

Fig. 2. ABC. Continuous record of activity in a carotid sinus baroreceptor afferent of dog (threshold pressure for continuous discharge = 70 mm Hg). A stimulus of 4 V, 2 msec and 6 Hz was applied to the peripheral end of the cut cervical sympathetic nerve (csn) during the time shown.

cases, interburst frequency; mean intraburst frequency did not alter (figure 2). These responses resulted in an increase in the total activity in that afferent fibre. At higher intrasinus pressures, where activity was converted to a steady discharge, sympathetic stimulation no longer altered afferent activity.

Discussion. One possible explanation of these results concerns the distribution of baroreceptor endings in the carotid sinus. Some of these lie close to isolated smooth muscle cells near the medio-adventitial border[18]. Presumably in this location they would be subjected to mechanical responses of the smooth muscle cell. It is quite reasonable to suppose that in the sympathetically-denervated sinus region smooth muscle cells may undergo cyclic spontaneous contraction. In the isolated rat aortic strip we have observed spontaneous smooth muscle contractions whose frequency increased during norepinephrine administration. Presumably sympathetic stimulation would evoke comparable changes in contractile activity in the smooth muscle cells of the sinus wall, increasing the frequency and duration of bursting activity of suitably located baroreceptor afferents.

In several rabbit preparations we observed that a single pulse to the cervical sympathetic nerve was able to initiate a burst of activity in a B-type afferent held at subthreshold pressure. This response showed refractoriness, but virtually continuous afferent activity could be obtained at any subthreshold pressure by application of a single stimulus to the sympathetic nerve just after the refractory period had ended.

These sympathetic-generated bursts of activity could also have been secondary to activation of adjacent smooth muscle cells, or might have been a response to the direct effects of noradrenaline on the afferent endings. If we are to believe that the spontaneous bursting of these B-type afferents was a consequence of their location adjacent to smooth muscle cells, then it would seem more reasonable that sympathetic modulation of this activity was secondary to sympathetic influence on the smooth muscle. It appears, therefore, that a single stimulus to the cervical sympathetic nerve can trigger a smooth muscle cell to contract.

In summary, low threshold carotid sinus baroreceptor afferents (presumptive A-fibres) are generally not susceptible to sympathetic modulation. Some of these fibres demonstrate a bursting discharge at subthreshold pressures and this activity is augmented by sympathetic nerve stimulation. It is likely that these afferent fibres have endings closely associated with smooth muscle cells. The profound baroreflex effects of sympathetic nerve stimulation, or of the systemic infusion or local administration of catecholamines, must be due to the direct influence of catecholamines on the high threshold unmyelinated C-fibre afferents.

1 This work was supported by the Medical Research Council of Canada and the British Columbia Heart Foundation.
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A transbasisphenoidal approach for selective occlusion of the middle cerebral artery in rats

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Summary. The authors report a new model of focal cerebral ischemia following a selective occlusion of the middle cerebral artery in rats, without additional insults of hypoxia, hypotension and handling of carotid and vertebral arteries, as required in previously described models.

At present, several experimental models are available to investigate the phenomena related to cerebral ischemia. Particularly, with reference to focal cerebral ischemia, the most used models consist of: a) ligation of the common carotid artery in gerbils[1]; b) occlusion of the middle cerebral artery (MCA) by transorbital approach in squirrel monkeys[2], cats[3], dogs[4], baboons[5], rabbits[6]; c) occlusion of the MCA in rats by transpalatine approach[7]; d) embolization by platelet aggregates in rabbits[8], by moulded silicone cylinders in primates[9], by carbon microspheres in rats[10]. Small animals can be used in large numbers because of their low cost and ease of accommodation. Rats have commonly been used in these studies[7,10–15]; the disadvantages of some of these models are due to hypoxia and/or hypotension which are required, in addition to the vascular occlusion, for producing cerebral ischemia. Recently, Pulsinelli and Brierley[16] introduced a new model of bilateral hemispheric ischemia in unanesthetized rats. In this model, cerebral ischemia is obtained by occlusion of the vertebral and carotid arteries. In the present paper we are reporting a model of focal cerebral ischemia in rats, following a selective occlusion of the MCA by a transbasisphenoidal approach.

For development of this technique, 26 albino rats (Sprague-Dawley), weighing 250–300 g were utilized. 10 of these animals were used to provide an anatomical view of the surgical procedure and to attain an adequate level of microsurgical skill. 4 rats were used for parallel sham operations. The animal, under ether anesthesia, is placed on its back; after an accurate exposure, the trachea is cannulated directly by a 16-gauge needle. By exposure and catheterisation of the femoral artery, the mean arterial