Depressor and Pressor Afferent Fibers in the Carotid Sinus Nerve of the Dog[1] (35855)

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It is well known that the carotid sinus nerve (CSN) contains fibers from both baroreceptors and chemoreceptors; however, few systematic studies appear to have been reported which establish the relative threshold of these different fiber groups to electrical stimulation in the dog. Douglas and Schauman (1) clearly illustrated three groups of fibers, two barosensory and one chemosensory, in the carotid sinus and aortic nerves of cats. We were able to completely confirm these results in cats but have directed the present studies to the dog. First we were interested in determining whether a similar functional separation of the fiber groups in the CSN of the dog could be shown and secondly we were interested in the feasibility of studying the cardiovascular effects resulting from such a selective activation of the different fibers in this nerve.

Methods. Twelve dogs weighing between 8 and 16 kg were anesthetized with chloralose (100 mg/kg iv) following premedication with morphine sulfate (3 mg/kg sc). The trachea was intubated and artificial ventilation provided during most of each experiment. The ventilatory rate was adjusted so that spontaneous breathing movements either ceased or only occurred occasionally. In some cases the animal was allowed to breathe spontaneously so that the inhibitory effects of CSN stimulation could be observed. Breathing movements were recorded as pressure changes in a pneumograph around the thorax. Both carotid sinus nerves were carefully isolated by finding their junction with the glossopharyngeal nerve and dissecting backward to the carotid sinus. Both were tied and cut close to the sinus and one was placed on silver electrodes for stimulation. The area was bathed in mineral oil to prevent drying of the nerves and to insulate nearby structures from the stimulus. Rectangular pulses from an AEL No. 104 stimulator were delivered to the CSN through an isolation transformer. Pulse duration and voltage were monitored on a cathode ray oscilloscope.

Initially the stimulus amplitude was adjusted to produce a maximum fall in blood pressure with a stimulus duration of 0.1 msec and at a frequency of 10 impulses/sec. This voltage and frequency were then used throughout the remainder of the experiment and the stimulus duration was varied. The duration of 0.1 msec was selected because maximum depressor effects were obtained with a 2–4-V stimulus with no evidence of changes in breathing. Approximately 5–10 times this voltage was required to produce increased breathing at this stimulus duration.

Systemic arterial blood pressure was measured from a branch of the femoral artery with a Statham P23Gb transducer recording on an Offner Dynograph. Heart rate was recorded continuously by a cardiotachometer triggered from the ECG.

The present data were obtained after bilateral cervical vagotomy. Flaxedil (1–2 mg/kg iv) was given to three animals to abolish the effects of the changes in breathing movements upon the blood pressure and heart rate responses in response to the stimuli of long duration. Bretylium tosylate (5–10 mg/kg iv) was given to two animals. In two other animals, tripelennamine (2–5 mg/kg iv) was given. One animal received atropine sulfate (2 mg iv).

Results. The average blood pressure and heart rate responses to stimulation of either the left or right CSN with electrical stimuli

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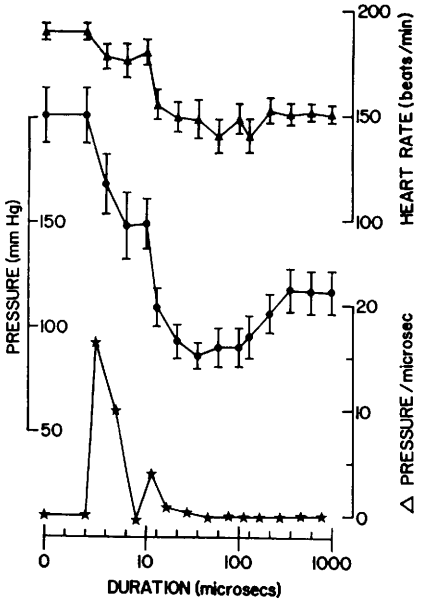

FIG. 1. Average ($N = 12$) blood pressure and heart rate responses in vagotomized dogs to progressively increasing stimulation of the CSN: stimulus frequency 10 impulse/sec, strength 2–4 V; duration was varied; standard error of the mean indicated by the vertical bars. (upper) heart rate; (middle) systemic blood pressure; (lower) rate of pressure change per microsecond increase in stimulus duration.

of progressively increased duration are summarized in Fig. 1. Stimulus frequency (10 impulses/sec) and voltage (2–4 V) remained constant throughout each experimental run. In every experiment a fall in blood pressure (35 ± 7 mm Hg) and cardiac slowing (12 ± 3 beats/min) occurred with stimuli of 5–6 μsec duration; however, little response occurred with stimulus durations below this value. The marked excitability of the CSN to the low duration stimuli is well illustrated by the rate of pressure fall per microsecond stimulus duration as shown in the lower curve of Fig. 1. Further increments in the stimulus duration caused a further fall in both pressure and heart rate; however, the rate of pressure change decreased rapidly to a minimum at about 10 μsec. Increasing the stimulus duration beyond 10 μsec resulted in a second increase in the response rate and a maximum lowering of the pressure and heart rate with a stimulus duration of about 60 μsec. These data suggest two groups of depressor fibers in the CSN with differing excitabilities. Whereas the response to stimulation of the most excitable fibers was often not well maintained, the responses resulting from the longer duration stimuli showed little recovery during stimulation. The curves in Fig. 1 represent the minimum values in all cases. Spontaneous breathing was unaffected by the stimuli of short duration but was inhibited by stimuli which produced the large depressor responses.

Stimulus durations of 200 μsec and greater caused a progressive increase in breathing effort and an increase in blood pressure and heart rate from the low levels which existed during maximum inhibition. Occasionally blood pressure and heart rate approached control values with stimuli of 1000 μsec duration. Blocking the breathing effort, caused by the long duration stimuli, with paralytic doses of Flaxedil (1–2 mg/kg) did not alter the direction or extent of the pressure responses. However, Flaxedil essentially blocked the tendency of the heart rate to increase, from the existing low rate, in response to the long duration stimuli. Thus it appears that the increase in heart rate observed in these experiments is the result of the indirect effect of chemosensory stimulation of breathing rather than a direct effect on the cardiac centers. Jacobs *et al.* (2) have recently pointed out that chemoreceptor stimulation causes cardiac slowing in the absence of breathing responses.

In two dogs, we were able to obtain essentially identical results by varying stimulus strength with a constant duration (20 μsec). Similar results were also obtained with a stimulus frequency of 100 impulses/sec instead of 10 impulses/sec in two experiments. At 100 impulses/sec the depressor responses were slightly larger than at 10 impulses/sec. This was particularly true when stimuli of the shortest duration were used.

Some recent evidence, presented by Heitz *et al.* (3), has suggested that part of the reflex response to CSN stimulation is mediated over histaminergic nerves. We considered the possibility that one group of the depressor fibers might involve histaminergic

or cholinergic efferent fibers. Tripelennamine (5–10 mg/kg iv) was given to two animals. In both cases the response to CSN stimulation was essentially abolished to all stimuli regardless of duration. Similarly bretylium (5 mg/kg iv) abolished the response to CSN stimulation in two different animals. Atropine had no effect on the responses in the one dog tested.

Discussion. Presuming a rough relationship between fiber diameter and excitability the data presented suggests that three fiber groups of different diameters exist in the CSN of the dog. Two fiber groups, one of large diameter and one of intermediate diameter, appear to be barosensory. The third fiber group, and the least excitable, appears to be small chemosensory fibers. Three similar fiber groups were described in the CSN of the cat (1); however, certain species differences exist. First, the most excitable (largest) barosensory fibers in the cat have a weak depressor effect; whereas, in the dog, activation of these fibers causes large changes in blood pressure. These changes are often not well maintained and a variable return toward control values occurs during stimulation. Secondly, the smaller barosensory fibers in the cat are less excitable than the chemosensory fibers, while in the dog the reverse is true. In both species, stimulation of the smaller barosensory fibers caused a large sustained reduction in blood pressure and heart rate. Speculation is unwarranted as to whether the role and mechanism of action of these two barosensory fiber groups in cardiovascular control is different. Landgren (4), in a detailed comparison of the action potentials from large and small barosensory fibers in the cat, concluded that the associated baroreceptors behaved similarly in response to intrasinusal pressure changes. If these two fiber groups made different efferent connections centrally this might result in a disengagement of some vascular beds to differing degrees. However, at the present time we have no evidence that this is the case.

Although the primary purpose of this investigation was to study the afferent characteristics of the CSN rather than its efferent limb, a few studies were conducted in an attempt to characterize the nature of the efferent connections made by the different afferent fiber groups. Based on this small number of experiments, it appears that no afferent fiber group is selectively blocked by cholinergic or histaminergic blocking drugs.

Tripelennamine and bretylium both block the response to CSN stimulation. This indicates a common interference point which seems unlikely to be histaminergic nerve endings. Tripelennamine has been shown by Isaac and Goth (5) to interfere with adrenergic nerve terminals. This may explain its blocking action in the present experiments. Further tests must be conducted to establish whether any component of the response to CSN stimulation involves efferent fibers other than sympathetic adrenergic fibers.

It is feasible that the judicious use of CSN stimulation can provide a tool to study the actions and interactions of the different fiber groups in cardiovascular control.

Summary. By progressively increasing the duration of an electrical stimulus, two barosensory and one chemosensory fiber groups have been illustrated in the CSN of the dog. Both barosensory fiber groups are more easily excited than the chemosensory fibers. In the cat, similar groups of fibers have been reported, but the chemosensory fibers are of intermediate excitability. All the fibers appear to exert their action on the sympathetic adrenergic system, since the response is blocked by bretylium, but not by atropine.

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