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Interaction between Depressor and Pressor Reflexes Arising from the Aorta in Dogs (41863)

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Abstract. In 18 dogs anesthetized with morphine–chloralose the interaction between the aortic nerve (AN) pressor and depressor reflexes was studied. Low-intensity, high-frequency electrical stimulation of the AN causes large decreases in heart rate and systemic pressure characteristic of baroreflex responses. High-intensity, low-frequency stimulation of the AN causes modest increases in heart rate and systemic pressure similar to the responses observed to intraaortic nicotine. Simultaneous electrical stimulation of these antagonistic reflexes results in much smaller ($P < 0.001$) reductions in heart rate and systemic pressure than can be explained on the basis of simple addition of the individual responses. Similarly the AN depressor reflexes are suppressed during intraaortic infusions of nicotine (40 μg/min). The results suggest that the inhibitory effects of the AN baroreflexes are suppressed by the aortic chemoreflexes. This interaction occurs in the CNS rather than at the level of the heart or vascular smooth muscle.

The aortic nerves in the dog carry afferent fibers arising from both baroreceptors and chemoreceptors of the aortic arch and adjacent arteries. Stimulation of the aortic baroreceptors produces a cardiovascular reflex response qualitatively similar to that produced by carotid baroreceptor stimulation (1); that is, decreased heart rate and ventricular performance (2) and a fall in systemic vascular resistance (3). In contrast, stimulation of aortic chemoreceptors produces a rise in blood pressure and an increased heart rate (4–9). Simultaneous stimulation of both the aortic baroreceptors and chemoreceptors would therefore give rise to antagonistic cardiovascular reflexes that would interact in some manner to determine the ultimate cardiovascular response.

In previous studies (10, 11) we investigated the interaction between the antagonistic responses to stimulation of the pressor afferents in the aortic nerve (AN) and the depressor afferents in the carotid sinus nerve (CSN) in dogs. From these studies we concluded that the aortic chemoreceptor reflex exerts its cardiovascular effects in part by directly increasing sympathetic outflow to the cardiovascular system and in part by suppressing the inhibitory effects of the carotid sinus baroreflexes on the autonomic output. In the present study we have extended these studies to examine the interaction between the aortic pressor afferents and the aortic baroreceptor reflex. The results suggest that the aortic chemoreflex suppresses the cardiovascular effects of the aortic baroreflex in a manner similar to that observed in the interaction with the carotid sinus baroreflex.

Methods. The experiments were conducted on a total of 21 dogs (10–20 kg). All animals were anesthetized with alpha-chloralose (100 mg/kg iv) 30 min after premedication with morphine sulfate (2 mg/kg sc). Anesthesia was maintained by a continuous intravenous drip of chloralose (approx 25 mg/kg/hr). The trachea was intubated and the animals were artificially ventilated with room air or oxygen. This generally eliminated spontaneous breathing movements in response to chemoreflex stimulation. In 8 animals a paralyzing dose of gallamine triethiodide (Flaxedil, 2 mg/kg iv) or pancuronium bromide (Pavulon, 0.2–0.5 mg/kg iv) was given to be certain that respiratory movements were abolished. This caused some reduction in the magnitude of the reflex responses but did not otherwise affect the results. In all animals ventilatory rate was adjusted to maintain end-expiratory CO_2 in the range of 4–5% as monitored by a LB-2 Beckman medical gas analyzer. Arterial pressure was measured from a catheter in a branch of the femoral artery with a Statham pressure transducer and was recorded on a Beckman polygraph. Heart rate was measured with a cardiotachometer triggered from the femoral arterial pulse. A second cannula in the femoral vein was used for intravenous drug infusion.

The AN were identified, carefully isolated, and in most experiments, cut and drawn into

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silver ring electrodes in the manner previously described (11). To exclude reflex changes from the carotid baroreceptors, both carotid sinus nerves were isolated and cut. The AN were stimulated with rectangular pulses from a dual-channel stimulator (Grass S-88). Low-intensity (0.01 msec, 1–3 V) stimuli were delivered to the AN from one channel of the stimulator. These stimuli primarily excite large, low-threshold baroreceptor afferents in the AN and are subthreshold to most of the chemoreceptor afferents (9). High-intensity stimuli (1.0 msec, 1–3 V) were delivered to the AN from the second channel of the stimulator. These stimuli activated both the baroreceptor and small chemoreceptor afferents in the AN. However, as we have shown (9), low-frequency (2 Hz) stimulation of the large baroreceptor afferents in the AN has minimal effects on the cardiovascular system. Thus the predominant reflex effect of low-frequency, high-intensity stimulation of the AN appears to result from the stimulation of chemoreceptor afferents. Similarly the response to low-intensity, high-frequency stimulation of the AN appears to predominantly arise from stimulation of large baroreceptor afferents (9).

In the present experiments, one channel of the stimulator delivered the low-intensity stimulus at high frequency (40 pulses/train, in 100-msec trains at two trains/sec), and the other channel delivered the high-intensity stimulus at low frequency (2 Hz). The strength of the high-intensity stimulus was adjusted to produce an increase of about 15 beats/min in the heart rate. In most experiments the two stimuli were delivered separately and then simultaneously to the same AN through the same electrode. During simultaneous stimulation the high-intensity stimulus was synchronized to the beginning of the low-intensity stimulus train. In six of the experiments, in addition to the usual method of stimulation, the high-intensity stimulus was delivered to one AN while the low-intensity stimulus was delivered to the other AN.

In eight animals, the number of low-intensity stimuli per train was varied in steps from 2 to 60. This series was then repeated with a high-intensity stimulus synchronized to the beginning of each train. The response curves thus obtained were compared.

In three animals intraaortic bolus injections (0.2 ml, 20 μg) or infusions (40 μg/min) of nicotine sulfate were given before cutting the AN. The infusions were made through a catheter placed in the aortic arch through the carotid artery. The response to low-intensity stimulation of one of the intact AN was then obtained in the presence and absence of nicotine infusion. In these experiments and in experiments reported earlier (9, 11) intraaortic nicotine causes variable responses following AN transection. Generally, the cardioacceleration and pressure rise are reduced or abolished but in some cases cardiac slowing and depressor responses occur.

Analysis of data. The sum of the sustained heart rate and blood pressure responses obtained to separate high- and low-intensity stimulation of the AN was compared to the sustained responses obtained during simultaneous stimulation of the AN with both high- and low-intensity stimuli. The standard paired t test was used. The 95% level of confidence was selected for significance. All responses are reported as mean values ± SEM.

Results. Figure 1 illustrates the heart rate and blood pressure responses obtained to AN stimulation. In this case, high-intensity, low-frequency stimulation caused an increase in heart rate of 8 beats/min and a systemic pressure rise of 40 mm Hg. This will be referred to as pressor stimulation. Low-intensity, high-frequency stimulation caused heart rate and blood pressure to fall by 84 beats/min and 75 mm Hg, respectively. We will refer to this as depressor stimulation. Simultaneous stimulation with both stimuli (combined stimulation) caused a decrease in heart rate of 42 beats/min and a 7 mm Hg increase in blood

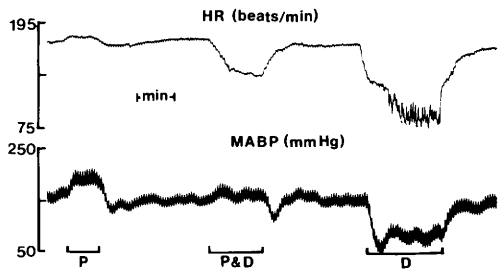

FIG. 1. Heart rate and systemic pressure responses to stimulation of AN pressor afferents (P) and depressor afferents (D) separately and in combination (P&D). Dog paralyzed with pancuronium.

pressure. This response is in contrast to the expected decrease in heart rate of 76 beats/min and a 35 mm Hg fall in pressure that would have occurred if these responses had summed in a simple algebraic manner. The average results of 37 trials in 18 dogs are shown in Fig. 2. Both the heart rate and blood pressure responses to combined stimulation were significantly smaller ($P < 0.001$) than the algebraic sum of the separate reflex responses.

The response curves shown in Fig. 3 illustrate the effect of increasing the frequency of depressor stimulation of the AN before and during simultaneous stimulation with a pressor stimulus. The upper curve illustrates the change in heart rate observed to depressor stimulation during ongoing pressor stimulation of the AN. In this case the initial heart rate was 173 ± 9 beats/min. The lower curve shows the change in heart rate to stimulation with the depressor stimulus alone. The initial heart rate in this case was 152 ± 20 beats/min. Each curve shows the change in heart rate due to depressor stimulation from the initial heart rate for that curve. The difference between these curves illustrates that during ongoing stimulation of the AN pressor reflex the effectiveness of the AN depressor reflexes is reduced over a wide range of stimulation. This difference was significant ($P < 0.05$) at all levels of stimulation above two stimuli per train. If simple addition of the reflex responses had occurred, the degree of slowing would have been the same in both cases and the curves would coincide.

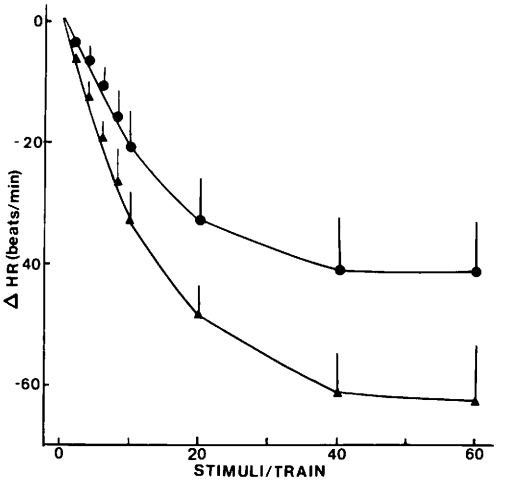

FIG. 3. Heart rate response curves (±SEM) to increasing depressor stimulation of the AN before (triangles) and during simultaneous pressor stimulation of the AN (circles). $N = 8$.

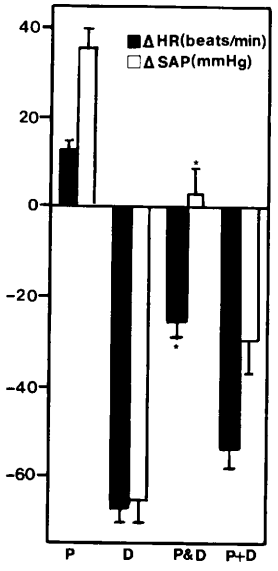

FIG. 2. Average heart rate and systemic pressure responses (±SEM) to separate pressor (P) and depressor (D) stimulation of the AN. The responses to combined stimulation (P&D) are compared to the algebraic sum (P + D) of the separate responses. This difference is significant ($P < 0.001$).

The possibility that the observed interaction was an artifact of two simultaneous stimuli being delivered to the same nerve was tested in six dogs. In these dogs one AN was stimulated with pressor strength stimuli while the other AN was stimulated with depressor strength stimuli. These responses are compared (Table I) to delivery of the pressor and depressor stimuli to the same AN in these dogs. The mode of stimulation had little effect on the results.

Figure 4 illustrates the heart rate responses to intraaortic nicotine (20 μg) before (4A) and during (4B) depressor stimulation of the AN. In the three animals tested in this study, intraaortic nicotine caused small increases in heart rate and systemic pressure. During depressor stimulation of the intact AN heart rate and systemic pressure fell. The responses to intraaortic nicotine were augmented such that they practically or completely offset the bradycardia and fall in systemic pressure. This is

TABLE I. HR RESPONSE TO DEPRESSOR AND PRESSOR STIMULATION OF THE SAME AN VS DEPRESSOR STIMULATION OF ONE AN AND PRESSOR STIMULATION OF THE OTHER AN (N = 6)

	Change in heart rate (beats/min ± SEM)			
Pressor stimuli delivered to:	Pressor	Depressor	Combined	Sum of separate pressor and depressor
Same AN as depressor	14 ± 7	−76 ± 9	−31 ± 8	−62 ± 9[a]
Opposite AN from depressor	15 ± 3	−76 ± 9	−36 ± 8[b]	−62 ± 10[a]

[a] Sum of the separate responses different ($P < 0.05$) from the response to combined stimulation.
[b] Not significantly different from response to delivery of both stimuli to the same AN.

further illustrated in Fig. 4C where the depressor response to stimulation of the intact AN is greatly reduced during nicotine infusion. Following transection of the AN, nicotine infusion had no effect on the AN depressor response.

Discussion. The results suggest that the aortic chemoreflex suppresses the inhibitory action of the aortic baroreflex as was previously observed in the interaction between the aortic chemoreflex and the baroreflex from the carotid sinus (10, 11). We recognize that electrical stimulation of the AN may not activate one afferent population in the nerve to the exclusion of all other afferents. However, in this and in our previous study we have obtained similar results with more physiological methods of reflex activation. Nicotine infusion into the aortic arch gives rise to reflex responses similar to those we observe in response to strong electrical stimulation of the AN. Both methods of AN pressor reflex activation reduce the response to stimulation of the aortic baroreflex to a greater degree than can be explained on the basis of simple addition of antagonistic reflexes. This suggests that an interaction between these reflexes is occurring centrally. This interaction is similar to that we have reported between the carotid baroreflexes and the aortic chemoreflexes (10, 11). In our earlier study (11) we suggested that the suppression of the carotid baroreflex occurred at the level of the medulla since this interaction still occurred following transcollicular decerebration. We also concluded that parasympathetic–sympathetic interactions at the heart level could not explain the results. We believe that these earlier arguments remain valid in the present study.

The suppression of the baroreflexes is not a unique action of the aortic chemoreflex. Somatic nerve pressor reflexes have been shown to suppress baroreflexes (12, 13) as have pressor reflexes arising from the thoracic aorta (14) and atrial volume receptors (15, 16). Thus it may be that all reflexes that cause cardioacceleration and vasoconstriction do so in part by suppressing the baroreceptor reflexes. The neuronal mechanisms involved in this suppression remain to be determined.

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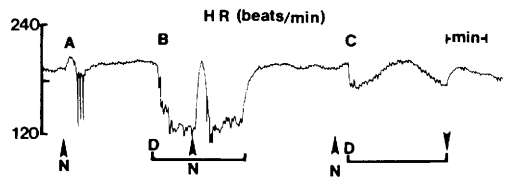

FIG. 4. (A) Heart rate responses to intraaortic bolus (20 μg) injections of nicotine (N). (B) Response to nicotine bolus during stimulation of AN depressor reflex (D). (C) Response to depressor stimulation of the AN during an intraaortic infusion of nicotine (40 μg/min, between arrows).

1. Donald DE, Edis AJ. Comparison of aortic and carotid baroreflex in the dog. J Physiol (London) **215**:521–538, 1971.
2. Levy MN, Ng ML, Zieske H. Cardiac and respiratory effects of aortic arch baroreceptor stimulation. Circ Res **19**:930–939, 1966.
3. Allison JL, Sagawa K, Kumada M. An open loop analysis of the aortic arch barostatic reflex. Amer J Physiol **217**:1576–1584, 1969.
4. Stern S, Rapaport E. Comparison of the reflexes elicited from combined or separate stimulation of the aortic and carotid chemoreceptors on myocardial contractility, cardiac output, and systemic resistance. Circ Res **20**:214–227, 1967.

5. Comroe JH, Mortimer L. The respiratory and cardiovascular responses to temporally separated aortic and carotid bodies to cyanide, nicotine, phenyldiguanide and serotonin. J Pharmacol Exp Ther **146**:33–41, 1964.
6. Biro GP, Hatcher JD, Jennings DB. The role of the aortic body chemoreceptors in the cardiac and respiratory responses to acute hypoxia in the anesthetized dog. Canad J Physiol Pharmacol **51**:249–259, 1973.
7. Karim F, Hainsworth R, Sofola OA, Wood LM. Responses of the heart to stimulation of aortic body chemoreceptors in dogs. Circ Res **46**:77–83, 1980.
8. Edis AJ, Shepherd JT. Selective denervation of aortic arch baroreceptors and chemoreceptors in the dog. J Appl Physiol **30**:294–296, 1971.
9. Kendrick JE, Matson GL. A comparison of the cardiovascular responses to stimulation of the aortic and carotid sinus nerves of the dog. Proc Soc Exp Biol Med **144**:404–411, 1973.
10. Kendrick JE, Matson GL. Interaction between carotid sinus baroreceptor and aortic nerve pressor reflexes in the dog. Amer J Physiol **237** (Heart Circ Physiol **6**):H662–H667, 1979.
11. Pisarri TE, Matson GL, Kendrick JE. Inhibition of baroreflex bradycardia by aortic nerve excitatory afferents in dogs. Amer J Physiol **243** (Heart Circ Physiol **12**):H607–H613, 1982.
12. Quest JA, Gebber GL. Modulation of baroreceptor reflexes by somatic afferent nerve stimulation. Amer J Physiol **222**:1251–1259, 1972.
13. Kumada M, Nogami K, Sagawa K. Modulation of carotid sinus baroreceptor reflex by sciatic nerve stimulation. Amer J Physiol **228**:1535–1541, 1975.
14. Pagani M, Pizzinelli P, Bergamaschi M, Malliani A. A positive feedback sympathetic pressor reflex during stretch of the thoracic aorta in conscious dogs. Circ Res **50**:125–132, 1982.
15. Stinnet HO, Bishop VS, Peterson DF. Reduction in baroreflex cardiovascular responses due to venous infusion in the rabbit. Circ Res **39**:766–772, 1976.
16. Vatner SF, Boettcher DH, Heyndrickx GR, McRitchie RJ. Reduced baroreflex sensitivity with volume loading in conscious dogs. Circ Res **37**:236–242, 1975.

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