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Beta-Adrenergic Influence on Cardiac Dynamics During Shock-Avoidance in Dogs[1,2]

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GRIGNOLO, A., K. C. LIGHT AND P. A. OBRIST. *Beta-adrenergic influence on cardiac dynamics during shock-avoidance in dogs.* PHARMAC. BIOCHEM. BEHAV. **14**(3) 313–319, 1981.—The role of beta-adrenergic receptors in the mediation of the cardiodynamic effects of a shock-avoidance task was evaluated in conscious dogs with the cardioselective beta-adrenergic antagonist practolol. The animals were chronically instrumented for the measurement of peak rate of change of left ventricular pressure (LV dP/dt), heart rate (HR), cardiac output (CO), systolic (SBP) and diastolic (DBP) blood pressure and total peripheral resistance (TPR), and were each subjected to brief bouts of shock-avoidance with and without practolol pretreatment (2–4 mg/kg). Shock-avoidance evoked reliable increases of LV dP/dt, HR, CO, SBP and DBP, and decreases of TPR. Beta-adrenergic blockade virtually eliminated LV dP/dt increases, attenuated HR and CO increases as well as the vasodilatation, diminished SBP increases in certain animals but did not affect DBP increases. Stable interindividual differences in the magnitude of LV dP/dt and HR increases during shock-avoidance were demonstrated; these differences were abolished by beta blockade. These findings indicate that a beta-adrenergic mechanism accounted for most of the rise of LV dP/dt during avoidance but contributed proportionally less to the elevations of HR and CO. Inter-individual differences in myocardial reactivity were however completely ascribable to beta-adrenergic factors.

Left ventricular dP/dt Heart rate Cardiac output Blood pressure Dobutamine Practolol Stress

BEHAVIORAL stimuli can elicit cardiodynamic changes. Shock-avoidance, for example, is associated with elevations of heart rate, stroke volume, cardiac output, left ventricular systolic pressure and peak rate of change of pressure in laboratory dogs [2, 8, 14]. The sympathetic nervous system has been implicated in the mediation of these responses. In fact, propranolol reduces the magnitude of the tachycardia [1]. However, no experimental evidence directly ascribing increases in the peak rate of change of left ventricular pressure (LV dP/dt, an indirect measure of cardiac contractility) or cardiac output (CO) to activation of beta-adrenergic receptors has been reported in conscious dogs during avoidance. The purpose of the present research was to gather this evidence. In addition, we sought to determine whether a beta-adrenergic mechanism might account for the presence of interindividual differences in cardiac responsivity to avoidance frequently observed in our laboratory (unpublished observations).

In the present study the cardiodynamic effects of a shock-avoidance task were evaluated in chronically instrumented dogs, with and without prior administration of the cardioselective beta-adrenergic antagonist practolol. Unlike propranolol, practolol has a relatively weak action on vascular beta receptors and minimal penetration of the blood-brain barrier [27]; the potential vasomotor and behavioral effects of beta blockade are thus reduced when practolol is used. In order to arrive at an effective dosage of practolol and to test the adequacy of the blockade, cardiac beta receptors were activated exogenously with intravenous boli of the cardioselective beta-adrenergic agonist dobutamine (a positive inotropic agent), with and without practolol pretreatment.

METHOD

Subjects and Instrumentation

Seven male mongrel dogs (12–20 kg) were obtained from the Division of Laboratory Animal Medicine at the University of North Carolina. They were screened to exclude the presence of microfilaria and were housed individually with free access to food and water.

A left thoracotomy at the level of the fourth intercostal space was performed aseptically using Metaphane or Nembutal anesthesia. A solid-state pressure microtransducer (Konigsberg, P-6.5) was inserted into the left ventricle via a stab incision at the apex; the incision was closed and the cable secured with a purse-string suture. The tips of two polyvinyl-chloride catheters (Bard, 8-French) were advanced to the descending limb of the aortic arch and to the right atrium via the internal thoracic artery and vein, respectively. The catheters had been pretreated with Tridodecylmethylammonium Chloride-Heparin Complex (TDMAC, 2% solution, Polysciences) to minimize the adhesion of clots to

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the lumen for the duration of the experiment. An electromagnetic flow transducer (Carolina Medical Electronics or Zepeda Instruments) was positioned on the ascending aorta; a dacron sleeve was first wrapped around the vessel to stimulate fibrosis and protect the wall against rupture by friction. All catheters and leads were tunnelled subcutaneously to the neck, where they were externalized and protected with a bandage. The catheters were flushed with a dilute 1000 U/ml) heparin solution three times a week. All dogs were treated with antibiotics and allowed to recover for 2–4 weeks. One animal (dog 7) was studied only in the pharmacological (dobutamine and practolol) portion of the experiment; the appearance of a severe infection led to the termination of the protocol.

All physiological variables were recorded on a Beckman Type RM 8-channel Dynograph. Left ventricular pressure (LVP) was obtained from the implanted microtransducer, and LV dP/dt via an active analog differentiator based on an operational amplifier (frequency range: 0.75–50 Hz). Left ventricular pressure was not quantified because of persistent drift in the recorded signal; LV dP/dt, on the other hand, could be quantified (in mm Hg/sec) because it was calibrated on the basis of the transducer sensitivity, which was shown to remain stable by performing *in vitro* manometric tests before implantation and after excision from each animal. Heart rate (HR) was derived automatically using a cardiotachometer in series with LVP, and was expressed in beats/min. Cardiac output (CO) was obtained as mean aortic flow (in L/min) from an electromagnetic flowmeter (Carolina Medical Electronics). The flow transducers were calibrated before implantation on an artificial system which pumped whole blood across the transducer at known rates of flow; one could thus set the flowmeter probe factors to yield the correct flow values. All transducers appeared to remain stable during implantation since baseline CO levels were relatively constant in a given dog. The arterial blood pressure was measured via the aortic catheter connected to an extra-corporeal transducer (MP-17, Micron Instruments); the systolic (SBP) and diastolic (DBP) values were quantified and expressed in mm Hg. During the experiments the pressure transducer lay approximately at heart level in the pocket of a jacket worn by the animals, thus minimizing any relative shift in position between the animal and the transducer. Blood pressure tracings were considered relatively damp-free if the dichrotic notch was visible. In any case, the catheter was flushed once or twice in the course of every experiment.

No flow transducer was implanted in dog 1, which served as a pilot for the left ventricular preparation. In addition, equipment malfunction prevented the recording of CO in dog 3, LVP and LV dP/dt in dog 5, and blood pressure in dog 6.

Procedure

Dogs stood during all phases of the experiment, fitted with a jacket (Alice Chatham Medical Arts, Los Angeles) and partially restrained in a custom-designed enclosure. This apparatus consisted of a treadmill platform (92×47 cm) enclosed on three sides by cloth-covered heavy wire mesh; one of these sides was hinged to permit access to the platform. Restraint was provided by a harness to which the jacket was secured; dogs could move forward and backward within the enclosure but could not sit or turn. The front of the apparatus consisted of a translucent response panel (30×37 cm). The dogs were visually isolated during the experiments. No studies were conducted until the animals, after recovering from surgery, became fully habituated to the apparatus and showed little restlessness or discomfort.

Each experimental session lasted approximately 90 min. Electrodes were applied to a shaved hind leg and connected to a constant-current generator (Grayson-Stadler, E6070B) for the delivery of shocks (1–5 mA, 0.5–1.0 sec). After 30 min of quiet adaptation a 40 W light bulb located behind the response panel and a white-noise generator connected to a speaker placed inside the apparatus were switched on and the shock-avoidance paradigm was instituted for 3 min. The S^D was a 1-kHz tone (Microtonics) which was followed by a shock after an interval of 10 sec unless the dog pressed the response panel; the tone was terminated following a response or a shock. The interval between response or shock and the following S^D was 20 sec. Dogs could avoid tones and shocks altogether by pressing the panel more or less continuously with the snout or a paw. Both the panel light and the noise were turned off at the end of each 3-min bout of avoidance. Experimental sessions were scheduled every other day and each comprised three 3-min bouts of avoidance spaced 15 min apart. The short duration of each bout and the spacing were intended to minimize habituation to the stressor. All of the scheduled avoidance bouts were subsequently analyzed; however, quantification of physiological variables began at either the third or the fourth training session, when dogs typically avoided most of the shocks and struggling had ceased.

The beta-adrenergic antagonist practolol (Ayerst) was infused intravenously (2–4 mg/kg) over 5 min during the baseline period on alternate experimental sessions. The half-life of practolol is reported to be 6–8 hours [27]. A test bolus of dobutamine (DBT, Lilly, 15 μg/kg) was infused intravenously on several occasions, with and without practolol pretreatment, before any avoidance training and again after dogs had been trained. Dobutamine was administered before and/or after the avoidance bouts.

Data Quantification and Analysis

Cardiovascular responses were quantified directly from the chart recordings by hand on a beat-by-beat basis. In addition to the variables obtainable directly from the implanted transducers, stroke volume (SV) was calculated as the ratio of CO to HR (in ml), mean arterial pressure (MAP) as DBP plus one-third of the pulse pressure, and total peripheral resistance (TPR) as the ratio of MAP to CO (in mmHg/L/min). An average resting value of each variable was calculated for either 10 or 20 sec immediately before each DBT bolus or bout of avoidance. Individual responses to these manipulations were quantified as follows.

For DBT, cardiovascular variables were averaged for the 10-sec time segment containing the peak response (between 10 and 20 sec after infusion). This procedure was identical to Intact and Blocked trials.

For shock-avoidance, variables were quantified beat-by-beat beginning at the onset of each bout and immediately following each resting period. Only the first 2 min of each bout were analyzed, since the ongoing physiological activity did not change noticeably after that point. Avoidance bouts with and without beta blockade were designated Blocked and Intact, respectively. Average values of each variable were calculated in each bout for the 10–20 sec resting period (REST) and for the 120-sec avoidance period (STRESS).

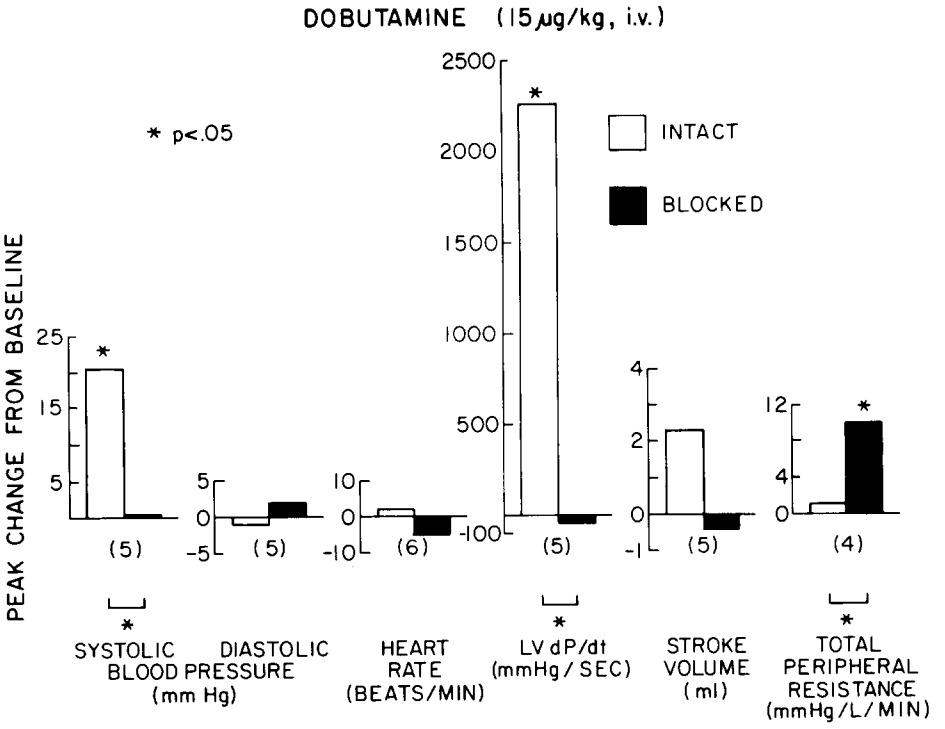

FIG. 1. Effects of beta-adrenergic blockade on cardiovascular responses to a bolus injection of dobutamine. Figures in parentheses refer to the number of dogs in which a given variable was measured. Significant differences between Intact and Blocked responses are indicated by brackets.

Statistical comparisons were carried out with Student's t-test; results were considered statistically significant at $p<0.05$. Subsequently, in order to obtain estimates of the covariation among the major cardiac parameters (LV/dP/dt, HR and CO) during avoidance in individual dogs, each STRESS period was subdivided into four 30-sec averages for these variables and bivariate correlation and regression coefficients were computed using the difference between each 30-sec STRESS segment and the corresponding REST period for both Intact and Blocked bouts. This analysis also tested the significance of the Intact and Blocked regression coefficients (slopes) and the significance of differences between slopes [13]. Bivariate, rather than multivariate, regression was used because the main concern was to determine whether the relationship between any two variables was altered by beta-adrenergic blockade. Besides, a multivariate approach would have been questionable because certain variables (e.g., CO, SV, BP) were not available in all dogs.

Dog 1 was a pilot animal and was exposed to a less elaborate behavioral task. No panel response was required. Tones were presented every 20 sec during 3-min bouts, beginning 40 sec after the onset of each bout, and unavoidable shocks were delivered 10 sec after tone onset. The cardiovascular responses to this task have already been described [22]; accordingly, the data quantification for this animal was limited to REST and to the first 40 sec of STRESS (before the delivery of any tones or shocks).

All the other dogs performed successfully on the shock-avoidance task and received only occasional shocks. Care was taken to match the number of shocks delivered during Intact and Blocked bouts. The cardiovascular activity within 5 sec after shock delivery was not quantified; the loss of data resulting from this policy was negligible because of the small number of shocks actually delivered.

RESULTS

Dobutamine

Figure 1 depicts the effects of DBT infusion as peak changes of each variable from baseline. With beta receptors intact, LV dP/dt rose significantly by an average +73%. Stroke volume rose 10–19% in all dogs except one, and CO rose 6–27% in four of five dogs. Systolic blood pressure increased significantly by 20 mmHg on the average, while HR, DBP and TPR did not change. With beta receptors blocked, LV dP/dt, HR, SV, CO and SBP did not change from baseline; TPR, however, rose significantly.

Shock-Avoidance

Table 1 shows the mean values of all cardiovascular variables obtained during Intact and Blocked shock-avoidance bouts in the REST (10–20 sec) and STRESS (120 sec) conditions.

Before the blockade, LV dP/dt rose significantly by an average +23% during avoidance; after blockade LV dP/dt also rose significantly, but only by +7%. Both REST and

TABLE 1

EFFECTS OF SHOCK-AVOIDANCE ON CARDIAC DYNAMICS, BLOOD PRESSURE AND TOTAL PERIPHERAL RESISTANCE WITH AND WITHOUT BETA-ADRENERGIC BLOCKADE

		Intact	Blocked	p[a]
Left ventricular dP/dt (mmHg/sec)	Rest	3326±120	2843±117	<0.01
	Stress	4104±169†	3029±135†	<0.01
	n	57	42	
Heart rate (beats/min)	Rest	92±3	85±3	
	Stress	121±4†	100±3†	<0.01
	n	69	48	
Cardiac output (L/min)	Rest	2.45±0.09	2.19±0.11	
	Stress	3.23±0.10†	2.63±0.11†	<0.01
	n	50	36	
Stroke volume (ml)	Rest	30±1	27±2	
	Stress	31±1*	28±2	
	n	50	36	
Systolic blood pressure (mmHg)	Rest	141±3	137±4	
	Stress	156±3†	148±4†	
	n	57	39	
Diastolic blood pressure (mmHg)	Rest	81±1	82±1	
	Stress	90±1†	90±2†	
	n	57	39	
Total peripheral resistance (mmHg/L/min)	Rest	47±3	54±3	
	Stress	38±2†	49±3*	<0.01
	n	38	27	

[a]Significant difference between Intact and Blocked values.

*$p<0.05$, †$p<0.01$ denote significant difference between Rest and Stress values.

n=number of bouts. Mean ± SE.

STRESS values of LV dP/dt were significantly lower after beta blockade.

Heart rate rose significantly during avoidance both before (+32%) and after (+18%) the blockade, but in the latter case the magnitude of the cardioacceleration was significantly reduced. Cardiac output, likewise, rose significantly before (+32%) and after (+20%) the blockade, which however reduced the magnitude of the response significantly. REST values of both HR and CO were unaffected by beta-adrenergic blockade. Stroke volume showed a small but significant increase before the blockade, and no change after the blockade, which had no effect on either REST or STRESS levels of SV.

Both SBP and DBP rose significantly during avoidance (+11%) with beta receptors intact; the magnitude of this pressor response was not affected by the blockade, which also failed to alter REST levels of either variable. Total peripheral resistance fell significantly during avoidance both before (−19%) and after (−9%) beta blockade; however the magnitude of this vasodilatation was significantly reduced by the blockade, which did not affect TPR levels at REST.

There were clear differences among dogs in cardiovascular reactivity to avoidance, particularly with respect to LV dP/dt and HR. Figure 2 illustrates these differences by showing the mean responses of LV dP/dt and HR during avoidance in individual animals. A repeated-measures analysis of variance tested whether (a) a particular response magnitude was a stable characteristic of a given dog and (b) whether beta-adrenergic mechanisms contributed to the difference in response magnitude among animals. In order to simplify the design, the number of Intact and Blocked bouts was matched in every animal by omitting the last few Intact bouts from the analysis; the means of the bouts which were included differed from the means of all bouts by 4% for LV dP/dt and by 8% for HR.

For LV dP/dt, there was a significant interaction, $F(4,37)=9.45$, $p<0.01$, between dogs and pharmacological treatment (Intact vs Blocked): post-hoc tests (Newman-Keuls) showed that before the blockade LV dP/dt rose consistently more in dog 2 than in all other dogs, and more in dogs 1 and 3 than in dogs 4 and 6. After beta blockade there were no significant differences in response magnitude among animals. Within-subject analyses of simple effects showed significant differences between Intact and Blocked responses in all except dog 6.

For HR, a significant interaction, $F(5,42)=5.12$, $p<0.01$, between dogs and pharmacological treatment was also demonstrated. Newman-Keuls test results showed that before the blockade HR rose consistently more in dog 1 than in all other dogs, and more in dogs 2 and 3 than in dogs 5 and 6. After the blockade, animals did not differ with respect to HR response magnitude. Within-subject analyses of simple effects again showed significant differences between Intact and Blocked responses in all except dogs 5 and 6.

In summary, the foregoing analysis demonstrated the existence of characteristic individual differences among dogs in LV dP/dt and HR responsiveness to shock-avoidance; these differences were completely eliminated by beta-adrenergic blockade.

The covariation among changes in LV dP/dt, HR and CO during shock-avoidance was examined with regression techniques (Table 2). Left ventricular dP/dt and HR changes were highly correlated both with and without beta blockade; in the Blocked condition, however, the slope of this relationship (with HR as predictor) was always significantly lower than in the Intact condition. This is illustrated for dog 3 (Fig. 3). Specifically, in each dog a given HR increase was associated with a smaller LV dP/dt increase after the blockade than before the blockade; this discrepancy grew more pronounced the larger the HR increase.

Left ventricular dP/dt and CO responses were also highly correlated both before and after the blockade. Again the slope of this relationship (with CO as predictor) was significantly lower by the blockade. Finally, the relationship between CO and HR responses was characterized by high correlations in both the Intact and Blocked conditions. The slope of this relationship was significantly lowered by the blockade in two dogs (4 and 6): in the remaining two dogs the slopes were identical.

DISCUSSION

The main purpose of this research was to gather evidence that beta-adrenergic influences on the heart associated with shock-avoidance affect not only HR but other cardiac parameters as well, specifically LV dP/dt and CO. The results indicate that beta-adrenergic mechanisms accounted for most of the increase in LV dP/dt during avoidance but contributed proportionally less to the elevations of HR and CO. Beta-adrenergic blockade consistently altered the relation-

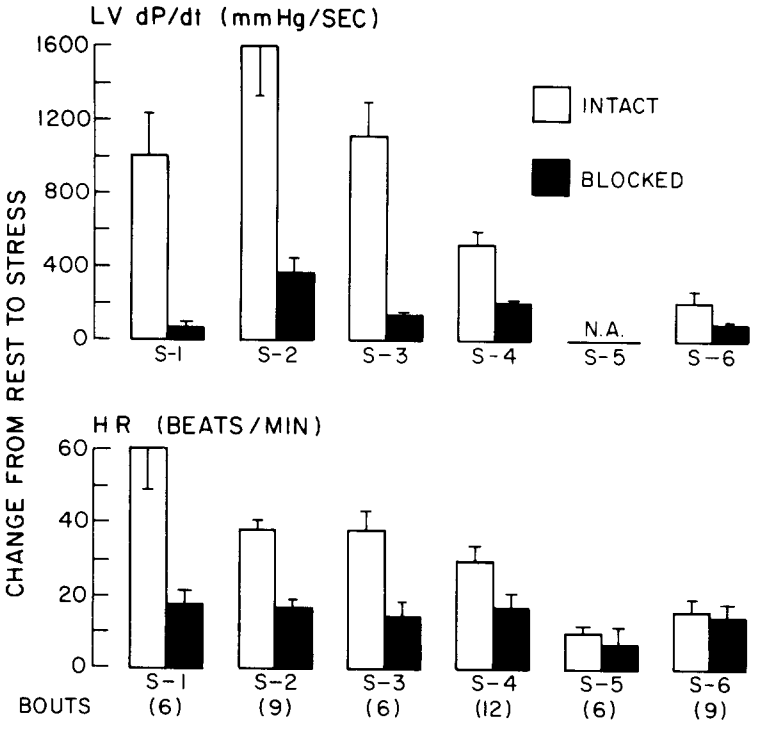

FIG. 2. Mean (±SE) change of LV dP/dt and HR from REST to STRESS in individual dogs (S-1, S-2, etc.) with and without beta-adrenergic blockade. Number of Intact and Blocked bouts was matched in every dog (see text) and is shown in parentheses at bottom. N.A.=not available.

ship among LV dP/dt, HR and CO changes, i.e., it suppressed LV dP/dt responses more effectively than either HR or CO responses. Finally, beta-adrenergic influences on the myocardium were the basis of individual differences among animals in LV dP/dt and HR responsivity to shock-avoidance.

The dose of practolol used in the present study led to an effective blockade of cardiac beta receptors. In fact, the large rise of LV dP/dt in response to DBT was completely abolished by the blockade. Our findings that DBT augments contractility, SV and CO via a beta-adrenergic mechanism and with little chronotropic effect agree with the literature [11, 30, 32]. In addition, these results indicate that changes in LV dP/dt reflect beta-adrenergically induced changes in myocardial contractility, and support similar contentions by others (e.g. [26]). Finally, the cardio-selectivity of practolol is questioned by the observation that TPR, which did not change in response to DBT alone, rose significantly after practolol pretreatment (Fig. 1); in addition, practolol reduced the magnitude of the vasodilatation during avoidance (Table 1).

Left ventricular dP/dt increases during shock-avoidance were greatly reduced by beta-adrenergic blockade. Left ventricular dP/dt has been shown to rise during cardiac sympathetic nerve stimulation [9] and during shock-avoidance [8]; LV dP/dt elevations occurring in anticipation of unavoidable shocks are reduced by propranolol [26] and are completely eliminated by transection of the cardiac nerves [25]. As recently reported [7], transection of the left ansa subclavia abolishes the rise of LV dP/dt during shock-avoidance. These results, complemented and extended by our own, are consistent with the hypothesis that during shock-avoidance in dogs there occurs an increase in myocardial contractility which is mediated largely by the left cardiac sympathetic nerves acting via a beta-adrenergic mechanism. In addition, beta blockade lowered significantly the resting levels of LV dP/dt; since practolol has little direct depressor action on myocardial tissue [16,29], this effect was probably due to the attenuation of a moderate degree of resting beta-adrenergic tone.

Cardiac output elevations during shock-avoidance were reduced by beta blockade, but to a lesser extent than LV dP/dt elevations. The regression analysis (Table 2) demonstrates that a given CO increase was associated with a smaller LV dP/dt increase after the blockade than before the blockade. Since SV did not change appreciably as a function of either avoidance or beta blockade, and since HR responses were highly correlated with CO responses in all animals, it was the altered relationship between LV dP/dt and HR which accounted for this phenomenon; specifically, the blockade reduced LV dP/dt increases significantly more than HR increases. This suggests a more substantial sympathetic contribution to LV dP/dt changes than to HR changes, and is consistent with the notion that the neural control of HR may be predominantly vagal [10]; on the other hand, beta-adrenergic blockade did in fact reduce the cardioaccel-

TABLE 2

CORRELATION COEFFICIENTS AND REGRESSION ANALYSIS OF CARDIAC RESPONSES DURING SHOCK-AVOIDANCE WITH AND WITHOUT BETA-ADRENERGIC BLOCKADE

Dog	r		slope		
	Intact	Blocked	Intact	Blocked	d
			HR vs LV dP/dt		
1	+0.93†	+0.89*	18.76†	6.69†	†
2	+0.64†	+0.48†	42.51†	15.26†	†
3	+0.85†	+0.77†	22.96†	10.59†	†
4	+0.68†	+0.44†	14.55†	3.11†	†
5	—	—	—	—	
6	+0.83†	+0.73†	24.43†	5.20†	†
			CO vs LV dP/dt		
1	—	—	—	—	
2	+0.69†	+0.61†	1274.04†	469.65†	†
3	—	—	—	—	
4	+0.76†	+0.55†	464.32†	170.46†	†
5	—	—	—	—	
6	+0.92†	+0.88†	740.46†	247.09†	†
			HR vs CO		
1	—	—	—	—	
2	+0.65†	+0.55†	0.023†	0.023†	
3	—	—	—	—	
4	+0.83†	+0.77†	0.029†	0.018†	†
5	+0.88+	+0.98†	0.037†	0.033†	
6	+0.93†	+0.89†	0.034†	0.022†	†

*$p<0.05$, †$p<0.01$, —not available, d=statistical significance of comparisons between slopes. Significance of correlation and regression coefficients is shown.

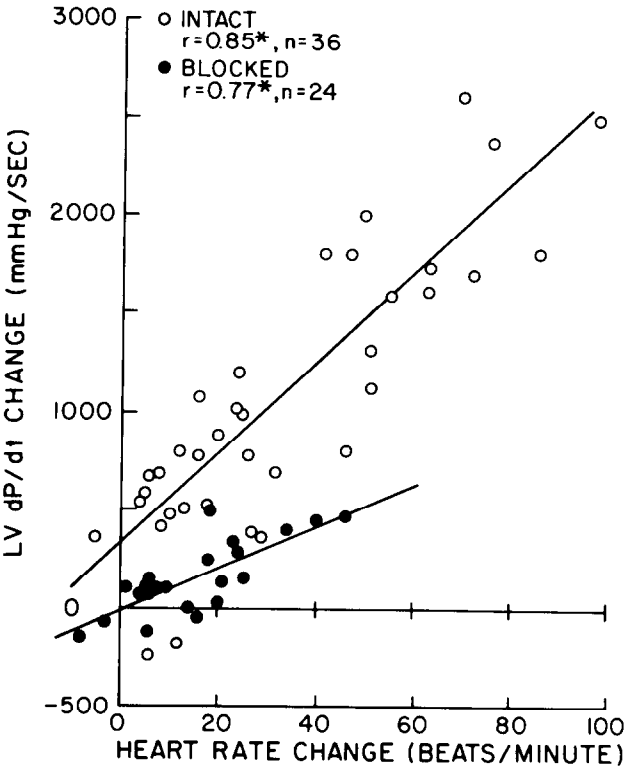

FIG. 3. Regression lines and correlation coefficients (r) depicting for dog 3 the relationship between HR and LV dP/dt changes during 9 Intact and 6 Blocked bouts of avoidance. Each point represents 30 sec of avoidance. *$p<0.05$.

cration engendered by shock-avoidance. Transection of the left ansa subclavia [7] abolishes both LV dP/dt and HR increases during avoidance, perhaps because afferent as well as efferent traffic is eliminated. In our study, blockade of only the efferent (beta-adrenergic) limb has unmasked a differential sympathetic effect on HR and LV dP/dt. More generally, the present findings corroborate the notion that alterations of CO are more readily ascribed to variations of HR than of SV [3,31].

The arterial pressure rose during avoidance. Beta blockade did not attenuate this response, on the average, but a beta-adrenergic contribution to SBP changes was evident, for example, in dog 3; in this animal a sharp rise of SBP in the initial portion of each bout was reduced by the blockade from +13.3 to +3.5 mmHg and was well correlated with the attenuation of marked chronotropic and inotropic changes. A beta-adrenergic link between cardiac and SBP changes has been reported in humans during a stressful reaction time task [23]. Failure of the blockade to affect the pressor response in general was probably due to the fact that practolol diminished both the CO elevation and the peripheral vasodilatation during shock-avoidance.

The behavioral paradigm employed in the present study differed somewhat from that used in other laboratories (e.g. [1,8]). Specifically, the duration of each trial of avoidance was limited to 3 min, to minimize progressive habituation to the paradigm. This was dictated by the necessity to maintain continued reactivity to the stressor, in order to study each animal repeatedly with and without beta blockade. In general, the physiological changes reported here are qualitatively similar to those observed by others and thus are not simply a function of the difference in the behavioral paradigm.

Individual differences in the reactivity of the heart to shock-avoidance were clearly apparent. Animals differed consistently with respect to the magnitude of LV dP/dt and HR increases in the Intact condition (CO was available in too few dogs to permit viable comparisons). Beta-adrenergic blockade eliminated these differences, even though it failed to completely abolish increases of LV dP/dt and especially of HR. These residual increases may be ascribed to parasympathetic withdrawal since both HR [10] and LV dP/dt [15] are sensitive to vagal influences. While the existence of interindividual differences in physiological responsivity may be intuitive, its functional basis is not obvious *a priori* because of the multiplicity of potential mediators. The present results suggest that interindividual variation in cardiac reactivity to a behavioral task is a consequence of varying degrees of

beta-adrenergic drive on the heart; these may be related to beta receptor density or sensitivity, or to differences in higher nervous integration. It is important to note that vagal disinhibition, while presumably responsible for residual increases in cardiac performance after beta blockade, did not adequately differentiate dogs with respect to response magnitude.

The sympathetic nervous system is a particularly important link to certain cardiovascular disorders, particularly cardiac arrhythmias [5, 21, 28] and borderline hypertension characterized by an elevated cardiac index [12]. Behavioral factors may contribute to cardiac electrical instability and overactivity [4, 17, 20] via neurogenic influences of sympathetic and parasympathetic origin [12]. The susceptibility of an individual to these disorders may well be related to the degree of cardiac beta-adrenergic drive engendered by behaviorally stressful situations. In man, individual differences in HR reactivity to a reaction time task which increases beta-adrenergic stimulation of the heart have been demonstrated [23,24]. Moreover, interindividual differences in the magnitude of cardiovascular response to a difficult cognitive task [19] have been shown to remain stable for as long as one year [18]. Collectively, these observations encourage the view that stable differences in beta-adrenergic reactivity to behavioral events may signal the susceptibility of certain individuals to abnormalities in the performance of the heart.

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