Instrumental Conditioning of Large-Magnitude, Daily, 12-Hour Blood Pressure Elevations in the Baboon

Abstract. *Blood pressure and heart rate were monitored continuously in four baboons during extended exposure to a daily 12-hour conditioning procedure providing food and shock-avoidance as contingent consequences of prespecified increases in diastolic blood pressure. Sustained and significant increases (30 to 40 mm-Hg) in both systolic and diastolic blood pressure were maintained throughout the daily 12-hour conditioning sessions, accompanied by elevated heart rates.*

Previous reports of instrumental blood pressure conditioning in laboratory animals and man have generally described cardiovascular changes limited, for the most part, in magnitude and duration. Typically, such conditioned blood pressure elevations in laboratory rats (*1*), squirrel monkeys (*2*), rhesus monkeys (*3*), and baboons (*4*) have been maintained for intervals limited to seconds or minutes, and, with few exceptions (*5*), only small-magnitude conditioned-pressure changes (less than 6 mm-Hg) have been described in human subjects (*6*). In addition, numerous theoretical and methodological questions have been raised concerning the role of "voluntary mediators" (for example, respiratory and skeletal responses) in the development and maintenance of such instrumental visceral-autonomic conditioning effects (*7*).

The present report describes sustained, large-magnitude elevations in blood pressure accompanied by elevated but progressively decreasing heart rates in baboons related to instrumental food-reward and shock-avoidance conditioning. Specifically, maintained elevations of 30 to 40 mm-Hg in both systolic and diastolic blood pressure were accompanied by elevated but decreasing heart rates during 12-hour conditioning sessions. Additionally, both blood pressure and heart rate were observed to decrease progressively during alternating 12-hour daily "rest" ("conditioning-off") intervals.

Four adult male dog-faced baboons (*Papio anubis*), each weighing approximately 35 lb (16 kg), served as subjects. Each animal was maintained in a primate restraining chair (*8*) housed in a sound-reducing experimental chamber provided with stimulus lights and an automatic food dispenser, as described in previous reports (*4*). Brief electric shocks (8 ma for 0.25 second) were administered through stainless steel electrodes applied with conducting paste to a shaved portion of the animal's tail. Each animal was surgically prepared (*9*) with two silicone-coated polyvinyl catheters, one implanted into the femoral artery to a point just above the level of the iliac bifurcation, and the other inserted into the vein and advanced to the inferior vena cava. The distal end of each catheter was tunneled under the skin, exited in the interscapular region, fitted with an 18-gauge Luer stud adapter, and connected to a Statham transducer (p23De) shock-mounted on the outside top of the experimental chamber. Patency of the catheter was maintained by continuous infusion of lightly heparinized saline (5000 USP units per liter) at a constant rate of approximately 4 ml/hour, and by a more rapid "flush" once each day. Periodic blood chemistry determinations of plasma sodium levels showed them to remain within the normal limits for the baboon (*10*) under these saline infusion conditions. Daily calibration of the system was accomplished without dismantling the components by integration of a mercury manometer through a series of three-way valves (*11*). Pressure signals from the transducer were amplified and displayed on an Offner polygraph (type R) which provided continuous heart rate and beat-by-beat blood pressure recordings. In addition, the pressure and rate signals were analyzed by an electronic averager (*12*) which provided on-line printout of heart rate (in beats per minute) and both systolic and diastolic blood pressure (in millimeters of mercury) over consecutive 40-minute intervals. Throughout the experiment, blood pressure and heart rate were measured continuously, 24 hours each day, and adjustable meter relays integrated with the physiological recording system provided for selection of criterion diastolic blood pressure levels and automatic programming of contingent food and shock events. Two "feedback" lights, mounted in front of the animal, signaled when diastolic blood pressure levels were above or below the prescribed criterion.

The instrumental conditioning procedure required the animals to maintain prespecified diastolic blood pressure levels in order to obtain food and avoid shock. Five 1-g food pellets were de-

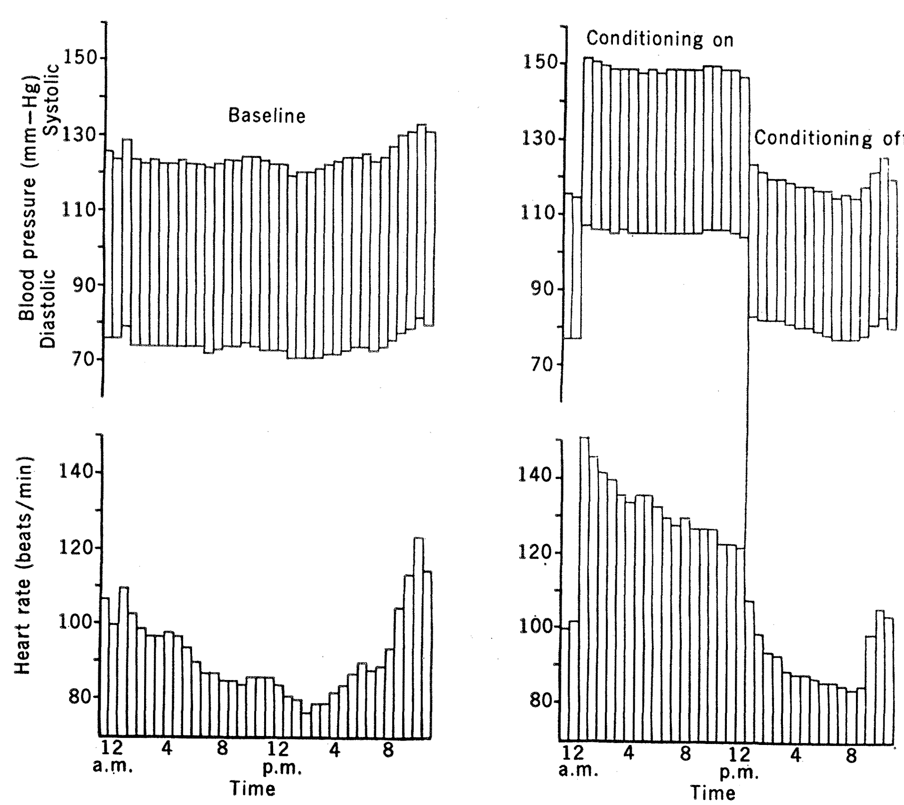

Fig. 1. Average blood pressure and heart rate values for four baboons over consecutive 40-minute intervals during sixteen preexperimental baseline determinations (left panel) compared with sixteen 12-hour conditioning-on, 12-hour conditioning-off ses sions (right panel).

Table 1. Average heart rate (HR, in beats per minute) and both systolic (Sys) and diastolic (Dia) blood pressures (in millimeters of mercury) for each baboon during the baseline determinations compared with the 12-hour conditioning-on, 12-hour conditioning-off sessions. Listed are the mean, the standard error of the mean (S.E.M.), and the number (*N*) of 40-minute intervals in each sample. All cardiovascular values are averages of the last 6 hours of the conditioning-on period, and of the first 6 hours of the conditioning-off period, with baseline entries for the corresponding 6 to 12 p.m. and 12 to 6 a.m. time periods. The asterisks indicate cardiovascular values that are significantly different ($P < .001$) from both the corresponding baseline and the conditioning-off cardiovascular determinations.

Animal	Baseline						Conditioning on			Conditioning off		
	6 p.m. to 12 p.m.			12 p.m. to 6 a.m.			6 p.m. to 12 p.m.			12 p.m. to 6 a.m.		
	Sys	Dia	HR	Sys	Dia	HR	Sys	Dia	HR	Sys	Dia	HR
Baboon 1												
Mean	127	77	108	120	69	96	146*	103*	134*	122	86	93
S.E.M.	0.9	0.9	2.0	0.8	0.9	1.1	0.5	0.2	1.8	0.6	0.6	1.5
N	36	36	36	36	36	36	36	36	36	36	36	36
Baboon 2												
Mean	130	74	75	135	77	81	149*	100*	144*	123	79	101
S.E.M.	0.9	0.8	0.8	1.3	1.0	2.4	0.2	0.1	3.1	0.6	0.4	2.1
N	36	36	36	36	36	36	36	36	36	36	36	36
Baboon 3												
Mean	123	76	96	119	74	88	161*	111*	121*	130	85	103
S.E.M.	0.6	0.5	0.7	0.6	0.6	1.0	0.4	0.3	2.4	0.7	0.5	1.6
N	27	27	27	27	27	27	45	45	45	45	45	45
Baboon 4												
Mean	114	67	63	116	68	63	140*	106*	105*	103	74	73
S.E.M.	0.5	0.6	0.5	0.9	1.0	0.9	0.5	0.3	1.6	0.5	0.4	1.9
N	45	45	72	45	45	72	27	27	27	27	27	27
Group												
Mean	123	73	85	123	72	82	149*	105*	126*	119	81	92
S.E.M.	0.7	0.7	1.0	0.9	0.9	1.4	0.4	0.2	2.2	0.6	0.5	1.8

livered to the animal for every 10 minutes of accumulated time that the diastolic blood pressure remained above criterion. Conversely, the animal received a single shock for every 30 seconds that the diastolic blood pressure remained below the criterion level. Additionally, each food reward delivery reset the shock timer (thus providing an additional 30 seconds of accumulated shock-free time), and each occurrence of an electric shock reset the food timer (thus postponing the delivery of food for at least an additional 10 minutes of accumulated time). Initially, the criterion diastolic blood pressure was determined by the animal's preexperimental resting baseline level (approximately 75 mm-Hg) with progressive increases programmed to occur at a rate approximating 4 mm-Hg per week over a period of 8 to 10 weeks. Within this 2- to 3-month interval, all four baboons attained diastolic blood pressure levels above 100 mm-Hg and maintained these elevated levels for more than 95 percent of each daily 12-hour conditioning-on period. During these daily conditioning sessions, the animals received, on the average, two electric shocks and 25 food pellets per hour.

Figure 1 compares the concurrent changes in blood pressure and heart rate during the 12-hour conditioning-on, 12-hour conditioning-off periods with the changes in blood pressure and heart rate during the preconditioning baseline period. The data plot in Fig. 1 is in the form of averages for three to five consecutive 24-hour experimental conditioning sessions (right panel) for each of the four baboons (that is, 16 total sessions) and three to five consecutive 24-hour preexperimental baseline sessions (left panel) for the same four animals before conditioning (that is, 16 total sessions). This figure shows consecutive 40-minute-interval averages, and summarizes, in the right-hand panel, the stable response pattern which developed after the baboons had been exposed to at least 40 daily 12-hour conditioning sessions. Characteristically, sustained elevations of 30 mm-Hg or more in both systolic and diastolic blood pressure were maintained throughout the 12-hour conditioning-on period, accompanied by elevated but progressively decreasing heart rates over the course of the same 12-hour interval. During the ensuing 12-hour conditioning-off recovery period, heart rate continued to fall, and blood pressure returned to approximately basal levels (or slightly above) within 6 to 8 hours. In contrast, cardiovascular changes during the preexperimental baseline period, summarized in the left-hand panel of Fig. 1, show virtually no change in blood pressure (save the minimal diurnal variation) throughout the 24-hour interval, and only moderate fluctuations in heart rate.

Table 1 summarizes the results of an analysis of these changes testing the statistical significance of the differences in blood pressure and heart rate between the last nine 40-minute intervals (6 hours) of the conditioning-on periods and the first nine 40-minute intervals (6 hours) of the conditioning-off periods for each animal individually and for the group as a whole. In addition, Table 1 shows the statistical significance of the difference in blood pressure and heart rate between the last nine 40-minute conditioning-on periods (6 hours) and the nine 40-minute intervals representing an identical time span (that is, 6 p.m. to midnight) during the preexperimental baseline period for each animal individually and for the group as a whole. Highly significant ($P < .001$) differences are shown for all measures in both individual and group averages.

That these large-magnitude, sustained elevations in blood pressure are related directly and specifically to the programmed contingency requirements of the instrumental conditioning procedure is further confirmed by the results obtained with two additional baboons exposed to virtually identical experimental conditions with the exception that concurrent food-reward and shock-avoidance were made contingent upon *decreasing* diastolic blood pressure. Over extended intervals (6 months or more) of daily exposure to this instrumental procedure for lowering blood pressure (involving electric shocks, food deprivation and reward, surgery and chronic catheterization, confinement and chair restraint) neither animal showed any change from baseline cardiovascular levels under the same general laboratory conditions obtaining for the four baboons which provide the basis for this report.

The results of this experiment show clearly that instrumental learning of cardiovascular responses can produce sustained large-magnitude changes in blood pressure which cannot be accounted for on the basis of short-term "voluntary mediators" (for example, the Valsalva maneuver) (*3*). All four baboons in this study showed daily elevations of 30 mm-Hg or more in both systolic and diastolic blood pressures and maintained such elevations for the entire 12-hour conditioning-on segment of each experimental session. These findings suggest the involvement of more durable adaptive mechanisms supporting the sustained pressure elevations, although the relative contributions of cardiac output and peripheral resistance to the establishment and maintenance of these hypertensive levels cannot be determined from the present data alone. In dogs anticipating (over a 15-hour interval) performance on a shock-avoidance procedure (*13*), and in rhesus monkeys during a 72-hour shock-avoidance procedure (*14*), similar blood pressure elevations have been reported, and concurrent measurements of cardiac output under such conditions (*15*) have revealed that the pressure elevations were determined by substantial increases in total peripheral resistance. Although the relationship of these sustained blood pressure elevations in the baboon to the circulatory changes characteristic of essential hypertension in humans (*16*) is far from clear, chronic exposure to aversive behavioral conditioning procedures has been reported to produce hypertensive patterns (*17*), with a bradycardia accompanying the chronic pressure elevations in at least some animals (*18*). The present findings with the baboon extend the range of potentially useful laboratory models for the analysis of environmental-behavioral influences upon the cardiovascular system, and call for further experimental scrutiny of the physiological mechanisms (for example, baroreceptor reflex) which mediate this significant alteration of the systemic circulation.

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Electrical Signs of Selective Attention in the Human Brain

Abstract. *Auditory evoked potentials were recorded from the vertex of subjects who listened selectively to a series of tone pips in one ear and ignored concurrent tone pips in the other ear. The negative component of the evoked potential peaking at 80 to 110 milliseconds was substantially larger for the attended tones. This negative component indexed a stimulus set mode of selective attention toward the tone pips in one ear. A late positive component peaking at 250 to 400 milliseconds reflected the response set established to recognize infrequent, higher pitched tone pips in the attended series.*

Human listeners are able to confine their attention to a single auditory message within a noisy environment and to disregard equally intense but "irrelevant" sounds. This feat of selective attention is accomplished by unknown brain mechanisms that act both to enhance the information received from selected sound sources and to suppress irrelevant, competing sensory input.

Attempts to identify neurophysiological mechanisms that uniquely subserve selective attention by recording sensory evoked potentials from animal brains have made little progress (*1, 2*). Human subjects offer distinct advantages in that their attentional processes can be accurately controlled and evaluated in conjunction with sensory evoked potentials that are recorded from the scalp. It is well established that the major components of the human auditory evoked potential—a negative component (N_1) peaking at 80 to 110 msec after an abrupt sound and a subsequent positive component (P_2) at 160 to 200 msec—are considerably larger when the sound is made "relevant" (to be attended) than when it is made "irrelevant" (to be ignored) (*3*). Naatanen (*2*) has pointed out, however, that relevant stimuli were delivered predictably in those studies, so that the effects of stimulus "relevance" upon evoked potentials could have been caused by nonselective preparatory states (for example, arousal or alertness) differentially preceding the stimuli. In experiments where the relevant and irrelevant stimuli were presented in randomized sequences that precluded differential preparatory states (*2, 4, 5*), only minimal differences were observed in N_1 and P_2.

We now report experiments in which randomized sequences of tone pips were delivered concurrently to the two ears at such a rapid rate that subjects were forced to restrict their attention to one ear at a time in order to perform a difficult pitch discrimination. Under these circumstances the N_1 evoked by tones in the attended ear was substantially larger than that evoked by tones in the opposite ear. This constitutes the first definite evidence that changes in an evoked potential component can specifically reflect selective attention as opposed to a preparatory or reactive change of nonselective state (*6, 7*).

Subjects sat in an acoustically shielded