Hemodynamic effects of acute stressors in the conscious rabbit

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Schadt, James C., and Eileen M. Hasser. Hemodynamic effects of acute stressors in the conscious rabbit. *Am. J. Physiol.* 274 (*Regulatory Integrative Comp. Physiol.* 43): R814–R821, 1998.—Chronically instrumented, conscious rabbits were used to test the hypothesis that sensory stimulation with an air jet or oscillation produces differential hemodynamic changes that may be appropriate for an active or a passive behavioral response, respectively. Both stressors increased arterial pressure, central venous pressure, and hindquarters blood flow and produced visceral vasoconstriction. Neither stimulus altered hindquarters conductance. Although air jet increased heart rate and cardiac output, oscillation did not. The two stressors affected arterial baroreflex control of heart rate differently. Oscillation reset arterial pressure to a higher level with no change in heart rate maximum or minimum, whereas air jet reset both heart rate and arterial pressure to higher levels. Neither stressor affected baroreflex sensitivity. We conclude that the conscious rabbit shows at least two distinct cardiovascular responses when exposed to acute stressors. Air jet produces a cardiovascular response including tachycardia, which resembles the defense reaction and appears appropriate for active defense or flight. The response to oscillation, on the other hand, appears better suited for a passive response such as "freezing" behavior. During exposure to either stressor, the baroreflex is altered to allow simultaneous increases in heart rate and arterial blood pressure, but the sensitivity is maintained, allowing normal moment to moment control of heart rate.

stress; cardiovascular control; regional blood flow; defense reaction; freezing behavior; vigilance

THE ACUTE RESPONSE to threatening or stressful sensory stimulation capable of producing active defense or flight is known as the defense reaction (12). The hemodynamic component of this response pattern includes increased arterial blood pressure and heart rate, skeletal muscle vasodilation, visceral vasoconstriction (12), and increased venous tone (15). Associated with the hemodynamic changes, there is a change in arterial baroreflex function which allows the simultaneous increase in arterial blood pressure and heart rate (12). These changes in cardiovascular function and control support somatic responses involving increased activity (i.e., fight or flight).

Under certain conditions in some species, stressful sensory input results in decreased motor activity. An example of this is the "freezing" behavior shown by many wild animals. During this behavior the animal remains motionless in an apparent attempt to escape detection by a predator. Freezing may also function as a prolonged alerting response to something novel in the environment. In this case the behavior may allow the animal to gather more information. The cardiovascular adjustments during this alternative response to threatening stimuli are less well understood and may differ significantly from those occurring during active defense or flight (12).

The rabbit is a species that shows both freezing and active defense behaviors in the wild. Most earlier studies of the cardiovascular response to stressful sensory input in the rabbit have involved brain stimulation in anesthetized (2, 3, 5, 6, 8–10, 12, 14, 17) or conscious (7) animals. These experiments demonstrated that stimulation at particular brain sites could produce the range of somatic adjustments to stressful sensory stimulation seen in wild rabbits (7). They also documented the associated cardiovascular (5, 6, 8, 17) changes. In anesthetized rabbits, electrical stimulation of the dorsomedial, posterior hypothalamus (the defense area) produces a pressor response, tachycardia, increased hindquarters blood flow, and decreased visceral blood flow (17). Electrical activation of the medial, lateral hypothalamus (the vigilance area) produces a pressor response accompanied by bradycardia and decreased hindquarters and visceral blood flow (17). In conscious rabbits, stimulation of the defense area increases and stimulation of the vigilance area decreases motor activity (7). Thus electrical activation of the defense area or vigilance area produces somatic and cardiovascular adjustments appropriate for active defense or freezing behavior, respectively. Activation of either area produces pupil dilation and eyeball protrusion (exophthalmos), signs of sympathetic activation (7). Although these studies have provided a framework within which to work, little is known about the integrated cardiovascular response to different environmental stressors in the conscious rabbit. To the best of our knowledge, this has not been systematically investigated.

The purpose of this study was to document the hemodynamic effects of acute exposure to stressful sensory stimulation in the conscious rabbit. Our general hypothesis was that acute exposure to different stressors in the conscious rabbit would produce the hemodynamic and cardiovascular reflex changes appropriate for either active defense or freezing behavior. On the basis of our preliminary studies (19, 20) and published data, we used air jet (4, 11, 21, 25) and oscillation (18) as sensory stimuli.

METHODS

Preparation. These studies were conducted in accordance with the NIH "Guide for the Care and Use of Laboratory Animals" [DHEW Publications No. (NIH) 85–23, Revised 1985, Office of Science and Health Reports, DRR/NIH, Bethesda, MD 20892] and were approved by the University of Missouri-Columbia Animal Care and Use Committee. Male New Zealand White rabbits (n = 39), weighing between 2.4

and 3.1 kg (2.74 ± 0.03 kg), were chronically instrumented with arterial and venous catheters, as well as Doppler flow probes. During abdominal surgery, rabbits were anesthetized with halothane. Following a midline abdominal incision, Doppler flow probes were placed at one or more of the following locations: distal abdominal aorta near the iliac bifurcation ($n = 17$), cranial mesenteric artery near its origin from the aorta ($n = 17$), or left renal artery ($n = 11$). Catheters were implanted in the abdominal aorta and abdominal vena cava to allow measurement of arterial pressure and removal of blood or injection of drugs, respectively. In some rabbits, a second vena caval catheter was implanted. The tip of this catheter was positioned for measurement of central venous pressure ($n = 6$). To measure cardiac output, we performed an additional surgical procedure in some rabbits to implant a Doppler flow probe on the ascending aorta ($n = 11$). This procedure was done while the rabbit was anesthetized with pentobarbital sodium (25–30 mg/kg, iv) and artificially ventilated and was done at least 2 wk prior to the abdominal surgery. Flow probe wires and catheters were tunneled subcutaneously and exteriorized in the dorsal cervical region. Antibiotics (60,000 IU im; Pen BP-48, Pfizer) were given the day before and the day after surgery. Animals were allowed to recover from the last surgical procedure for at least 10 days. Multiple experiments were done on each rabbit. The actual number varied from rabbit to rabbit. Experiments in the same animal were separated by at least 2 days. We systematically alternated the order of experiments among rabbits to yield a balanced design. That is to say, a systematic attempt was made to have an equal number of animals exposed to the stressors in each possible order.

General. During experiments, the arterial catheter was connected to a pressure transducer (Statham model P23Dc), and the flow probe wires were connected to pulsed Doppler flow meters (Triton model 100). Heart rate (triggered by the arterial pressure wave), pulsatile and mean arterial blood pressure, and pulsatile and mean blood flow velocities were monitored on a chart recorder (Gould model 3800). The experimental information was also recorded (Neuro-Data model DR-886) on VHS videotape and analyzed on- or off-line using a microcomputer and commercially available data acquisition and analysis hardware and software (RC Electronics).

Heart rate, arterial blood pressure, and mesenteric blood flow are higher in rabbits that have eaten recently. In addition, all hemodynamic parameters are more variable (unpublished observations). Therefore, rabbits were fasted 15–23 h prior to experimentation. Since rabbits usually finished eating before the food was removed (around 1730), the day before the experiment, fasting was accomplished by simply feeding rabbits 2–3 h later than usual. Rabbits were not restrained during experiments. They were placed in a box (33 × 15 × 18 cm, inside dimensions) which restricted their movement. They had previously been acclimated to the box. Rabbits were treated with heparin (sodium heparin, 2,000 U iv; Eli Lilly) before the experiment to prevent blood clotting in the venous or arterial lines.

Experimental protocol for effects of stressors. Before the experiment, we allowed 10–30 min for the rabbit to reach a stable baseline in terms of heart rate and blood pressure. Once stable, the experiment consisted of a 1-min control period, followed by 20 min of either air jet or oscillation or sham stimulation (time control), then finally a 1-min poststimulation period. Hemodynamic data were monitored throughout the experiment.

Two forms of sensory input were used to produce stress: air jet and oscillation. For air jet, a continuous stream of room air from a polyvinyl chloride tube (9 mm OD; 5 mm ID) was directed at the rabbit's nose through a 6-cm diameter hole in the front of the box. The tube was positioned 4–6 cm from the box. For oscillation, the rabbit box was positioned on an oscillating shaker. When the oscillating shaker was turned on, the box moved counterclockwise in 2-cm circles at a rate of 48 cycles/min. During sham stimulation, rabbits were treated the same as during air jet or oscillation, but no stimulus was applied.

Experimental protocol for baroreflex studies. Baroreflex function was assessed by recording the maximum heart rate changes at the maximum increases and decreases in arterial blood pressure produced by bolus injections of phenylephrine (3, 7, and 10 μg/kg) and nitroglycerin (5, 40, and 80 μg/kg), respectively. The bolus of phenylephrine or nitroglycerin was given 2 min after the onset of the stressor or sham stimulation. One dose of one drug was administered per day. Experiments were performed every other day. Exposure to the stressors and sham stimulation were alternated to provide a balanced design. Thus, for each animal, there were three pressor and three depressor experiments with each form of stimulation (i.e., air jet, oscillation, and sham). In addition, there were six baseline values, one for each pressor or depressor injection, for each of the three types of stimulation. The resulting twelve experimental data points from each animal for each form of stress were fit to the following equation (13)

$$\text{heart rate} = P_4 + \left[(P_1)/1 + \exp\left[P_2(\text{mean arterial pressure} - P_3)\right]\right] \quad (1)$$

where P_1 is heart rate range, P_2 is coefficient for calculating gain, P_3 is arterial pressure at the midrange of the curve, and P_4 is minimum heart rate. For the purpose of assessing differences in baroreflex sensitivity, the gain at the midpoint of the linear portion of the relationship was calculated as follows: gain $= P_2P_1/4$. A mean value for each parameter was calculated from the individual animal values, and the resulting equation was used to describe the group response.

Analysis of data. Statistical analysis of data was by repeated measures analysis of variance (ANOVA). Treatment (air jet, oscillation, or sham stimulation) and time after applying the stimulation were the independent variables in the ANOVA. Treatment was the independent variable for the baroreflex ANOVA. When the ANOVA demonstrated a significant primary effect of treatment or the interaction of treatment and time, differences between individual means were assessed by a least-significant difference (LSD) test (24). Significant differences were determined when $P < 0.05$. The dashed lines in Figs. 1–4 represent the time control (no stimulation) ± 1 LSD ($\alpha = 0.05$). If the ANOVA demonstrated significant main or interaction effects (see RESULTS), then points outside the dashed lines were significantly different from the vehicle control values.

Data in the text and representative points in Figs. 1–4 and Table 1 are shown as means ± SE. The SE was computed from the pooled estimate of the sample variance, the error mean square, calculated in the associated ANOVA. Regional vascular conductances were calculated as mean blood flow velocity divided by mean arterial pressure. To facilitate comparison of flow velocities in different vascular beds, we normalized flow and conductance data to prestimulation levels. Thus all flows and conductances are shown as percent of prestimulation (baseline) values.

RESULTS

Hemodynamic effects of air jet or oscillation. Air jet or oscillation increased mean arterial pressure (Fig. 1).

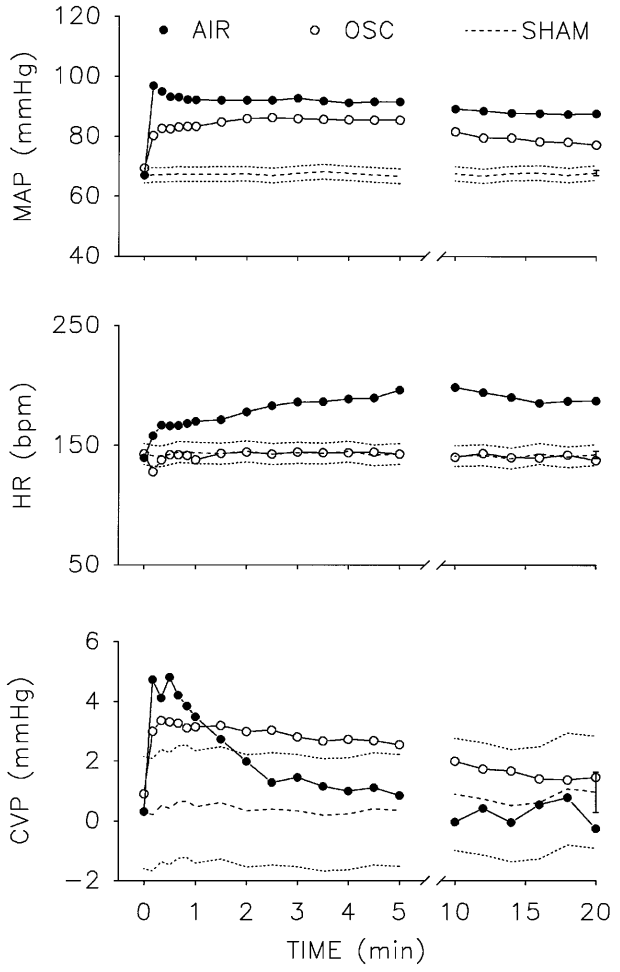

Fig. 1. Hemodynamic effects of 20 min of air jet (●), oscillation (○; OSC), or sham (dashed line) stimulation on mean arterial pressure (MAP; n = 33–38), heart rate (HR; n = 33–38), and central venous pressure (CVP; n = 6). Values are means. SE values are from pooled estimate of sample variance by ANOVA and are shown on last symbol of the sham stimulation curve. Dotted lines, values after sham stimulation ± 1 least-significant difference (LSD) (α = 0.05). Stimulation began at *time 0*. bpm, Beats/min ANOVA demonstrated significant interactions between time and treatment (stimulus) for MAP [F(44,2,516) = 13.31], HR [F(44,2,516) = 8.14], and CVP [F(44,340) = 1.92].

During air jet, mean arterial pressure rose from 67 ± 1 mmHg before the stimulus to a peak of 97 ± 1 mmHg 10 s later. Pressure declined slightly after this point, but was still 88 ± 1 mmHg at 20 min after stimulus onset. During oscillation, mean arterial pressure increased rapidly from 69 ± 1 to 80 ± 1 mmHg at 10 s after stimulus onset. Mean arterial pressure was 77 ± 1 mmHg at the end of the 20-min oscillation period. There was a significant interaction between time and treatment (the stimulus) for mean arterial pressure (Fig. 1). Both stimuli increased arterial blood pressure. However, the increase was significantly greater in magnitude during air jet than during oscillation.

Heart rate rose rapidly from 140 to 167 ± 3 beats/min at 20 s after air jet onset (Fig. 1). It reached a peak of 201 ± 3 beats/min at 8 min after stimulus onset and was still significantly elevated (187 ± 3 beats/min) at the end of the air jet exposure. In contrast, heart rate transiently decreased at the onset of oscillation but was otherwise statistically similar to that during sham stimulation. The interaction effect of treatment and time for heart rate was significant (Fig. 1). Thus, whereas air jet stimulation resulted in a significant, sustained tachycardia, oscillation did not produce any sustained change in heart rate.

Central venous pressure was increased by air jet or oscillation. During the first 10 s of air jet, central venous pressure increased from 0.3 to 4.7 ± 0.7 mmHg. This effect was transient, and central venous pressure was similar between the sham and air jet experiments by 2 min after stimulus onset. Oscillation also increased central venous pressure from 0.9 ± 0.7 mmHg before the stimulus to 3.4 ± 0.7 mmHg at 20 s after stimulus onset. However, the increase during oscillation was sustained compared with that during air jet and was still significantly above sham experiment levels 6 min after stimulus onset. There was a significant effect of the interaction between time and treatment on central venous pressure (Fig. 1). Thus central venous pressure was transiently increased by air jet or oscillation. The increase was sustained significantly longer during oscillation than during air jet.

Air jet increased cardiac output, whereas oscillation did not change cardiac output (Fig. 2). There was a 29 ± 5% increase in cardiac output 20 s after air jet onset. This increase was sustained and cardiac output was 34 ± 5% above prestimulus levels at the conclusion of the 20-min stimulation period. Oscillation did not significantly affect cardiac output. Thus there was a primary effect of treatment on cardiac output, but there was not a significant effect of time or the interaction of treatment and time (Fig. 2). Air jet or oscillation increased hindquarters blood flow (Fig. 2). During air jet, hindquarters blood flow increased rapidly and was 35 ± 6% above prestimulus levels after 20 s. This increase was sustained, and hindquarters flow was still 23 ± 6% above prestimulus levels at the conclusion of the stimulation. In contrast, hindquarters flow increased more gradually during oscillation reaching a maximum 41 ± 6% above prestimulation levels 3.5 min after the onset of oscillation. It then declined but was still above the prestimulation baseline (21 ± 6%) at the end of the oscillation period. The interaction of treatment and time significantly affected hindquarters blood flow (Fig. 2). Mesenteric blood flow did not initially change but was increased 5 min (15 ± 4%) after the onset of air jet (Fig. 2). Mesenteric blood flow continued to increase and was 24 ± 4% above prestimulus levels at the conclusion of air jet. During oscillation, mesenteric blood flow was transiently reduced (77 ± 4% of prestimulus) 10 s after stimulus onset. After this point, mesenteric flow gradually increased and was not different than the sham experiments from 2.5 min through the end of the stimulation. There was a significant interaction between time and treatment in their effects on mesenteric blood flow (Fig. 2). Renal flow decreased to 58 ± 5% of prestimulus baseline immediately after air jet onset and then rapidly increased, reaching a peak 19 ± 5% above prestimulation levels 1 min after

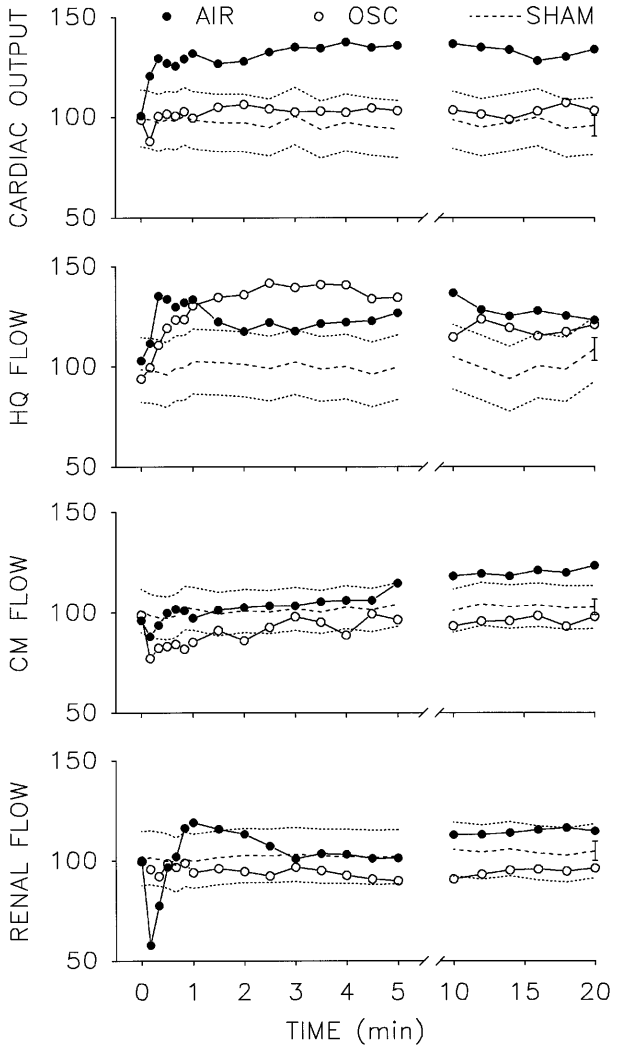

Fig. 2. Effects of air jet, oscillation, or sham stimulation on cardiac output (n = 11) and hindquarters blood flow (HQ flow; n = 13–17), cranial mesenteric blood flow (CM flow; n = 13–17), and renal blood flow (n = 8–11). Flows are normalized to percent of prestimulus baseline. Values are means. SE values are from pooled estimate of sample variance by ANOVA and are shown on last symbol of the sham stimulation curve. Dotted lines, values after sham stimulation ± 1 LSD (α = 0.05). Stimulation began at *time 0*. ANOVA demonstrated significant interactions between time and treatment (stimulus) for HQ flow [F(44,1,088) = 2.38], CM flow [F(44,1,088) = 2.05], and renal flow [F(44,680) = 3.36] but not for cardiac output [F(44,680) = 0.97]. Only the main effect of treatment was significant for cardiac output [F(2,680) = 280.4].

the stimulus (Fig. 2). Renal flow then decreased and was not significantly affected by air jet for the duration of the stimulus. Oscillation did not have a significant effect on renal blood flow. The interaction of time and treatment significantly affected renal blood flow (Fig. 2). Thus, whereas air jet significantly increased cardiac output, oscillation did not. Both air jet and oscillation increased hindquarters blood flow. Changes in blood flow to visceral structures during air jet and oscillation were small, transient, and complex.

Either air jet or oscillation reduced total peripheral conductance by ~25% at 10 s after the onset of either stimulus (Fig. 3). This vasoconstriction was somewhat transient. Total peripheral conductance during air jet or oscillation was not different from sham stimulation after 1 min and 3.5 min of stimulation, respectively. Although time and treatment significantly affected total peripheral conductance, their interaction did not (Fig. 3). After 10 s of air jet or oscillation, hindquarters vascular conductance had decreased to 83 and 86 ± 5% of prestimulus levels, respectively (Fig. 3). However, the changes in hindquarters conductance were quite transient, and hindquarters conductance was not significantly different from the sham experiment at any other time points. There was a significant interaction of time

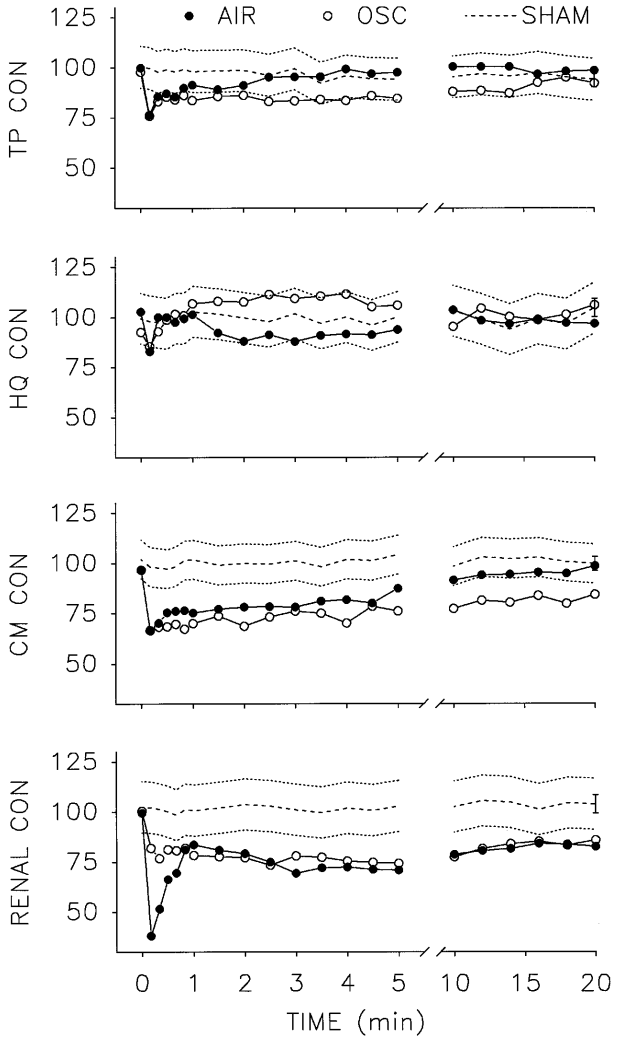

Fig. 3. Effects of air jet, oscillation, or sham stimulation on total peripheral (TP; n = 11), hindquarters (HQ; n = 13–17), cranial mesenteric (CM; n = 13–17), and renal (n = 8–11) conductance (CON). Conductances are normalized to percent of prestimulus baseline values. Values are means. SE values are from pooled estimate of sample variance by ANOVA and are shown on last symbol of the sham stimulation curve. Dotted lines, values after sham stimulation ± 1 LSD (α = 0.05). Stimulation began at *time 0*. ANOVA demonstrated significant interactions between time and treatment (stimulus) for HQ conductance [F(44,1,088) = 1.49], CM conductance [F(44,1,088)=2.14], and renal conductance [F(44,680)=2.72] but not for TP conductance [F(44,680)=1.28]. Only the main effects of time [F(22,680)=1.89] and treatment [F(2,680)=112.2] were significant for TP conductance.

and treatment in their effects on hindquarters conductance (Fig. 3). The peak decrease in mesenteric conductance during air jet or oscillation was the same (67 ± 4 of prestimulus) and was reached after 10 s of stimulation (Fig. 3). The mesenteric vasoconstriction was not sustained during air jet and after 6 min of stimulation was similar to the sham stimulus experiment. The mesenteric vasoconstriction during oscillation was sustained longer than during air jet and was 84 ± 4% of prestimulation after 20 min of oscillation. The interaction of time and treatment significantly affected mesenteric conductance (Fig. 3). Renal conductance decreased to 38 ± 5% of prestimulation after 10 s of air jet (Fig. 3). Although it increased rapidly from this peak level, renal conductance was still significantly reduced (83 ± 5% of prestimulus) at the conclusion of air jet. Renal conductance decreased rapidly to 82 ± 5% of prestimulation after 10 s of oscillation and was still reduced (86 ± 5% of prestimulation) 20 min after the start of oscillation. The interaction of time and treatment significantly affected renal conductance (Fig. 3). Thus either air jet or oscillation produced systemic vasoconstriction reflected as a decrease in total peripheral conductance. This vasoconstriction appeared to be concentrated in visceral structures (i.e., cranial mesenteric and renal vasculatures) as opposed to skeletal muscle (i.e., hindquarters).

Effects of air jet or oscillation on the arterial baroreflex. Both stressors increased mean arterial pressure (Table 1), but only air jet increased heart rate. Neither stimulus affected the maximum gain (gain at the midpoint of the curve) nor the range of the heart rate response (Fig. 4; Table 1). Air jet increased the minimum and maximum heart rate to a similar degree and shifted the midpoint of the curve to a higher pressure. Although oscillation did not affect the minimum or maximum heart rate, it did shift the midpoint of the curve to a higher arterial pressure. The shift for oscillation was less than for air jet (Fig. 4). Thus air jet shifted the arterial pressure-heart rate relationship upward and to the right, whereas oscillation resulted in only a shift to the right.

Table 1. *Effects of air-jet and oscillation on baroreflex control of heart rate*

	Control	Air Jet	Oscillation	ANOVA Values
Baseline MAP, mmHg	71 ± 1	91 ± 1*	83 ± 1*†	$F(2,18) = 52.2$; $P < 0.001$
Baseline HR, beats/min	143 ± 4	179 ± 4*	146 ± 4†	$F(2,18) = 20.3$; $P < 0.001$
Minimum HR, beats/min	105 ± 5	143 ± 5*	105 ± 5†	$F(2,18) = 17.4$; $P < 0.001$
Maximum HR, beats/min	257 ± 5	304 ± 5*	261 ± 5†	$F(2,18) = 24.1$; $P < 0.001$
HR range, beats/min	153 ± 5	161 ± 5	156 ± 5	$F(2,18) = 0.54$; $P > 0.50$
MAP midpoint, mmHg	64 ± 2	80 ± 2*	73 ± 2*†	$F(2,18) = 14.2$; $P < 0.001$
Gain, beats·min^{-1}·mmHg^{-1}	5.3 ± 0.5	5.2 ± 0.5	5.1 ± 0.5	$F(2,18) = 0.05$; $P > 0.50$

Values are means ± SE. MAP, mean arterial pressure; HR, heart rate. *$P < 0.05$ with control. †$P < 0.05$ with air jet.

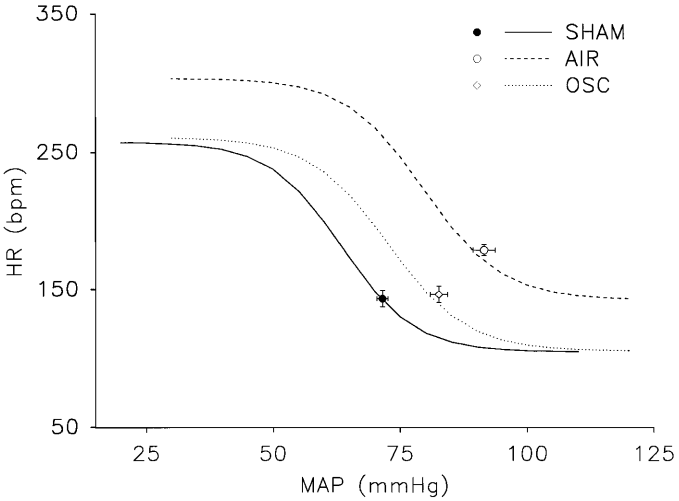

Fig. 4. Effects of air jet, oscillation, and sham stimulation on arterial baroreflex modulation of heart rate (n = 10 for all). Twelve data points (3 pressor, 3 depressor, and 6 control) from each animal were fit to *Eq. 1* in METHODS (see *Experimental protocol for baroreflex studies*). Mean values for each parameter were calculated from individual rabbit values, and the resulting equation was used to generate the curves shown. Mean baseline values (±SE) for each treatment are shown by the symbols.

DISCUSSION

Exposure to dangerous or otherwise stressful sensory stimulation may result in increased or decreased somatic activity. If the stimulus results in active defense or flight, then cardiovascular changes appropriate to support the somatic response (e.g., an increase in heart rate) will precede and accompany the increase in motor activity. This autonomic response is known as the defense reaction. In other situations, hiding or freezing might be an alternative response to an environmental stressor. During this less-active response to a stressful stimulus, the accompanying cardiovascular changes are quite different than those during active defense or flight. Thus the response to stressful sensory stimulation depends on the nature of the stimulus and the biological needs of the animal. A particular species might rely almost totally on one of these behavioral and autonomic alternatives. However, a behavioral and autonomic repertoire including more than one alternative is possible (23) and might provide a survival advantage. In the conscious rabbit, we were able to identify two stimuli that elicit cardiovascular responses that appear to be similar to those shown during active defense and during freezing or hiding.

We examined the hemodynamic response to air jet and oscillation. Each stimulus produced some of the hemodynamic changes characteristic of the defense reaction. Both air jet and oscillation increased arterial blood pressure, although the increase with air jet was significantly larger. Both stimuli also resulted in redistribution of blood flow from visceral structures to skeletal muscles as indicated by the mesenteric and renal vasoconstriction and increase in hindquarters blood flow. However, there were differences in the hemodynamic response to the two stimuli. First, air jet resulted in sustained tachycardia, whereas oscillation

did not change heart rate. Second, air jet significantly increased cardiac output, whereas oscillation did not. Third, the increase in central venous pressure was sustained longer during oscillation than during air jet. Finally, the effects of the two forms of sensory stimulation on baroreflex control of heart rate were different. Thus air jet appeared to result in hemodynamic changes characteristic of a defense reaction, whereas oscillation produced hemodynamic changes more appropriate for a less active response such as freezing.

A major difference between the two stressors was that air jet increased heart rate, and oscillation did not. The heart rate responses to these two stimuli are similar to the heart rate effects produced by stimulation of the hypothalamic defense and vigilance areas as described by Schneiderman and colleagues (5, 6, 8, 17). In anesthetized rabbits, electrical stimulation of the dorsomedial, posterior hypothalamus (the defense area) produces a pressor response, tachycardia, increased hindquarters blood flow, and decreased visceral blood flow (17). However, electrical activation of the medial, lateral hypothalamus (the vigilance area) produces a pressor response accompanied by bradycardia and decreased hindquarters and visceral blood flow (17). In conscious rabbits, stimulation of the defense area promotes motor activity, whereas stimulation of the vigilance area leads to decreased motor activity. Activation of either area produces signs of sympathetic activation (e.g., pupil dilation and exophthalmos) (7).

Bradycardia in response to stressful sensory input has been reported in conscious cats during immobile confrontation (1) and during freezing behavior in conscious, wild rabbits (22) and conscious, free-ranging woodchucks (23). It appears that the direction of the heart rate response to a particular stimulus can be influenced by the circumstances under which it is presented. For example, in rats physical restraint has a directional effect on the heart rate response to a conditioned stimulus paired with an electric shock (16). In unrestrained rats, increased heart rate accompanies the conditioned stimulus, whereas decreased heart rate accompanies the conditioned stimulus in restrained rats. Interestingly, in woodchucks, the same stimulus can produce either flight or a freezing response depending on the setting in which it is presented. When the woodchuck is close to the burrow, the presence of a potential predator results in bradycardia and increased vigilance. However, if the same stimulus is presented when the woodchuck is some distance from its burrow, the result is tachycardia and flight (23). The experiments reported here did not allow us to observe the behavioral response to either of the stimuli. It is, therefore, possible that our restriction of the rabbits movement during the stimuli influenced the heart rate response. However, it is also possible that air jet and oscillation produced two distinctly different cardiovascular response patterns compatible with active (i.e., defense or flight) and passive (freezing) behavioral responses, respectively.

Dilation of skeletal muscle resistance vessels and the associated increase in skeletal muscle blood flow is considered one of the hallmarks of the defense reaction (12). In the present study, the increase in hindquarters blood flow during either form of stimulation likely reflects increases in skeletal muscle blood flow. However, the increase in hindquarters blood flow appeared to be driven primarily by the increases in arterial pressure resulting from vasoconstriction in other vasculatures rather than hindquarters vasodilation (i.e., there was no change in vascular conductance). During air jet, the increase in cardiac output probably also contributed to the increase in hindquarters blood flow. This is similar to results in conscious cats during preparation for fighting (1). Adams et al. (1) reported hindquarters vasoconstriction during confrontation without fighting and hindquarters vasodilation only during actual fighting. In addition, they reported that the hemodynamic changes produced by fighting were similar to those observed during treadmill exercise. These authors felt that the hindquarters vasodilation observed during the defense reaction in conscious cats was linked to an increase in motor activity (1). We did not address this specific issue in the present experiments, as increases in motor activity were limited by the size of the experimental box. Nevertheless, it seems likely that if increases in motor activity had occurred in the present experiments, then they might have been accompanied by hindquarters vasodilation. In the present study, rabbits achieved 30–40% increases in hindquarters blood flow with no change in vascular conductance. With an increase in hindquarters conductance, the reserve available for responding during stressful situations would be even greater.

Central venous pressure was increased by both stimuli. The increase was more transient with air jet than with oscillation. This increase in central venous pressure could be due to increased thoracic blood volume secondary to peripheral venoconstriction, decreased central venous compliance, or both. Venoconstriction with the resultant increase in mean circulatory filling pressure during air jet has been reported for the rat (15). It is interesting to note here that if sensory stimulation resulted in mobilization of blood centrally, then this was apparently a more transient phenomenon during air jet than during oscillation. It is tempting to speculate that the increase in central venous pressure is more transient during air jet because of the increase in heart rate and more long lasting during oscillation because heart rate does not increase. Consistent with this idea, cardiac output increased during air jet but not during oscillation.

Stressful sensory stimuli modulate arterial baroreflex function. A simple illustration of this is the simultaneous increase in heart rate and arterial blood pressure. This would appear to be inconsistent with normal baroreflex function. A variety of stress- or defense reaction-related changes in baroreflex function have been reported, including inhibition (12), facilitation (9), differential effects on the heart rate and pressor components (6), and most recently, a shift in the set points for arterial pressure and heart rate with no change in baroreflex sensitivity (11, 21). A decrease in baroreflex

sensitivity during exposure to stressors has most commonly been reported (12). In our experiments, both types of stimulation altered the relationship between arterial blood pressure and heart rate. However, the two forms of stimulation affected this relationship differently. Oscillation appeared to reset the maintained pressure to a higher level with no change in heart rate maximum or minimum. Air jet also reset the maintained arterial pressure to a higher level but also increased the heart rate maximum and minimum. Neither stimulus affected the range of the relationship. In other words, the presence of a stressful stimulus resulted in a relative tachycardia at any arterial pressure and the relative tachycardia was greater for air jet. Neither air jet nor oscillation affected baroreflex sensitivity. Therefore, although there were changes in the regulated levels of arterial blood pressure and/or heart rate, there was no change in the slope at the midpoint of the linear portion of the relationship between the two variables. Although these results differ from earlier studies (12), they are in close agreement with two recent reports on the effects of stressful sensory stimulation in conscious rats (11, 21). These authors reported an air-jet-induced rightward and upward shift in the relationship between heart rate and arterial pressure with no change in baroreflex sensitivity. Thus recent evidence appears to suggest that arterial baroreflex control of heart rate is not compromised during the defense reaction. Rather, normal control of heart rate appears to be the rule, although at increased arterial pressure values.

It is possible that the difference between the hemodynamic effects of air jet and oscillation are due to quantitative rather than qualitative differences in the stimuli. In conscious rats, stimulation of the midbrain tectum produces hemodynamic response patterns appropriate to support somatic responses to stressors. In this situation, the intensity of brain stimulation determines the qualitative nature of the heart rate response. Threshold levels of stimulation produce bradycardia and freezing behavior, whereas higher levels of stimulation in the same area result in tachycardia and flight (21). In preliminary experiments, we observed a dose-response relationship between the strength of the air jet and the magnitude of the heart rate and arterial blood pressure increase (unpublished observations). This could also be true for oscillation. In other words, the failure of oscillation to increase heart rate or cardiac output may be due to the less stressful nature of the oscillation stimulus rather than a qualitative difference between the stimuli. This same explanation could relate to stimuli in the wild that produce freezing or defense.

In summary, air jet stimulation and oscillation produced hemodynamic responses appropriate for active defense (fight or flight) and a more passive response to stress such as freezing, respectively. Both stressors increased arterial blood pressure and hindquarters blood flow and produced visceral vasoconstriction. Air jet stimulation increased heart rate and cardiac output, whereas oscillation did not. Neither stressor decreased the sensitivity of baroreflex control of heart rate.

Perspectives

The hemodynamic responses to the two stimuli used in this study appear well designed for meeting the biological needs of animals in different situations. Rabbits responded to air jet with hemodynamic changes characteristic of an active somatic response to a threatening stimulus. Mean arterial pressure, hindquarters blood flow, heart rate, and cardiac output increased, presumably to supply the blood flow necessary to support flight or defense. This hemodynamic response appears well designed to meet the needs created by a sudden increase in skeletal muscle activity. The response to oscillation was quite different. Whereas mean arterial blood pressure and hindquarters blood flow increased, heart rate and cardiac output did not. This response may be analogous to freezing in wild animals and to the vigilance response elicited by hypothalamic stimulation (5, 6, 8, 17). This somewhat passive alternative appears well suited as either a response to something novel in the environment or an attempt to remain undetected by a predator. The animal is prepared for an active response involving defense or flight, but if the need doesn't materialize, then the biological cost to the animal has been minimized and unnecessary energy has not been expended. Importantly, most animals are not limited to only one of these choices in response to stressful stimuli. Rather, they can show more than one and, in some cases, may show different responses sequentially. Although the observation of unchanged baroreflex sensitivity with shifts in the set points of the reflex after exposure to stressors appears somewhat controversial, it also appears biologically relevant. A stressful situation is likely to demand normal moment-to-moment control of arterial blood pressure. Thus the increased arterial pressure and heart rate (at least in the case of air jet) provide for meeting the increased demands, whereas maintained baroreflex sensitivity provides for normal control of arterial pressure, albeit at a higher level.

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