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Maintenance of Arterial Pressure in Infant Rats during Moderate and Extreme Thermal Challenge

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ABSTRACT: *It has recently been demonstrated in week-old rats that extreme cold challenges that lead to significant bodily cooling result in decreased cardiac rate. To determine whether pups are able to maintain arterial pressure in the face of decreasing cardiac rate in extreme cold, we measured blood pressure in unanesthetized week-old rats. Instrumented pups were thermally challenged and thermoregulatory and cardiovascular responses were monitored. Despite pronounced decreases in cardiac rate in the cold, pups were able to maintain mean arterial pressure (MAP), presumably by increasing peripheral resistance. At the lowest air temperature (17°C) pups emitted ultrasonic vocalizations, and these emissions were accompanied by pulsatile increases in intraabdominal pressure (IAP) and MAP. We hypothesize that these pulsatile increases in IAP during extreme cooling reflect the use of the abdominal compression reaction to increase venous return during periods of diminished cardiac output.*
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Keywords: *blood pressure; brown adipose tissue; thermoregulation; abdominal compression reaction; cardiac rate; laryngeal braking; ultrasound; vocalization; rat; neonate*

INTRODUCTION

When the thermogenic function of brown adipose tissue (BAT) was first confirmed in the early 1960s, it was suggested that the delivery of warmed blood from BAT to the heart is important in the selective regulation of heart temperature (Smith, 1964). Indeed, recent observations of cardiac rate during cold challenge in infant rats support this notion (Blumberg, Sokoloff, & Kirby, 1997). Specifically, cardiac rate was effectively maintained by pups when BAT thermogenesis increased at moderate air temperatures, but pronounced bradycardia resulted when BAT's ability to produce additional heat was exceeded at extreme air temperatures. It was concluded that, in addition to the modulatory role of the autonomic nervous system, heart temperature may also play a significant role in the control of cardiac rate in infant rats.

Because modulation of stroke volume may be limited in infant rats as it is in the young of other species (Shaddy, Tyndall, Teitel, Li, & Rudolph, 1988; Teitel et al., 1985), the decrease in cardiac rate during extreme cooling may indicate a decrease in cardiac output. This leads to the question as to whether rat pups maintain blood pressure in the cold. Therefore, the

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goal of the present study was to monitor arterial pressure during varying levels of cold exposure in 7- to 9-day-old rats. To do this, it was first necessary to develop a method for the continuous monitoring of blood pressure in unanesthetized pups at ages younger than had heretofore been successfully studied (Shair, Brake, Hofer, & Myers, 1986; Smith, Poston, & Mills, 1984). In addition to blood pressure, we also monitored cold-induced ultrasonic vocalizations and their relationship with blood pressure changes; it has been hypothesized that these vocalizations are by-products of laryngeal braking during extreme thermal challenge (Blumberg & Alberts, 1990). Our results indicate that pups maintain blood pressure across a wide range of air temperatures and can increase blood pressure acutely during extreme thermal challenge.

METHODS

Detailed descriptions of the test environment and the collection of thermal and metabolic measures have been provided elsewhere (Blumberg et al., 1997). Brief descriptions, however, are provided below.

Subjects

Eight 7- to 9-day-old male rat pups from eight litters were used. At the time of surgery, the pups weighed 17.6–22.4 g. They were born to Harlan Sprague-Dawley females in the animal colony at the University of Iowa and were raised in litters that were culled to 8 pups within 3 days after birth (day of birth = Day 0). Litters and mothers were housed in standard laboratory cages (48 × 20 × 26 cm) in which food and water were available ad libitum. All animals were maintained on a 12 : 12 hr light : dark schedule with lights on at 6:00 a.m.

Surgery

For direct recording of arterial pressure, the femoral artery was catheterized on the day of testing. The catheter was constructed from Micro-Renathane tubing (MRE-040; Braintree Scientific, Inc., Braintree, MA) with a 1-cm tip hand-drawn under a hot air stream; the catheter was filled with heparinized (50 IU/ml) isotonic saline. For catheter implantation, pups were anesthetized with Metofane and the left femoral artery exposed under a Nikon dissecting microscope. The catheter was introduced into the artery through a small hole made with a 27-g needle and advanced 1 cm into the artery. This distance placed the tip at the level of the branching of the femoral arteries from the abdominal aorta. After checking for adequate blood flow, the catheter was sutured in place and stabilized with a drop of cyanoacrylate at the juncture of the catheter and femoral artery. The catheter was then tunneled subcutaneously to exit on the left flank and plugged with a 23-g obturator. The incisions were then sutured closed and the animal was allowed to recover in an incubator at an air temperature of 35–36°C.

Test Environment

Pups were tested inside a double-walled glass chamber. Air temperature (T_a) within the chamber was controlled by passing temperature-controlled water through the chamber walls. Pups were allowed to move freely inside the chamber on a platform constructed of polyethylene mesh.

Blood Pressure Measurements

Polyethylene tubing was used to connect the arterial catheter to a pressure transducer (Argon, Athens, TX). The entire length of tubing from pup to transducer was filled with heparinized saline. The output of the transducer passed through an analog-to-digital converter, whose signal was then fed into a computerized data acquisition system. Before each pup was tested, the system was calibrated using a sphygmomanometer with a resolution of 1 mm Hg.

Temperature Measurements

Physiological and air temperatures were measured using chromel-constantan thermocouples. Average T_a within the metabolic chamber was determined using two thermocouples located beneath the platform. Physiological temperatures were attained by attaching thermocouples to the skin surface using collodion as an adhesive. One thermocouple was attached on the midline in the interscapular region above the brown fat pad, thus providing a measure of interscapular temperature (T_{is}). A second thermocouple was attached on the midline in the lumbar region, thus providing a measure of back temperature (T_{back}).

Oxygen Consumption Measurements

Compressed air passed through a two-stage regulator and was split into two lines, one of which was circulated through the metabolic chamber. After passing through the chamber, the exhaust air was drawn through one of two channels of an electrochemical oxygen analyzer. The second line of air traveled directly from the air cylinder to the second channel of

the oxygen sensor. The percent difference in oxygen between the chamber's effluent airstream and the nonrespired airstream was used to determine the amount of oxygen consumed by the pup. All oxygen consumption values are presented as ml O_2/kg/min.

Ultrasonic Vocalizations

Ultrasonic vocalizations were detected using a microphone sealed inside the metabolic chamber. The microphone was connected to a "bat detector" (Model SM100, Ultra Sound Advice, London, England) tuned to a ± 5 kHz range centered on 40 kHz. The output of the microphone was amplified and fed into the same data acquisition computer that was used for acquiring blood pressure measurements.

Data Acquisition

T_a, T_{is}, T_{back}, and oxygen consumption were acquired at least twice each min using a customized data acquisition system for the Macintosh computer. A second data acquisition system was used to acquire blood pressure and ultrasonic vocalization data at the rate of 200/s.

Procedure

While the pup was recovering from surgery in the incubator, thermocouples were attached in the interscapular and lumbar regions. To ensure that the pup was in a postabsorptive state at the time of testing, each pup was intubated and given commercial half-and-half at a volume of 3–3.5% body weight.

Of the 7 pups implanted with femoral artery catheters, 2 failed to show thermogenic responses to cooling as defined by increases in oxygen consumption accompanied by increases in T_{is} in relation to T_{back}. Because these 2 pups responded inadequately to cold challenge, they were eliminated from the study and are not discussed further.

After at least 50 min of recovery in the incubator, the pup was transferred to the metabolic chamber maintained at 35.5°C. The pup was given 45–58 min to acclimate to the chamber and exhibit stable thermal and metabolic measures. The test then began by acquiring baseline blood pressure data for 1 min. Next, air temperature was decreased in succession to 29°C and 23°C. Pups were given at least 45 min to stabilize at each T_a, at which time blood pressure data were acquired for 1 min.

After data were acquired at 23°C, T_a was decreased one last time to 17°C. There were two experimental aims during this final period of cooling: (a) to acquire MAP data as interbeat interval (IBI) increased at an extreme T_a; and (b) to acquire data during periods when ultrasound production was high enough so that the vocalization could be related to changes in MAP and IBI. When T_a had reached 17°C, data were collected for at least 5 min beginning 13 to 60 min after the decrease in T_a was initiated.

After the test, the pup was removed from the chamber and the oxygen consumption system was allowed to rezero to verify minimal drift in the system over the course of the test.

Intraabdominal Pressure and Respiration

One 8-day-old was prepared for the measurement of intraabdominal pressure (IAP) by inserting a piece of PE-50 tubing into the abdominal cavity under light ether anesthesia. The catheter was filled with heparinized saline and pressure measured as described earlier for blood pressure. Respiration was also measured in this animal by placing a mercury-filled strain gauge around the thorax as described elsewhere (Sokoloff & Blumberg, 1997).

Data Analysis

Thermal and metabolic measures were imported into StatView 4.5 for the Macintosh. The values of T_a, T_{is}, T_{back}, and VO_2 at each phase of the experiment were determined. Blood pressure and ultrasound data were imported into DataDesk 5.0 for the Macintosh. A scatterplot of the data was produced for each session, and each point in the scatterplot was linked to a row number that represented the passage of 1/200 s. The time at which maximum systolic and minimum diastolic pressures occurred were determined and, from these data, interbeat interval (IBI) was determined to a resolution of ± 2.5 ms. Mean arterial pressure (MAP) was calculated as $P_d + \frac{1}{3}(P_s - P_d)$, where P_s and P_d are systolic and diastolic pressure, respectively. Paired *t* tests were used to test for significant changes in the variables at different phases of the experiment. α was set at .05 and a Bonferroni correction procedure was used to adjust α for multiple pairwise comparisons. All means are presented with their standard errors.

RESULTS

For the 5 pups in the study, the thermal, metabolic, and cardiovascular responses at four air temperatures are presented in Figure 1. The cardiovascular data (i.e., MAP, IBI) were calculated from the means of 200

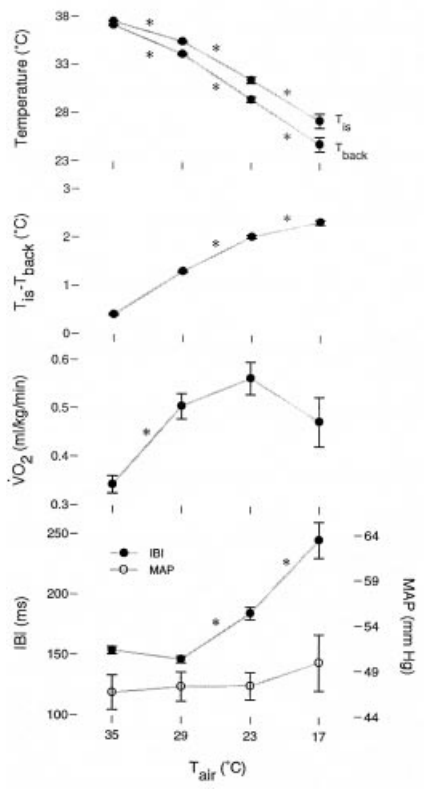

FIGURE 1 Thermoregulatory, metabolic, and cardiovascular responses of five 7- to 9-day-old rats to decreases in T_a. It can be seen that MAP was maintained even as IBI increased in the cold. Mean ± *SEM*. *Significant, $p <$ .017, difference between adjacent points using paired *t* test.

values from every pup at each T_a, which were then averaged across pups. The thermal and metabolic data are single values acquired simultaneously with the cardiovascular data.

Pups increased BAT thermogenesis in response to a decrease in T_a from 35°C to 29°C as indicated by (a) an increasing differential between T_{is} and T_{back} and (b) an increase in oxygen consumption. When T_a was decreased to 23°C and then to 17°C, however, limitations in BAT thermogenesis resulted in more pronounced decreases in T_{is} and T_{back}. These results are consistent with those reported elsewhere using similar experimental procedures (Blumberg & Stolba, 1996).

IBI did not change as T_a was decreased from 35°C to 29°C. In contrast, and as reported previously (Blumberg et al., 1997), when T_a was decreased to 23°C and then to 17°C, IBI increased dramatically. MAP did not decrease, however, in the face of this dramatic bradycardia. In fact, no two values of MAP differ from one another in Figure 1, suggesting that pups adjusted to the decreasing cardiac rate (and thus perhaps cardiac output; e.g., Teitel et al., 1985) by increasing peripheral resistance.

Extended 5-min periods of data collection in which high levels of ultrasound production were detected allowed for the assessment of cardiovascular changes that accompany the emission of the vocalization. An example of a 5-min period for 1 pup at a T_a of 17°C is shown in Figure 2. The *x* axis for these plots represents the occurrence of approximately 1400 heartbeats. For each beat, moving time averages (with a window of 25 beats) were calculated for IBI, MAP, and ultrasound production; a value of 1 for ultrasound production indicates 25 successive interbeat intervals in which the vocalization exceeded an arbitrary threshold voltage.

Figure 2 indicates an overall trend of increasing IBI during this 5-min period of cold exposure. Even as IBI increased, however, MAP was maintained between 52 and 60 mm Hg throughout the period, although there was marked lability in MAP. This lability was driven by peaks in MAP that corresponded with the emission of ultrasound. Moreover, increases in ultrasound production and MAP were related to IBI such that periods of increased pressure and ultrasound emission corresponded with decreases in IBI.

The correspondence between ultrasound production and MAP suggests a mechanistic connection. In fact, observations of the arterial pressure records and ultrasound production indicated a clear relationship between the emission of the vocalization and instantaneous increases in blood pressure. A typical record of these two variables is shown in Figure 3, in which blood pressure exhibits a stable pattern until ultra-

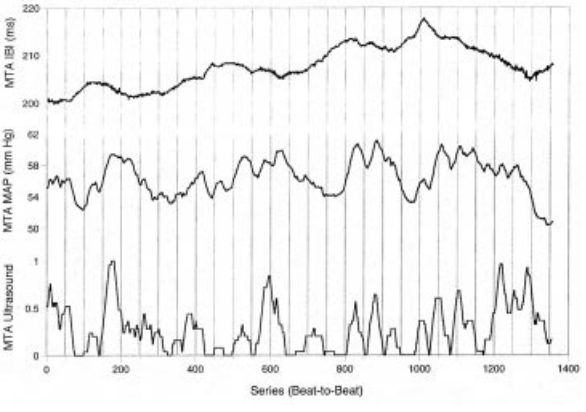

FIGURE 2 Moving time averages (MTA) of IBI (ms), MAP (mm Hg), and ultrasound production (arbitrary units) during a 5-min period for an individual 8-day-old rat. The moving time window was 25 beats long. During the time of data recording, T_a was 17°C and T_{is} was decreasing from 29.0°C to 28.3°C. While IBI increased during the period of recording, the animal was able to maintain MAP. Significant pressor responses often occurred during periods of ultrasound production.

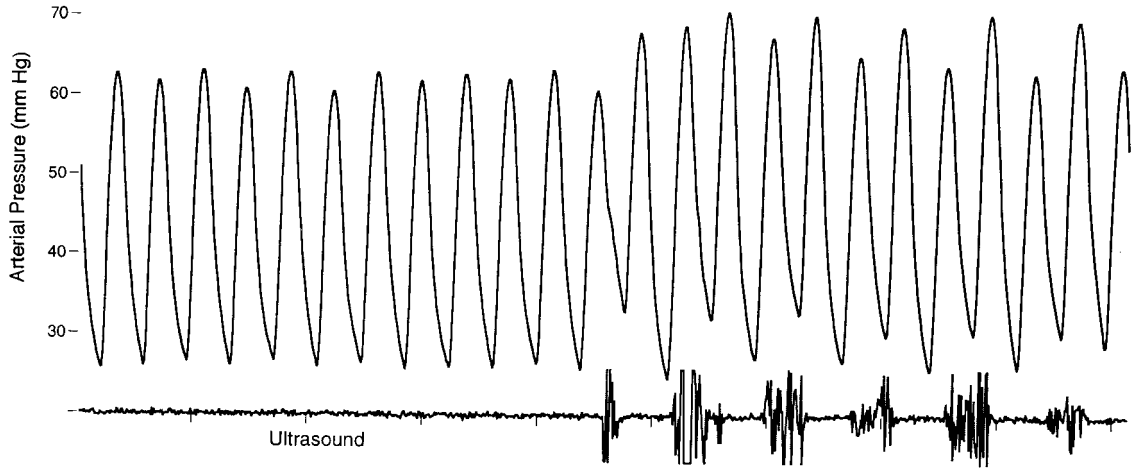

FIGURE 3 Real-time record of arterial pressure (mm Hg) and ultrasound production (arbitrary units) for an individual 8-day-old rat. As can be seen, each ultrasonic pulse was followed by a rise in arterial pressure.

sound emission occurs, at which time there is an approximately 4 mm Hg increase in blood pressure with each ultrasonic pulse. Quantitative analysis of this relationship for all 5 animals showed that when an ultrasound was detected, MAP averaged 57.2 ± 1.3 mm Hg, whereas when ultrasound was not detected, MAP averaged 53.4 ± 1.8 mm Hg. This mean difference of 3.8 mm Hg (range: 2.6–5.5 mm Hg) is statistically significant, $t_4 = 7.34$, $p < .002$.

Ultrasonic vocalizations are accompanied by pronounced contractions of the abdominal muscles. Therefore, to assess the possibility that the increases in MAP described above are initiated by increases in intraabdominal pressure (IAP), we recorded IAP, respiration, and ultrasound production in an individual 8-day-old rat during cold exposure. Figure 4 presents a 50-s period during which T_a was approximately 17°C. It can be seen that there is a very strong correspondence between bouts of ultrasound production and pulsatile increases in IAP.

The rectangular box in Figure 4 indicates a 7.5-s portion of data that is presented in expanded form in

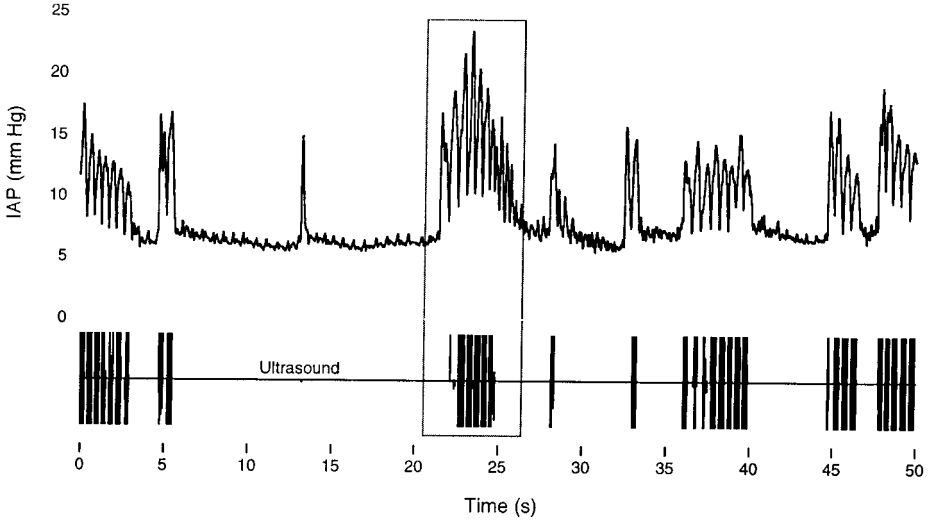

FIGURE 4 Intraabdominal pressure (IAP; mm Hg) and ultrasound production (arbitrary units) for an individual 8-day-old rat at a T_a of approximately 17°C. Data were acquired at a rate of 200/s. Note that IAP increased with each bout of ultrasound production. The data within the box are shown in expanded form in Figure 5.

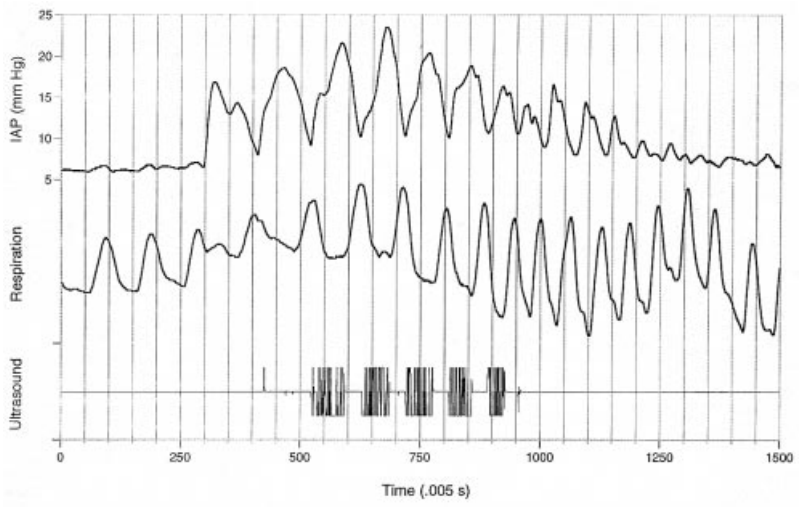

FIGURE 5 Expanded view of the portion of data indicated in Figure 4. In addition to intraabdominal pressure (IAP; mm Hg) and ultrasound production (arbitrary units), respiration (arbitrary units; inspiration upward) has been included. Note that IAP increased during the expiratory phase of breathing. In many cases, clear indications of laryngeal braking can be seen. Increases in IAP are sometimes but not always accompanied by the emission of ultrasound.

Figure 5. In this figure, the respiratory data have been added. First, it can be seen that the third breath in the figure is different from the previous two in that there is a "shoulder" on the expiratory curve; this shoulder is indicative of laryngeal braking (Andrews, Symonds, & Johnson, 1991) and the initiation of braking coincides with a pronounced increase in IAP. Second, with each successive breath, peak IAP increases progressively. Third, although there are many instances of breaths that are accompanied by increases in IAP, only five breaths are associated with detectable levels of ultrasound. Finally, as peak IAP decreases progressively toward the end of the record, ultrasound production is no longer detectable but expiratory shoulders can still be seen during some of the expirations. In general, while we noted many instances of increased IAP without ultrasound production in this pup, the converse was not observed.

DISCUSSION

The present study is the first to demonstrate in infant rats that arterial pressure is regulated during cold exposure. Across the range of air temperatures examined, infant rats were able to maintain arterial pressure at basal levels, even when the limits of BAT thermogenesis were exceeded and cardiac rate decreased. For infant mammals that are limited in their ability to modulate stroke volume (Teitel et al., 1985), a falling cardiac rate indicates decreasing cardiac output (Shaddy et al., 1988) and thus decreasing venous return (Berne & Levy, 1977; Guyton & Hall, 1996). If infant rats, like other infant mammals, cannot modulate stroke volume, then they must elevate peripheral resistance to maintain arterial pressure during bradycardia induced by cold exposure. Adult mammals maintain arterial pressure in the cold primarily by increasing sympathetic vasoconstrictor influences on the arterioles and arteriovenous anastomoses in the skin surface (Toner & McArdle, 1996; Wasserstrum & Herd, 1977). At the present time, however, it is unknown whether infant rats can selectively elevate resistance in the skin surface.

While the regulation of arterial pressure has not previously been examined in unanesthetized infant rats, evidence suggests that neural control of the vasculature is present during the early preweanling period. Smith and colleagues (1984) demonstrated that ganglionic blockade decreases arterial pressure in anesthetized 5- and 9-day-old rats. They also found that both direct- and indirect-acting α_1-adrenoceptor agonists (i.e., methoxamine and tyramine, respectively) produced significant pressor responses. These data demonstrate that in anesthetized infant rats there is a basal level of sympathetic tone maintaining arterial pressure and that catecholamines released from sympathetic terminals can induce increases in vascular resistance. Therefore, a sympathetically mediated vasoconstriction may serve as one mechanism allowing for the maintenance of arterial pressure during cold exposure found in the present study.

In addition to a chronic mechanism for maintaining arterial pressure, an acute pressor mechanism is suggested by the transient increases in MAP observed during extreme cooling (Figures 2 and 3). These pressor responses may be the result of the abdominal compression reaction (ACR; Youmans et al., 1963; Youmans, Tijoe, & Tong, 1974), a maneuver that improves venous return during periods of decreased cardiac output and venous pooling. The ACR entails compression of the abdominal muscles during expiration, resulting in increased intraabdominal and intrathoracic pressures. In turn, such increased pressures enhance venous return by decreasing the capacitance of the venous system and raising the mean systemic filling pressure in relation to right atrial pressure. Although the ACR has received little experimental attention for the last 20 years, the efficacy of externally applied abdominal compression as a means of enhancing venous return during cardiopulmonary resuscitation is now appreciated (Einagle, Bertrand, Wise, Roussos, & Magder, 1988).

It is possible that elevated IAP during the ACR may have artificially elevated our measurement of arterial pressure by influencing the arterial catheter within the abdominal cavity. This is not, however, supported by an analysis of the present data. Specifically, during periods of elevated IAP which include periods of ultrasound production, the tracings of arterial pressure maintain an artifact-free, sinusoidal waveform typical of pulsatile arterial pressure recordings (e.g., Figure 3). In contrast, the recordings of IAP and respiration become highly irregular during periods of ultrasound production (see Figure 5). It should also be stressed that other investigators have demonstrated increased arterial pressure during abdominal compression when arterial pressure was measured using a catheter placed in the thoracic or abdominal cavities (e.g., Abel & Waldhausen, 1969; Einagle et al., 1988). Altogether, these observations argue against the possibility that elevations of IAP contaminated the measurement of arterial pressure in this experiment.

There is now strong evidence that abdominal contractions accompany respirations in which ultrasounds are produced and that these contractions result in increases in intraabdominal pressure (this study) as well as tracheal pressure (Hofer & Shair, 1993). During these breaths, sound is produced by the forced expiration of air through a constricted larynx (Roberts, 1975). Laryngeal constriction during expiration may be an indication of laryngeal braking, a maneuver that is thought to enhance oxygen transport in the lungs (Blumberg & Alberts, 1990). Laryngeal constriction, by providing resistance to airflow, could also make the ACR more effective at generating increased intraabdominal and intrathoracic pressures. Interestingly, respiratory records of adult dogs exhibiting the ACR (see Figure 18, Youmans et al., 1974, and Figure 3, Gilfoil, Youmans, & Turner, 1959) bear a striking resemblance to records that are commonly described as indicative of laryngeal braking, that is, such records contain a shoulder on the expiratory curve (e.g., Andrews et al., 1991; Davis & Bureau, 1987; Symonds et al., 1995). Direct experimental tests will be necessary to determine if laryngeal braking and the ACR serve as integrated responses to improve respiratory and cardiovascular function during extreme thermal challenge.

Recent investigations have highlighted the regulation of BAT thermogenesis and its importance for the physiological and behavioral adaptations of infant rats to cold exposure (Blumberg et al., 1997; Blumberg & Sokoloff, 1997; Blumberg & Stolba, 1996; Sokoloff & Blumberg, 1997). The present results extend these observations to demonstrate that infant rats maintain arterial pressure during moderate cold exposure and even during extreme cold exposure when cardiac rate decreases dramatically. Determining the mechanisms used to maintain arterial pressure remains for further study. Regardless, it is becoming increasingly clear that pups isolated in the cold recruit a variety of physiological mechanisms to maintain thermoregulatory and cardiovascular function.

NOTES

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REFERENCES

Abel, F. L., & Waldhausen, J. A. (1969). Respiratory and cardiac effects on venous return. *American Heart Journal, 78*, 266–275.

Andrews, D. C., Symonds, M. E., & Johnson, P. (1991). Thermoregulation and the control of breathing during N-REM sleep in the lamb. *Journal of Developmental Physiology, 16*, 27–36.

Berne, R. M., & Levy, M. N. (1977). *Cardiovascular physiology*. St. Louis: C. V. Mosby.

Blumberg, M. S., & Alberts, J. R. (1990). Ultrasonic vocalizations by rat pups in the cold: An acoustic by-product of laryngeal braking? *Behavioral Neuroscience, 104*, 808–817.

Blumberg, M. S., & Sokoloff, G. (1997). Dynamics of brown fat thermogenesis: Evidence of stable regulation during moderate cold exposure. *Physiological Zoology, 70*, 324–330.

Blumberg, M. S., Sokoloff, G., & Kirby, R. F. (1997).

Brown fat thermogenesis and cardiac rate regulation during cold challenge in infant rats. *American Journal of Physiology, 272*, R1308–R1313.

Blumberg, M. S., & Stolba, M. A. (1996). Thermogenesis, myoclonic twitching, and ultrasonic vocalization in neonatal rats during moderate and extreme cold exposure. *Behavioral Neuroscience, 110*, 305–314.

Davis, G. M., & Bureau, M. A. (1987). Pulmonary and chest wall mechanics in the control of respiration in the newborn. *Clinics in Perinatology, 14*, 551–579.

Einagle, V., Bertrand, F., Wise, R. A., Roussos, C., & Magder, S. (1988). Interposed abdominal compressions and carotid blood flow during cardiopulmonary resuscitation. *Chest, 93*, 1206–1212.

Gilfoil, T. M., Youmans, W. B., & Turner, J. K. (1959). Abdominal compression reaction: Causes and characteristics. *American Journal of Physiology, 196*, 1160–1162.

Guyton, A. C., & Hall, J. E. (1996). *Medical physiology*. Philadelphia: W. B. Saunders.

Hofer, M. A., & Shair, H. N. (1993). Ultrasonic vocalization, laryngeal braking, and thermogenesis in rat pups: A reappraisal. *Behavioral Neuroscience, 107*, 354–362.

Roberts, L. H. (1975). Evidence for the laryngeal source of ultrasonic and audible cries of rodents. *Journal of Zoology, London, 175*, 243–257.

Shaddy, R. E., Tyndall, M. R., Teitel, D. F., Li, C., & Rudolph, A. M. (1988). Regulation of cardiac output with controlled heart rate in newborn lambs. *Pediatric Research, 24*, 577–582.

Shair, H., Brake, S., Hofer, M., & Myers, M. (1986). Blood pressure responses to milk ejection in the young rat. *Physiology & Behavior, 37*, 171–176.

Smith, P. G., Poston, C. W., & Mills, E. (1984). Ontogeny of neural and nonneural contributions to arterial blood pressure in spontaneously hypertensive rats. *Hypertension, 6*, 54–60.

Smith, R. E. (1964). Thermoregulatory and adaptive behavior of brown adipose tissue. *Science, 146*, 1686–1689.

Sokoloff, G., & Blumberg, M. S. (1997). Thermogenic, respiratory, and ultrasonic responses of week-old rats across the transition from moderate to extreme cold exposure. *Developmental Psychobiology, 30*, 181–194.

Symonds, M. E., Andrews, D. C., Buss, D. S., Clarke, L., Darby, C. J., Johnson, P., & Lomax, L. A. (1995). Environmental effects on thermoregulation and breathing patterns during early postnatal development in hand-reared lambs. *Experimental Physiology, 80*, 779–792.

Teitel, D. F., Sidi, D., Chin, T., Brett, C., Heymann, M. A., & Rudolph, A. M. (1985). Developmental changes in myocardial contractile reserve in the lamb. *Pediatric Research, 19*, 948–955.

Toner, M. M., & McArdle, W. D. (1996). Physiological adjustments of man to the cold. In K. B. Pandolf, M. N. Sawka, & R. R. Gonzalez (Eds.), *Human performance physiology and environmental medicine at terrestrial extremes* (pp. 361–400). Indianapolis: Benchmark Press.

Wasserstrum, N., & Herd, J. A. (1977). Elevation of arterial blood pressure in the squirrel monkey at 10°C. *American Journal of Physiology, 232*, H459–H463.

Youmans, W. B., Murphy, Q. R., Turner, J. K., Davis, L. D., Briggs, D. I., & Hoye, A. S. (1963). Activity of abdominal muscles elicited from the circulatory system. *American Journal of Physical Medicine, 42*, 1–70.

Youmans, W. B., Tjioe, D. T., & Tong, E. Y. (1974). Control of involuntary activity of abdominal muscles. *American Journal of Physical Medicine, 53*, 57–74.