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Do Infant Rats Cry?

Mark S. Blumberg and Greta Sokoloff
University of Iowa

In the current revival of interest in the emotional and mental lives of animals, many investigators have focused attention on mammalian infants that emit distress vocalizations when separated from the home environment. Perhaps the most intensively studied distress vocalization is the ultrasonic vocalization of infant rats. Since its discovery, this vocalization has been interpreted both as a communicatory signal for the elicitation of maternal retrieval and as the manifestation of emotional distress. In contrast, the authors examined the cardiovascular causes and consequences of the vocalization, and on the basis of this work, they hypothesized that the vocalization is the acoustic by-product of the abdominal compression reaction (ACR), a maneuver that results in increased venous return to the heart. Therefore, the vocalization may be analogous to a sneeze, serving a physiological function while incidentally producing sound.

> cry, *n*, (1) a loud vocal sound uttered by either a man or an animal, expressing pain, anger, fright, etc. (2) any loud utterance; shout (9) a sobbing and shedding of tears; a fit of weeping (10) the characteristic vocal sound of an animal
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> —*Webster's Unabridged Dictionary*

When the infants of many mammalian species are separated from the comfort and security of the nest, they emit loud vocalizations. These vocalizations are often referred to as cries. As the dictionary definition above indicates, there are multiple definitions of *cry*. For example, *cry* is defined as the expression of an emotional state (first definition) or as the mere production of sound (10th definition). These definitional contrasts mirror the scientific dispute that has arisen over the last decade regarding the significance of one particular cry—the infant rat's ultrasonic vocalization. Specifically, researchers have strongly disagreed as to whether the infant rat's cry should be interpreted as the expression of an emotional state or as the acoustic by-product of an underlying physiological maneuver. In this article, we provide evidence that supports the latter view—specifically, that the ultrasonic vocalization of infant rats is the acoustic by-product of a maneuver that promotes cardiovascular function. The significance of this dispute, details of which are reviewed here at length, goes far beyond the particularities of the infant rat and touches on numerous evolutionary, conceptual, and methodological issues. We begin with Darwin's contribution to the dispute's intellectual foundations.

Mark S. Blumberg and Greta Sokoloff, Program in Behavioral and Cognitive Neuroscience, Department of Psychology, University of Iowa.

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Correspondence concerning this article should be addressed to Mark S. Blumberg, Department of Psychology, Program in Behavioral and Cognitive Neuroscience, University of Iowa, Iowa City, Iowa 52242. Electronic mail may be sent to mark-blumberg@uiowa.edu.

The Revitalization of Anthropomorphism

Darwin's *Expression of the Emotions in Man and Animals* (Darwin, 1872) was a critical analysis of facial expressions and physiological responses commonly associated with such emotions as fear, sadness, and anger. A century after its publication, Ghiselin (1969), noting the lack of scholarship inspired by the book, declared it "a historical dead end" (p. 187) because of the tendency of Darwin's critics "to cast aspersions by quoting his so-called anthropomorphic statements out of context" (pp. 188–189). For example, Ghiselin pointed out that Darwin, when writing about climbing plants, "refers to branches recoiling with 'disgust' " (p. 189), implying that Darwin used anthropomorphic language for literary effect.

Although Darwin was once widely criticized for this use of anthropomorphic language, Kennedy (1992) noted recently that "we are witnessing a new swing of the theoretical pendulum, now back towards anthropomorphism" (p. 5). For example, in an article devoted to reviving the long-neglected study of animal emotion, Panksepp (1982) argued that "recent advances in brain research may permit anthropomorphism to become a more useful strategy for understanding certain primitive psychological processes in animals than it has been in the past" (p. 407). Cheney and Seyfarth (1990) were more emphatic, declaring: "Anthropomorphizing works" (p. 303).

More important than Darwin's use of anthropomorphic language is the thematic approach that he adopted throughout *Expression* (Darwin, 1872) and his other works. As Ghiselin (1969) pointed out with respect to the passage in which Darwin refers to a disgusted plant, "this statement occurs as an integral part of a strictly physiological explanation" (p. 189). *Expression* is densely packed with attempts by Darwin to provide physiological explanations for various facial expressions. For example, in his discussion of intense screaming in small children, Darwin focused his attention on firm closure of the eyelids and contraction of the surrounding muscles as a mechanism to protect the eyes from excessive pressures generated by the screaming. He also discussed the upturning of the lip as a by-product of this response, noting how similar movements of the upper lip are elicited in adults when

squinting on a bright day. The motive for providing such explanations is clear: Although Darwin was interested in the communicatory effects of facial expression, he also wished "to combat the notion . . . that certain muscles in man are present solely 'for' [i.e., have the function of] expressing certain attitudes" (Ghiselin, 1969, p. 205).

Darwin's appreciation for the distinction between functions and effects can be seen even in his considerations of the vocal productions of animals. For example, in *The Descent of Man, and Selection in Relation to Sex* (Darwin, 1871), in a section devoted to voice, he noted

> Animals of all kinds which habitually use their voices, utter various noises under any strong emotion, as when enraged and preparing to fight; but this may merely be the result of their nervous excitement, which leads to the spasmodic contraction of almost all the muscles of the body, as when a man grinds his teeth and clenches his hands in rage or agony. (p. 275)

As Ghiselin (1969) summarized Darwin's view, the "mere fact of communication does not suffice to demonstrate the origin of an expression through natural selection" (p. 206). This simple observation has been a driving force in the work that is reviewed here.

The field of animal communication is experiencing a period of rapid growth, including the infusion of many new ideas and perspectives from psychologists, ethologists, evolutionary biologists, and neurobiologists (Guilford & Dawkins, 1993; Hauser, 1996; Owings & Morton, 1998). Perhaps the most visible feature of this rapid growth is the explosion of interest in the function and design of animal signals (Hauser, 1996). However, there is growing appreciation for the fact that investigation of such ultimate evolutionary issues cannot be divorced from the study of proximate mechanisms (Owings & Morton, 1998; Stamps, 1991). In this article, we illustrate how attention to proximate mechanism has altered and enhanced our understanding of one communicatory behavior.

The behavior that is the focus of this review—the ultrasonic "distress cry" of infant rats—touches on all of the above issues: functions and effects, communication, emotion, anthropomorphism, physiology, by-product, and historical origin. It is perhaps surprising that a sizable debate has emerged concerning the cause and significance of such a seemingly trivial behavior. However, the thematic, conceptual, and methodological issues at the heart of this debate are not trivial. On the contrary, they are vitally connected with many aspects of the cause, significance, and evolution of the behavior of humans and nonhumans alike.

Ultrasound Production in Infant Rodents: A Brief History

Ultrasound production is a widespread behavioral feature of the neonates of the Murid (e.g., mice, rats) and Cricetid (e.g., hamsters, gerbils) rodents (de Ghett, 1978). In this review, we focus on infant Norway rats (*Rattus norvegicus*). Rat pups are altricial, which means that they are born in a relatively undeveloped state. Specifically, newborn rats lack fur and subcutaneous fat, cannot hear or see, and have limited thermoregulatory and locomotor abilities. These limitations persist until they are at least 12 days of age. In the meantime, a pup relies on its mother for nutrition and upon its mother and littermates for warmth.

The traditional interpretation of ultrasound production and its significance is as follows: If a pup is separated from the nest, it will cool rapidly. This cooling produces imminent danger to the pup if it is not retrieved quickly. With limited thermoregulatory and locomotor capabilities, the pup has only one option: It must call for help. The pup's call is ultrasonic, emitted at a frequency of approximately 40 kHz, 20 kHz above the range of human hearing. The mother, however, is particularly sensitive to this call and will retrieve the pup to the nest when she detects it. Therefore, "ultrasonic vocalization is the neonate's way of achieving behavioral thermoregulation before it develops physiological thermoregulation" (de Ghett, 1978, p. 361).

Beginning in the mid-1950s when it was discovered that infant mice emit ultrasonic vocalizations (Zippelius & Schleidt, 1956), these calls have been interpreted within the general context described above and, over time, the broad outline of this story has been supported and refined. Specifically, we now know that cold exposure is a particularly potent stimulus for ultrasound production (Allin & Banks, 1971; Okon, 1971), that mothers will investigate the source of the vocalization and will retrieve pups to the nest (Allin & Banks, 1972; Sewell, 1970; Smotherman, Bell, Starzec, Elias, & Zachman, 1974), and that although the infants cannot hear their own vocalization, mothers have bimodal hearing curves that are tuned to the frequency of the vocalizations of conspecific young (Brown, 1970, 1973a, 1973b). In addition, investigators reported on the modulation of the vocalization in the presence of social stimuli (Hofer & Shair, 1978, 1980; Oswalt & Meier, 1975). A perspective emerged in which the vocalization was viewed by many as a sign of emotional distress and that the pup could be comforted (and thereby quieted) through replacement of sensory stimuli (e.g., odors) associated with the nest. In this way, the vocalizing pup came to be seen as a candidate for an animal model of separation anxiety, thereby providing a glimpse into the emotional lives of animals and, ultimately, providing a tool for investigations of the pharmacological bases of emotion (Brain, Kusumorini, & Benton, 1991; Miczek, Weerts, Vivian, & Barros, 1995; Panksepp, 1982).

That ultrasounds are detected by the dam and elicit maternal retrieval is well established. It also seems clear that pups have an obvious motivation for calling their mother. Moreover, it seems reasonable to assume that a helpless pup, isolated from the thermal, olfactory, and tactile cues that characterize its nest environment, would feel panic, distress, and anxiety (Brain et al., 1991; Miczek et al., 1995; Panksepp, 1982) and would not be comforted until those cues were restored. Therefore, it hardly seems unreasonable to posit that the vocalization is an acoustic signal produced by an emotionally distressed infant to gain the attention and assistance of the mother.

The fact that the mother rat retrieves a vocalizing pup is important in the interpretation of the pup's vocalization as a cry of distress. However, recall Ghiselin's (1969) summary of Darwin's view, that the "mere fact of communication does not suffice to demonstrate the origin of an expression through natural selection" (p. 206). For example, the fact that a human mother hands over a tissue when her child sneezes does not tell us why the child sneezed. Similarly, the fact that a mother rat retrieves a vocalizing pup does not tell us why the pup vocalized.

Although most vocalizations have been and continue to be analyzed from a functional perspective, we have adopted a mech-

anistic perspective in our investigations of the infant rat's vocalization, specifically focusing on the physiological responses that accompany cold exposure and emission of ultrasound. This work has led to a fundamentally different view of the cause of this vocalization and its significance. Before presenting this work, however, it is helpful to review the arguments that have for many years buttressed the interpretation of ultrasound production as a communicatory act and as an expression of emotional distress.

Infant Rat Ultrasound: Production, Communication, and Emotional Distress

Many aspects of the ultrasonic vocalization of infant rats and other rodents—including the mechanism by which it is produced, its communicatory effects, and its modulation by drugs that are presumed to mediate anxiety—have contributed to a broad consensus that emission of this vocalization reflects an emotionally distressed animal that is calling its mother. The arguments that, in their totality, have contributed to this consensus are addressed below.

Argument #1: Infant Ultrasounds Are Produced by the Larynx, and The Larynx is a Vocal Organ

The identification of the larynx as the vocal cords or as the organ of voice overlooks the function and evolutionary history of this organ. As documented in Negus's (1929) classic treatment, the larynx evolved first as a mechanism to prevent substances (e.g., food, water) from entering the lungs but was then modified for a number of other functions, of which only one was sound production. For example, the larynx has been modified to subserve such functions as locomotion, olfaction, swallowing, and independent use of the forelimbs. With respect to sound production, Negus (1929) is clear:

> The larynges of animals do not show any marked relation to the vocal powers of their possessors; the development of those structures which in human anatomy we call vocal cords is no indication of the amount or kind of noise made by the animal. Cords similar to those of Man are to be seen in many animals which are naturally silent, and, conversely, many animals which are naturally noisy have no true vocal cords. (p. 245)

One particularly salient example of a nonvocal use of the larynx that, nonetheless, produces sound is the Valsalva maneuver. This maneuver, referred to colloquially as "bearing down," entails constriction of the larynx accompanied by prolonged abdominal straining and is used during heavy lifting as well as during defecation and childbirth. As most of us are aware from personal experience, such straining is accompanied by audible, and often loud, grunts. Similarly, coughing entails constriction of the larynx accompanied by strong abdominal contraction, a combination that clears the throat while also incidentally producing a sound.

Vibration of the laryngeal folds (i.e., the vocal cords) produces most mammalian vocalizations, including the audible (i.e., nonultrasonic) vocalizations of rodent pups (Roberts, 1975a). However, although the larynx produces ultrasonic vocalizations (Roberts, 1975a), it does not produce them in the conventional way. Specifically, the rat pup's ultrasonic vocalization is produced during expiration by the passage of air under high pressure between constricted laryngeal folds, causing emission of a pure tone similar to that produced by a bird whistle (Roberts, 1972; Roberts, 1975c); the cords themselves do not vibrate. Despite the uniqueness of this sound production mechanism, no special modifications of the rodent larynx can explain it (Roberts, 1975b).

Argument #2: Emitting Distress Calls at an Ultrasonic Frequency Is Ideally Suited to the Needs of the Infant

Why do rodents in general, and infant rodents in particular, emit sounds at ultrasonic frequencies? Some have speculated (Nyby & Whitney, 1978) that such high frequency sounds are used because they are above the hearing range of predators. Ultrasounds attenuate rapidly with distance and are readily deflected by small objects, thereby preventing the long-distance alerting of predators while providing the mother with information regarding the pup's location.

One might suggest, therefore, that rodents "have been evolutionarily selected to communicate ultrasonically because of predatory pressures" (Nyby & Whitney, 1978, p. 3). This suggestion, however, overlooks one fundamental fact: Body size influences sound production and detection. That is, smaller bodies emit higher frequency sounds, whereas larger bodies emit lower frequency sounds. To appreciate this fact, consider a musical instrument such as a pipe organ, with the small pipes that produce high frequency sounds and the large pipes that produce low frequency sounds. On the same principle, the elephant, the largest land animal, emits infrasonic vocalizations, that is, vocalizations below the range of human hearing (Payne, Langbauer, & Thomas, 1986). This relationship between size and vocalization frequency holds even within species. For example, we have found in infant rats that the dominant frequency of ultrasound production decreases linearly from 45 kHz in 2-day-olds to 25 kHz in the larger 20-day-olds (Blumberg, Sokoloff, & Kent, 2000).

Argument #3: Rodent Mothers Respond Appropriately to Infant Vocalizations

This argument, discussed to some extent above, uses the behavior of the receiver to help explain the behavior and intentions of the sender. It is becoming increasingly appreciated, however, that receivers are not passive respondents to the needs of senders but rather are active participants in the development and evolution of communicatory relationships (Blumberg & Alberts, 1997; Guilford & Dawkins, 1993; Owings & Morton, 1998). This perspective views communication as a dynamic interplay between sender and receiver, rather than simply an exchange of information from sender to receiver (Owings & Morton, 1998).

The important role of the receiver in driving many communicatory relationships can be seen in a variety of systems. For example, it has been argued that preexisting perceptual biases in receivers have shaped the development of the sword in swordtail fish (Basolo, 1990) and the evolution of the "chuck" vocalization in Tungara frogs (Ryan, Fox, Wilczynski, & Rand, 1990). Sometimes, receivers are members of a different species than a sender, such as in the parasitoid female fly that has evolved an auditory sensitivity to the mating call of the male cricket. This sensitivity guides the fly to the cricket, where she deposits her offspring on or near the cricket, whereupon they burrow inside it, grow, and

eventually eat their host (Robert, Amoroso, & Hoy, 1992). This system appears well designed for the provision of ready nourishment to the fly's offspring, including the advertisement of the location of the meal. However, would anyone argue that the fact that the fly responds to the cricket's call provides insight into the function of the call or its evolutionary or mechanistic origins?

We alluded earlier to the sneezing child eliciting delivery of a tissue, and how children do not emit the sneezing sound specifically to evoke delivery of a tissue; the sneezing sound is a by-product of a maneuver whose function is to expel irritants from the respiratory tract. We have little trouble appreciating the likelihood of this conclusion because we all have personal experience with sneezing, what it is for, and the sound that it happens to make. We lack such direct experience with regard to ultrasound production. Nevertheless, ultrasound production may be akin to a sneeze—that is, an incidental by-product of a physiological maneuver that, through the response of the mother, has clear communicatory effects (Blumberg & Alberts, 1997).

Argument #4: Agents With Known or Presumed Anxiolytic Properties Suppress Ultrasound Production

Consideration of the vocalizing infant rat as an animal model of separation anxiety or distress led to the appreciation that this model could be used to examine the pharmacological bases of emotion in infants (Gardner, 1985a; Miczek et al., 1995; Winslow & Insel, 1991b). Various classes of drugs have now been examined, including benzodiazepines (Gardner, 1985b; Insel, Gelhard, & Miller, 1989) and opioids (Kehoe & Blass, 1986; Winslow & Insel, 1991a), with mixed results. Regardless of the results, however, important interpretive issues need to be addressed.

One issue arises from ambiguity concerning the use of ultrasound production as an experimental variable. If we are not careful, we enter the following vicious circle: Why does a pup vocalize? Because it is emotionally distressed. And how do we know it is emotionally distressed? Because it is vocalizing. Within the context of a psychopharmacological study, if emission of ultrasound is to be used as an operational definition of anxiety, then one may be interested in testing a variety of compounds for their anxiolytic or anxiogenic effects as determined by their ability to modulate expression of the vocalization. Alternatively, if one is interested in testing the hypothesis that the ultrasonic vocalization is produced by a state of anxiety, then drugs with known anxiolytic or anxiogenic properties should be used. Too often, failure to appreciate the distinction between (a) using ultrasound as an operational definition of anxiety and (b) testing the hypothesis that ultrasound reflects a state of anxiety results in both meanings being invoked simultaneously.

Another issue raised by psychopharmacological investigations of ultrasound involves the assignment of particular functions to classes of drugs (e.g., benzodiazepines, opioids) and then the assumption that there is an isomorphism between the drug and a particular function. For example, when investigators are interested in the mediating effects of pain on behavior, they often turn to the opioids; conversely, when a behavioral or physiological effect of opioids is discovered, it is generally assumed that pain is involved. However, as reviewed by Moss and Inman (1989), opioids play important roles in other systems as well, such as in modulating respiratory function during development. Therefore, failure to consider the panoply of effects that drugs might have on physiology and behavior can lead to erroneous conclusions.

Argument #5: Separation Calls Have Been Documented in Many Species

The favored interpretation of the infant rat vocalization as a sign of emotional distress appears to gain support from research on the infants of other species. It has been suggested that "[m]ost mammalian young cry when separated from their mothers and homes" (Carden, Barr, & Hofer, 1991, p. 17). Investigators have documented separation calls from a variety of animal young, including ducks (Gaioni, DePaulo, & Hoffman, 1980), chickens (Rajecki, Eichenbaum, & Heilweil, 1973), guinea pigs (Pettijohn, 1979), dogs (Gurski, Davis, & Scott, 1980), and human (Michelsson, Christensson, Rothgänger, & Winberg, 1996) and nonhuman (Newman, 1985) primates.

Although the infants of many mammalian and avian species produce vocalizations during separation and although it may even be obvious that some of these vocalizations are emitted for the benefit of their communicatory effects (e.g., maternal care), it certainly does not follow that all infant vocalizations are emitted for a communicatory purpose. Many (if not all) infant animals, including humans, emit so-called vegetative sounds in a variety of contexts whose communicatory significance is, at best, secondary. Indeed, in human infants, such vegetative sounds (e.g., coughs, burps, snorts, grunts) are as prominent as cries in the neonatal period (Stark, Rose, & Benson, 1978). Grunting is a particularly interesting behavior: In lambs (Johnson, Harding, McClelland, & Whyte, 1977) and human infants (Davis & Bureau, 1987), grunting is an acoustic by-product of laryngeal braking, a respiratory maneuver that enhances gas exchange in the lungs; in addition, in human infants, a grunt vocalization can accompany effortful movements and focal attention before it acquires communicative significance (McCune, Roug-Hellichius, Vihman, Delery, & Gogate, 1996).

Even when focusing on separation-induced vocalizations, more complexity exists than meets the eye. For example, infant dogs exhibit two kinds of separation distress calls: One vocalization occurs soon after birth and for many weeks thereafter and results from discomfort (i.e., cooling); a second vocalization is first detected beginning around the second week postpartum and results from separation (Gurski et al., 1980). Of interest, it is this second vocalization that is thought to coincide with the ontogeny of attachment. Thus, in dogs, it is possible to identify developmentally discriminable responses to separation that are evoked by different contexts and are governed perhaps by different physiological mechanisms, thus highlighting the importance of avoiding labels that merely categorize vocalizations and thereby gloss over potentially important differences.

Argument #6: Why Else Would Pups Vocalize?

As is well appreciated, theories are only replaced by other theories. Thus, in the absence of an alternative explanation for ultrasound emission by infant rats, the above arguments in support of the conventional interpretation of ultrasound production may in their entirety seem reasonably compelling, even if each argument individually has weaknesses. Therefore, the remainder of this

article is devoted to describing an alternative theory of the significance of ultrasound production in infant rats and the evidence in support of it. We begin by first discussing the methods currently used by investigators to evoke emission of the vocalization.

Evoking Ultrasound Production in the Laboratory

There are three common methods for evoking ultrasound production in infant rats (we introduce a fourth method later in the article). Two of these methods are nonpharmacological (i.e., isolation and cold exposure) and the other is pharmacological (i.e., clonidine administration). Because any theory of ultrasound production must address all three of these methods, they are described in detail below.

Isolation Procedure

In the isolation procedure, a pup is removed from the nest, transported by hand across a room or down a hall to a second room, and then placed in a container, whereupon ultrasound production is monitored for a period of time. Different labs use very different procedures in these tests. For example, the temperature of the testing environment can be 10 °C (Naito & Tonuoe, 1987), 20 °C (Vivian, Barros, Manitiu, & Miczek, 1997), 22 °C (Hofer & Shair, 1980), 24 °C (Goodwin & Barr, 1997), or 32 °C (Kehoe & Blass, 1986). After the pup is isolated in the test container, which is usually covered with bedding, the test is concluded after 2–6 min (Goodwin & Barr, 1997; Hofer & Shair, 1980; Kehoe & Blass, 1986; Naito & Tonuoe, 1987; Vivian et al., 1997).

The isolation test, in its many incarnations, reflects the interpretation of the behavior that it was designed to examine. In other words, because the vocalization is widely interpreted as an isolation distress call, the isolation method is designed to mimic the sensory experiences of a rat pup during isolation, including thermal, vestibular, and tactile stimulation. According to this perspective, these stimuli are merely signs or tokens, of significance only to the extent that they signal to the pup that it is no longer in the nest. Therefore, whether pups are tested at 10 °C or 32 °C, on bedding or on an aluminum plate, placed immediately in the test chamber or walked down a hallway with the pup cradled in bare hands, or even shaken before testing, has little relevance to the goal of eliciting the distress call and investigating the stimuli or pharmacological agents that modulate its expression.

The isolation procedure elicits high rates of ultrasound production that then taper off over the next 5–10 min, the exact time course depending on the methods used. For example, in one experiment, the experimenter handled pups with rubber gloves, completed the transfer within 5 s, and transferred the pups from the nest to a 35 °C test chamber (Blumberg, Efimova, & Alberts, 1992). In this experiment, rates of vocalization declined to near-zero levels within 3 min of the transfer. However, these pups also exhibited heat production immediately after transfer, leaving open the possibility that thermal factors had not been removed completely. Therefore, in a second experiment, pups were acclimated in an incubator maintained at 35 °C and then transferred to a test chamber maintained either at 35 °C or 22 °C. Only transfer to the 22 °C test chamber evoked ultrasound production. These experiments suggested that, in the isolation procedure, thermal stimuli contribute significantly to the elicitation of ultrasound production.

Cold Exposure

The uncontrolled nature of the isolation procedure makes it difficult to assess the relationship between cold exposure and ultrasound production. Therefore, a second method was developed to remove nonthermal stimuli from the procedure (Blumberg & Alberts, 1990). In this procedure, a pup is removed from the nest and placed in a chamber at thermoneutral (i.e., approximately 35 °C for a 1-week-old rat). After a period of acclimation of at least 45 min, chamber air temperature is decreased to a subthermoneutral temperature without handling or transporting the pup. In addition, the pup is tested on a mesh platform constructed of a material that minimizes conductive heat loss. Using this procedure, many physiological variables can be measured, including oxygen consumption, skin and rectal temperatures, cardiac rate, and blood pressure. As we find, this procedure yields highly reliable and reproducible results and has significantly altered our understanding of the causes and consequences of ultrasound production.

Just as the isolation procedure entails significant thermal stimulation of the pup, the cold exposure method entails isolation of the pup from mother and littermates. However, for many investigators, the controlled procedure just described removes exactly those features that make the vocalizing rat pup a subject of interest. For these investigators, the isolation procedure more accurately captures the context of isolation distress and thus gets to the heart of the vocalization's functional significance; in other words, it is the acute response to separation that is believed to reflect the emotional component of the vocalization, perhaps justifying the use of 2-min to 6-min tests. For example, Hofer and his colleagues (Hofer, Masmela, Brunelli, & Shair, 1998) have recently investigated a phenomenon, maternal potentiation, in which isolated infant rats provided with brief periods of maternal contact exhibit increased rates of vocalization when the mother is subsequently removed. Drawing a direct analogy to human infant behavior, they state

> If the mother of a toddler returns briefly to the day-care center for some reason soon after dropping off her child on the way to work and then starts to leave again after this brief visit, she may be startled by a frantic outburst of crying from her child, very unlike the mild response to her initial departure earlier in the day. This intense vocal response to the second separation can be inexplicable to the mother and is a powerful inducement to give up her plans for the morning and remain with her child. (Hofer et al., 1998, p. 200)

Clonidine Administration

As mentioned above, psychopharmacologists have largely focused on the ability of benzodiazepines and opioids to modulate ultrasound production evoked by separation of the pup from the nest. One agent, however, can evoke ultrasound production on its own. That agent is clonidine, an α_2 adrenoceptor agonist (Hård, Engel, & Lindh, 1988; Kehoe & Harris, 1989). Clonidine is able to evoke ultrasound in quiet pups isolated at a thermoneutral temperature (Hård et al., 1988; Sokoloff, Blumberg, Mendella, & Brown, 1997), an essential finding for concluding that it acts independently of cold exposure. Curiously, clonidine has been used widely as an anxiolytic in adults, suggesting that its apparent anxiogenic activity in infants undergoes reversal, probably around 3 weeks postpartum when the cataleptic effects of clonidine first become

noticeable (Hård et al., 1988; Kehoe & Harris, 1989; Reinstein & Isaacson, 1977). Finally, it is interesting that the clonidine-injected pup is not quieted when presented with sensory cues from the nest or even when returned to the nest (Hansen, 1993; Kehoe & Harris, 1989), indicating that clonidine's psychological or physiological effects are profound indeed.

For an agent that has such a substantial impact on the infant's vocal behavior, clonidine has received relatively little attention from psychopharmacologists, especially when compared with that given to the modulatory effects of benzodiazepines and opioids. Perhaps it has been difficult for researchers to reconcile the incongruity of a sympathoinhibitory agent like clonidine (Gillis, Gatti, & Quest, 1985; Luft et al., 1986) inducing a state of anxiety. Nonetheless, this incongruity has not called into question the usefulness of the infant's vocalization as a measure of anxiety.

Any complete theory regarding the significance of ultrasonic vocalizations must account for the contexts and conditions with which they are associated. Our theory unifies the methods outlined above into a single mechanistic explanation. Because our theory relies on the unambiguous use of the distinction between products and by-products, we now examine that distinction in detail.

Products and By-Products

The hypothesis presented below posits that the infant rat's ultrasonic vocalization is an acoustic by-product of a physiological maneuver that is evoked in response to a cardiovascular challenge. Before embarking on the path toward this hypothesis, it is first necessary to define what is meant by the term *by-product,* because it can be so easily misunderstood.

Webster's Unabridged Dictionary (1983) defines *by-product* as "something produced in the process of making another thing; secondary or incidental product or result." In a classic example, a car engine's primary function is to produce the work needed to turn the car's wheels; the heat produced by the engine is a by-product of the engine's primary function. The heat itself does not contribute to the work performed by the engine and, in fact, must be controlled by a radiator system so that the engine does not overheat.

Distinguishing products from by-products is useful when trying to understand the relationship between mechanism and function. The distinction is also important in the historical sciences, including evolutionary biology. Indeed, in Gould and Lewontin's (1979) now-famous critique of the adaptationist programme, they state that the "immediate utility of an organic structure often says nothing at all about the reason for its being" (p. 593). These issues were discussed with particular clarity more than three decades ago by Williams (1966) who, in *Adaptation and Natural Selection,* stated

> It is often easy, in practice, to perceive functional design intuitively, but unfortunately disputes sometimes arise as to whether certain effects are produced by design or merely as by-products of some other function. The formulation of practical definitions and sets of objective criteria will not be easy, but it is a problem of great importance and will have to be faced. (p. 9)

As we saw earlier, Darwin acknowledged that even some vocal behaviors can be incidental by-products of exertion or other processes. Indeed, how could he not have acknowledged this given the numerous acoustic behaviors that humans exhibit—including sneezing, coughing, snoring, wheezing, and gurgling—in which sound production is known to be incidental to an underlying physiological process? However, how do we know, for example, that the sound produced by coughing is a by-product of the maneuver that produces the cough? The answer, it would seem, is that a linkage exists between the cause and consequence of coughing. Specifically, coughing is caused by the presence of an irritant in the throat, and the consequence of coughing is the forcible expulsion of the irritant; once the irritant has been expelled, coughing ceases. Similarly, sneezing is caused by an irritation of the mucous membrane of the nose, and the consequence of sneezing is removal of the irritant. In other cases, however, this linkage does not exist; for example, snoring and wheezing are simply forms of noisy breathing. In such cases, it appears that the vocalization has a cause but no physiological or communicatory consequence (although, see Welsch, 1993, for a humorous perspective on these issues).

Of course, many vocalizations appear to have arisen for their signaling function per se. In such cases, there are causes and consequences of the vocalization, but there is no direct mechanistic link between them. For example, birds may sing more often in the morning with the rising sun, and the coming of heat and light may even evoke physiological changes in birds, but there is no evidence that the production of bird songs, including the complex arrangement of syllables that make up many of them, plays a homeostatic, regulatory role.

Therefore, for a vocalization that has demonstrated communicatory effects, the discovery of a linkage between physiological cause and consequence suggests that the vocalization is an incidental by-product of a more fundamental process. Unfortunately, resolution of these issues may sometimes be impossible, in part because the answers may be buried in the evolutionary past. It is even possible for a vocalization to begin as an acoustic by-product but become ritualized to serve primarily a communicatory function (Morris, 1956). Regardless, investigations of a signal's evolutionary and mechanistic origins can only enrich our understanding of any communicatory system.

Infant Rat Ultrasound Production: Toward a New Perspective

Those who have investigated the ultrasound production of infant rats will readily acknowledge the preeminent role played by temperature. Differences arise, however, as to the nature of that role: Is temperature merely a sign to the pup that it is out of the nest, or does cold exposure evoke physiological responses that in turn play a causal role in the production of ultrasound? The former perspective emerged from and was reinforced by a long-held view of the infant rat as an inadequate thermoregulator. As we see, this view is no longer tenable, and the foundation on which the classic interpretation of ultrasound production has rested loses much of its strength.

The Infant Rat as Poikilotherm and a New Interpretation

Fifty years ago, as investigators sought to document the development of thermoregulation in small infants such as rats, they concluded that homeothermy (i.e., the ability to maintain body

temperature at a high level across a range of cold air temperatures) does not develop until infants are more than 2 weeks of age (Blumberg, in press; Blumberg & Sokoloff, 1998). Because rectal temperature was considered the sine qua non of body temperature and because these investigators tested pups at extremely cold temperatures, they were not aware that pups are able to produce heat internally on the day of birth, as was later discovered (Taylor, 1960). In time, it was found that the infants of most mammalian species, including rats and humans, possess a heat-producing organ, called brown adipose tissue (BAT), that is located primarily under the skin in the interscapular region and is capable of producing heat in response to cold exposure (Hull, 1966; Smith & Horwitz, 1969). Nonetheless, because infant rats are small and are poorly insulated, the presence of BAT was not considered adequate to offset the drastic heat loss experienced by infants during seemingly moderate cold exposures, thus forcing the infant's dependence on behavioral thermoregulatory mechanisms (Satinoff, 1996).

The physiologist's view of infant thermoregulation described above has played a seminal role in shaping the psychobiologist's view of ultrasound production:

> The phenomenon of ultrasound production occurs at a time when the pups' own capacity to alleviate such conditions [i.e., hypothermia during cold exposure] is relatively undeveloped. They can neither prevent progressive loss of body heat nor find their way back to the nest or to the mother. This indicates that distress calls are oriented primarily toward the mother and suggests that one function of the calls is to induce the latter to search for calling pups. (Allin & Banks, 1971, p. 155)

> Since rats are born blind and deaf and without the ability to forage or regulate their own internal temperature, the capability of an isolate to summon the dam may be crucial to survival. (Carden et al., 1991, p. 17)

If, as was commonly understood, any degree of cooling of an infant rat below thermoneutrality results in hypothermia, then ultrasound production makes adaptive sense as a form of behavioral thermoregulation. Recent work, however, calls into question this long-held assessment of infant thermoregulation (Blumberg, in press; Blumberg & Sokoloff, 1998).

A series of studies that began 5 years ago (Blumberg & Stolba, 1996) has addressed the physiological and behavioral responses of infant rats to varying levels of cold exposure. We began by distinguishing three categories of air temperature: at thermoneutral temperatures (approximately 35–37 °C in a week-old rat), BAT thermogenesis is minimal; at moderate temperatures (approximately 25–35 °C in a week-old rat), BAT thermogenesis increases with each successive decrease in air temperature; and at extreme temperatures (< 25 °C in a week-old rat), BAT thermogenesis can increase no further, resulting in hypothermia.

Contrary to the view that any subthermoneutral air temperature results in thermoregulatory failure, we found that the distinction between moderate and extreme cold exposure is significant. Specifically, during moderate cold exposure and as pups gradually increased BAT thermogenesis, thermoregulation was effective as evidenced by the pups' ability to maintain cardiac rate and remain asleep (Blumberg, Sokoloff, & Kirby, 1997; Blumberg & Stolba, 1996; Sokoloff & Blumberg, 1998; Sokoloff, Kirby, & Blumberg, 1998). In contrast, as pups were exposed to extreme air temperatures, their cardiac rate plummeted and the pups woke up. In addition, whereas pups did not vocalize at moderate air temperatures, they vocalized increasingly at extreme air temperatures (Blumberg, Sokoloff, & Kent, 1999; Blumberg & Stolba, 1996; Sokoloff & Blumberg, 1997), a finding that was unexpected on the basis of our own previous research (Blumberg & Alberts, 1990).

The work summarized above provided evidence for unexpected thermoregulatory capabilities in infant rats, resulting in a changed perspective. In addition, this work weakened one of the pillars on which the standard interpretation of ultrasound production has long rested: that the infant vocalization is a behavioral thermoregulatory response to elicit maternal retrieval and compensates for the infants' inability to regulate temperature physiologically. However, even though the pillar is weakened, it is not toppled, because one could reasonably respond that pups vocalize at extreme air temperatures because it is only at these temperatures that the pups' thermoregulatory abilities are overwhelmed, and thus it is only then that maternal retrieval is truly needed.

Therefore, our next step in assessing the mechanistic origins of ultrasound production was to determine the causal linkages between the physiological and behavioral responses that we had observed. For example, the cardiac rate response to moderate and extreme cooling was particularly interesting because it had been hypothesized over 30 years ago that BAT is ideally suited for the delivery of warm blood to the heart (Smith, 1964). As has been known for many years, the heart (like any muscle) is highly temperature sensitive (Lyman & Blinks, 1959); the warmer the heart, the faster it beats. When we found that pups are able to maintain cardiac rate during moderate cold exposure, it was of interest to determine whether this maintenance is dependent on heat production by BAT and the delivery of warm blood to the heart. We found BAT thermogenesis does indeed contribute to the regulation of cardiac rate (Blumberg et al., 1997; Sokoloff et al., 1998), thus supporting Smith's hypothesis and providing evidence that heat produced by BAT is dedicated to the maintenance of thoracic temperature, rather than of body temperature per se. As it turned out, consideration of cardiac rate and its response to cold was a key finding for the development of our interpretation of ultrasound production in infant rats.

Cardiovascular Concomitants of Ultrasound Production and the Abdominal Compression Reaction

Cardiac rate is one of the two primary determinants of cardiac output (i.e., the volume of blood ejected by the heart per unit time). The second major determinant is stroke volume (i.e., the amount of blood ejected by the heart per cardiac cycle). Infant mammals appear to be limited in their ability to increase stroke volume when cardiac rate decreases, thus creating a situation whereby changes in cardiac rate evoke concomitant changes in cardiac output (Shaddy, Tyndall, Teitel, Li, & Rudolph, 1988). Therefore, when infant rats experience a decrease in cardiac rate during extreme cold exposure, it is likely that they are also experiencing a decrease in cardiac output. A decrease in cardiac output will decrease the amount of blood returning to the heart (Guyton & Hall, 1996), resulting in venous pooling and threatening overall cardiovascular function.

An additional factor working against the infant rat during extreme cold exposure is increased blood viscosity. Blood viscosity

is a major determinant of venous return to the heart (Goslinga, 1984). As infant rats become hypothermic, blood temperature also decreases, and because blood viscosity is inversely proportional to temperature, hypothermia results in increased blood viscosity (Blumberg et al., 1999). This increase in viscosity will then conspire with the decrease in cardiac output to produce an infant whose ability to return blood to the heart is severely compromised.

What physiological options are available to an infant rat facing hypothermia and decreased venous return? The answer to this question was unclear until researchers began measuring arterial and venous pressures in young rats. In the first such study (Kirby & Blumberg, 1998), the authors were primarily interested in determining whether infant rats are able to regulate arterial pressure across the transition from moderate to extreme cold exposure. Surprisingly, pups were able to maintain arterial pressure even during extreme cold exposure as cardiac rate (and cardiac output) plummeted. Because arterial pressure is a function of cardiac output and peripheral resistance, this result suggested that pups can increase peripheral resistance substantially to compensate for the decreased cardiac output. In addition, as pups emitted ultrasonic vocalizations, arterial pressure pulses occurred synchronously with vocalizations. Next, when the pressure in the abdominal cavity was measured during ultrasound production, it was clear what might be causing the arterial pressure changes: With each ultrasonic pulse, intra-abdominal pressure (IAP) increased 200–300% (see Figure 1A). All together, these findings suggested a causal relationship between ultrasound production, IAP, and cardiovascular function.

That the maneuver producing ultrasound may play a role in the maintenance of cardiovascular function first emerged upon consideration of a series of studies performed on dogs over 30 years ago. Specifically, Youmans and his colleagues (Gilfoil, Youmans, & Turner, 1959; Youmans et al., 1963; Youmans, Tjioe, & Tong, 1974) examined the physiological causes of a maneuver, called the abdominal compression reaction (ACR), and the consequences of this maneuver for cardiovascular function. The ACR occurs in animals when venous return is decreased and entails compression of the abdominal muscles during or after expiration. The increased IAP that ensues compresses the abdominal veins and thereby propels blood back to the heart. Although these early studies of the ACR did not address the role of the larynx (these studies were usually performed on anesthetized and intubated dogs), Kirby and Blumberg suggested that laryngeal constriction during expiration contributes to the increased IAP observed during ultrasound production, thereby increasing the effectiveness of the maneuver. Indeed, as indicated above, when IAP and ultrasound production were measured simultaneously (Kirby & Blumberg, 1998), it was clear that initiation of increased IAP occurred as ultrasound production commenced (see Figure 1A). Therefore, on the basis of such findings in infant rats as well as those of Youmans and his colleagues in adult dogs (Youmans et al., 1963, 1974), it was hypothesized that (a) ultrasound production is the acoustic by-product of the ACR during periods when venous return is compromised (such as in conditions of extreme cooling), and that (b) as a result of the ACR, venous return is increased.

As noted in a prominent textbook of medical physiology (Guyton & Hall, 1996), the ACR "is probably much more important than has been realized in the past" (pp. 217–218), and, in fact, there have been relatively few investigations of the ACR since the

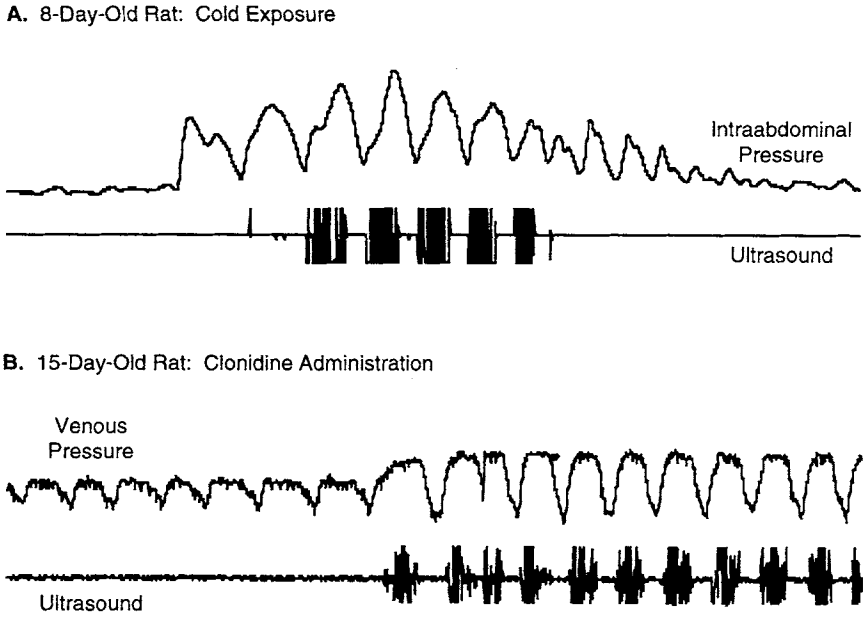

Figure 1. A: Intra-abdominal pressure (IAP) and ultrasound production records for an 8-day-old rat during cooling to an air temperature of 17 °C. When ultrasound is detected, IAP increases more than twofold. Data are from Kirby and Blumberg (1998). B: Venous pressure (measured near the right atrium) and ultrasound production records for a 15-day-old rat after administration of clonidine hydrochloride (0.5 mg/kg). When ultrasound is detected, venous pressure increases substantially, indicative of increased venous return. Data are from Blumberg et al. (2000).

last review of the subject by Youmans and colleagues in 1974 (Youmans et al., 1974). Of interest, the topic has surfaced in a somewhat altered form among researchers studying cardiopulmonary resuscitation (CPR). Specifically, these researchers, usually working on anesthetized dogs, have noted that CPR is more effective when there is application of external pressure to the abdomen asynchronously with the rhythm of chest compression (Babbs, 1985). The idea is simple: Pumping blood from the heart using chest compressions is more effective when abdominal compressions are also used to increase the amount of blood returning to the heart.

Further Insights Gained From the Study of Clonidine's Effects on Ultrasound Production and Cardiovascular Function

We have already described the ability of clonidine to evoke ultrasound production in infant rats and that this result is surprising because anxiogenic agents generally are not sympathoinhibitory. What was not emphasized is the intense and widespread interest among physiologists in the cardiovascular effects of clonidine. Specifically, clonidine is widely known for its ability to withdraw sympathetic tone and thereby dilate blood vessels and decrease cardiac rate (Gillis et al., 1985; Luft et al., 1986). Therefore, we wondered whether clonidine has similar cardiovascular effects in infants and whether these effects occur simultaneously with ultrasound production. When we measured cardiac rate in week-old rats while monitoring ultrasound production, we found that the two responses did indeed occur together (Blumberg et al., 2000; Sokoloff et al., 1997). We also found that developmental changes in clonidine's effects on cardiac rate and ultrasound production mirror each other, suggesting that the infant rat's dependence on sympathetic outflow for the maintenance of autonomic function is an important factor in clonidine's ability to initiate ultrasound production.

To move beyond a mere correlation between clonidine's effects on cardiac rate and ultrasound production, we pretreated week-old rats with prenalterol, a β_1 adrenoceptor agonist that acts peripherally to increase cardiac rate (Blumberg, Kreber, Sokoloff, & Kent, 2000). If clonidine's cardiovascular effects are indeed causal to its ultrasound effects, then prenalterol pretreatment should inhibit clonidine-induced ultrasound production. As predicted, prenalterol pretreatment did significantly inhibit clonidine-induced ultrasound production. It is particularly difficult for the anxiety hypothesis to explain this result because of the oddity of a sympathomimetic like prenalterol acting as an anxiolytic, preventing a putative distress response elicited by clonidine, a sympathoinhibitory agent. Typically, clinical anxiety in humans is characterized by excitation of the sympathetic nervous system, with one consequence being tachycardia, not bradycardia (Berkow, 1987).

A Critical Test

The ACR hypothesis predicts that emission of the ultrasonic vocalization is associated with increased venous return to the heart. It is difficult to measure venous blood flow directly, but we reasoned that an increase in venous blood flow would be detected as an increase in venous pressure. Because venous pressure is more difficult to measure than arterial pressure, we could not perform such an experiment on week-old rats. Therefore, we used 15-day-olds instead, taking advantage of the fact that clonidine has a maximal stimulatory effect on ultrasound production at this age (Blumberg, Sokoloff, Kirby, & Kent, 2000). We predicted that each ultrasonic pulse would be associated with pronounced increases in venous pressure.

To perform this experiment, a catheter was inserted in the subject's right jugular vein and threaded down until it was within 1 mm of the right atrium. After recovery, the infant rat was injected with clonidine while venous pressure and ultrasound production were recorded. As predicted, after clonidine administration, there was a close correspondence between emission of ultrasound and pulsatile increases in venous pressure; as ultrasound production was initiated, venous pressure increased significantly (see Figure 1B).

This critical test of the ACR hypothesis is notable because it forms a link between the hypothesized cause of the maneuver that produces ultrasound—that is, decreased venous return as a result of extreme cold exposure or clonidine administration—and the consequence of the maneuver that produces ultrasound—that is, increased venous return. Accordingly, this linkage suggests that the emission of ultrasound is merely a by-product of the ACR, produced by forced movement of air between constricted laryngeal folds under high pressure created by contraction of the abdominal muscles. The result is a whistle, not unlike that produced by water boiling in a kettle on a stove.

Figure 2 presents our working model of the cardiovascular causes and consequences of the ACR. This model is able to account for the ability of both clonidine administration and extreme cold exposure to decrease venous return and thereby elicit the ACR and ultrasound production. As detailed above, we now have substantial direct and indirect evidence to support most of the elements of this diagram.

One prediction of the model presented in Figure 2 is that it should be possible to trigger the ACR and ultrasound production through any manipulation that causes a decrease in venous return. We have tested this prediction by administering sodium nitroprusside to 15-day-old rats (Sokoloff, Blumberg, Gorby, Lewis, & Kirby, 2000). Sodium nitroprusside is metabolized within the blood vessel walls, producing nitric oxide that in turn directly causes these vessels, especially the veins, to dilate (Hardman & Limbird, 1996). Venodilation then results in decreased venous return as blood is redistributed from central to peripheral veins. In adult rats, administration of nitroprusside results in rapid initiation of a tachycardia as baroreceptor mechanisms attempt to counter falling blood pressure (Kirby, Woodworth, Woodworth, & Johnson, 1991); these mechanisms contribute to the recovery of blood pressure, usually within 10 min. When infant rats are administered nitroprusside (400 μg/kg), they also exhibit a rapid tachycardia that dissipates within minutes. Most important for the present discussion, these infants vocalize for the first few minutes after nitroprusside administration when venous return is likely to be compromised. This effect of nitroprusside is especially noteworthy because of this agent's specific and short-lived dilatory action on veins.

Therefore, we have now added a new manipulation to the list of those capable of evoking ultrasound in infant rats, one that was chosen for its known cardiovascular effects and that supports the prediction that manipulations that decrease venous return are suf-

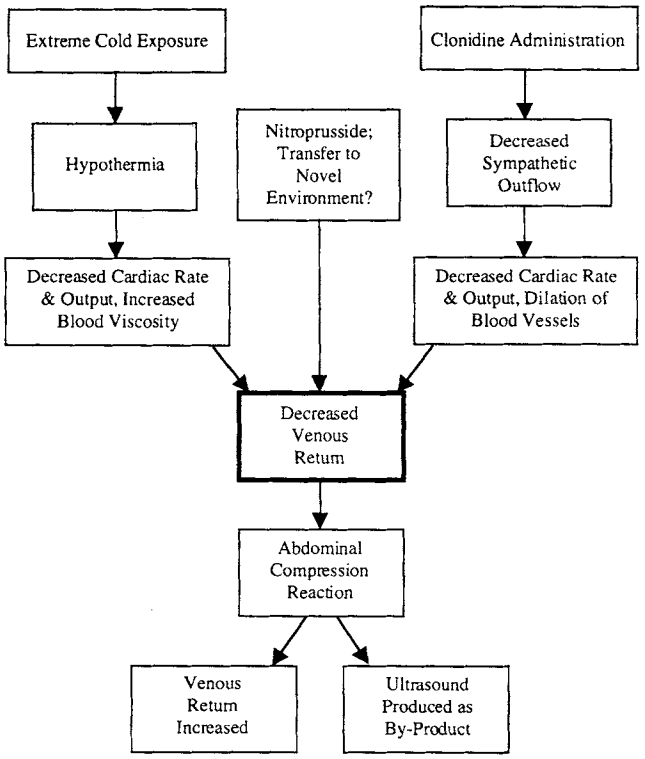

Figure 2. Flow diagram depicting a working hypothesis for how extreme cold exposure and clonidine administration result in decreased venous return, thereby triggering the abdominal compression reaction and ultrasound production. Nitroprusside administration might trigger ultrasound production through a more direct influence on venous return, as might transfer to a novel environment.

ficient to trigger ultrasound production. A corollary to this view is that once ultrasound has been evoked, any stimulus capable of modulating autonomic nervous system outflow to the cardiovascular system should be capable of modulating ultrasound production as well.

The working model presented in Figure 2 does not specifically address the emission of ultrasound that follows removal of pups from the nest and their transfer to a novel environment. This paradigm, although perhaps the most common of all experimental procedures for eliciting ultrasound, is also the most difficult to assess because it entails so many simultaneously changing variables. Although some might argue that separation-induced ultrasound production is a qualitatively different phenomenon than that produced by cold exposure alone or by clonidine or nitroprusside administration, it is more parsimonious to suggest that decreasing venous return underlies all of these ultrasound-related contexts. For example, as noted above, the separation paradigm entails thermal, tactile, and vestibular stimuli. When the thermal stimuli are controlled, ultrasound production decreases dramatically (Blumberg et al., 1992). In addition, because pups are often picked up by the nape of the neck or by cupping them in the hand in a head-up orientation, there is likely to be an alteration of blood flow due to the effect of gravity. Youmans and his colleagues (Youmans et al., 1963) used tilting procedures to explore such gravitational effects on venous return and expression of the ACR; in general, head-up tilting increased expression of the ACR. Therefore, we mimicked the separation paradigm in infant rats but, instead of transferring pups to a flat surface, we transferred them to a small container that permitted the pups to be oriented at an angle of 25° in a head-up or head-down orientation (Blumberg, Sokoloff, Mendella, & Brown, 1996). The findings were striking: For the 10 pairs of week-old rats tested, those tilted head-up vocalized more than four times as much over the 10-min test as those tilted head-down, once again suggesting that venous return is a critical factor in the elicitation of ultrasound production.

Concluding Comments

The standard definitions of *cry* presented at the beginning of this article encompass the many meanings that we have considered here regarding the infant rat's ultrasonic vocalization. Although one definition of *cry* specifies the mere emission of sound, the first definition adds the expression of emotion, such as pain or fear. Therefore, the infant rat's vocalization can be considered a cry in the sense that it is a characteristic vocal sound. In contrast, it is clear that many investigators view the vocalization as an emotional expression of distress or anxiety.

It is very important to define explicitly the terms that we use to describe the infant rat's vocalization, as well as the implications of those terms. For example, the vocalization may be a communicative act in that it conveys reliable information regarding the pup's physiological state, and the mother responds appropriately to this information by retrieving the pup to the nest. The act of communicating, however, does not imply the intention to communicate—this simple yet important point was illustrated above with regard to the human mother's response to a sneezing child. Furthermore, in the specific case of the ultrasounding rat pup, a lack of intentionality is implied by two observations: First, infant rats are unable to hear their own vocalizations until they are 12 days of age, and second, when pups are frozen in ice water and are allowed to rewarm, ultrasonic vocalizations are detected while pups are still unconscious (Hofer & Shair, 1992).

The term *distress* is also problematic because it is used variously by different investigators. If *distress* implies only that an animal has been pushed beyond its physical and physiological limits or that its homeostatic regulatory capabilities have been exceeded, then the infant rat during extreme cold exposure is in distress. Therefore, because the vocalization is associated with extreme cold exposure, it could reasonably be designated a distress vocalization. In this case, there need be no mention of emotion as an intervening, causative variable. However, whatever term we use to describe the vocalization, we must not lose sight of the mechanisms that are causative to its emission. Thus, although the pup's vocalization can be designated as a distress call, it would be a mistake to then conclude that any stimulus that is commonly thought to cause distress is capable of evoking the vocalization. For example, week-old starved pups do not vocalize, and neither starvation nor hypoxia exacerbate ultrasound production during cold exposure (Blumberg & Alberts, 1991).

Explicitly distinguishing between the mechanistic, functional, and emotional interpretations of distress is important to avoid needless confusion. For example, defining a distress call as any vocalization emitted on separation of an infant from a nest pre-

sumes the existence of a function that may not apply. Moreover, categorizing all such vocalizations in this way glosses over important differences, both within and across species. For example, as discussed earlier, infant dogs appear to exhibit two different vocalizations that are evoked by different stimuli at different times during development (Gurski et al., 1980). On the basis of these and other observations, it may be the case that altricial infants (e.g., rats, dogs) emit primarily vegetative sounds during early development followed by emission of true separation calls in older infants, while precocial infants (e.g., guinea pigs, nonhuman primates) begin emitting separation calls soon after birth. However, even if such a suggestion was found to have merit, investigations of separation calls may still benefit from the kind of mechanistic approach described here for the infant rat.

Even if the infant rat's vocalization is the acoustic by-product of a maneuver that serves a physiological function, we cannot preclude the possibility that the pup is also experiencing emotions such as fear or anxiety. Specifically, although the perspective promoted here suggests that an explanation in terms of emotional states is not necessary to explain emission of ultrasound, it may be that the relationship between the ACR (and the vocalization) and any accompanying emotional state is analogous, for example, to reflexively withdrawing one's hand from a hot stove seconds before pain is experienced. In the end, however, for obvious reasons, we cannot prove that emotional distress is not the cause of this vocalization.

Our interpretation also does not preclude the possibility that the infant rat's vocalization has been modified by natural selection to enhance its detectability or discriminability by the mother (Guilford & Dawkins, 1991), nor does this interpretation preclude the possibility that the vocalization can be modified by learning or modulated by stimuli associated with the dam, littermates, and nest (Hofer, Brunelli, & Shair, 1994; Hofer & Shair, 1980). For example, if the vocalization is akin to an autonomic reflex, then modification of its expression using the procedures of classical conditioning should be possible. Whether presentation of olfactory cues alone can modulate ultrasound production remains an important area for further study.

Any scientific theory can be judged on a number of dimensions, such as parsimony and empirical fruitfulness, and on those dimensions the theory outlined here—that a common physiological event triggers ultrasound production regardless of the context or manipulation used—has been successful. Nonetheless, more work needs to be done to establish the proximate physiological mechanisms that stimulate the ACR and evoke ultrasound production, as well as to determine whether similar processes are common in the infants and adults of other species, including humans. Much may also be learned regarding the possibility that these physiological processes are modified throughout ontogeny and are modulated by cues in the social environment. Therefore, the perspective encouraged here should be viewed not as removing a phenomenon from psychological scrutiny but rather as an opportunity to understand the diverse and complex ways in which physiological, behavioral, and psychological processes interact during development.

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