

## Autonomic Changes in Affective Behavior

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The purpose of this chapter is to review what is known about the autonomic responses that accompany affective behavior and to provide a description of the neural mechanisms that integrate autonomic and somatic motor functions. In attempting this task, it is necessary to compare the neural sites responsible for producing patterns of behavior with those responsible for patterns of autonomic response. The discussion focuses on how these behavioral and autonomic sites coincide and interact to provide integrated responses appropriate for particular physiological situations. Much of the experimental work in this area has been done on awake animals in the laboratory. This is an important point since many of the responses evoked under these experimental conditions may not compare equally with those evoked by natural stimuli. The chapter concludes with a discussion of how the integrated response to fear or other emotions can be conditioned to occur on presentation of previously neutral stimuli; the focus here is on the neural pathways mediating such responses. Further discussions of this field can be found in reviews by Kaada (1967), Mancia and Zanchetti (1981), Smith et al. (1980, 1982, 1986), Hilton (1986), and LeDoux (1986, 1987).

### DEFINITION OF AFFECTIVE BEHAVIOR

Affective behavior involves integrated somatic and visceral responses elicited by emotions, which are triggered by various stimuli. These responses are generally directed toward a particular object. However, this type of behavior is difficult to define in precise terms. Since much of the experimental work has been carried out on animals, the problem becomes even more difficult when we are asked to define what emotions animals experience. For this reason, research in this field has concentrated on stereotyped

behavior patterns, particularly those related to aggression or territorial defense.

At least three different types of behavioral patterns are termed *aggressive behavior*: affective attack, predatory attack, and the flight reaction. On studying the literature, it is often unclear whether the same term is used by different investigators to describe the same behavioral response pattern. This problem of terminology may explain at least some of the inconsistencies in the literature, and it has been discussed at length elsewhere (Glusman, 1974; also see reviews by Kaada, 1967; Siegel and Edinger, 1981).

Affective attack, commonly referred to as the *defense reaction*, is the most commonly described aggressive behavior. For example, cats manifest a stereotypic response by crouching, retracting their ears, vocalizing, and exhibiting pupillary dilation. There is no directed attack at any particular prey or individual. Rather, the attack is directed against any moving object. This contrasts with a predatory attack, in which the behavior pattern is directed against an aggressor or a prey. In this case, autonomic activity is reduced as the animal stalks its prey. Following a period of stalking, the animal will pounce on its prey and bite it.

The type of aggressive behavior elicited in any particular situation depends on the stimulus presented. For example, a defense response can be elicited by a wide range of different environmental stimuli that could be considered a threat to the survival of the individual. It is, therefore, considered a multifactorial process, whereas predatory attack is clearly a response to a specific stimulus (e.g., sight of prey) that has a specific goal. When challenged with the same stimulus, an animal may show a defense reaction if placed in an enclosed environment or if faced with a smaller adversary. However, if an exit is present or if faced with a dominant opponent, the animal will escape. During this flight reaction, au-

tonomic responses such as piloerection and pupillary dilation are still evident.

One question that has yet to be answered is how independent the attack and flight responses are. Under natural circumstances, there are clearly close similarities in the type of stimuli that elicit them. In addition, evidence from electrical stimulation studies suggest that the anatomical substrates in the brain that control the fight and flight areas are closely apposed. Increasing the intensity of stimulation in either the attack or the flight area has been shown to convert an attack response to escape, or vice versa (Hunsperger, 1956), but verification of this result has been controversial (Romaniuk, 1965; Wasman and Flynn, 1962). Two possibilities may account for the differences in results. First, distinct and independent mechanisms for the initiation of flight and fight may exist that when activated would each lead inevitably to such an end result. Alternatively, it is possible to envisage a common system of output, the pattern of which can be switched, depending on the information presented to the integrating system. The second system would allow the individual to both grade the intensity of the responses and provide the flexibility to modify the response if environmental cues change. As yet, no evidence is available to substantiate either possibility.

## NEURAL SITES MEDIATING AFFECTIVE BEHAVIOR

A wide range of neural sites have been considered to be important in the initiation and mediation of affective behavior. The three behavior patterns appear to be controlled by separate, but overlapping sites within the brain. Much of this work has been carried out on decerebrate cats, with only the midbrain, lower brain stem, and spinal cord intact. These animals can be induced to produce a pattern of somatic activity regarded as imitating anger and defense when exposed to painful stimulation of the skin; the responses have been termed pseudoaffective reactions (Woodworth and Sherrington, 1904). Higher neural centers such as the limbic system and cerebral cortex are not involved in these reactions and the animal cannot evaluate the significance of the stimulus or the appropriateness of the response. Thus, it is generally thought that the midbrain and lower brain stem provide the minimal neural circuits capable of producing an organized pattern of affective behavior. The behavioral responses elicited in animals with brain stem transections caudal to the midbrain are not well organized (Bard and Macht, 1958 for review).

The central gray matter appears to be a key area integrating the defense response. Electrical or chem-

ical stimulation of this region elicits behavioral and autonomic responses similar to the naturally evoked defense reaction (Hunsperger, 1956; Bandler and Carrive, 1988). This includes pupillary dilation, piloerection, hissing, and cardiovascular changes. Electrolytic lesions of this area abolish defense behavior evoked by electrical stimulation of more rostral CNS sites such as the hypothalamus. In contrast, more rostral lesions do not alter responses evoked by stimulation of the central gray matter. Although the central gray matter appears to be a central site of integration for these behavioral patterns, this region may also subserve other functions including pain perception (see Chapter 7). Since it has not yet been possible to determine if there are spatially separate functional centers within the central gray matter, the possibility remains that the autonomic responses evoked from this region are a reflection of activation of neuronal systems involved in nociceptive functions.

The hypothalamus is another site thought to be involved in the integration of affective behavior. Electrical stimulation of specific hypothalamic loci in free moving animals elicits certain patterns of somatic and autonomic responses that are typical of a range of affective behaviors. The three distinct aggressive behavior patterns can be evoked from the hypothalamus: the defensive reaction can be evoked from the perifornical hypothalamic area and the region just dorsal to the ventromedial hypothalamic nucleus (Hunsperger, 1956). This defense region extends from the anterior to the posterior hypothalamus (Nakao, 1958; Romaniuk, 1965; Wasman and Flynn, 1962). Dorsal to it, there is a hypothalamic region that on electrical stimulation evokes the flight reaction (Romaniuk, 1965). Escape can also be elicited by electrical stimulation of rostral sites in the anterior hypothalamus (Nakao, 1958) as well as lateral hypothalamus (Wasman and Flynn, 1962) and the ventral tegmental area in the mesencephalon (Hunsperger, 1956). Finally, electrical stimulation of the lateral hypothalamic area has been shown to evoke an attack response that is considered to be predatory attack behavior (Wasman and Flynn, 1962). It is of interest that this reactive region in the lateral hypothalamic area overlaps other functional areas like the "feeding center". However, since electrical stimulation methods have been used to define these functional regions, as we will see later in this chapter, uncertainty exists over whether the cell bodies mediating these responses really lie in this region and if the hypothalamus per se is the critical site generating this activity. Although the hypothalamus has been thought to be the major site for initiation and integration of these behaviors, this view has not been substantiated with more contemporary methods (Bandler, 1982; Hilton and Redfern, 1986).

Many of the earlier studies documenting the importance of the hypothalamus in aggressive behavior were carried out in decorticate or high decerebrate cats (in which the hypothalamus is left intact). In these animals, rage behavior was easily evoked by mild stimuli such as stroking the skin (Goltz, 1892). This stereotyped pattern of response included lowering of the head, arching of the back, hissing, growling, retraction of the ears, piloerection, pupillary dilation, and retraction of the nictitating membranes. Cannon and Britton (1925) termed this pattern *sham rage* to denote the lack of higher brain involvement. Animals with this type of lesion appear to lack true perception of their environment and seem to respond inappropriately to innocuous stimuli. Bard (1928) showed that the caudal hypothalamus is critical for the production of sham rage; removal of all tissue rostral and lateral to this area leaves the response intact. These studies implied that the activity of the caudal hypothalamus is inhibited by forebrain areas such as the cerebral cortex or amygdala. These higher centers keep the rage initiating region in check. This is not to deny, as some investigators appear to do, that rostral regions can also facilitate aggressive forms of behavior. More restrictive ablations demonstrated that widespread removal of the cerebral cortex resulted in a behaviorally placid animal whose threshold to aggression was markedly increased (Bard and Mountcastle, 1948). Furthermore, electrical stimulation of cortical and limbic regions can elicit behavioral responses similar to those evoked from the hypothalamus (see Siegel and Edinger, 1981 for review).

The amygdala has often been implicated as another site regulating behavior. In unanesthetized cats, stimulation of this area with low levels of electrical current elicits attentive behavior. With prolonged stimulation, the response progresses to either flight or anger depending on the area of stimulation (Ursin and Kaada, 1960). Fernandez de Molina and Hunsperger (1959, 1962) showed that the region from which defensive behavior could be elicited extended as a continuum from the amygdala through the level of the caudal hypothalamus. This reactive zone coincided with the efferent pathways emanating from the amygdala. In fact, in subsequent investigations, this pathway was traced further caudally in the brain stem where it coincides with the amygdalofugal pathway arising from the central nucleus of the amygdala (Price and Amaral, 1981).

Although it is clear that the behaviors evoked from the amygdala and hypothalamus are similar, they differ in several important respects. One characteristic of the amygdaloid response is the manner in which it gradually builds up during the stimulus and its persistence after the stimulus ceases (MacLean and Delgado, 1953; Hilton and Zbrozyna,

1963). This contrasts with the rapid onset and stimulus locking of the hypothalamically evoked response. In addition, unlike reactions evoked from the hypothalamus or central gray matter, directed attack is not evoked from the amygdala.

The results of electrical stimulation of amygdaloid structures must be questioned, since such stimulation is frequently followed by after-discharges, which spread throughout the tissue and complicate any question of localization of function. More importantly, since the amygdala is reciprocally connected with the cerebral cortex, forebrain, hypothalamus, and brain stem (see Price et al., 1987 for review), electrical stimulation of any site in this nuclear complex will simultaneously antidromically and orthodromically activate multiple CNS areas. In fact, it may be these extra-amygdaloid sites that control behavioral or autonomic responses. However, the contribution of the amygdala to emotion behavior has also been demonstrated by studies that show that ablation of the amygdala results in a reduction of escape behavior (Downer, 1961; Ursin, 1965) and more recent investigations by LeDoux and his associates (see below) also support its role in affective responses.

In addition to the amygdala, other forebrain areas such as the cingulate gyrus and septum have been studied, however, the results from these areas are more equivocal (see Siegel and Edinger, 1981 for review).

## NEURAL SITES MEDIATING AUTONOMIC RESPONSES

The studies considered so far have been concerned with somatic and autonomic responses. There is also a wealth of data concerning the effects of studies of electrical stimulation on other specific autonomic responses including blood pressure, heart rate, sympathetic nerve activity, regional blood flow, gastrointestinal motility, and adrenal catecholamine secretion. The discussion here will be restricted to the midbrain, the hypothalamus, and the amygdala.

Before these studies are summarized, the reader should be aware of the limitations of their methodology. Electrical stimulation activates both cell bodies and fibers of passage. Thus, studies of this nature do not provide definitive evidence that a response is due to activation of either the cells at a particular locus, fibers traveling to, or through it. In addition, they cannot be used to determine whether a response is due to orthodromic or antidromic activation of fibers. However, these studies serve as a useful if rather general guide to central autonomic pathways; they are the first systematic studies aimed specifically at providing a functional neuroanatomy of

central autonomic circuits. Electrical stimulation of a large zone stretching from the anterior to the posterior hypothalamus elicits marked pressor responses due to vasoconstriction of mesenteric, renal, and cutaneous vascular beds, tachycardia, and increased ventricular contraction. These changes result from increased sympathetic nervous discharges to the heart and resistance vessels. However, in addition to these sympathoexcitatory effects, stimulation at a restricted range of sites rostral to the anterior hypothalamus evokes depressor responses, bradycardia, and vasodilation in many vascular beds. These responses are primarily due to inhibition of sympathetic activity but the heart rate response includes augmentation of parasympathetic drive to the heart. These results have led to the idea of a functional division within the hypothalamus of a posterior sympathoexcitatory region and a rostral sympathoinhibitory/parasympathoexcitatory region. However, this interpretation must be viewed as premature and needs confirmation with chemical microinjection techniques.

Stimulation within the pressor/sympathoexcitatory region evokes a marked vasodilation of resistance vessels in skeletal muscle of cats (Eliasson et al., 1951). In certain species such as the cat, activation of this specialized sympathetic cholinergic vasodilatory system results in a marked increase in blood flow to limb skeletal muscle. This pathway is thought to utilize acetylcholine at the vascular smooth muscle junction because the response can be blocked by the cholinergic antagonist atropine. However, even in those species that do not exhibit this cholinergic vasodilation, increased muscle blood flow is still observed when the hypothalamic sympathoexcitatory region is stimulated. In these cases, vasodilation could result from combinations of inhibition of sympathetic vasoconstrictor fibers, the activation of vasodilator fibers with a noncholinergic mediator, and increased secretion of adrenaline from the adrenal medulla.

In addition to these wide-ranging effects on the cardiovascular system, other autonomic effects can be demonstrated after hypothalamic stimulation such as pupillary dilation, retraction of the nictitating membrane, piloerection, increased sudomotor activity, and a wide range of alterations in gastric and intestinal motility (see Mancina and Zanchetti, 1981 for review).

A variety of autonomic responses can also be elicited by electrical stimulation of the amygdala (Kapp et al., 1983 for review). For example, Ursin and Kaada (1960) described a range of autonomic and somatomotor responses evoked from different amygdaloid nuclei. These included piloerection, pupillary dilation, micturition, defecation, salivation, licking, and a range of respiratory responses.

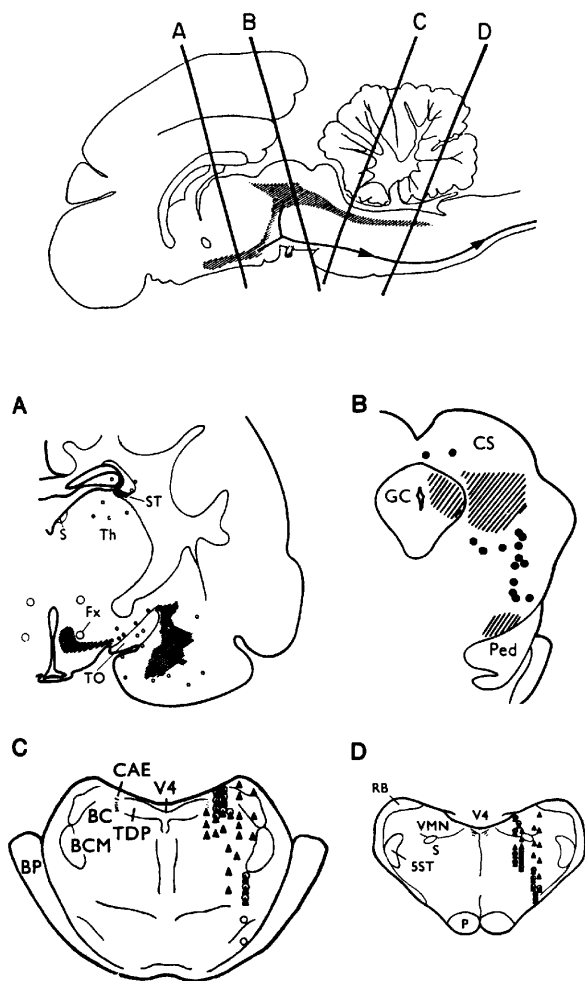
Whether these are due to activation of efferent or afferent systems remains unknown.

## THE BRAIN AS A MEDIATOR OF INTEGRATED BEHAVIOR AND AUTONOMIC ACTIVITY

There are two major concerns with the experiments described so far: (1) the extent to which they relate to real life situations and (2) the accuracy of experimental findings based in large part on electrical stimulation methods. Both of these issues will be discussed in this section.

Although the electrical stimulation mapping studies described above have considered individual autonomic or behavioral variables, it is now clear that the stimulation sites that alter cardiovascular function also modify activity of other autonomic, endocrine, and behavioral functions. This concept developed as a result of studies in which multiple recordings of a range of autonomic and somatomotor activities were made in animals. The responses were studied in free-moving awake cats, which allowed for a correlation with the somatomotor, autonomic, and behavioral responses elicited by the same stimuli (see Mancina and Zanchetti, 1981 for review). The experiments demonstrated that on electrical stimulation, the hypothalamus was capable of producing complex integrated patterns of behavioral, somatomotor and autonomic responses that mirrored the physiological patterns of visceral activity seen in freely moving animals undergoing a variety of motivational behaviors. It is important to stress that although these results do not prove that the response is due to neurons originating within the hypothalamus, they illustrate that the neural system(s) that regulate these physiological patterns of visceral activity are present in conscious animals. Although this concept has now been extended to explain a variety of patterns of activity seen during feeding, drinking, thermoregulation, and exercise, its development was initiated by studies of defense behavior and the autonomic responses accompanying it. Since the concept itself is so clearly applicable to other areas of autonomic control, it is useful to consider in detail its development and standing in relation to our current understanding of autonomic control.

In 1943, Hess and Brugger used electrical stimulation methods in conscious cats to delineate the hypothalamic regions from which a coordinated behavior pattern could be evoked. This response was initially one of alerting, but culminated, if the electrical stimulation was intense, in flight or attack. The response could not be distinguished from those evoked by natural aversive environmental stimuli



**Figure 19-1** Top: A schematic diagram of a parasagittal section of a cat's brain. The diagonal shaded areas represent regions in the hypothalamus, mesencephalon, pons, and medulla oblongata, which integrate defense reactions; the solid line indicates the location of the efferent pathway for the cardiovascular pattern of response and other visceral components. Coronal sections taken at the planes indicated A–D are shown below as indicated. Four representative transverse sections of the cat brain illustrating reactive sites in which electrical stimulation elicits the defense reaction. (A) The reactive zone included the perifornical hypothalamic area (diagonal screening) and the amygdala (cross-hatching). (Reproduced from Hilton and Zbrozyna, 1963, with permission of the authors and publisher.) (B) Regions in the mesencephalon from which active muscle vasodilation is obtained on stimulation. Hatching indicates areas from which vasodilation was regularly obtained; the dots indicate sites of large responses in individual experiments. (Reproduced from Abrahams et al., 1960, with permission of the authors and publisher.) (C) Regions in the pons from which increases in blood pressure were obtained, with (open circles) and without (triangles) muscle vasodilation. (Reproduced from Coote et al., 1973, with permission.) (D) Regions in the medulla oblongata from which increases in blood pressure were obtained, with (open circles) and without (triangles) muscle vasodilation. (Reproduced from Coote et al., 1973, with permission.) BC, brachium conjunctivum; BCM, parabrachial nucleus (nucleus of brachium conjunctivum); BP, brachium pontis; CAE, locus coeruleus; CS, superior colliculus; GC, central gray matter; FX, fornix; P, pyramidal tract; Ped, cerebral peduncle; RB, restiform body; S, solitary tract; ST,

and was termed the *defense reaction* (*Abwehrreaktion*). It was most easily evoked from the perifornical hypothalamic area (Figure 19-1A). Stimulation of this region in anesthetized cats evokes an atropine-sensitive vasodilation in skeletal muscle accompanied by sympathetically mediated vasoconstriction in cutaneous and intestinal vascular beds and a rise in arterial blood pressure (Eliasson et al., 1951; Abrahams et al., 1960), renal vasoconstriction (Feigl et al., 1964), increased heart rate and cardiac contractility (Rosen, 1961), and a rise in cardiac output (Kylstra and Lisander, 1970). In addition, pupillary dilation, retraction of the nictitating membrane, piloerection, and rapid, shallow breathing are features of this response (Abrahams et al., 1960). This same coordinated pattern of response can be evoked from a series of sites extending caudally from the hypothalamus into the midbrain (Figure 19-1B) (Abrahams et al., 1960). In particular, an excitable region is found in the dorsolateral part of the central gray matter (Figure 19-1B). Further laterally in the tegmentum and underlying the superior colliculus, similar responses are obtained, except that the pressor response is particularly large and associated with bradycardia. Finally, electrical stimulation of a small area in the mesencephalon dorsal to the cerebral peduncle produces only hindlimb vasodilation. Small lesions of this most ventral region abolish hypothalamically evoked vasodilation, whereas lesions of much of the midbrain, including the central gray matter and the appropriate region of the tegmentum, have little effect. Thus, this ventral region may be part of an efferent pathway controlling muscle vasodilation.

If any site along the pathway from the amygdala to medulla oblongata mediating muscle vasodilation was stimulated in unanesthetized cats (except the area dorsal to the cerebral peduncle), it produced a fairly constant pattern of behavior (Abrahams et al., 1960). A threshold stimulus evoked an alerting reaction. The animal would raise its head to look about and dilate its pupils. With stronger stimulation, the animal would show increased pupillary dilation, piloerection, stand, hiss, or growl, retract its ears, and unsheath its claws. This culminates in attack behavior. With electrodes implanted in either the hypothalamus, central gray matter, or midbrain tegmental area, the behavioral and cardiovascular patterns of response were always evoked in concert. This coordinated response was thought to be due to activation of common regions that subserved integrative cell groups or pathways from which all components of the defense reaction were produced. How-

stria terminalis; TDP, dorsal tegmental nucleus; Th, thalamus; TO, optic tract; VMN, medial vestibular nucleus; V4, 4th ventricle; 5ST, spinal trigeminal tract.

ever, the correlation between the autonomic and behavioral responses elicited from the hypothalamus may be due to the inability of the electrical stimulation technique to discretely stimulate separate populations of neurons or fiber systems controlling these different functional components. The chemical stimulation experiments also have the same problem of spatial resolution. Thus, the brain stem defense region extends from the amygdala complex into the lower brain stem.

Electrical stimulation of the amygdala in unanesthetized cats causes behavioral and autonomic responses qualitatively identical to those evoked by hypothalamic stimulation (Hilton and Zbrozyna, 1963). The area of the amygdala producing defense responses includes part of the anterior amygdala, the magnocellular component of the basal nucleus, and medial part of the central nucleus (Figure 19-1A). However, unlike the responses elicited from the hypothalamus, stimulation within the amygdala produces the entire pattern of response only in awake, or very lightly anesthetized animals (Stock et al., 1978). In addition, Timms (1981) has demonstrated the useful properties of the steroid anesthetic, alphaxalone/alphadolone (Althesin), which is thought not to interfere with the integrative activities of the forebrain in the same way as conventional anesthetics. In Althesin-anesthetized cats, the visceral changes characteristic of a defense reaction can be evoked by stimulation of the amygdala or even reflexly by stimulation of afferent inputs (see Marshall, 1987 for review). Thus, these results clearly show the marked effects anesthetics have on these responses—a factor that has been largely ignored in this area of research.

Stimulation of two regions of the rostral part of the rhombencephalon yields complete patterns of behavioral and autonomic response similar to those seen on hypothalamic stimulation (Figure 19-1C and D). The first area lies in the dorsolateral central gray matter just medial to the parabrachial nucleus. When stimulated in awake or anesthetized animals, it evokes both the behavioral and visceral components of the defense response (Coote et al., 1973). This region may represent the caudal trajectory of the active region identified in the lateral tegmental area of the midbrain. Only two differences are apparent between the responses evoked by stimulation at this site, and those evoked from the hypothalamus or by natural stimuli. First, the brain stem-evoked response is less well integrated and, second, the muscle vasodilation is the result of a reduction in sympathetic vasoconstrictor activity. The second area lies in the ventrolateral tegmentum near the region of the ventral nucleus of the lateral lemniscus.

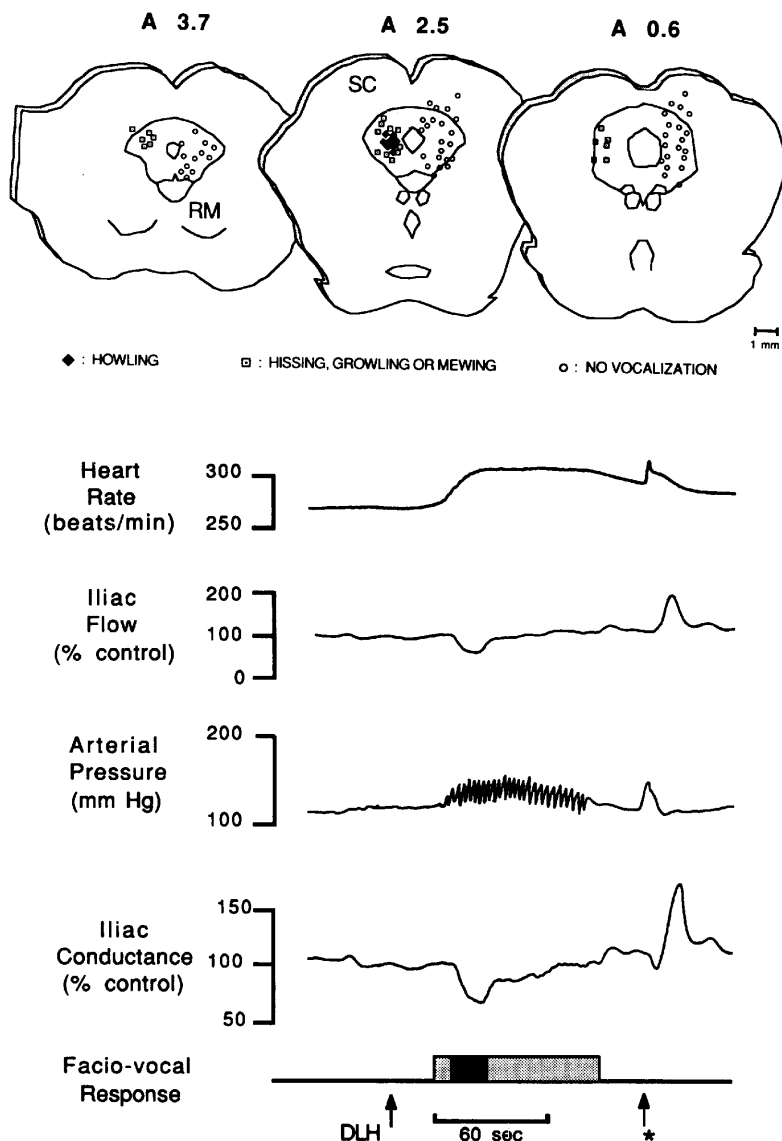
Electrical stimulation of the medulla oblongata at several loci elicit rises in arterial pressure along with

muscle vasodilation (Figure 19-1D). These areas include the dorsal medial medulla (medial vestibular nucleus), the dorsal reticular formation, and the ventral medulla. Only the last area has been studied in detail. Electrical stimulation of the ventral medulla elicits the characteristic cardiovascular patterns of defense response (Hilton et al., 1983). In cats, this narrow pathway runs as a strip about 3 mm lateral to the pyramidal tract. At more caudal medullary levels, the pathway lies ventral to the facial nucleus, very close to the surface of the medulla and coincides with the "rostral ventrolateral medulla." This is considered one of the key autonomic regulatory regions in the brain. It receives inputs from the hypothalamus, central gray matter, and nucleus tractus solitarius and gives rise to a major projection to the intermediolateral cell column (for review see Ciriello et al., 1986). Bilateral disruption of synaptic transmission in this area totally abolishes the cardiovascular, respiratory, and pupillary responses evoked by stimulation within the defense areas of the amygdala, hypothalamus, or midbrain (Hilton et al., 1983) or by peripheral nerve stimulation (Marshall, 1986).

Neurons in this region are important in the maintenance of vasomotor tone (see Chapters 8 and 9). In a 1986 review, Hilton hypothesized that ongoing activity in the brain stem defense regions is responsible for the tonic activity of the rostral ventrolateral medullary neurons, and, hence, ultimately responsible for vasomotor tone. In contrast, however, Guyenet (Chapter 9) argues that this tonic activity is more likely to be the result of intrinsic pacemaker properties of the neurons themselves. However, the actual neural mechanism(s) responsible for generating vasomotor is still not resolved.

Although electrical stimulation throughout a large continuum of neural tissue can evoke the complex integrated pattern of activity now considered characteristic of affective behavior, the question of which site(s) is important in coordinating and initiating such a response remains unanswered. The hypothalamus, or sites caudal to it have been implicated as the neural centers mediating this behavior because peripheral stimuli can reflexly initiate an almost entire repertoire of responses in the high decerebrate animal. Since the response was produced most reliably by electrical stimulation of the perifornical region of the hypothalamus, the idea arose that this region was of prime importance. However, studies using microinjections of excitatory amino acids that activate only nerve cell bodies and dendrites have cast serious doubt on the accuracy of this hypothesis.

In anesthetized or awake cats and rats, chemical stimulation of midbrain central gray matter can evoke both the behavioral and the cardiovascular patterns of the defense response (Figure 19-2); com-



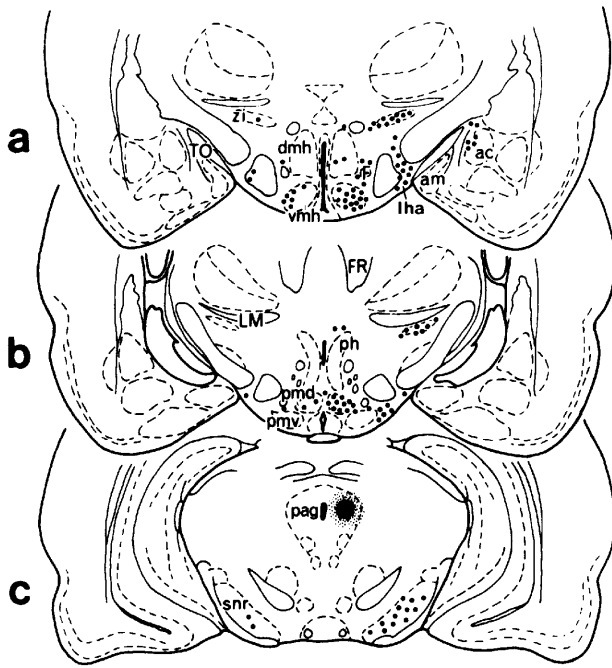
**Figure 19-2** Top: Three representative transverse sections of the mid-brain of the cat to show location of D,L-homocysteic acid injection sites that elicited vocal reactions (left side). Sites from which no vocal reaction was produced are plotted on the right side. RM, red nucleus (magnocellular division); SC, superior colliculus. Bottom: Example of the cardiovascular changes that accompany vocal reactions after excitatory amino acid injections in the central gray matter. The period of intense vocal reaction is indicated by the dark shading. This was preceded and followed by periods during which the animal exhibited a moderate vocal reaction (indicated by the lighter shading). Note that only the intense reaction was accompanied by a marked decrease in iliac conductance. The first arrow indicates the point at which a micro-injection of D,L-homocysteic acid (0.2  $\mu$ l of 0.2 M solution) was made. The second arrow, marked by an asterisk, indicates the point at which the hindlimb of the animal showed a spontaneous movement. (Reproduced from Carrive et al., 1987, with permission of the authors and publisher.)

parable injections into the hypothalamus and mid-brain tegmentum are ineffective (Bandler, 1982; McDougall et al., 1985; Carrive et al., 1987; Hilton, 1986; Bandler and Carrive, 1988; Hilton and Redfern, 1986). This suggests that it is neurons within the midbrain central gray matter that are responsible for coordinating and initiating the responses seen during affective behavior. However, any chemical stimulus must activate a pool of neurons large enough to evoke a measurable peripheral response. Since it is possible that the particular neural architecture of the central gray matter makes it easier for such a pool of functionally homogeneous neurons to be activated by chemical stimuli, even these results must be considered with care.

The midbrain central gray matter (also called the periaqueductal gray matter) receives afferent inputs from the central nucleus of the amygdala, zona incerta, lateral hypothalamic area, substantia nigra, as

well as numerous other sites, including the nucleus tractus solitarius and rostral ventrolateral medulla (see Figure 19-3; rat: Beitz, 1982; Luiten et al., 1987; rabbit: Meller and Dennis, 1986; cat: Bandler and McCulloch, 1984; Bandler et al., 1985). These inputs may subserve autonomic, somatomotor, and sensory functions. For example, the afferents from the central nucleus of the amygdala, the lateral hypothalamic area, and the zona incerta may mediate changes in cardiovascular function, since stimulation of each of these areas produces cardiovascular response (Stock et al., 1978; Spencer et al., 1988, 1989) and each connects with autonomic centers of the brain stem and/or spinal cord. The inputs from the substantia nigra may regulate somatomotor functions.

This region of the central gray matter from which defense reactions may be evoked provides descending projections to both medullary and spinal cord



**Figure 19-3** The central gray matter receives afferent projections from a variety of forebrain nuclei. Following an injection of the retrograde cell body marker horseradish peroxidase in the midbrain central gray matter of a rat (c), retrogradely labeled cell bodies are found in the central nucleus of the amygdala (ac), zona incerta (zi), lateral hypothalamic area (lha), and a number of other hypothalamic nuclei (a and b). In addition to the substantia nigra, the pars reticulata (snr) also contains retrogradely labeled cells (c). am, medial amygdaloid nucleus; dmh, dorsomedial hypothalamic nucleus; F, fornix; FR, fasciculus retroflexus; LM, medial lemniscus; pag, periaqueductal gray matter; ph, posterior hypothalamic area; pmd, dorsal premammillary nucleus; pmv, ventral premammillary nucleus; vmh, ventromedial hypothalamic nucleus. (Reproduced from Luiten et al., 1987, with permission of the authors and publisher.)

nuclei involved in both autonomic and somatic motor functions (Figures 19-4 and 19-5). It projects to the ventrolateral medulla and the caudal raphe nuclei (Luiten et al., 1987); these two latter areas project to the spinal nuclei containing sympathetic preganglionic neurons and somatic motor neurons (Loewy et al., 1981; Loewy, 1981). However, these projections are considerably less dense than the projection to the rostral ventrolateral medulla (Figure 19-4), so it is likely that the central gray matter projection to the ventral medulla is of prime importance. Thus, this system may influence both sympathetic and somatic responses via direct and indirect pathways.

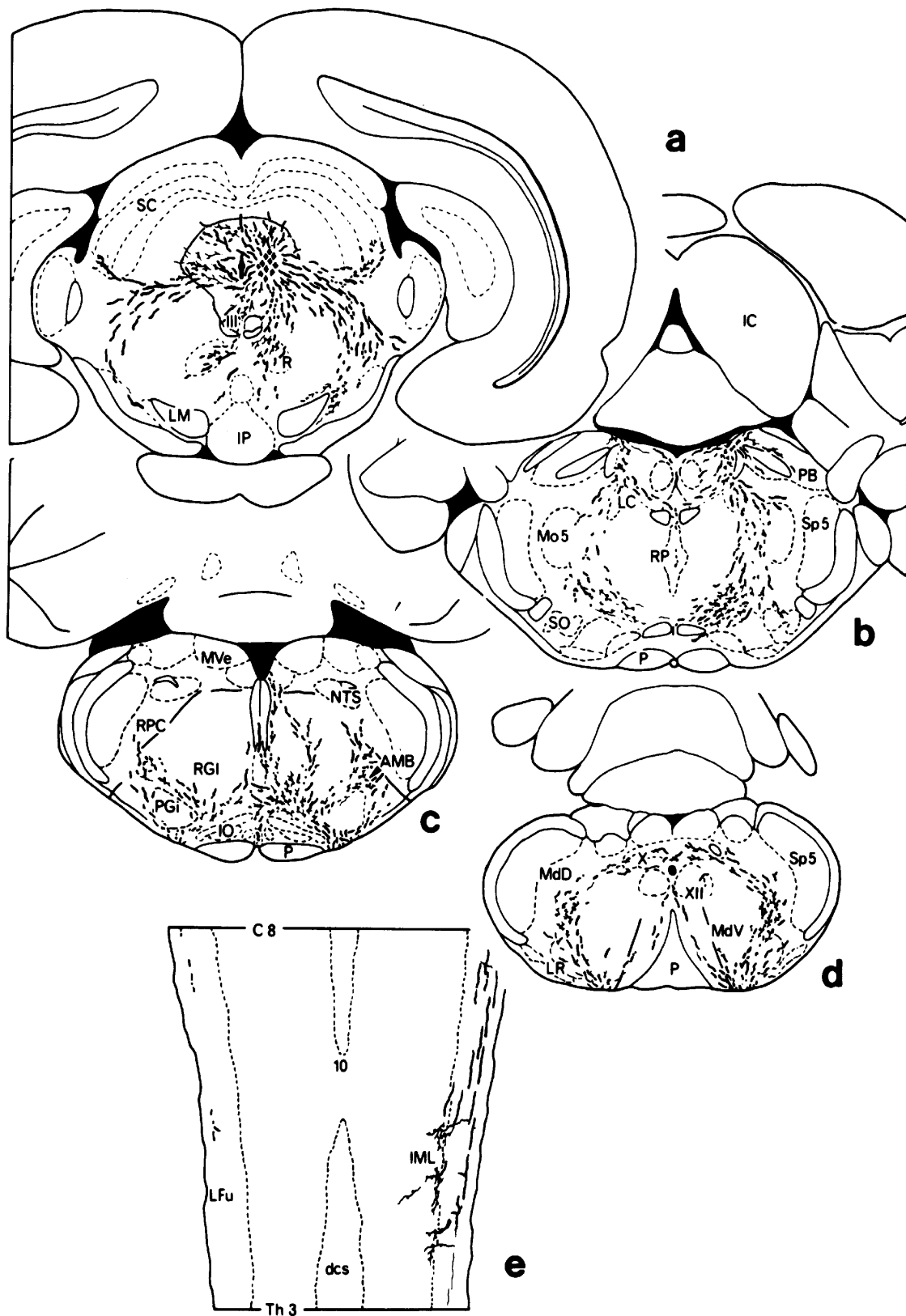
If the effects of electrical stimulation within the hypothalamus are due to activation of axons arising elsewhere, the origin of these fibers remains to be determined. Numerous neuronal systems project to and through this defense hypothalamic zone. One possibility is the amygdala. However, when this area

is stimulated with the excitatory amino acid D,L-homocysteic acid in conscious rats, none of the behavioral or cardiovascular changes seen under anesthesia is observed (Gelsema et al., 1987). Another possibility is the prefrontal and insular regions of the cerebral cortex, which is known to play a role in control of autonomic function. However, functional studies in conscious animals have not yet been reported. Additional sites that provide inputs to the hypothalamus may be involved as well, but the search for the cell group controlling this response will require systematic mapping studies using excitatory amino acids combined with lesions to pinpoint the critical loci.

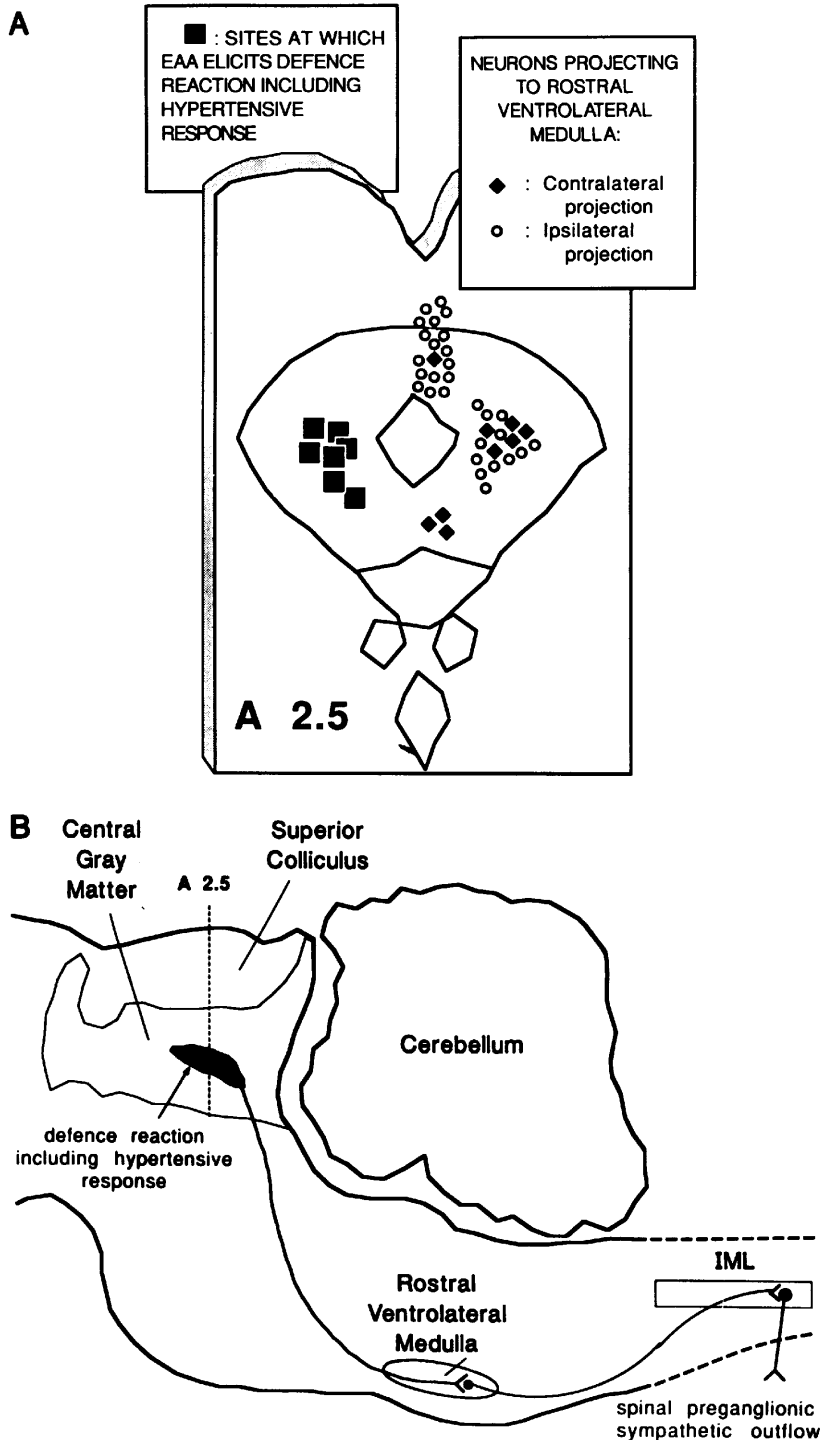
### AFFECTIVE BEHAVIOR AND AUTONOMIC RESPONSES TO NATURAL STIMULI

So far, consideration of the defense reaction has been restricted to those responses that could be elicited by electrical or chemical stimulation of neural tissue. Although this has been productive in providing a conceptual framework, we must now look at how such patterns of response compare to those exhibited by awake animals when confronted with stimuli that would evoke such affective behavior.

When cats are chronically instrumented to measure a range of cardiovascular and motor variables and then studied during confrontation of an aggressor, they display a variety of emotional behavior and cardiovascular responses (Mancia and Zanchetti, 1981). When the aggressor cat was allowed to attack, the instrumented cat would engage in a bout of fighting in which all four limbs were involved. This was termed supportive fighting (as opposed to nonsupportive fighting, which occurred if the subject was initially lying). In this latter case, the subject tended to fight using only the forelimbs to strike out. When the aggressor approached without attacking, the cat was immobile, vocalized, and showed signs of pupillary dilation. During supportive fighting, the pattern of cardiovascular response was similar to that evoked by hypothalamic stimulation. This included tachycardia, a small increase in arterial blood pressure, marked decreases in mesenteric and renal blood flows, and an increased iliac blood flow (Figure 19-6). The vasoconstriction in the mesenteric and renal beds was primarily the result of increased sympathetic vasoconstrictor activity and, indeed, a similar sympathetic vasoconstriction in the iliac bed was occasionally seen at the onset of the response. However, this was overridden at the onset of the muscle movement by vasodilation, which was a consequence of local metabolic factors and activation of sympathetic cholinergic fibers.



**Figure 19-4** The central gray matter sends efferent projections to a number of sites in the brain stem and the spinal cord. After an injection of the anterograde axonal marker *Phaseolus vulgaris* leucoagglutinin (PHA-L) in the central gray matter of a rat (a), labeled axons and terminals can be traced to autonomic centers of the lower brain stem (b-d), including the parabrachial nucleus, the ventral medulla, and the caudal raphe nuclei. The latter two areas project to the intermediolateral cell column (e). Fibers can also be traced to the intermediolateral cell column (IML) in the upper thoracic spinal cord. AMB, ambiguus nucleus; IC, internal capsule; IP, interpeduncular nucleus; IML, intermediolateral cell column; LC, locus coeruleus; LFu, lateral funiculus; MdV, ventral reticular nucleus; MVe, medial vestibular nucleus; NTS, solitary tract nucleus; P, pyramidal tract; PB, parabrachial nucleus; PGI, paragigantocellular reticular formation; RGI, gigantocellular reticular formation; RP, raphe pontis nucleus; RPC, parvocellular reticular formation; SC, superior colliculus; SO, superior olivary nucleus; XII, hypoglossal nucleus. (Reproduced from Luiten et al., 1987, with permission of the authors and publisher.)

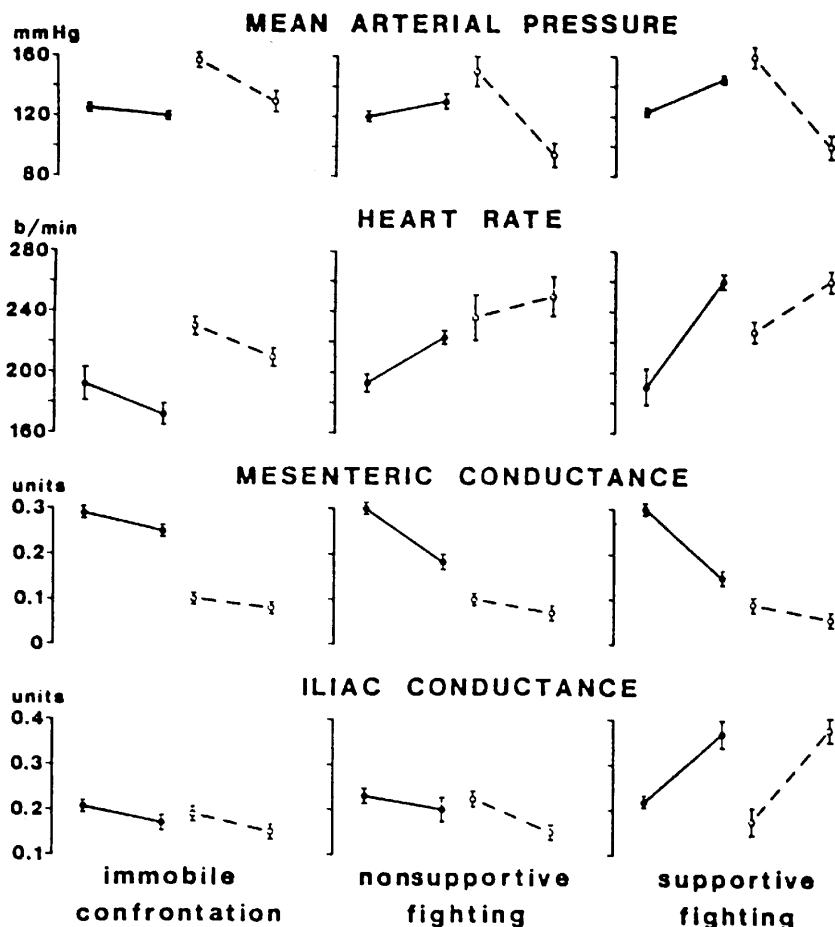


**Figure 19-5** (A) Transverse section of the central gray matter showing that the area from which the defense reaction can be elicited with microinjections of excitatory amino acids (EAA) overlaps the same area that projects to the rostral ventrolateral medulla. (Reproduced from Carrive et al., 1988, with permission of the authors and publisher.) (B) Schematic diagram of the postulated pathway that mediates the cardiovascular response component of the defense reaction. IML, intermediolateral cell column.

During nonsupportive fighting, small increases in heart rate and blood pressure were noted. In addition, mesenteric and renal vasoconstriction occurred (Figure 19-6). Since there was no hindlimb muscle movement, vasoconstriction was also prominent in the iliac bed (see also Figure 19-2). This was also the case during immobile confrontation, but in this situation small decreases in blood pressure and heart rate were usual.

Clearly then, during naturally evoked affective behavior, the pattern of evoked response can very de-

pending on how the stimulus is presented, only one of the patterns mirroring that evoked by electrical stimulation of the hypothalamus. Comparing the natural and hypothalamic evoked responses shows some similarities but also some major discrepancies. First, during immobile confrontation, the heart rate and cardiac output often fall. Second, blood pressure responses are never as large during natural responses as during hypothalamic-evoked responses. This may be due to less intense increases in cardiac output and vasoconstrictor activity being evoked during natural



**Figure 19-6** The cardiovascular changes recorded during emotional behavior before (filled circles and solid lines) and after (open circles and dashed lines) bilateral sinoaortic deafferentation. Circles on the left of each line indicate values immediately before the onset of emotional behavior; circles on the right indicate maximum changes during emotional behavior. Each panel refers to the type of behavior indicated at the bottom of the figure. Data are shown as means and standard errors of the mean of six trials of each behavior in one cat. (Reproduced with permission from Baccelli et al., 1976.)

confrontation. Third, it may also result from the fact that the baroreceptor reflex remains functional during natural stimulation (see Mancina and Zanchetti, 1981 for review). Finally, the most contentious issue concerns the observation that during natural stimulation active muscle vasodilation occurs only when muscle movements participate in the response. This is clearly different from hypothalamically evoked responses in which muscle vasodilation is so often present that it was considered a feature characteristic of the defense reaction.

Hilton (1982), in his review, has argued that results discussed by Mancina and Zanchetti (1981) can be explained in the following ways: (1) there was selection of subjects on the basis that they showed strong behavioral responses to the stimuli used; and (2) since multiple tests were carried out in each animal, the experiments could be criticized because the subjects were not naive to the stimuli, and the confrontations were not associated with actual noxious stimulation or physical attack. These are important issues since when a cat is confronted by a dog, a threatening reaction is elicited in which the cat remains in the sitting position with its hindlimbs immobile (Martin et al., 1976). During this response, only small changes in blood pressure and heart rate are seen, accompanied by vasoconstriction in the

iliac bed. However, this response occurs only after multiple confrontations, the earlier, naive confrontations being associated with hindlimb vasodilation, and larger increases in blood pressure and heart rate. These responses become habituated on repeated stimulation, the hindlimb vasodilation being most easily extinguished. Although this may, in fact, explain the discrepancies between the two sets of data, it is important to consider that in the natural environment in which we live, by far the majority of aversive or alerting stimuli with which we are confronted are not novel but have been the subject of many previous experiences. Indeed, as attested by the large array of conditioning paradigms studied (see below), the alerting response evoked by a novel tone soon habituates so that the tone can then be employed as a conditioned stimulus.

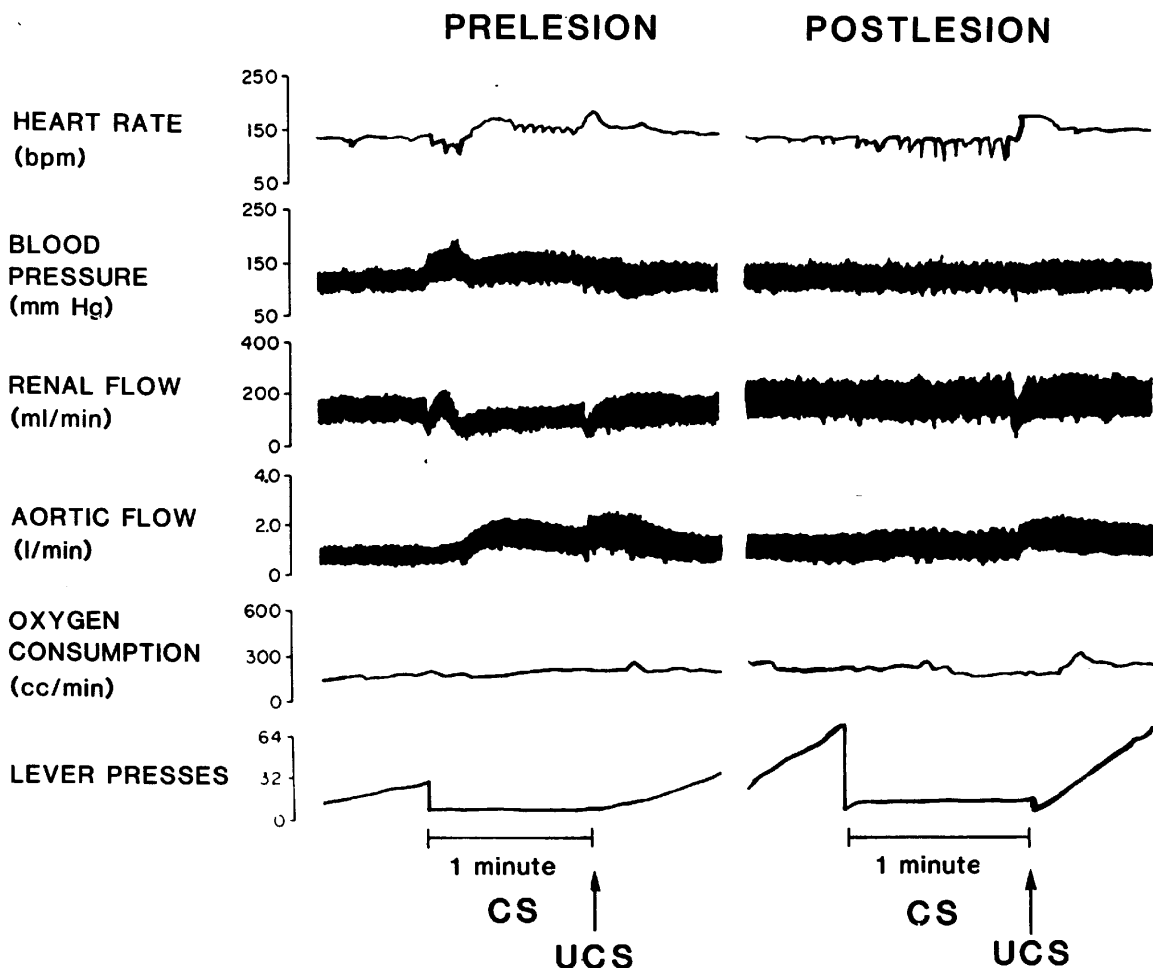
## CONDITIONING OF AFFECTIVE BEHAVIOR

The studies considered so far have suggested a role for the hypothalamus-midbrain axis in the integration of the behavioral and autonomic responses to alerting and defense. However, these experiments have not discounted the possibility that two, or

more, anatomically adjacent pathways may separately mediate behavioral and/or autonomic effects and that during electrical or chemical stimulation these pathways are simultaneously activated.

An answer to this problem has been forthcoming in a wide range of species where the combination of autonomic and behavioral responses typical of fear or defense has been conditioned to occur in response to the presentation of a previously unrelated, non-aversive, and emotionally insignificant stimulus such as an acoustic tone or a particular colored light. In particular, Smith and his colleagues have investigated the hypothesis that the hypothalamus influences a variety of different behaviors and that specific cardiovascular responses accompany them (see reviews by Smith et al., 1980, 1986). Using awake baboons that have been chronically instrumented to monitor a range of cardiovascular variables, the effects of various interventions have been studied on a range of behaviors and accompanying autonomic re-

sponses. The instrumented animals are trained by operant (reinforcement) techniques to respond to colored lights by either performing mild leg exercise or by pressing a lever, a successful performance being rewarded by applesauce. After a stable performance has been reached a classical conditioning series is carried out to develop what Smith terms the *conditioned emotional response*, which is an electric shock to the abdominal skin. During data collection sessions the animal would be signaled to exercise, lever press, or feed, or the conditioned stimulus would be applied during a period of lever pressing. During the conditioned emotional response, a rapid response initiates a neurally mediated renal vasoconstriction and pressor response, followed by secondary increases mediated by adrenal catecholamine secretion. In addition, this mediates the tachycardia, and increased aortic blood flow, that probably represents a hindlimb vasodilation (Figure 19-7).



**Figure 19-7** The cardiovascular pattern recorded from a chronically instrumented baboon during a conditioned emotional response evoked by presentation of a conditioned stimulus (CS). The panels show the pattern of response evoked before (prelesion) and after (postlesion) destruction of the perifornical region of the hypothalamus. Note that the lesion abolishes the changes evoked by the CS, but not those evoked by the unconditioned stimulus (UCS). (Reproduced with slight modification from Smith et al., 1982, with permission of the authors and publisher.)

Associated with this response, there was inevitably a behavioral suppression of the ongoing lever pressing. When the conditioned emotional response was repeated following localized bilateral lesions of the perifornical hypothalamic region, the cardiovascular response was totally abolished or severely attenuated, even though baseline cardiovascular variables were unaltered. However, these small hypothalamic lesions had no effect on the behavioral suppression of lever pressing (Figure 19-7).

These studies led to the conclusion that this definable area of the hypothalamus controls the whole pattern of cardiovascular response specifically associated with emotional behavior, since animals were still able to evoke the appropriate cardiovascular responses during exercise, feeding, and lever pressing. Although a similar effect may have been expected had the animal simply lost its ability to assess the significance of the conditioned stimulus, this is clearly not the case since behavioral suppression of lever pressing was still effective after the lesions (Figure 19-7).

These studies of chronically instrumented animals have been extended by recording the autonomic response patterns in response to normal environmental stimuli (Smith et al., 1986 for review). Results from studies of a social group of baboons, in which a representative blood pressure recording was taken from a submissive male who was eating, is shown in Figure 19-8. As he was briefly approached by a dom-

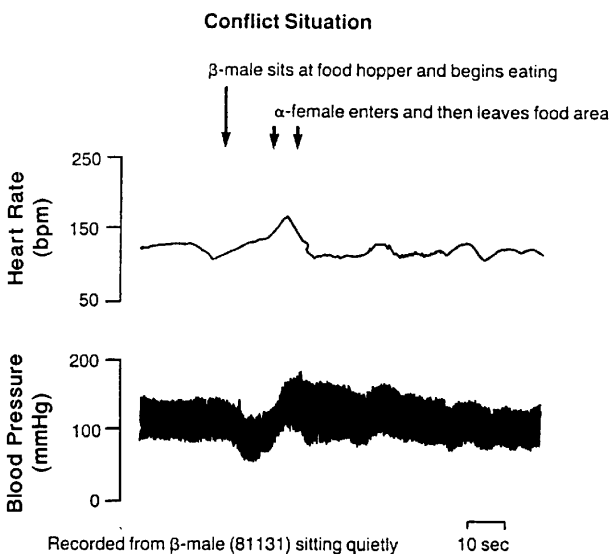
inant female, he was placed in a situation of conflict between leaving the area and his desire to remain and continue eating. Although his somatic activity during this encounter was minimal, the emotionally evoked cardiovascular responses were marked. Although this is a preliminary report, the results that may be expected to emanate from extensions of this study should be of immense importance in understanding cardiovascular control during normal behavioral activities.

## NEURAL PATHWAYS MEDIATING CONDITIONED RESPONSES

Although it is now well known that aversive conditioning to a variety of auditory or visual stimuli can be easily performed, the neural pathways underlying such a procedure are only now being uncovered. One major question arises at this point—at which neural locus is the emotional significance applied to an otherwise insignificant tone or light? A discussion of how the emotional significance of any particular stimulus is encoded, the factors that determine it, and the neural regions required for its implementation forms a major part of the review on emotion by Le Doux (1987). Only a summary of the main points will be included here.

With regard to visual stimuli, the search for an answer goes back to ablation experiments performed by Kluver and Bucy (1937). They demonstrated that temporal lobe lesions endowed monkeys with what has been termed “psychic blindness” (the Kluver–Bucy syndrome); although able to see, the monkeys were unable to recognize objects (visual agnosia) and were passive or unresponsive to external stimuli. Although these lesions clearly involved the amygdala, subsequent studies in monkeys with more restricted lesions limited to the amygdala have implicated this nuclear complex in emotional processing. If the amygdala is destroyed on one side after sectioning the cerebral commissures then visual stimuli evoke normal emotional reactions. If the optic chiasm is subsequently sectioned, then the monkeys show normal emotional responses if the stimulus is presented to the eye ipsilateral to the intact amygdala, but are “tamed” if the stimulus is applied only to the opposite eye (Downer, 1961).

The pathways mediating the conditioned response to auditory stimuli in rats have been reviewed by Le Doux (1986, 1987). Such emotional responses are unaffected by large ablations of the auditory cortex. However, using microinjections of ibotenic acid (which destroys neuronal cell bodies but not axons) they have demonstrated that emotional responses are disrupted by localized destruction of neurons of the auditory pathway. Lesions of the inferior collic-



**Figure 19-8** Heart rate and blood pressure records from a chronically instrumented submissive male baboon living in a family situation with four other baboons. Heart rate and blood pressure decrease while sitting and eating. When a dominant female walks toward him, there is an increase in blood pressure and heart rate. (Reproduced with slight modification from Smith et al., 1986, with permission of the authors and publisher).

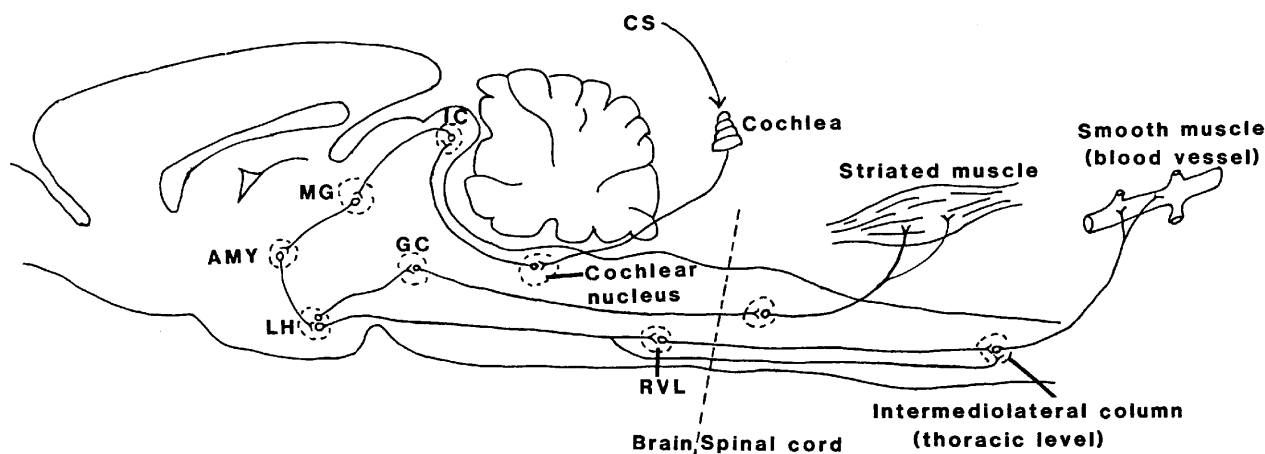
ulus or in the medial geniculate nucleus blocked the response.

Medial geniculate nucleus lesions were specific for the conditioned response to auditory stimulation, but unconditioned responses to auditory stimuli or footshock were unaffected. In addition, the lesioned animals can still learn to associate visual stimuli with footshocks (Le Doux et al., 1986). This implies that the medial part of the medial geniculate nucleus is part of the afferent pathway for learning the emotional significance of auditory stimuli. The ascending pathway from the medial geniculate nucleus projects to several regions in the brain of which the pathway to insular cortex and central nucleus of the amygdala may be of importance in the current context. In addition, the outflow from the central nucleus of the amygdala seems important in this response. Ibotenic acid lesions of the dorsal part of the central nucleus of the amygdala abolish both the behavioral and blood pressure responses to auditory conditioned stimuli, whereas lesions of the lateral central nucleus or medial part of the lateral nucleus of the amygdala disrupt only the behavioral responses. The neurons in the central nucleus of the amygdala project to the bed nucleus of the stria terminalis, lateral hypothalamic area, midbrain central gray matter, and possibly directly to brain stem nuclei. Ibotenic acid lesions of the bed nucleus of the stria terminalis have no effect on blood pressure or somatomotor activity elicited by classical conditioning of fear to an acoustic stimulus, whereas lateral hypothalamic area lesions affect the blood pressure response and central gray matter lesions disrupt the behavioral response (Le Doux et al., 1988). This sug-

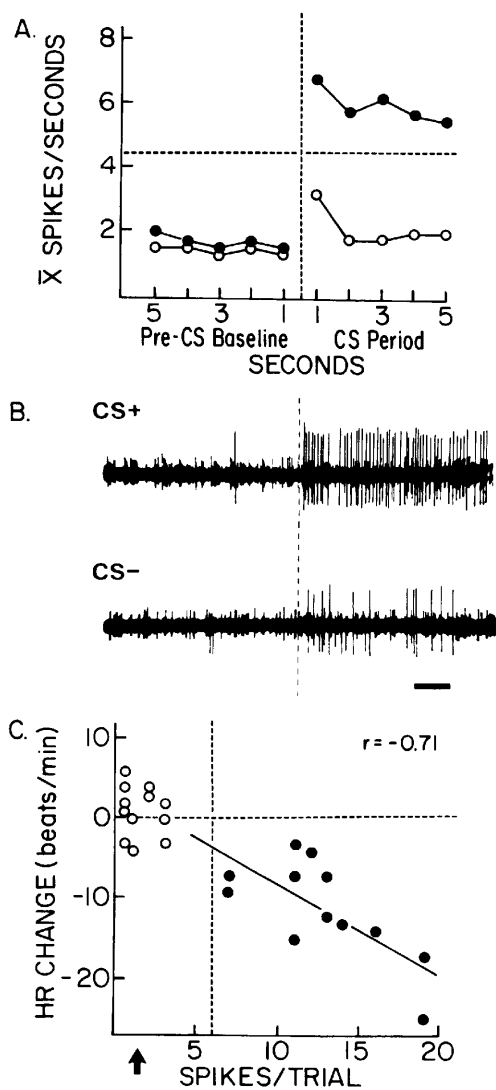
gests that the lateral hypothalamic region, which overlaps with a region of neurons projecting to the intermediolateral cell columns, forms part of the efferent pathway, mediating the cardiovascular response (Figure 19-9), whereas the pathways for the behavioral response are controlled separately by the central gray matter. However, if this is the case, it does not resolve the question of the role of the direct pathways from the amygdala to many brain stem nuclei. In addition, although the efferent pathway for the behavioral response may well pass via the midbrain central gray matter, it is known that chemical stimulation of this site also evoked the autonomic components of defensive behavior (Bandler and Carrive, 1988; Carrive et al., 1987; McDougall et al., 1985).

Conditioning of the emotional responses to auditory stimuli appears to be mediated by a direct thalamic-lymbic pathway that bypasses the auditory cortex (Figure 19-9). However, this does not necessarily mean that corticolimbic pathways cannot, or do not, normally influence such conditioned responses. Indeed, it is possible that the direct subcortical pathways may provide for conditioned responses to primitive sensory stimuli, whereas thalamocorticolimbic pathways may mediate responses requiring perceptual discrimination between stimuli (Le Doux, 1987). If this is indeed the case, even within the subcortical pathway, neurons must exist that are able to assign affective significance to different stimuli.

Neurons within both the medial geniculate nucleus and the central nucleus of the amygdala receive convergent input from both conditioned and uncon-



**Figure 19-9** Thalamoamygdaloid pathways mediating learned fear responses in the rat. A schematic drawing of sections through the rat brain illustrating the pathways essential for autonomic activity and emotional behavior. The two pathways overlap through the auditory system and the amygdala but different efferent pathways mediate the effects from the amygdala. AMY, amygdala; CS, conditional stimulus; GC, central gray; IC, inferior colliculus; LH, lateral hypothalamus; MG, medial geniculate; RVL, rostral ventrolateral medulla. (Adapted and reproduced from LeDoux, 1987, with permission of the author and publishers.)



**Figure 19-10** Characteristics of a neuron recorded extracellularly in the central nucleus of the amygdala of an anesthetized rabbit during Pavlovian fear conditioning. The positive conditioning stimulus (CS+) involved presentation of a two-tone stimuli followed by an electrical shock to the eyelid (unconditioned stimulus). The negative conditioned stimulus (CS-) situation also involved a two-tone stimulus, without electrical shock. (A) Cumulative records of the activity of 13 of these neurons during the course of 114 presentations of each of the CS+ (closed circles) and CS- (open circles). Shown are the mean spike counts during CS and pre-CS periods. The dashed horizontal line indicates the level above which unit activity is significantly elevated above pre-CS baseline rates. (B) Oscilloscope traces showing the response of a neuron to presentations of each CS (at the dashed line). Calibration bar = 1 sec. (C) The relationship between the heart rate change and the activity of an amygdala neuron during the course of 12 presentations of each of the CS+ (closed circles) and CS- (open circles). The dashed vertical line indicates the point above which the activity is significantly elevated over the spontaneous firing rate of the neuron (shown by the arrow). (Reproduced with slight modification from Pascoe and Kapp, 1985, with permission of the authors and publisher.)

ditioned stimuli. Some neurons in the amygdala can respond differently to stimuli signifying food and shock, and others can distinguish between edible and inedible objects (Ono et al., 1983; Sanghera et al., 1979). In addition, neurons in both the cat medial geniculate nucleus (Ryugo and Weinberger, 1978) and rabbit central nucleus of the amygdala (Pascoe and Kapp, 1985) (Figure 19-10) change their ongoing activity during the development of fear conditioning. Of course, because any neuron in the efferent pathway of a conditioned response would be expected to demonstrate such differential responses, the question still remains of whether the amygdala complex is simply an outflow pathway or is integrally involved in the development of the emotional significance of stimuli.

### PLAYING DEAD: A FURTHER BEHAVIORAL AND AUTONOMIC PARADIGM?

During the development of fear conditioning, rabbits, unlike cats, show a marked bradycardic response. This has been used as a model to describe the contribution of the central nucleus of the amygdala in the acquisition of conditioned response in this species (see review by Kapp et al., 1983). Such a role was proposed since the bradycardic response is attenuated by lesions in the central nucleus of the amygdala, or by injection of opiate agonists or  $\beta$ -adrenoceptor antagonists into this region. In addition, electrical stimulation of the central nucleus of the amygdala evokes a marked, vagally mediated bradycardia.

Although the major part of this chapter has discussed experimental paradigms in which tachycardia and other sympathoexcitatory responses served as a marker of affective behavior, the reader may be puzzled about the use of bradycardia as a functional indicator of this behavior. The reason for this is the observation that electrical stimulation of the central nucleus of the amygdala in awake rabbits evokes an arrest of ongoing behavior, pupillary dilation, rapid shallow breathing, and bradycardia (Applegate et al., 1983), which in the anesthetized animals is associated with a fall in blood pressure and a hindlimb vasodilation (Cox et al., 1987). This pattern of behavior and autonomic responses is considered to be typical of that seen during what has been termed "playing dead." This is often encountered when animals are faced with a threat outside their own territory. They freeze, crouch, and remain immobile. Although this is commonly seen in rabbits, they too can show aggressive behavior in response to some stimuli. Stimulation of regions of the hypothalamus and midbrain in unanesthetized rabbits can evoke

flight or escape type behavior. When these animals are anesthetized, the same stimulus then evoked pupillary dilation, exothalamus, hyperventilation, a pressor response, tachycardia, hindlimb vasodilation, and renal vasoconstriction (see Azevedo, 1987 for review).

These results define another pattern of matched autonomic and behavioral responses appropriate to the context of the stimulus. An important question still unanswered is whether in every individual there are always two or more different preprogrammed patterns of behavior and associated autonomic responses that can be switched in and out at will depending on the environmental cues presented? An alternative explanation is that the different patterns of response all rely on one basic efferent outflow pattern that can be modified to suit the particular stimulus. Only a more detailed analysis of the individual components of the neural networks involved will allow this to be answered.

## SUMMARY

The autonomic nervous system plays a full and coordinated part in providing an appropriate pattern of activity to complement somatic alterations associated with evoked behavioral patterns. The most widely studied activity, affective attack (defense response), has been used as a model on which general concepts of behavioral-autonomic integration have been based.

The defense response is evoked in a wide range of species when presented with threatening or aversive stimuli. In cats, the animal retracts its head and ears, crouches, vocalizes, and is generally alert. The stereotyped pattern of autonomic activity that accompanies this behavior mediates dilation of the pupils, piloerection of the back and tail, increases in blood pressure and heart rate, and vasoconstriction in renal, mesenteric, and skin beds with increased blood flow to hindlimb muscles.

These behavioral and autonomic patterns of activity can both be evoked by electrical, and sometimes, chemical stimulation of the same parts of a longitudinal continuum of brain tissue stretching from at least the level of the amygdala, through the hypothalamus and midbrain to the medulla. A unified site—probably the midbrain central gray matter—organizes and integrates both the behavior and the autonomic outflow appropriate for that behavior, and this general phenomenon could be extended to other behavior patterns such as feeding, temperature regulation, or exercise.

An output similar to the defense response is evoked in awake animals presented with threatening stimuli, and it can also be conditioned to occur on presentation of a previously nonsignificant stimulus.

The neural networks underlying the conditioning of such affective responses include both cortical and subcortical pathways. In the latter case, the amygdala nuclei seem to be of importance as a site for assessing the emotional significance of the stimuli.

In rabbits, the "playing dead" reaction is a common response to an aggressor. This involves arrest of ongoing locomotor activity, pupillary dilation, rapid shallow breathing, decreases in heart rate and blood pressure, and increased hindlimb muscle blood flow. However, in certain situations, rabbits can also exhibit the classical defense response as described in the cat. It is suggested that in all animals there are always several different preprogrammed patterns of behavior and their associated autonomic responses and that these can be switched in and out at will, depending on the environmental cues provided.

## REFERENCES

### Reviews

- Azevedo, A. D. (1987). The defense reaction in different animal species. In: *Neuroscience and Behaviour*, M. L. Brandao (ed.), Grafica de UFES, Vittoria, Brazil, pp. 263–296.
- Bard, P., and Macht, M. B. (1958). The behavior of chronically decerebrate cats. In: *Ciba Foundation Symposium on the Neurological Basis of Behavior*, G. E. W. Wolsteinholme and C. M. O'Connor (eds.), Little, Brown, Boston, pp. 55–75.
- Ciriello, J., Caverson, M. M., and Polosa, C. (1986). Function of the ventrolateral medulla in the control of the circulation. *Brain Research Reviews* 11, 359–391.
- Hilton, S. M. (1982). The defence-arousal system and its relevance for circulatory and respiratory control. *Journal of Experimental Biology* 100, 159–174.
- Hilton, S. M. (1986). The central nervous contribution to vasomotor tone. In: *Central and Peripheral Mechanisms of Cardiovascular Regulation*, A. Magro, W. Osswald, D. J. Reis, and P. Vanhoutte (eds.), Plenum, London, pp. 465–486.
- Kaada, B. (1967). Brain mechanisms related to aggressive behaviour. In: *Aggression and Defense*, C. D. Clemente and D. B. Lindsey (eds.), University of California Press, Los Angeles, pp. 95–133.
- Kapp, B. S., Pascoe, J. P., and Bixler, M. A. (1983). The amygdala: A neuroanatomical systems approach to its contribution to aversive conditioning. In: *The Neuropsychology of Memory*, N. Butters and L. R. Squire (eds.), Guilford Press, New York, pp. 473–488.
- LeDoux, J. E. (1986). Sensory systems and emotion: A model of affective processing. *Integrative Psychology* 4, 237–248.
- LeDoux, J. E. (1987). Emotion. In: *Handbook of Physiology—The Nervous System V*, F. Plum (ed.), American Physiological Society, Bethesda, MD, pp. 419–459.
- Luiten, P. G. M., ter Horst, G. J., and Steffens, A. B. (1987). The hypothalamus, intrinsic connections and outflow pathways to the endocrine system in relation to

the control of feeding and metabolism. *Progress in Neurobiology* 28, 1–54.

Mancia, G., and Zanchetti, A. (1981). Hypothalamic control of autonomic functions. In: *Handbook of the Hypothalamus*, Vol. 3B, P. J. Morgane and J. Panksepp (eds.), Dekker, New York, pp. 147–202.

Marshall, J. M. (1987). Contribution to overall cardiovascular control made by the chemoreceptor-induced alerting/defense response. In: *Neurobiology of the Cardiorespiratory System*, E. W. Taylor (ed.), Manchester University Press, Manchester, pp. 222–240.

Price, J. L., Russchen, F. T., and Amaral, D. G. (1987). The limbic system. II. The amygdaloid complex. In: *Handbook of Chemical Neuroanatomy*, Vol. 5, *Integrated Systems in the CNS*. Part I, A. Bjorklund, T. Hokfelt, and L. W. Swanson (eds.), Elsevier, Amsterdam, pp. 279–388.

Siegel, A., and Edinger, H. (1981). Neural control of aggression and rage behaviour. In: *Handbook of the Hypothalamus*, Vol. 3B, P. J. Morgane and J. Panksepp (eds.), Dekker, New York, pp. 203–240.

Smith O. A., Astley, C. A., DeVito, J. L., Stein, J. M., and Walsh, K. E. (1980). Functional analysis of the hypothalamic control of the cardiovascular responses accompanying emotional behavior. *Federation Proceedings* 39, 2487–2494.

Smith, O. A., DeVito, J. L., and Astley, C. A. (1982). The hypothalamus in emotional behaviour and associated cardiovascular correlates. In: *Changing Concepts of the Nervous System*, A. R. Morrison and P. L. Strick (eds.), Academic Press, New York, pp. 569–584.

Smith, O. A., Astley, C. A., Chesney, M. A., Taylor, D. J., and Spelman, F. A. (1986). Personality, stress and cardiovascular disease: Human and non-human primates. In: *Neural Mechanisms and Cardiovascular Disease*, B. Lown, A. Malliani, and M. Prosdociami (eds.), Liviana Press, Padua, Italy, pp. 471–484.

### Research Papers

Abrahams, V. C., Hilton, S. M., and Zbrozyna, A. (1960). Active muscle vasodilation produced by stimulation of the brain stem; its significance in the defence reaction. *Journal of Physiology (London)* 154, 491–513.

Applegate, C. D., Kapp, B. S., Underwood, M. D., and McNall, C. L. (1983). Autonomic and somatomotor effects of amygdala central nucleus stimulation in awake rabbits. *Physiology and Behavior* 31, 353–360.

Bacelli, G., Albertini, R., Mancia, G., and Zanchetti, A. (1976). Interactions between sino-aortic reflexes and cardiovascular effects of sleep and emotional behaviour in the cat. *Circulation Research* 38, Suppl. 2, 30–34.

Bandler, R. (1982). Induction of 'rage' following microinjections of glutamate into midbrain but not hypothalamus of cats. *Neuroscience Letters* 30, 183–188.

Bandler, R., and Carrive, P. (1988). Integrated defence reaction elicited by excitatory amino acid microinjection in the midbrain periaqueductal gray region of the unrestrained cat. *Brain Research* 439, 95–106.

Bandler, R., and McCulloch, T. (1984). Afferents to a midbrain periaqueductal grey region involved in the 'defence-reaction' in the cat as revealed by horseradish peroxidase. II. The diencephalon. *Behavioural Brain Research* 13, 279–285.

Bandler, R., McCulloch, T., and Dreher, B. (1985). Afferents to a midbrain periaqueductal grey region involved in the 'defence reaction' in the cat as revealed by horseradish peroxidase. I. The telencephalon. *Brain Research* 330, 109–119.

Bard, P. (1928). A diencephalic mechanism for the expression of rage with special reference to the sympathetic nervous system. *American Journal of Physiology* 84, 490–515.

Bard, P., and Mountcastle, V. B. (1948). Some forebrain mechanisms involved in expression of rage with special reference to suppression of angry behaviour. *Research Publications of the Association for Nervous and Mental Diseases* 27, 362–404.

Beitz, A. J. (1982). The organization of afferent projections to the midbrain periaqueductal gray of the rat. *Neuroscience* 7, 133–159.

Cannon, W. B., and Britton, S. W. (1925). Studies on the conditions of activity in endocrine glands. XV. Pseudoaffective medulladrenal secretion. *American Journal of Physiology* 72, 283–294.

Carrive, P., Dampney, R. A. L., and Bandler, R. (1987). Excitation of neurones in a restricted portion of the midbrain periaqueductal grey elicits both behavioural and cardiovascular components of the defence reaction in the unanesthetized decerebrate cat. *Neuroscience Letters* 81, 273–278.

Carrive, P., Bandler, R., and Campney, R. A. L. (1988). Anatomical evidence that hypertension associated with the defence reaction in the cat is mediated by a direct projection from a restricted portion of the midbrain periaqueductal gray to the subretrofacial nucleus of the medulla. *Brain Research*, 460, 339–345.

Coote, J. H., Hilton, S. M., and Zbrozyna, A. W. (1973). The ponto-medullary area integrating the defence reaction in the cat and its influence on muscle blood flow. *Journal of Physiology (London)* 229, 257–274.

Cox, G. E., Jordan, D., Paton, J. F. R., Spyer, K. M., and Wood, L. M. (1987). Cardiovascular and phrenic nerve responses to stimulation of the amygdala central nucleus in the anesthetized rabbit. *Journal of Physiology (London)* 389, 541–556.

Downer, J. L. deC. (1961). Changes in visual gnostic functions and emotional behaviour following unilateral temporal pole damage in the 'split-brain' monkey. *Nature* 191, 50–51.

Eliasson, S., Folkow, B., Lindgren, P., and Uvnas, B. (1951). Activation of sympathetic vasodilator nerves to the skeletal muscles in the cat by hypothalamic stimulation. *Acta Physiological Scandinavica* 23, 333–351.

Feigl, E., Johansson, B., and Lofving, B. (1964). Renal vasoconstriction and the 'defence reaction'. *Acta Physiological Scandinavica* 62, 429–435.

Fernandez de Molina, A., and Hunsperger, R. W. (1959). Central representation of affective reactions in forebrain and brain stem: Electrical stimulation of amygdala, stria terminalis and adjacent structures. *Journal of Physiology (London)* 145, 251–265.

Fernandez de Molina, A., and Hunsperger, R. W. (1962). Organization of the subcortical system governing defence and flight reactions in the cat. *Journal of Physiology (London)* 160, 200–213.

Gelsema, A. J., McKittrick, D. J., and Calaresu, F. R.

