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State-Dependent Amygdala Stimulation-Induced Cardiovascular Effects in Rats

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Abstract

Stimulation of the amygdala is known to produce pressor, depressor, or has no effects. The present study was performed to test whether amygdala cardiovascular effects are influenced by consciousness states and by different types of anesthetics. Adult rats were set up for stimulation amygdala and measurement of blood pressure in a chronic preparation. After recovery, same sites of the amygdala were stimulated electrically for several trials with the rat under conscious or anesthetic states induced by pentobarbital, urethane, ketamine, α-chloralose and urethane plus α-chloralose, respectively. The interval between any two stimulation trials was at least 2 days. The stimulation was an 80-Hz, 0.5-ms, 100-μA square wave pulse train lasting for 15 s. Cardiovascular responsive sites were found in the central, medial, and basolateral nuclei of the amygdala. In stimulating these responsive sites, significantly different cardiovascular effects were induced under a conscious state and an anesthetized state of the animal, yet no significant differences were found among the various anesthetic agents. We conclude, that the cardiovascular influence of the amygdala is state-dependent in the rat.

Key Words: amygdala, anesthesia, blood pressure, heart rate, electrical stimulation, ketamine, pentobarbital, chloralose, urethane

Introduction

Different emotional states are accompanied with different cardiovascular reactions. Blood pressure and heart rate change as an animal faces different conditions (18, 23, 25, 27, 33, 41, 52) such as fear, reward, stress, aversive stimulus and a prey or a predator. This is also the case for humans (40, 48). In animals, there are many different paradigms to address emotional issues especially those concerning fear. In classical fear conditioning, an initially harmless conditioned stimulus (CS) like tone or light is paired with an aversive unconditioned stimulus (US), usually a foot-shock, the CS eventually elicits a conditioned fear responses (CRs) which, in rodents, include freezing, enhancement of muscular reflexes to any abrupt stimulus (*e.g.* startle) and alterations in autonomic activities, such as blood pressure, heart rate and respiration rate.

The amygdala plays an important role in fear conditioning (3, 8, 15, 20, 31, 32, 47). Various types of fear conditioning fail after amygdala lesions (3, 15, 20, 32, 47). The amygdala has also been implicated in the control of many autonomic functions including cardiovascular functions such as blood pressure and heart rate. As an animal acquires fear conditioning,

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its blood pressure and heart rate are elevated in response to the CS (22, 25, 27, 41, 52). As lesions in the central nucleus of the amygdala abolish these conditioned cardiovascular responses (22, 25, 52), the data are interpreted as that the amygdala or some of its nuclei mediate the association between the CS and the US with the latter eliciting various responses indicative of fear through amygdala outputs (7). It follows that stimulation of the amygdala should induce a response similar to CR. Indeed, direct stimulation of the amygdala activates cardiovascular responses. However, it was found that the stimulation elicited either pressor or depressor responses (11, 13, 14, 16, 19, 21, 34, 36, 37). This lack of parsimony in the existing literature might be due to differences in the animal species, parameters or sites of the stimulation, and most importantly states of the animal studied because the stimulation studies were done mostly in anesthetized animals whereas the conditioning experiments were mostly done under a conscious state. As pentobarbital, urethane, α-chloralose, ketamine and combinations of them have been used in different stimulation experiments (5, 6, 11, 13, 14, 21, 29, 36, 37, 42), the various anesthetics used may further exacerbate the different effects on the cardiovascular system (9, 26, 29, 30, 39, 44, 51).

To formally address this concern, the present study was performed to examine whether the amygdala stimulation effects on the cardiovascular functions could be influenced by the conscious conditions and the anesthetics applied. To repeatedly examine effects of the same stimulation site, stimulation electrodes and recording sensors were chronically implanted, and amygdala stimulation-induced cardiovascular effects were measured and compared under different anesthetics and in different sites in different experimental sessions.

Materials and Methods

Adult male Wistar rats weighing 370~603 g (n = 31) were used in accordance with guidelines approved in the *Codes for Experimental Use of Animals* of the Council of Agriculture of Taiwan based on the *Animal Protection Law* of Taiwan. All experimental protocols were approved by the Institutional Animal Care and Use Committee of the National Taiwan University. Rats were obtained from the Animal Center, National Taiwan University Hospital, Taipei. Rats had free access to laboratory chow and water. The implantation surgeries were performed with sodium pentobarbital (50 mg/kg, i.p.). Two methods were used to record blood pressure. One was through femoral artery cannulation. In these rats, the femoral cannulation was also utilized for drug administration. The other method used telemetric sensors (TL11M2-C50-PXT, DSI, St. Paul, MN, USA) implanted in the descending aorta in the abdomen. In these rats, anesthetics were administered intraperitonealy. For implantation of amygdala electrodes, the head of the rat was fixed in a Kopf stereotaxic apparatus in the prone position. Small holes were drilled in the skull to expose the cortex overlying the amygdala. Two tungsten microelectrodes (parylene-insulated monopolar microelectrodes) were implanted in the amygdala, one on each side. These two microelectrodes were fixed in place using dental cement. In rats with femoral artery cannulation, stimulation electrodes were implanted 1 week before the artery cannulation surgery; in the telemetric experiements, the stimulation electrodes were implanted into the amygdala of rats 1 week after the telemetric sensor implantation. After the surgery, rats were allowed to rest for at least 24 h before undergoing stimulation trials. The blood pressure and heart rate were acquired through the Dataquest A.R.T. program in the telemetric rats. All blood pressure and heart rate data were saved as txt files and imported into the Chart program to calculate changes in blood pressure and heart rate.

A total of 6 different states (awake, pentobarbital anesthesia, ketamine anesthesia, urethane anesthesia, urethane+α-chloralose anesthesia, and α-chloralose anesthesia) were tested in this study. Each rat was stimulated under at least 3 anesthetic states. Two anesthetic trials were separated by at least 48 h. Before each anesthetic trial, the conscious state trials were first run. Rats were stimulated in the home cage under resting conditions. Before stimulation, the resting blood pressure and heart rate were recorded for 3 min. After 15 s of stimulation, the rats were allowed to rest for at least 3 min. Then they were anesthetized by one of the 5 anesthetics, and the same stimulation procedure was repeated. The anesthetic order was random. Dosage of anesthetics was 50 mg/kg for pentobarbital, 100 mg/kg for ketamine, 1,300 mg/kg for urethane, 80 mg/kg for α-chloralose and 450 mg/kg + 60 mg/kg for urethane plus α-chloralose. Electrical stimulation consisted of a 15-s train of an 80-Hz 0.5-ms square wave anodal current delivered by a Grass S48 simulator *via* an isolation unit. Current intensities were 100 μA. The indifferent electrode was implanted in the frontal bone. The extent of the amygdaloid area stimulated was 2.5~3.0 mm caudal to the bregma, 3.0~5.0 mm lateral to the midline and 6.5~9.0 mm deep from the bone surface.

At the end of the anesthesia experiment, the stimulated sites were electrically lesioned to verify the exact locations of the electrode. The rat was then sacrificed by an intracardiac perfusion of saline followed by a 10% formalin solution. The brain was removed and blocked for serial frozen sections in 100 μm thickness in the coronal plane. Sections were

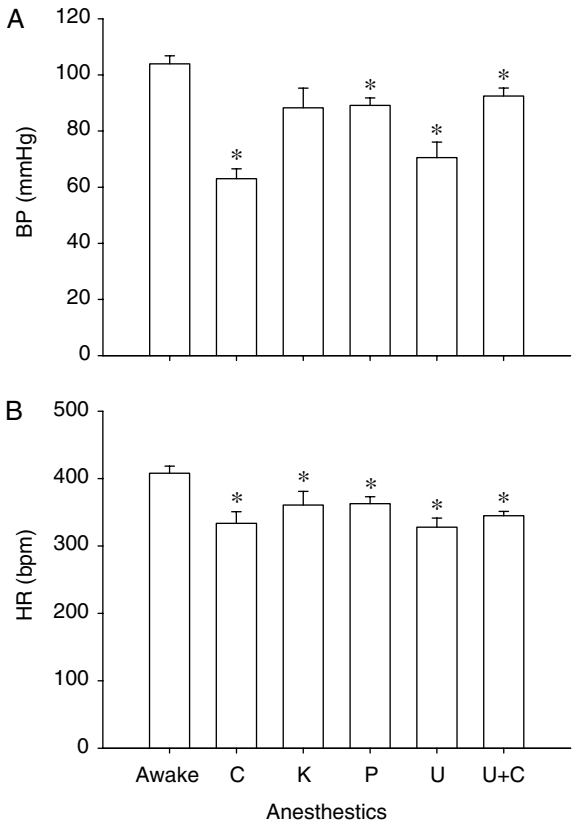

Fig. 1. Baseline values of blood pressure and heart rate in conscious or anesthetized states. *$P < 0.05$, compared with the awake state. C, α-chloralose anesthesia; K, ketamine anesthesia; P, pentobarbital anesthesia; U, urethane anesthesia; U+C, urethane + α-chloralose anesthesia.

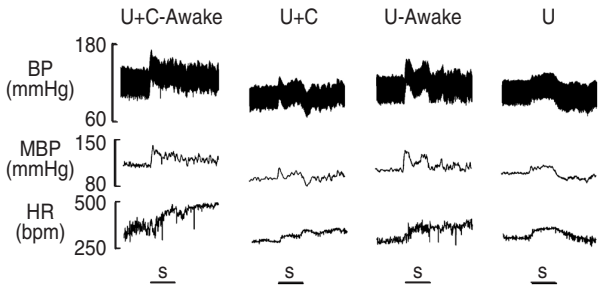

Fig. 2. Representative example of blood pressure (BP) and heart rate (HR) responses produced by electrical stimulation of the central amygdala nucleus (CE). BP was measured through a telemetric sensor connected to a cannula in the descending aorta. HR was calculated online through the BP trace. MBP, mean arterial blood pressure; U, urethane anesthesia; U+C, urethane + α-chloralose anesthesia; s, stimulation; bar, 15-s stimulation period.

stained with cresyl violet and were examined for stimulation sites.

Two types of stimulation responses were discriminated: transient or sustained. If the response did not last for at least half the stimulation period, it was characterized as transient; otherwise it was defined as sustained. Only sustained responses were considered. Changes in the cardiovascular responses were normalized to the baseline before stimulation. All values are expressed as the means ± standard error (SE). For statistical analysis of the amygdala-stimulation responses, used the *t*-test and multi-factorial analysis of variance (ANOVA) were used. The criterion for statistical significance was set at $P < 0.05$.

Results

Baseline Values

The resting baseline blood pressure and heart rate of the rats in the conscious state were 103.9 ± 2.9 mmHg and 407.8 ± 10.6 beats/min, respectively. After anesthetic induction, the resting blood pressure and heart rate significantly decreased from the awake state for all anesthetics except ketamine under which the blood pressure did not decrease (Fig. 1). The blood pressure and heart rate responses to amygdala stimulation in 1 rat are presented in Fig. 2. Electrical stimulation of the left central nucleus of the amygdala produced a pressor response and tachycardia in the awake state. Stimulation of the same site elicited the same responses under urethane and α-chloralose anesthesia. The rat then underwent another conscious trial and the responses were pressor and tachycardia. After the conscious trial, the rat was anaesthetized with urethane, and pressor and tachycardia responses were again recorded. In this case, the heart rate continued to increase after the end of the stimulation.

Response Pattern in the Conscious State

The stimulation sites were tested in the central nucleus, medial nucleus and basolateral nuclei of the amygdala (Fig. 3). In a conscious state, amygdala stimulations applied to the right- or left-central and basolateral nuclei caused pressor or no responses (Fig. 3A). The responses to stimulation of the medial amygdala nucleus resulted in different patterns. On the right side, it produced pressor, depressor or no responses. On the left side, it only caused pressor responses. For heart rate control, stimulation of the central amygdala nucleus produced tachycardia, bradycardia, biphasic or no responses (Fig. 3B). Stimulation of the medial amygdala nucleus did not produce dual responses whereas stimulation of the right basolateral amygdala nucleus produced the same responses as that of the central nucleus, but stimulation of the left basolateral nucleus produced bradycardia or no responses.

Table 1. Changes in blood pressure (BP) following electrical stimulation at various nucleus sites of the amygdala under different states (values are percentage changes normalized to the baseline values)

	RCE	RM	RBL	LCE	LM	LBL	Total
Awake	17.9 ± 4.01 (22)	15.1 ± 5.6 (16)	18.6 ± 3.8 (20)	21.1 ± 4.12 (21)	25.7 ± 4.96 (12)	9.3 ± 3.77 (12)	18.2 ± 1.82 (103)
C	-11.4 ± 13.4 (4)	9.71 ± 19.0 (3)	–	-5.7 ± 12.2 (5)	-30.5 ± 0 (1)	–	-5.8 ± 7.48* (13)
K	-0.9 ± 0.91 (5)	-3.4 ± 4.41 (3)	5.1 ± 4.56 (6)	-0.6 ± 0.60* (4)	1.8 ± 4.97 (3)	-3.2 ± 3.22 (3)	0.4 ± 1.48* (24)
P	-17.0 ± 4.3 (9)	-6.9 ± 4.28 (8)	-4.0 ± 2.56 (5)	-6.4 ± 10.7 (9)	-8.9 ± 5.02 (4)	0.0 ± 0.0 (3)	-8.4 ± 2.93* (38)
U	-2.7 ± 4.51 (8)	8.2 ± 5.78 (7)	11.4 ± 13.6 (5)	5.5 ± 5.02 (7)	16.2 ± 6.83 (3)	-6.8 ± 3.87 (3)	4.9 ± 2.98* (33)
U+C	-10.8 ± 4.5 (5)	-2.0 ± 4.21 (3)	6.02 ± 3.36 (6)	4.09 ± 6.61 (4)	6.42 ± 11.7 (3)	5.45 ± 11.9 (3)	1.2 ± 2.73* (24)

Values are the means ± SE. RCE, right central nucleus; RM, right medial nucleus; RBL, right basolateral nucleus; LCE, left central nucleus; LM, left medial nucleus; LBL, left basolateral nucleus; P, pentobarbital anesthesia; K, ketamine anesthesia; U, urethane; U+C, urethane and α-chloralose anesthesia; C, α-chloralose anesthesia. *$P < 0.05$, vales compared to the awake ones.

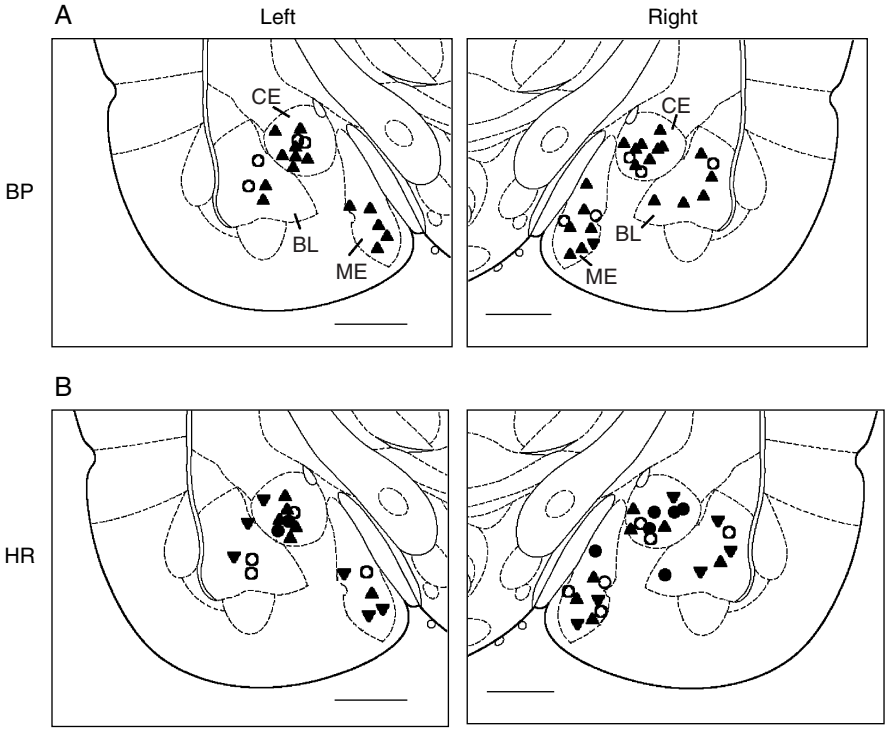

Fig. 3. Coronal section of the amygdala depicting the stimulation sites. Observations were obtained from conscious animals. Panels A and B represent BP and HR responses, respectively. Solid triangles represent increasing responses; inverted triangles, decreasing responses; open circles, no responses; closed circles, biphasic increasing and decreasing. Scale bar: 1 mm. CE, central nucleus; BL, basolateral nucleus; ME, medial nucleus. The nucleus in panels B is the same as in panels A.

Comparison of Response Patterns

The total results of stimulation responses in different nuclei under different anesthetic states are shown in Tables 1 and 2. Blood pressure responses are shown in Fig. 4A. The responses were pressor or depressor under anesthetized and awake states. Electrical stimulation had little influence on the heart rate compared with the blood pressure responses (Fig. 4B). For an overall analysis of these data, an ANOVA

Table 2. Changes in the heart rate (HR) following electrical stimulation of the various nucleus sites in the amygdala under different states (values are percentage changes normalized to the baseline values)

	RCE	RM	RBL	LCE	LM	LBL
Awake	4.38 ± 3.68 (22)	10.6 ± 6.77 (16)	-8.36 ± 3.55 (20)	7.43 ± 4.72 (21)	-12.1 ± 5.9 (12)	-3.69 ± 1.94 (12)
C	-10.30 ± 3.0 (4)	4.84 ± 10.9 (3)	–	7.07 ± 7.17 (5)	10.1 ± 0 (1)	–
K	-5.9 ± 4.88 (5)	-2.43 ± 2.43 (3)	-3.35 ± 1.68 (6)	-9.68 ± 8.7 (4)	-6.04 ± 4.74 (3)	-2.57 ± 2.57 (3)
P	-2.86 ± 0.94 (9)	0.33 ± 1.22 (8)	-1.38 ± 1.38 (5)	2.0 ± 2.67 (9)	-2.98 ± 3.13 (4)	-1.12 ± 1.12 (3)
U	7.4 ± 4.74 (8)	4.04 ± 2.35 (7)	2.66 ± 5.48 (5)	11.8 ± 7.1 (7)	3.35 ± 3.35 (3)	-6.74 ± 6.74 (3)
U+C	4.41 ± 4.58 (5)	3.05 ± 3.05 (3)	3.73 ± 2.37 (6)	12.3 ± 5.64 (4)	11.6 ± 3.89 (3)	0.15 ± 4.5 (3)

Values are the means ± SE. RCE, right central nucleus; RM, right medial nucleus; RBL, right basolateral nucleus; LCE, left central nucleus; LM, left medial nucleus; LBL, left basolateral nucleus; P, pentobarbital anesthesia; K, ketamine anesthesia; U, urethane; U+C, urethane and α-chloralose anesthesia; C, α-chloralose anesthesia. *$P < 0.05$, values compared to the awake ones.

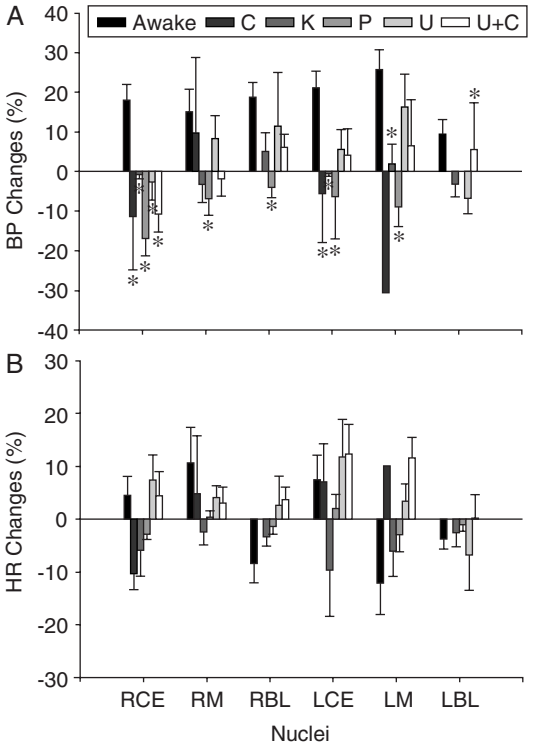

Fig. 4. Blood pressure and heart rate responses produced by electrical stimulation of the amygdala under 6 different states. *Differs from the awake state ($P < 0.05$). LCE, left central nucleus; RCE, right central nucleus; LM, left medial nucleus; RM, right medial nucleus; LBL, left basolateral nucleus; RBL, right basolateral nucleus; AWAKE, conscious state; C, α-chloralose anesthetized; K, ketamine anesthetized; P, pentobarbital anesthetized; U, urethane anesthetized; U+C, urethane + α-chloralose anesthetized.

with stimulation sites and anesthetized states was carried out. A statistically significant difference was found between the conscious and anesthetized states ($P < 0.05$). There were no significant differences between stimulation applied to the right and left side for the central, medial or basolateral nuclei. In comparisons among the various anesthetics, amygdala stimulation caused an overall depressor response under pentobarbital anesthesia (-8.4 ± 2.93%; n = 38). In contrast, the stimulation produced an overall pressor response under urethane anesthesia (4.9 ± 2.98%; n = 33). The difference is statistically significant ($P < 0.05$, ANOVA).

Comparison among the Nuclei

Further comparisons of the effects induced by stimulating the individual nuclei were made. Stimulation of the right central nucleus produced an overall pressor response under an awaked state (17.9 ± 4.01%; n = 22). However under the α-chloralose, pentobarbital, ketamine, urethane and urethane + α-chloralose anesthesia, stimulation in the right central nucleus caused an overall depressor response (-11.4 ± 13.4%; n = 4, -17.0 ± 4.3%; n = 9, -0.9 ± 0.91%; n = 5, -2.7 ± 4.51%; n = 8, -10.8 ± 4.5%; n = 5, in order). The difference is of statistical significance ($P < 0.05$, *t*-test). Stimulation of the right-medial and basolateral nuclei under an awake state produced pressor responses (15.1 ± 5.6%; n = 16, 18.6 ± 3.8%; n = 20) significantly different from that under pentobarbital-anesthetized state (-6.9 ± 4.28%; n = 8, -4.0 ± 2.56%; n = 5) ($P < 0.05$, *t*-test). In the left-central

Table 3. Motion patterns during stimulation of the various amygdala nuclei

Stimulation site (n)	Rat # \ Order	1	2	3	4
Central (13)	1	Stage 4	Stage 4 (30 μA)	Stage 4 (30 μA)	(30 μA) Stage 4
	2	Spasm	–	–	–
Medial (15)	1	Stage 2	Stage 2	–	–
	2	X	Stage 4 (100 μA)	Stage 4 (100 μA)	Stage 4 (50 μA)
	3	Spasm	Spasm	–	–
	4	Spasm	Spasm	–	–
Basolateral (6)	1	Stage 4	Stage 4	Stage 4 (50 μA)	(30 μA) Stage 2
	2	X	X	X	Stage 2

Stage 1: automatisms of the facial musculature, Stage 2: head nodding, Stage 3: clonic movements of the forelimbs, Stage 4: rearing on the hind limbs, Stage 5: loss of postural control. X: no movement. –: not tested. The stimulation intensity in the table before the motion patterns means the movement happening during the stimulation, the intensity after the movement means the movement happening after the stimulation ends.

nucleus, stimulation under an awake state (21.1 ± 4.12%; n = 21) produced an effect significantly different from that under pentobarbital-, ketamine-, and α-chloralose-anesthetized states (-6.4 ± 10.7%; n = 9, -0.6 ± 0.6%; n = 4, -5.7 ± 12.2%; n = 5) ($P < 0.05$, *t*-test). For stimulating the left-medial nucleus, the effect observed under an awake state (25.7 ± 4.96%; n = 12) differed from that under the pentobarbital- and ketamine-anesthetized states (-8.9 ± 5.02%; n = 4, 1.8 ± 4.97%; n = 3) ($P < 0.05$, *t*-test). For stimulation of the left-basolateral nucleus, the effect induced under an awake state (9.3 ± 3.77%; n = 12) differed from that observed under a urethane-anesthetized state (-6.8 ± 3.87%; n = 3) ($P < 0.05$, *t*-test). On the contrary, stimulation of the various amygdala nuclei did not produce a significant difference in the responses of the heart rate under the 6 states.

Body Movements

Stimulation under the conscious state sometimes induced movements (Table 3). Out of the 13 rats tested, two exhibited body movements with the central nucleus stimulation. One rat exhibited kindling-like behavior immediately upon the first stimulation. Even when the stimulation intensity was lowered to 30 μA, the rat continued to convulse after termination of the stimulation. The other rat exhibited whole-body spasm during the stimulation. Among the 15 rats receiving stimulation of the medial amygdala nucleus, two rats exhibited kindling-like behavior with one rat showing head nodding at the first stimulation and the other rats showing rearing on the hind limb at the second stimulation. Two additional rats exhibited whole-body spasm during stimulation of the medial nuclei. During stimulation of the basolateral nucleus, 2 out of 6 rats exhibited body movements: one produced rearing on the hind limb at the first stimulation and the other exhibited head nodding at the fourth stimulation.

Discussion

The two most important findings emerging from the present study are as follows: [1] cardiovascular responses produced by amygdala stimulation were altered by various anesthetics; and [2] the effect was most affected by anesthetics for stimulation sites in the central nucleus.

Iwata *et al.* (21) have previously used the same experimental design to contrast the effects of amygdala stimulation under wakefulness and anesthesia, but they only made comparisons between awake and chloralose-anesthetized states. They found that amygdala stimulation elicited a depressor response sometimes accompanied by bradycardia under anesthesia. Because only one anesthetic was used, it was not certain if this effect was specific to chloralose per se or anesthesia in general. We compared pentobarbital-, ketamine-, urethane-, urethane + α-chloralose-, and α-chloralose-anesthetized and awake states. We found that the effects were due to anesthetics but not to specific influence of chloralose.

Stimulation in the conscious state can produce responses without confounding of anesthetics. However, under this situation, the animals had to be in a calm state, and the test environment needed to be

quiet to avoid disturbing the animals. It presumably reflects the direct results from the stimulation itself. Yet this presumption may not be fully warranted. First of all, the amygdala is implicated in emotional processes in addition to autonomic functions (4, 24, 38, 46). When we electrically stimulated the amygdala of rats in a conscious state, we may also activate the emotional function of the amygdala. Consequently, the blood pressure and heat rate would contribute to the observed effects. Additionally, stimulation of the amygdala induced some body movements in our experiments. These movements would affect the cardiovascular responses and further complicated the stimulation results.

Our stimulation pattern and that used to generate kindling are very much alike: application of a brief train of electrical pulses once daily through a thin wire electrode implanted chronically. Kindling has been taken as an experimental model of epilepsy resulting from repeated application of electrical stimulation or pharmacological agents to brain tissues (2) and the amygdala is the most sensitive site for kindling induction. Kindling involves, electrophysiologically, amygdala after discharges and behaviorally, 5 stages of convulsive behaviors involving automatisms of the facial musculature, head nodding, clonic movements of the forelimbs, rearing on the hind limbs and loss of postural control during a generalized convulsion at stage 5. We did not record neuronal activities and thus, cannot observe after-discharges after stimulating the amygdala. In our studies, we observed kindling-like behavior after medial, central, and basolateral stimulation in rats. Stimulation of the medial nucleus is prone to produce body movements from head nodding to whole-body spasm. The reactions evoked by stimulation of the central and basolateral nuclei were mostly slight shaking of the head, mild walking and changing of body positions. The various motor responses may contribute to the cardiovascular changes observed under an awake state.

Anesthetics produce their effects partly by inhibition of spontaneous mechanical activity in venous and arterial smooth muscles. This inhibition lowers the resting tension of arteries and arterioles and results in a blood pressure decrease (1, 28). This might explain decrease in resting blood pressure. Anesthetics also attenuate contractile responses of both arteries and veins to catecholamine, serotonin, angiotensin, vasopressin and potassium ions. Thus, after anesthesia, the stimulation-induced responses of the amygdala decreased in anesthetized rats. Anesthetics act *via* both depression of the excitatory and enhancement of the inhibitory receptors. Urethane potentiates the functions of $GABA_A$ receptors and inhibits NMDA receptors (17). Pentobarbital and α-chloralose enhanced the GABA-induced chloride conductance of $GABA_A$ receptors (10, 12, 43) thereby increasing the duration of the opening of the chloride channels. Ketamine exerts its anesthetic effects by inhibiting N-methyl-d-aspartate (NMDA) receptors (10, 50). Their inhibiting actions were obviously duplicated. According to Takayama *et al.* (45), after anesthetic induction, several brain regions, including the solitary tract nucleus, dorsal motor nucleus of the vagus nerve, caudal ventrolateral medulla, rostral ventrolateral medulla, and paraventricular nucleus of the hypothalamus expressed the Fos protein. These brain regions are the most important areas implicated in the central cardiovascular control. Before stimulating the amygdala, the anesthetics already affect these cardiovascular-related regions, and these effects might be more than a simple inhibition.

Pentobarbital anesthesia did not greatly alter the resting values but changed the responses to amygdala stimulation from pressor to depressor and decreased the response magnitude regardless of which nucleus was stimulated. Pentobarbital can directly bind to the GABA receptor; this may be why it is a potent inhibitor and has a greater effect on cardiovascular control than the other anesthetics. Urethane anesthesia significantly decreased the resting blood pressure and heart rate in our results, yet Wildt *et al.* (49) reported that urethane anesthesia did not greatly change the baseline. This discrepancy may have been due to different routes of administration (28). Yet it should be noted that in our studies, the intravenous application of urethane increased the death rate. While urethane anesthesia and α-chloralose anesthesia decreased the response values, their combined administration caused a greater decrease than their separate application. Their inhibiting actions were obviously duplicated.

Stimulating the medial nuclei and the basolateral nuclei induces cardiovascular effects (14). They did not show differences in stimulation results compared to the central nucleus stimulation. But the responses to stimulation of the central nucleus were affected by most of the anesthetics; this reveals that the central nucleus is most sensitive to these anesthetics in terms of its cardiovascular control. Fibers from the central nucleus project to the hypothalamus, midbrain, pons and medulla. Many of these projection areas are involved in cardiovascular control. Through connections to preganglionic neurons and premotor neurons of sympathetic and parasympathetic in the medullary oblongata and hypothalamus, the central nucleus exerts direct control over the cardiovascular functions. The major outputs of the medial nucleus are to the olfactory system, bed nucleus of the stria terminalis, thalamus and hypothalamus. The basolateral nucleus provides substantial projections to the medial prefrontal cortex, hippocampal formation,

bed nucleus of the stria terminalis, substantia innominata, nucleus accumbens and caudate-putamen. A few projections from the basolateral nucleus to the hypothalamus terminate in the lateral hypothalamic area and the ventromedial nucleus (35). Medial and basolateral nuclei might pass through the hypothalamus and other higher-order cardiovascular related central structures and influence cardiovascular functions indirectly.

In summary, we have found no major differences among stimulation-produced cardiovascular effects elicited by either central, basolateral or medial nuclei of the amygdala. No major difference in stimulation effect was found among different anesthetics either. In contrast, the present study demonstrated a significant difference in the stimulation-produced blood pressure response between conscious state and anesthetized states. We conclude is that the amygdala cardiovascular control may be state dependent.

Acknowledgments

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