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INHIBITION OF POSITIVELY REWARDING BEHAVIOR BY THE HEIGHTENED AGGRESSIVE STATE EVOKED EITHER BY PAIN-INDUCING STIMULUS OR SEPTAL LESION

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soored either as threat (T), or attack (A) re

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Abstract: Using a footshock elicited aggression paradigm, aggressive responses were scored in normal and in septal-lesioned adult male Wistar rats. Septal lesions were made electrolytically to include the medial and lateral septal nuclei. The lesion was confirmed by behavioral criteria (septal aggression) and post-mortem histology. The aggressive response types (threat, attack) of the septal animals were compared with their corresponding age and weight matched controls. Results showed a statistically significant increase (P = 0.05) in the number of attack responses but not the threat responses in septal animals.

The modulatory role of the aggressive experience on responsiveness to positively rewarding or hedonic stimuli was assessed by quantifying the intracranial self-stimulation (SS) rates that were obtained before and after an aggression schedule. For testing the SS behavior bipolar electrodes were implanted in the ventral tegmental area - substantia nigra (VTA-SN). Results showed a decrease in SS pedal press rates in post-aggression schedule as compared to the pre-aggression period in the normal subjects. This depressing effect lasted for over a week. In septal lesioned rats the SS rates were virtually abolished even without having an aggressive schedule.

These experiments revealed the effect of environment and of a brain area in provoking aggressive mood and its inhibitory consequence on responding for positive experience.

Key words:	self-stimulation behavior	aggression state	responding to positive reward		
	septum lesion		ventral tegmental area		

INTRODUCTION

Aggression in organisms is known to serve various biological functions (1), and no single experimental model is sufficient enough to explain these functions. Inappropriate or pathological forms of aggression also exist. The neural mechanisms of aggression remain to be understood (2). Some progress occurred about brain regions involved in hedonic behavior (3-5). While the aggressive behavior could be said to be helpful to the organism in preservation of self, the hedonic behavior is involved with survival and propagation of species. Both these behaviors represent two strong forces that enable the organism to deal with the environment advantageously. However, if an experimental situation is created where one of these forces comes into prominence how would the other behavior get affected? This is an interesting question to explore, and rather forms the aim of this study.

One of the common experimental paradigms of aggression is the pain-inducing foot-shock elicited fighting. It was first described in rats by O'Kelly and Steckle (6). It is produced by brief duration electric shock pulses of moderate intensity (2 mA) and scrambled polarity presented every second via the basis of grid floor of a small experimental chamber that accommodates a pair of rats (7).

On the other hand, hedonic behavior (3) is the tendency to learn pedal pressing to switch on electrical stimulation of certain regions in the brain via implanted electrodes, thereby exhibiting the

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self-stimulation (SS) behavior. This behavior seems to be more preferred than even the otherwise available natural reward of food (5, 8). The SS behavior can be varied by altering the primary locus of stimulation, or making lesions in various brain structures, or varying the parameters of stimulation (9).

METHODS

Adult male Wistar rats (270-340g body weight) were used as subjects. They were housed in pairs and provided with ad libitum food and water. For aggression study a well ventilated standard box of $30 \times 30 \times 30$ cm with a one-way viewing window and having a shocking grid floor was used as a testing chamber. The inter-bar distance of the grid floor was 2.5 cm. Aggression behavior was provoked by placing a pair of rats in the chamber and shocking them by passing current in floor grid bars. A total of 100 electric shocks per session were administered with scrambled polarity at the rate of 13 shocks per minute. Each electric shock was 0.5 second in duration (220 V, 50 Hz frequency). For each pair of rats the optimal shock current intensity was determined by taking into

consideration the mean tail flinch threshold and mean jump threshold (7).

Aggressive responses in a pair of rats were scored either as threat (T), or attack (A) responses (7, 10). In the threat responses (T), subjects assumed an upright posture facing each other, but made no physical contact, whereas in attack response one or both subjects made a physical contact by boxing, jumping, lunging and striking or biting. During threat and attack responses the subjects invariably kept their mouths open and squealed. The sum total of the threat and attack responses constituted the total aggression scores (10). Each pair of rats was observed in the testing chamber for 3 minutes prior to onset of shocking and 5 minutes after the last shock was delivered. This was to verify the presence of any spontaneous aggression in the pair during nonshock periods.

Results are expressed as the probability of attack or threat responses which represents number of attacks or threats per shock delivered (Table I). It was calculated as the total number of responses divided by total number of shocks delivered (11).

Grou	4p n		wher got all	Aggresion scores		Pre- Aggression	Post- Aggression
	no extreminentel na		T Case of th		Total	SS ratel min	SS rate/ min
hile	inducing foot-shock	the pain	grosslop is	al forms ag	of pathologic	mendan Ment	ese functions
A)	Control (C)	8	0.321	0.273	0.593	1130 CHISE FILE	t aggresnon i
			±0.179	±126	±0.270		egression to
	Experimental (E)	8	0.288	0.55*	0.84	lor (3-51) Whi	adonic-hehav
	or of a small cape		±0.19	±0.16	±0.07	e said to be he	
B)	Normal (N)	8	0.435	0.237	0.66	130.25	60.02**
	badonic behavior (3		±0.04	±0.06	±0.08	±10.04	±12.09
	Lesigned (1)	6 (1)	dency to	(anna) 68 abalia	oal with the		
	Lesioned (L)	0 (b	enavior as in E	group) 55 abous	ned		

TABLE I

T : threat responses

^{**} P 0.01

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For self-stimulation or hedonic behavior study, bipolar electrodes were stereotaxically implanted in ventral tegmental area - substantia nigra (VTA-SN) and the rate of pedal presses per minute was used as a quantitative assessment for SS behavior. Each session of SS lasted for 15 minutes. The self-stimulation intensity was set at optimal level to elicit maximal possible pedal pressing rate under 50 Hz sine wave stimulus train of 0.25 sec duration delivered with each pedal pressing.

The experiment was done in two parts -

- A) Effect of septal lesions on aggressive behavior. Bilateral electrolytic lesions of lateral and medial septal nuclei were done in the experimental group (E), while the controls (C) were sham-operated. The site of lesion was confirmed by behavioral criteria (12) (septal irritability), and postmortem histological studies of the lesion site. Aggression scores of the two groups compared and significance tested with Student's t-test.
- B) To assess the modulatory role of aggressive experience on hedonic behavior (SS). Normal subjects (N) and an additional group (L) of subjects from the category (E) were implanted with bipolar electrodes in VTA-SN to study SS behavior. Preaggression and post-aggression SS behavior assessments were done in both the groups. The SS rates obtained before and after the aggression were evaluated by Student's 't' test.

RESULTS

A) A statistically significant increase (P = 0.05) was seen in the number of attack responses (100.87%) in the experimental group (E) as compared to controls (Table I, Fig. 1). In comparison the threat responses remained almost unchanged (10.3%). In total, there was an increase in the number of aggressive responses (41.62%).

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B) The post-aggression SS pedal pressing rates showed a statistically significant decrease (P = 0.01) over the pre-aggression SS rates in the normal group (N) (Fig. 2). The effect persisted for a week, during







Fig. 2 : Rate of pedal pressing for self-stimulation through electrode implanted in ventral tegmental area substantia nigra, before and after an aggression episode. L = rats with septal lesions. Rest of legend as in Fig. 1.

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which time the subjects regained the pedal pressing intermittently. However, in subsequent sessions the ICSS rates returned back to near normals.

In the lesioned group (L) the ICSS behavior was virtually abolished and could not be restored back. Hence, the aggression scoring was not needed to be done in this lesioned group (L), since this was already quantified in the similar group (E) mentioned before. The septal lesions caused enhanced aggressive tendency and diminished responding to the positive reward of SS. During the initial training and priming for SS, the lesioned subject would jump out of the SS chamber. The animal had to be put back in the test chamber and given sufficient time to orient itself before priming could again be given. A step-wise increase or decrease in current intensity of stimulation also did not show much improvement.

DISCUSSION

The salient results of this study were that the attack responses significantly increased in septal lesioned experimental group (E), and also that in such a group of subjects (L) the SS behavior for positive reward was abolished.

Furthermore, in the normal group (N) of subjects without lesions, post-aggression SS pedal pressing rates showed a 50% decrease over the pre-aggression rates. In the lesioned group (L), the SS behavior was virtually abolished, but the animal seemed to be aware of the pedal pressing reward since priming evoked a few responses of pedal pressing at a stretch after which the animal stopped again. Several studies have been reported in past literature on aggressive behavior or SS behavior, but in none of them the effect of aggression generated mood on hedonic behavior was studied. The observation of the increased number of attack responses and total aggressive responses in septal lesioned rats is in accordance with the previous studies (11).

The brain lesion-induced decrease in SS rate could be due to a loss of the mechanism of the reward, or due to a disability of the subject to perform the task because of a motor deficit (9). Since the septal lesioned rats showed good motor ability and also a high aggressive behavior in a suitable environment, there is no basis to suspect a motor disability as the cause of reduced SS pedal pressing behavior in these rats, but to suspect only the loss of the rewarding mechanisms of the SS as an underlying cause of reduction of the SS. Moreover, the lesion seemed to have tilted balance in favor of proneness to excessive state of aggression which might also cause an inhibitory effect on the positive reward mechanisms. This type of an inference is imperative because even in the normal rats with intact septum, the SS was reduced following an aggression experience. Thus the present experiments showed that aggression provoking environment could have a considerable influence on positive reward dependent behavior.

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Abstract: The local analgesic efficacy of EMLA Cream (a eutectic mixture of lidocaine and prilocaine) Astra pharmaccuticals, Sweden) in reducing the pain at Venous cannulation was investigated in a trandomized blind study in 75 children scheduled for elective surgery. In 25 children placeho cream and in 50 children, EMLA cream was applied at the site of venous cannulation 1 hour prior. EMLA Cream was found to be highly effective (84% patients in contrast to 16% patients in placeho group; P<0.005). Local side effects of EMLA Cream were negligible.

Key words: EMLA Cream local

local analgesic cream

painless venous cannulation

INTRODUCTION

A topical anaesthetic can be of great help for a number of painful procedures, but it is difficult to obtain a suitable anaesthetic agent which penetrates deep into the superficial tissues. Although, many local anaesthetic agents have been tried, none has demonstrated a clinical satisfactory efficacy.

EMLA Cream, a recently introduced eutoctic mixture of lidocaine base and prilocaine base in an emulsifier (Arlectone) contains high concentration of active local anaesthetics (80%). This composition (ASTRA pharmaceuticals, Sodertalje, Sweden) is an emulsion and thereby achieves adequate penetration and concentration in the superficial tissues. It has shown promise in relieving the pain associated with short surgical procedures i.e., split skin grafting without additional anaesthesia (1), skin grafting without additional anaesthesia (1), gery (2). It has also been used to provide painfree venous cannulation in some of the studies done abroad (3-7). Due to the paucity of any report on eMLA Cream in Indian literature and the recent availability of this cream to the investigators, we designed the present study to evaluate the efficacy

of EMLA Cream in providing a painfree venepucture in children in our set up.

METHODS

In the present prospective, blind, randomised study, 75 children between the ages of 19,-10 yrs who were scheduled to undergo elective surgery were included. After obtaining the ethical committice clearance, an informed consent was taken from local anaesthetic agents were not included in this study. Patients were premedicated with morphine subplate (0.2 mg/kg i m) 90 min prior to surgery. At this stage patients were divided into 2 groups, i.e., Group A consisting of 25 children (6 males and 6 females in age group 19,-3 yrs; 9 males and placebo cream was applied to the skin over a vein stolected for venous cannulation and Group B males) in age group 14,-3 yrs; 10 males and 15 consisting of 50 children (15 males and 15 females in age group 3-10 yrs) in whom EMLA males) in age group 14,-3 yrs; 10 males and 15 consisting of 50 children (15 males and 15 females in age group 3-10 yrs) in whom EMLA males) in age group 14,-3 yrs; 10 males and 15 consisting of 50 children (15 males and 15 females in age group 3-10 yrs) in whom EMLA females in age group 3-10 yrs) in whom EMLA cream was applied at the similar site. The creambase used in EMLA Cream as well as the placebo

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