

SHORT COMMUNICATION

EFFECT OF MID-DORSAL CAUDATE NUCLEUS ON CONDITIONING FOR PAIN STIMULUS IN RATS

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Abstract : Male rats were subjected to conditioning, with light source as conditioned stimulus, followed by a noxious stimulus applied to the tail as unconditioned stimulus. There was development of conditioned response after a few days, which was inhibited later on.

Bilateral destruction of mid-dorsal caudate nucleus decreased the period of development of conditioned response, but did not alter the period for inhibition of this developed conditioned response, suggesting the role of neostriatum in learning behaviour.

Key words : unconditioned stimulus pain conditioned response caudate nucleus

INTRODUCTION

Pain-induced vocalization in animal is a behavioural response (1, 2). A noxious stimulus applied to an animal elicits varied response in vocalization, depending upon the intensity of the stimulus. The vocalization after-discharge is obtained on increasing the stimulus intensity above the threshold that produces a single vocalization component and depends significantly on the affective state of the animal (3, 4). The conditioned response elicited in an animal to a noxious stimulus disappears after a few days due to activation of intrinsic analgesic circuit (5).

Previous experiments conducted by us on rats with mid-dorsal caudate nuclear lesions have shown interesting responses on hoarding behaviour (6), male sexual behaviour (7) pain threshold alteration (4), sensorimotor orientation (8) and body-weight maintenance (9). However, the role of this area of neostriatum on the learning behaviour in rats (such as conditioning of the animal) has not been studied extensively. The present study was therefore

undertaken to determine its role on conditioning to a noxious stimulus.

METHODS

The study was carried out in 20 male albino rats of ages between 100 to 150 days. Each animal was kept in a separate cage, and food (Hindustan Lever supplemented by vitamins) and water were provided *ad libitum*. The experimental procedure commenced ten days after adaptation to this cage. During this period the animals maintained normal food and water intake and exhibited growth pattern in terms of body weight.

All the experiments were conducted in the morning at about 10 a.m. in a dimly lit air-conditioned room. The experimental design consisted of restraining the animal daily for 60 minutes in a specially made wire-mesh cylindrical cage (length 15 cms diameter 6 cms) with its tail being kept out, without any discomfort to the animal. A period of 4 days was allowed for adaptation in the restraining position for all the animals. It was

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observed that the animals remained quiet for the period of restraint and did not exhibit any distress in the form of vocalization, body movements, urination, defecation, or signs of suffocation.

Electrical stimulation was then applied as a nociceptive stimulus following the method described by Vidal & Jacob (3) with slight modification. For this purpose two small stainless steel needles (gauge 30) were introduced subcutaneously into the middle of the tail, the distance between the two points of the needles being kept at 5 mm. These needle electrodes were stimulated with a Medicare Research Stimulator Model SS44.

The animals underwent a classical conditioning paradigm, consisting of 5 seconds of light as conditioned stimulus (CS), followed immediately by electrical stimulation of the tail as unconditioned stimulus (UCS). The light source consisted of an electric torch bulb kept at a distance of 15 cms in front of the rat. The electrical stimulus consisted of a train of impulses with pulse width of one msec and frequency of 100 Hz applied for 1 second duration. The intensity of this UCS was adjusted for each rat to be just sufficient to obtain vocalization after-discharge response.

Each rat received 20 trials per day on successive days with two minutes interval between trials.

Vocalization after-discharge emitted during the light stimulus constituted conditioned response (CR), while that emitted by shock constituted unconditioned response (UCR).

The CR deemed to have been acquired when the light elicited vocalization in 9 out of 10 consecutive trials. It was likewise deemed to have been inhibited when the light elicited no vocalization for 6 consecutive trials in rats that had previously shown the above stated response (4).

This conditioning procedure was continued till the inhibition of CR that was obtained during the initial period. Those animals which were not conditioned even after 10 days were discarded from

the study. The number of days for development of CR and later its inhibition were recorded.

The animals were then grouped in two groups one group of 14 rats in which bilateral caudate lesioning was done and second group of 6 rats, which had sham operation

Operative procedure : The animals were anaesthetised with ether inhalation. In first group of 14 animal the skull was exposed and stainless steel electrodes (gauge 26), varnished except at the tips and having tip diameter of 150 microns, were passed stereotaxically into right and then left mid-dorsal caudate nuclei at A 7.4 to 8.2, L2 to 3 and H+2 to +3 (10). On each side cathodal current of 2 mA was passed for 60 seconds. In the second group of 6 animals, electrodes were lowered in mid-dorsal caudate nuclei and kept for 60 seconds but no current was passed (Sham operation).

Eight days after the operative procedure the animals were again subjected for conditioning, as carried out before the lesioning. The number of days for the development of CR and its inhibition were noted.

At the completion of study the animals were sacrificed and the locations of the lesions histologically confirmed. Fig. 1 displays the anteroposterior extent of lesion in all the animals belonging to the first group.

RESULTS

In all the animals belonging to the group with caudate lesion, the intensity of the stimulus to produce vocalization afterdischarge increased after destruction of mid-dorsal caudate nuclei. As compared to this, the strength of the stimulus to produce this response did not change in animals with the sham operation.

Of the 14 animals in the lesioned group, there was decrease in period of days for conditioning in 12 animals while there was no change in 2 animals.

TABLE I

	<i>Animals with caudate lesion</i>		<i>Animals with sham operation</i>	
	<i>Before lesion</i>	<i>After lesion</i>	<i>Before operation</i>	<i>After operation</i>
Development of conditioned reflex	4.6 ± 1.28	3.4 ± 1.34*	3.7 ± 0.82	3.2 ± 0.75
Inhibition of developed CR	3.0 ± 0.78	3.6 ± 2.73	3.2 ± 0.75	2.5 ± 0.55

Reading in mean number of days ± standard deviation. *P < 0.05

This decrease in the period of days was statistically significant (P < 0.05).

In the sham operated group of animals, though there was decrease in number of days for conditioning in 4 animals, it was not statistically significant.

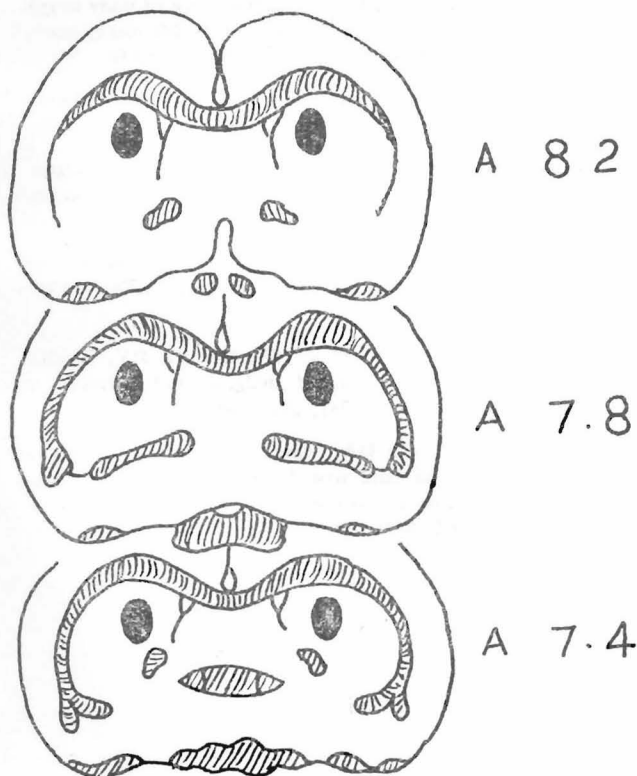
However, there was no significant change in the period of inhibition of the developed conditioned response, in both the lesioned and the sham operated animals.

Table I shows the mean results for the development and inhibition of the conditioned response in lesioned and sham operated groups.

DISCUSSION

Application of pain stimulus to the tail of a rat produces different responses depending upon the intensity of the stimulus. With low voltage stimulus there is tail withdrawal which is a spinal reflex. With further increase in strength of this stimulus the response, in addition, is simple vocalization, a reflex involving lower brain stem. Vocalization afterdischarge response is obtained at still higher voltage of the stimulus due to activity in higher centers of the brain (3). Conditioning, being a learning process in an animal, will occur only when higher functions of the brain are involved to influence the affective state of the animal. Hence the response of vocalization afterdischarge elicited by tail stimulation with higher voltage in a restrained animal is taken as a criterion for conditioning in the present study.

Bilateral lesions of mid-dorsal caudate nuclei increase the pain threshold resulting from electrical stimulation of the tail (7). This is in conformation with the present study as after bilateral destruction of this brain region the intensity of stimulus required to obtain vocalization afterdischarge increase.



Coronal section of rat's brain at the levels A8-2, A7-8 and A7-4 (De Groot stereotaxic coordinates). The extent of lesion is shown in block on both sides.

The stress produced by immobilization of the animal and the stronger noxious stimulus (thus creating learned helplessness) activates the endogenous opiate mediated analgesic circuit (11, 12, 13, 14). Once activated this analgesic circuit suppresses pain on presentation of the conditioned stimulus, through its effect on the affective state of the animal (4).

In the present study mid-dorsal caudate lesion diminished the period of conditioning. This suggests the possible role of this part of caudate nucleus

over learning behaviour of conditioning during association between light and noxious stimuli.

However, bilateral mid-dorsal caudate destruction does not significantly alter the period of inhibition of the developed conditioned response. The inhibition of this conditioned response is the result of activation of endogenous opiate mediated analgesic circuit, due to presentation of noxious stimulus in a stressful environment (i.e. immobilization). Thus it appears that mid-dorsal caudate nucleus does not play any role in modifying the activity of this analgesic circuit.

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