EFFECT OF BILATERAL CAUDATAL LESION ON PAIN THRESHOLD IN RATS

V. K. MULGAONKER AND M. G. GOGATE

Department of Physiology,
Goa Medical College,
Bambolim, P.O.-Santa-Curz Goa - 403 005

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Summary: Pain threshold was determined in eleven adult male rats (Haffkine strain) on electrical stimulation of midpart of tail. Three responses, namely tail withdrawal, vocalization and vocalization afterdischarge were studied. Of these eleven animals, seven in experimental group were subjected to bilateral electrolytic lesion of mid-dorsal caudate nucleus while remaining four animals were sham operated. The increase in pain threshold after caudatal destruction for all the three responses suggests the possible modulatory role of mid-dorsal caudate nucleus in the mechanism of pain.

Key words: pain threshold, electrical stimulation, tail, mid-dorsal caudate nucleus, electrolytic lesion

INTRODUCTION

The role of different structures in Central Nervous System in modulating the pain sensation to various types of noxious stimuli has been extensively studied and reported by many workers. Electrical stimulation of Nucleus Raphe Magnus (17, 18, 19), Ventrolateral aspect of Midbrain Periaqueductal Gray (12, 14, 21) and Periventricular Thalamic sites (22) causes profound analgesia without any behavioral depression. Stimulation of Medial Forebrain Bundle and Lateral Hypothalamus also reduces threshold to pain (2, 5, 23, 30). Stimulation of Dorsal Column in man causes varied threshold responses to painful stimuli (16, 25). Other areas in brain such as Internal Capsule and Ventrobasal Thalamic Nucleus in man (1, 8) Septum in primates, man and rat (24, 9, 4) and cerebellum in primates (27) are also reported to have caused varied threshold responses to pain. Reports are also available on the role of Caudate Nucleus on modulation of pain threshold in monkey (13, 24) and man (7, 11). However these workers have not been manipulating the same area in Caudate Nucleus as regards its influence on pain threshold.

In most of the studies reported so far the modulation of pain threshold was observed to be brought about after stimulation of different subcortical areas. Alteration in pain threshold has not been extensively studied after destroying localized areas in the brainstem other than Medical Hypothalamus (28) and Raphe Magnus (20).
The present work is therefore, carried out to study the effect of bilateral destruction of Mid-dorsal Caudate Nucleus in rats in modulation of pain threshold. This area of neostriatum has been manipulated because there were other interesting responses from this area (9, 15).

MATERIAL AND METHOD

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

All the experiments were started in the morning at about 10 A.M. The experimental pattern consisted of restraining the animals for 30 min in the talcum powder tin cut longitudinally so as to accommodate the average animal, head and tail being kept out without any discomfort to the animal. A period of four days was allowed for adaptation in the restraining position for all the animals. It was observed that the animals remained quiet for the period of restraint and did not exhibit distress in the form of vocalization, body movements, urination, defecation or signs of suffocation.

Electrical stimulation was then used as a nociceptive stimulus as employed by Vidal and Jacob (28) with slight modification. For this purpose two small stainless steel needles (gauge 30) were introduced into the middle of the tail subcutaneously and the distance between these two points of needle introduction was kept at half a centimeter. The points where the needles were introduced were marked by India Ink.

At the end of adaptation the tail sites were stimulated by rectangular wave stimulator delivering stimuli to these needles for nociceptive testing.

The stimuli consisted of a train of fixed one second duration, with pulse width of 1.5 msec at a frequency of 100/sec. In order to determine the threshold for the tail withdrawal, vocalization and vocalization afterdischarge the voltages were progressively increased in steps by 0.1 volt. An interval of five minutes was kept between two electric shocks in the same animal.

Three types of pain threshold were determined as indicated below

1. A low intensity stimulation producing motor response - tail withdrawal - regarded as spinal reflex.
2. A higher voltage causing a simple vocalization or squeak considered as reflex involving the lower brain stem and 

3. A still higher voltage producing vocalization afterdischarge—persisting after cessation of stimulus. This may represent the affective component of pain responses (involving hypothalamus and rhinencephalon).

The above procedure was carried out thrice in a day in the same rat with an interval of 15 min between the two procedures, for six days. The threshold remained nearly constant during the last four days. The mean reading of last three days was taken as the mean threshold for the three nociceptive responses.

Operative procedure:

The animals were randomly grouped into operated and sham. All the animals were anaesthetized with nembutal intraperitoneally. The skull was exposed and stainless

![Fig. 1: Coronal sections of Rat's brain at the levels A 8.2, A 7.8 and A 7.4 (De Groot Stereotaxic Coordinates). The extent of the lesion is shown in black on both sides.](image)
steel electrodes (gauge 26) varnished except at the tip and having tip diameter of 150 microns were passed stereotaxically into right and left mid-dorsal caudate at A 7.4 to 8.2, L 2 to 3 and H +2 to +3 (6) and anodal current of 2 mA was passed for thirty seconds in seven animals (operated series). Electrodes were lowered in the mid-dorsal caudate in four animals without producing lesion (Sham series).

Nociceptive testing was done in both series after 5th, 8th, 12th and 15th day of lesion. The post lesion stimulation was repeated three times in a day as was done before the lesion, and mean threshold for each response was determined. At the end of the experiment the animal was sacrificed and histological confirmation of the lesion was done as per Prussian Blue Technique (26) as shown in Fig. 1.

RESULTS

All the seven animals in experimental series showed a rise in pain threshold for the three nociceptive responses tested as compared to the four sham operated series. The mean results of caudate nucleus on pain threshold before and after caudatal lesion are listed in Table I. Statistical analysis of these results show that of the three nociceptive

<table>
<thead>
<tr>
<th>Tail withdrawal</th>
<th>Vocalization</th>
<th>Vocalization afterdischarge</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>E</td>
</tr>
<tr>
<td>Before lesion</td>
<td>0.79±0.2382</td>
<td>0.58±0.1746</td>
</tr>
<tr>
<td>5 days after</td>
<td>0.76±0.3808</td>
<td>1.11±0.2609*</td>
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<tr>
<td>lesion</td>
<td>0.75±0.3738</td>
<td>1.19±0.4176*</td>
</tr>
<tr>
<td>8 days after</td>
<td>0.6±0.228</td>
<td>1.1±0.4317*</td>
</tr>
<tr>
<td>lesion</td>
<td>0.82±0.3629</td>
<td>1.5±0.5435*</td>
</tr>
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Pain threshold (Mean±standard deviation) in volts in experimental and sham operated animals.

S = Sham operated series. E = Experimental series. * = P<0.05
responses studied, the increase in pain threshold for pain withdrawal and vocalization was significant \((P<0.05)\). Though the third response, namely vocalization afterdischarge, also showed a rise in pain threshold after the lesion it was not found to be statistically significant.

Separate groups of rats showed that there were arousal disturbances manifested in akinesia, somnolence, hypophagia, hypodipsia and a few sensorimotor disturbances for two to three days after the lesion. All these changes disappeared subsequently.

**DISCUSSION**

Irrespective of type of response, the present study indicates that in rats, lesion of mid-dorsal caudate nucleus produced analgesic effect as manifested by sustained increase in pain threshold after electrical stimulation of the tail.

Manipulation of caudate nucleus is known to alter the emotional and motor behaviour associated changes in the EEG activity. It could therefore be argued that the increased pain threshold after the mid-dorsal caudatal destruction was due to reduction in the overall levels of arousal and motor activity. However, in the present study, the animals did not exhibit any change in motor activity, food and water intake four to five days after the bilateral caudatal lesion.

Caudate nucleus is known to have opiate receptors which are concerned with modulation of pain sensation. High concentration of encephalin is present in caudate nucleus (29). It has also been documented that caudate nucleus in monkey has both facilitatory as well as inhibitory influences on pain reactivity depending upon the site (13).

It thus suggests that in addition to opiate analgesic system there is probably also an antagonistic system in caudate nucleus which feeds back on opiate analgesic system and thus maintains a balance in pain threshold. The nature of this antagonistic system has not been still resolved. This antagonistic system may be inhibiting the activity of local opiate system. Caudate nucleus has different sets of neurons present in it such as dopaminergic, GABAergic and cholinergic and those releasing some other transmitter substance such as substance P, cholecystokinin and angiotensin II as caudate has been found to be containing the necessary converting enzyme. It is likely that a few of these neurones might inhibit the opiate analgesic system.

It has also been documented that the output system of the neostriatum can be divided into two functional efferent systems since spiny I cell with its neurotransmitter GABA exerts inhibitory action while spiny II cell identified with substance P exerts excitation (10). Stimulation of neostriatum exerts either an excitatory or inhibitory influence via its efferent pathway.
It thus appears that caudate nucleus in rat has both facilitatory and inhibitory effects on pain threshold. The nature of control between these two opposing effects remains a problem to be investigated. It can thus be hypothetized from these observations that each structure in the brain has both facilitatory and inhibitory control over any particular behaviour in an animal. Such effects are comparable with feeding and satiety as controlled by different structures in the hypothalamus. Inhibition or super-normal stimulation of one control system is the final deciding factor in any behavioral change in that animal.

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REFERENCES


