EFFECT OF NIALAMIDE INFUSION INTO THE THIRD CEREBRAL VENTRICLE ON SEX BEHAVIOUR OF MALE RATS

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Summary: Sex behaviour of randomly selected adult albino male rats was assessed by observing items like pursuit of the female mounting, intromission and ejaculation in terms of their respective frequency and latency with the help of a multichannel event recorder. A number of rats though exhibited the pursuit, did not mount the female even when tested on 10 consecutive trials. They had a low level of sex drive score (SDS) i.e. 1.09±0.09 inspite of a normal locomotor activity. These were designated as non-mounter rats. The mounter rats exhibited a wide variation in various items of sex behaviour, mean values being: SDS = 6.95±0.23, mount frequency = 22.4±0.76, intromission frequency = 20.1±0.7, mount latency = 22.27±1.72 sec, intromission latency = 23.06±1.72 sec. Ejaculation latency varied between 3 and 22 min.

Infusion of nialamide into the III ICV produced an initial inhibition (within 5 min to 2 hr) followed by an excitation of sex behaviour (2 hr and later). At the time of inhibition frequencies of various sex items were markedly reduced and latencies markedly increased. This was accompanied by a marked fall in the SDS. The reverse effects were obtained at the time of excitation. The inhibitory and excitatory effects were also noted in the non-mounter rats, the inhibitory effect manifested in terms of decrease in the pursuit of female and increase in rest percentage. The excitatory effect manifested by converting the non-mounters into mounters some of whom also intromitted and ejaculated. These effects when tested at two different dose levels of 50 μg and 200 $\mu g/kg$ were found to be dose-dependant.

Since nialamide, a monoamine oxidase inhibitor when injected in III ICV would increase the concentration of all amines i.e. 5 HT, noradrenaline, adrenaline and dopamine in hypothalamic sites controlling sex behaviour, the dual inhibitory-excitatory effect on sex behaviour would possibly be due to differential accumulation of various amines in these brain regions at any particular time.

Key words: male sex behaviour, nialamide, hypothalamic controls, brain amines

INTRODUCTION

Neuropharmacological agents affecting the synthesis (1,19,20,23,27), storage (10,17), release (7), and breakdown (11,19) of monoaminergic neurotransmitters and those which cause the stimulation (3,6,7,19), and blockade (19) of the monoaminergic receptors have been shown to modify the copulatory behaviour of male rats. It has been suggested that an increase in the dopaminergic tone stimulates the male copulatory behaviour, serotonin inhibits it while any change in the noradrenergic tone has no direct effect (14,19,22,23).

Since long the lesion and stimulation studies have indicated a pivotal role for hypothalamus especially the medial preoptic areas and the medial forebrain bundle over its

antero-posterior extent in the control of male sex behaviour of rats (13,18,21,25). Interes tingly the majority of the ascending monoaminergic pathways converge and pass in th median forebrain bundle (2,17,37). The effect on the male sex behaviour elicited by th peripheral administration of various neuropharmacological agents as mentioned above ar probably brought about by the changes in the activity of the monoaminergic pathways cours ing in or projecting to the hypothalamus and telencephalon. However, there does not seem to be any significant evidence whereby these central nervous areas have been directl manipulated by neuropharmacological agents to affect the activity of central amines an show corresponding changes in the male sex behaviour.

The present study was undertaken to investigate the role of monoaminergic pathway in the control of male sex behaviour in rat by directly infusing some neuropharmacologica agents into the 3rd cerebral ventricle so as to manipulate the neurones and pathways coursin in the hypothalamus. This paper reports the effects of nialamide, a monoamine oxidase inhibitor when infused in this manner.

MATERIALS AND METHODS

Male albino rats weighing 250-300 g supplied by the rodent colony of the All India Institute of Medical Sciences, New Delhi were housed in individual polypropylene cages and maintained at controlled temperature and light. Tap water and synthetic pellet diet were provided *ad lib*.

Preparation of sexually receptive female

Bilaterally ovariectomised female rats weighing 150-200 g were treated with 25 *µg* of 17-beta-oestradiol benzoate subcutaneously (s.c.) followed by 1 *mg* of progesterone s.c. after 48 hr. These animals were used as receptive females 6-10 hrs after the progesterone injection. With this method female rats were brought into a fairly stable level of sexual receptivity at a time when behavioural testing was performed.

Test procedure for male sex behaviour

A wooden cage (45x30x30 cm) with one side made of glass to facilitate visual observations and provided with a round window in the ceiling to provide light and ventilation served as the test cage. Only dim and diffuse light was allowed. Sudden and strong sound was avoided. Test male rat was transferred and allowed to adjust to the cage at least for 5 min or more and until it stopped urination or/and defaecation that sometimes occurs during this period. After such adjustment the rat usually exhibited exploratory activity and some self-grooming. Introduction of a receptive female rat into the test cage at this time marked the beginning of the test.

Behavioural events were recorded on an event recorder consisting of a series of signal markers, tap keys and a kymograph providing the recording surface. Recording was carried out for a period of 10 min as a rule. However, ejaculation latency was noted if it took more than 10 min. If the animal did not ejaculate by 30 min after the initiation of the test, it was returned to its home cage.

Parameters recorded for the male sex behaviour in each rat were (i) pursuit of the female (ii) mounting (iii) genital licking by the male (iv) intromission and (v) ejaculation. In addition observations were also made on the motor activity of the rate if it was oriented towards self or the environment (Fig. 1-A,B).

DEFINITIONS

Pursuit: Male approaching the female, nibbling at the head or the body of the female, examining or sniffing her anogenital region, or placing the forelimbs on her body from any direction but without any pelvic thrusts are included in this parameter (Fig.1-C,D).

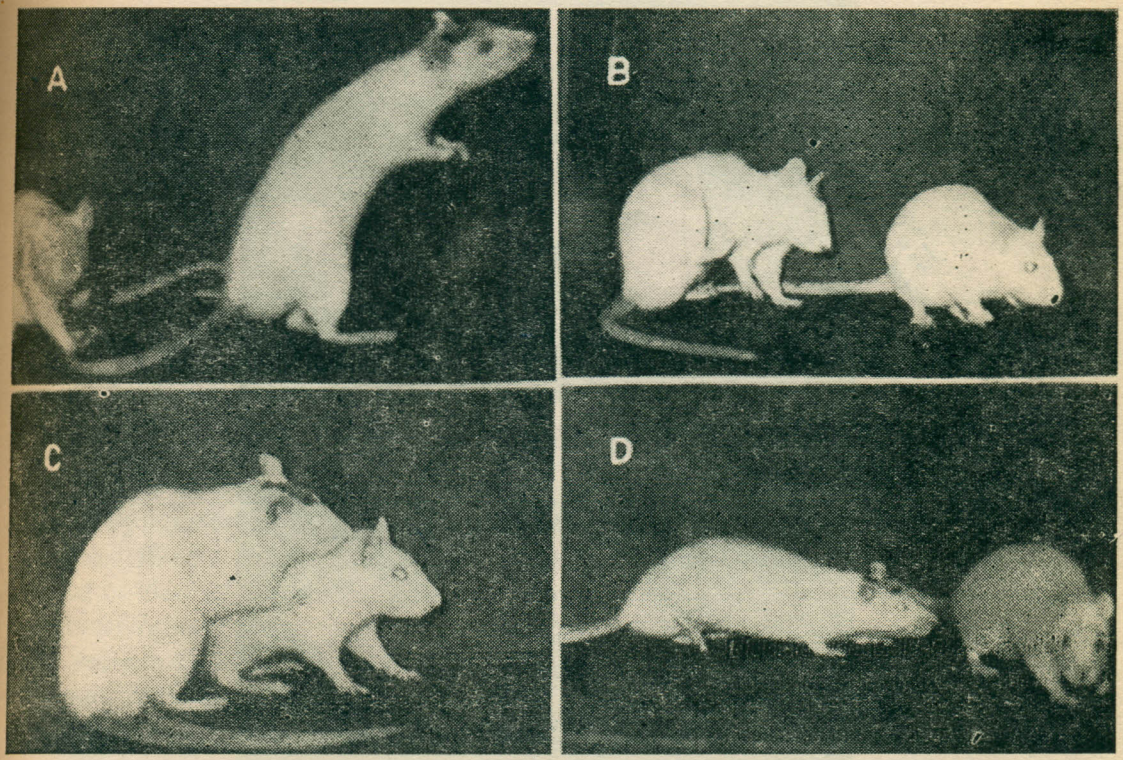


Fig. 1 : Shows various types of extra-coital activity observed in the male rat at the time of a test trial. (a) Environment-oriented activity. (b) Self-oriented activity (self-grooming), (c) Pursuit of the female involving licking and biting. (d) Pursuit of the female involving ano-vaginal sniffing.

Mounting: Male clasping and palpating the female's sides with simultaneou pelvic thrusting from the rear (Fig.2).

Intromission : Mounting followed by sudden backward lunge fol owed by genita licking (Fig.2).

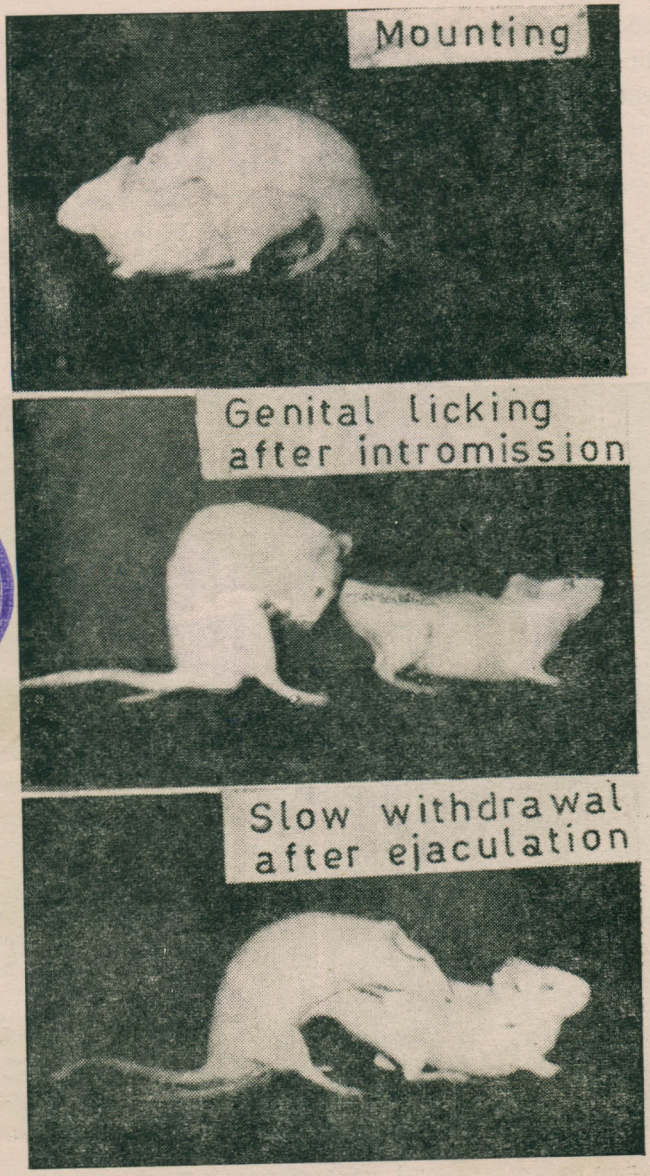


Fig. 2 : Snaps taken during a test procedure showing the three events representing mounting, intromission and ejaculation.

Ejaculation: Spasmodic pelvic thrusting and prolonged intromission followed by slow withdrawal from female's back was recognised as ejaculation (Fig.2).

Mount latency: Time in seconds from the time of introduction of the female into the test cage to the first mount.

Intromission latency: Time in seconds from the time of introduction of the female into the test cage to the first intromission.

Ejaculation latency : Time in minutes and seconds from the time of introduction of the female into the test cage to ejaculation.

Mount frequency: Number of mounts per 10 min were calculated. If the animal took more than 10 min to ejaculate, the number of mounts achieved in the first 10 min were counted. If the animals ejaculated in less than 10 min, the frequency was calculated as follows:

$$10 \times \frac{\text{Number of mounts}}{\text{Time taken for ejaculation (min)}}$$

Intromission frequency: Number of intromission per ten minutes calculated in the same way as in case of mount frequency.

Rest percentage: The percentage of 10 min during which the animals did not show any activity.

Sex drive score (SDS)

For the purpose of quantification of the male sex behaviour weightage was given to different components of male sex behaviour. Pursuit (A), pursuit plus mount (B) pursuit plus intromission (C) and pursuit plus ejaculation (D) were the four 'sexual behaviour patterns' considered to be indicating an increasing degree of sex drive. If the pursuit was not followed by mounting a score of 1 was given with the condition that pursuit was continued for at least 15 sec. A score of 2 for B, 3 for C and 4 for D was given. This order is justified in view of the observations that these elements appear in this sequence during sexual maturation (31); disappear in the reverse order after castration and reappear in the same sequence with androgen treatment after castration (4,32). The weighted counts of all events were added up and divided by the test period. The resultant sum was taken as indicative of sex drive and termed as *Sex Drive Score* (SDS).

Besides these observations the number of animals which exhibited mounting, intromission, ejaculation and rest pauses in each group of ten animals was also noted.

Stereotaxic implantation of the cannula into the 3rd ventricle (Fig.3)

The cannula was prepared from 22 gauge stainless steel tubing of 22 mm length. A trocar reaching the lower tip of the cannula was locked in position with the help of a loop soldered approximately 6 mm below the top of the cannula. All the test males were implanted with the cannula into the 3rd ventricle according to the co-ordinates of the de-Groot atlas (9). These were : antero-posterior = 1.4 mm anterior to lambda at the midsagitta

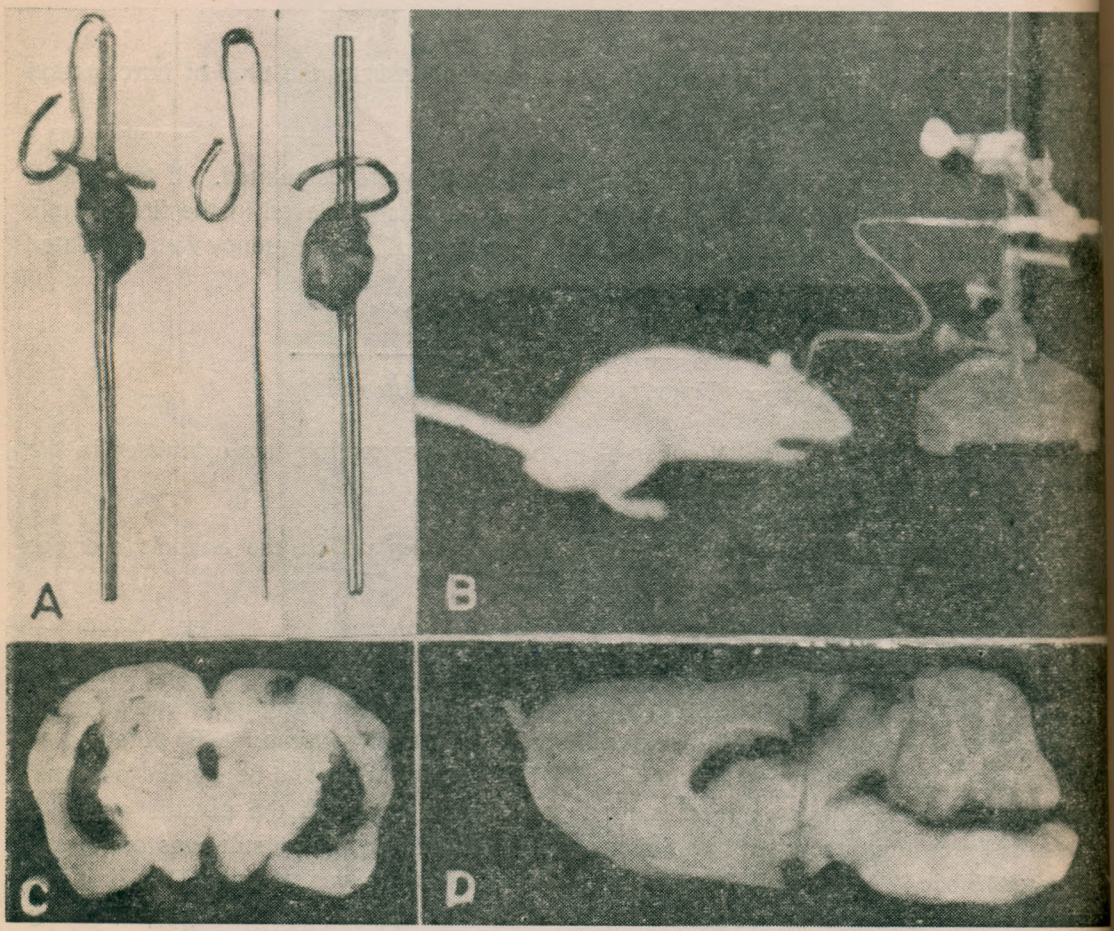


Fig. 3 : (A) Shows (i) a cannula with the trocar inserted into it and locked in position (left), (ii) the trocar that fits snugly into the cannula (middle) and (iii) the cannula without the trocar on which a loop of steel wire is soldered to provide anchorage for the trocar (right).

(B) Rat with a permanently implanted cannula in the 3rd cerebral ventricle. The cannula is connected with a Hamilton syringe through a polyetheyline tube for microinfusion of various solutions.

(C) Coronal section of the rat brain showing deposits of India ink in the cerebral ventricles.

(D) Saggital section of the rat brain. The deposits of India ink can be noted in various ventricles. Note also the track made by the cannula leading to the third ventricle.

line, and vertical 8.3 - 8.5 mm from the surface of the cortex, the cannula directed anteriorly 30 to the vertical plane while the incisor bar was positioned 5 mm above the interaural line. The cannula was fixed to the skull surface by slowly building up the dental cement around the cannula and the anchors. At the end of implantation the trocar was removed to find the reflux of the cerebrospinal fluid (CSF) through the cannula. If the CSF was not leaking the animals were discarded. At the end of the experiment at the time of sacrificing the animal, India ink was injected into the 3rd cerebral ventrical and the brain was fixed in all animals. Sections of approximately 1 mm thickness were cut by hand to find India ink in the ventricles and 10 μ thick sections were also made to verify the position of the cannula in 2 out of 10 animals in each group.

Infusion of substances into the 3rd ventricle (ICV)

An inner infusion cannula of 28 gauge was inserted through the chronically implanted 22 gauge outer cannula to reach the third ventricle. Through a light weight teflon tubing (Small Parts Inc., USA) the inner perfusion cannula was connected to 20 μl Hamilton syringe. Infusion into the 3rd ventricle was done slowly each infusion taking a period of about 5 min.

The 3rd ventricular cannulated test male rats, at least 10 days after the surgical operation, were tested with the sexually receptive female on successive days until they showed a regular pattern of sex behaviour. Tests were then carried out after infusing nialamide (Sigma Chemical Co., USA) at two different doses of 50 and 200 $\mu g/kg$ in 20 μl of saline, at intervals of 5 min, 2 hr, and 24 hr and on subsequent days. After the infusion controls were kept by the infusion of 20 μl of normal saline which was the vehicle for dissolving nialamide.

Data analysis

The control and experimental scores were compared with the normal scores. Percentage change from normal of all the parameters was calculated. Median values were used for evaluation and the data were statistically analysed using Friedman's two way analysis of variance, a non-parametric test as per Siegel (29).

RESULTS

SEX BEHAVIOUR OF RANDOMLY SELECTED MALE RATS

There were some rats which did not show any mounting when trials were performed on ten consecutive days (10 trials). These animals did show pursuit of the female thus acquiring a low level of SDS (1.09 ± 0.09). Such animals evidently did not show any intromission and ejaculation. Their locomotor activity however, remained within the normal range without showing any rest pauses. These rats were designated as *non-mounter rats.*

On the other hand there were rats which showed mounting on the very first contr trial and were designated as *mounter rats.* These animals showed sex behaviour of variou grades with an SDS ranging between 2.5 and 16.0 (mean value 6.95±0.23). The numbe of rats at the extremes of scale was very small. Out of a total of 120 mounter rats onl 4 had an SDS less than 4 and 6 had more than 10. Thus an overwhelming majority i.e. 91.7% had an SDS between 4.0 and 10.0. The sex events of an average rat as charte from the event recorder are reproduced in Fig.4.

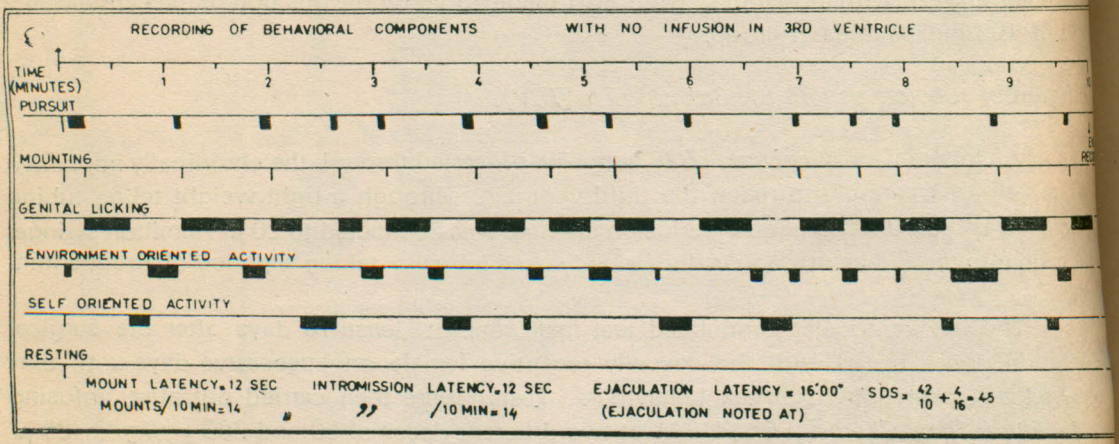


Fig. 4 : Shows the various events of sex behaviour as charted from an event recorder. The sex drive score was calculated from such records.

The mount frequency in these rats ranged between 6 and 55/10 min (mean 22.4 ±0.76). Only 3 animals had a frequency of less than 10 and 14 had more than 30. Thus 85.8% of the 120 rats had a mount frequency between 10 and 30/10 min. Similar was the situation with respect to intromission frequency which had a mean value of 20.1±0.7 10 min.

Similarly most rats (92.5%) had a mount latency between 5 and 60 sec (mean value 22.27±1.72), and intromission latency also between 5 and 60 sec (mean value 23.06±1.72). The ejaculation latency varied between 3 and 22 min, but was less than 4 min only in 5 rats and more than 15 in only 18 rats leaving a vast majority which ejaculated within a period of 4 to 15 min after the start of the trial.

EFFECT OF NIALAMIDE

The effect of III ICV infusion of nialamide was assessed at 50 as well as 200 $\mu g/kg$ in both mounter and non-mounter rats. Besides the control trials, tests were performed at intervals of 5 min, 2, 24, 48 and 72 hours after infusion.

Nialamide at 50 μg/kg: The results obtained are given in Table I. The significant decrease in the mount and intromission frequencies leading to a decrease in SDS that occurred at 2 hr after infusion may be noted. Such inhibition is also reflected in the marked increase in various latencies that occured in trials conducted at that time. Group analysis showed that out of 10 animals one animal did not exhibit mounting at all, 2 did not show intromission and 6 did not ejaculate. Three of these animals exhibited frequent rest pauses during the trial. In the non-mounter rats in which the sex activity is already at very low level, further inhibitory effects were not so marked. Even so the SDS was reduced to half the control level which was due primarily to the partial loss of even the pursuit of the female and 8 of the 10 non-mounters showed rest pauses during the trials. After the initial inhibition observed in these trials the animals recovered and started showing sex activity which

TABLE I : Effect of infusion of nialamide 50 μg/kg into the III ventricle (ICV) on copulatory behaviour of male mounter (A) and non–mounter (B) rats (median values).

Parameters	*Normal*	*After ICV saline 5 min*	*After ICV nialamide*				
			5 min	*2 hr*	*24 hr*	*48 hr*	*72 hr*
(A)							
SDS	5.5	5.9 (−7.0)	5.2 (−6.2)	2.3* (−62.9)	7.6* (+30.6)	7.2 (−1.1)	5.5 (−4.8)
Mounts/10 min	17.5	18.5 (−5.1)	16.5 (−4.1)	7.0* (−56.3)	25.0* (+27.7)	24.5 (−1.7)	17.5 (−5.0)
Intromissions/10 min	17.5	17.0 (−1.8)	16.0 (−4.7)	4.0 (−77.6)	24.0** (+34.3)	22.5 (+4.5)	17.0 (0)
Mount latency (sec)	13.5	13.5 (−5.0)	15.0 (0)	77.5** (+185)	7.5** (−53.6)	10.0 (−26.8)	12.5 (−4.8)
Intromission latency (sec)	13.5	13.5 (0)	15.0 (0)	77.5* (+446)	7.5* (−50.0)	10.0 (−22.5)	12.5 (0)
Ejaculation latency (min)	14′00″	13′38″ (+1.1)	13′45″ (−1.2)	—* (+α)	9′53″* (−25.5)	10′53″ (−0.5)	11′50 (0)
Rest percentage	0	0	0	0	0	0	0
(B)							
SDS	1.1	1.0	1.0	0.5*	1.8*	1.0	1.0
Mounts/10 min	0	0	0	0	6.0*	0	0
Intromissions/10 min	0	0	0	0	5.0*	0	0
Mount latency (sec)	—	—	—	—	82.5*	—	—
Intromission latency (sec)	—	—	—	—	87.5*	—	—
Ejaculation latency (min)	—	—	—		—	—	—
Rest percentage	0	0	0	52.0**	0	0	0

*P<0.05; **P<0.01

Values in brackets indicate the median of percentage change from normal.

was more vigorous than the controls. Thus in trials conducted at 24 hr after III IVC in fusion of nialamide the SDS increased to 7.6 i.e. increase of 30.6% over the control value which was due to an increase in the mount and intromission frequencies. All latencie registered a marked decrease. Such excitatory effects were also observed in the non mounter rats six of whom out of a group of ten exhibited mounting and intromissio and three even ejaculated. While the mounter rats slowly recovered from this excitato phase showing near normal values at 72 hr, some of the non-mounter rats continued exhibi ing mounting even at 72 hr after infusion of nialamide (2 out of 10).

Nialamide at 200 μg/kg: The results are given in Table II. It may be noted that with th dose the inhibitory effect was immediate. Group analysis showed that in 9 out of 10 animal there was a complete abolition of mounting, intromission and ejaculation. All these

TABLE II : Effect of infusion of nialamide 200 μg/kg into the III ventricle (ICV) on the copulatory behaviour of male mounter (A) and non–mounter (B) rats (median values).

Parameters	Normal	After ICV saline 5 min	After ICV nialamide 5 min	2 hr	24 hr
(A)					
SDS	4.2	4.2 (+1.0)	0.1** (−94.1)	8.1** (+75.1)	4.2 (−0.1)
Mounts/10 min	13.0	13.0 (−2.3)	0** (−100)	25.0** (+79.8)	13.0 (0)
Intromissions/10 min	12.5	12.5 (0)	0** (−100)	24.5** (+75.9)	13.0 (−3.4)
Mount latency (sec)	33.5	50.0 (−5.0)	—** (+α)	5.0** (−81.6)	52.0 (−8.4)
Intromission latency (sec)	36.0	50.0 (+10.0)	—* (+α)	5.0** (−84.2)	52.0 (+8.3)
Ejaculation latency (min)	17'25"	17'30" (+1.2)	—** (+α)	7'43"** (−57.3)	17'10" (+1.5)
Rest percentage	0	0	75.5**	0	0
(B)					
SDS	1.2	1.3	0.2**	3.6*	1.1
Mounts/10 min	0	0	0	15.0**	0
Intromissions/10 min	0	0	0	11.5**	0
Mount laency (sec)	—	—	—	70.0**	—
Intromission latency (sec)	—	—	—	85.0*	—
Ejaculation latency (min)	—	—	—	16'00"*	—
Rest percentage	0	0	61.0***	0	0

*P<0.05; **P<0.01; ***P<0.001

Values in brackets indicate the median of percentage change from normal.

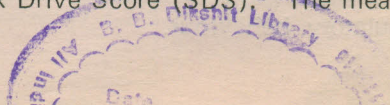
animals showed markedly decreased motor activity and continued rest pauses. The SDS dipped down to a rather low level of 0.1 as against the control value of 4.2. Eight of the 10 non-mounter rats also showed decreased motor activity and marked resting abolishing the pursuit of the female. This led to a decrease of SDS from a control level of 1.3 to as low a figure as 0.2 within five minutes of nialamide infusion.

But in these animals recovery was also quicker and the excitatory effects became manifest when trials were conducted at 2 hour after nialamide infusion. Mount and intromission frequencies increased markedly. Latencies showed a marked decrease and the SDS registered a level of 8.1 as against the controls standing at 4.2. Similarly with respect to the 10 non-mounters tested at 2 hr, 8 became mounters and exhibited intromission, their frequencies very nearly reaching the averages achieved by the mounter controls, and their SDS increased from the control levels of 1.2 and 1.3 to 3.6. These excitatory effects in mounters as well as non-mounters did not persist longer than 24 hours for when tested at that time the values of various sex events had already come back to the near normal levels.

It may also be noted from Table I and II that the values of various items of male sex behaviour after the III ICV infusion of 0.85% saline in the same volume as the nialamide solution remained practically the same as obtained in the normal controls.

DISCUSSION

Methods used in the assessment of copulatory behaviour of rats for testing the effects of drugs have been critically reviewed by Dewsbury (10). In some experimental designs, male-to-male mounting has been used to indicate the hypersexuality (27,28,36), which of course does not occur under normal conditions. Using male-to-female copulation method, some authors allowed continuous mating until exhaustion took place (1,5,11). This method though allowed a consideration of large number of sexual parameters, tests could be repeated only after recovery from exhaustion. Therefore, the time course of action of the drug is difficult to assess by this method. Malamnas (19) used castrated rats treated with suboptimal doses of testosterone and allowed only 3 min for testing which is a rather short period. No wonder information on ejaculation is missing often from this paper. Scoring procedures for determining sex drive have been used earlier (15,31-33). We have followed a procedure in which mount and intromission frequencies and time of ejaculation could be noted on an event marker and latencies to mount, intromission and ejaculation could be calculated with precision. Extracoital activity was also recorded. For comprehensive projection of the sex drive, a quantitative method was devised in which the extracoital activity (pursuit of the female), mount without intromission, intromission and ejaculation were allotted suitable weights in an ascending order and the integrated score was calculated per min which was termed as Sex Drive Score (SDS). The measurement



of time spent in complete lack of any activity, sexual or locomotor which was termed as res percentage enabled us to assess inhibitory effects on the locomotor activity, giving also a indication of the arousal state of the animal. In addition the number of animals in each grou of 10 which showed mounting, intromission, ejaculation and resting were also noted t enhance the significance of observations. Sufficient time was allowed for ejaculation t occur. Since there was no sexual exhaustion, the tests could be conducted more naturall every day.

A number of studies have been reported in which neuropharmacological agent affecting monoamine metabolism have been systemically administered to assess the effec on sex behaviour (10-13, 19,20,22,23,26,30,34-36). Systemic administration of thes agents presumably modified the activity of monoaminergic pathways in brain areas controll ing the male sex behaviour. However, a more exact correlation of this nature may be achiev ed if such neuropharmacological agents are introduced directly into the 3rd ventricle fro where these could permeate specifically into brain areas controlling sex behaviour.

In the earlier studies, systemic administration of monoamine oxidase inhibitors have consistently demonstrated an inhibitory effect on male copulatory behaviour. Dewsbur and colleagues (10-12) demonstrated increases of mount and intromission latencies latencies of successive ejaculations and postejaculatory interval without much effect o mount and intromission frequencies with 50 and 100 *mg/kg* nialamide administered intra peritoneally. Other reports indicate that with the administration of 100-125 *mg/kg* o nialamide there is no effct on copulatory behaviour except a small decrease in locomoto activity but at 250 *mg/kg* i.p. it caused a reduction in the mount and intromission percentage and an increase in the mount and intromission latencies. With such high doses inhibitio was accompanied by increased motor activity (19,23). Pargyline too has been used t assess the effect of MAO inhibition on male copulatory behaviour (1,35). In all these studies, inhibition in the male sex behaviour occurred along with an increase in the locomoto activity. However, with daily administration of iproniazid over a number of days Soulaira and Soulairac demonstrated a facilitation followed by inhibition (30). Nailamide i.p. 20 *mg/kg* in mice quadruples brain serotonin while dopamine is doubled and norephinephrin is elevated to a fairly high level at 6 hr after administration (24). Nialamide induced in hibition in male sex behaviour occurring at 6 hr after systemic administration of rats therefore corresponds to this time frame. The inhibitory effect thus may be mainly produced by a higher rise in the serotonin levels of the brain than that of the catecholamines. Pargylin induced inhibition in male sex behaviour can be reversed by para-chlorophenylalanine which in turn inhibits the snythesis of serotonin (1,20,26,27,28). Such a reversal is associated with a marked drop in the brain serotonin but not catecholamines (35). It is also shown that MK-486, an extracerebral decarboxylase inhibitor and L-dopa which allow a proportionately higher increase in the levels of brain catecholamines cause a facilitation of copulatory behaviour.

In our experiments, we have infused the 3rd ventricle with nialamide at dosages which were several hundreds of times less than the dose used in i.p. administration and demonstrated that ICV infusion of nialamide initially produced an inhibition followed by facilitation. In view of the fact that nialamide was given into the III cerebral ventricle to allow a quick and direct access to the hypothalamic neurones controlling sex behaviour, the inhibitory effect occurred almost immediately i.e. within 5 min to 2 hr depending on the dose of nialamide. The extent of inhibition and facilitation were also dependent on the dose. At the time of inhibition while copulation was abolished, the pursuit of female was also fairly inhibited. Assessing from the rest pauses to which such rats resorted one may conclude that these animals were not very alert. This finding is contrary to the earlier observations in which inhibition of the sex behaviour was accompanied by an increase in the locomotor activity (19).

The facilitation that followed the inhibition of sex behaviour by ICV infusion of nialamide can be explained by the time dependent differential increase in the serotonin gradually followed by a higher increase in the catecholamines. The inhibitory effect may be due to a higher rise in the serotonin levels of the brain than that of catecholamines. The suppression of alertness and locomotor activity at the time of inhibition of sex behaviour supports such a formulation. In addition, there may be a slow, gradual or delayed rise in the catecholamines which upon reaching a proportionately higher levels than serotonin produce the facilitation of sex behaviour thus annulling the inhibitory effect due to high serotonin levels. It could thus be that the level of male sex behaviour depends upon the relative ratio of brain catecholamines versus serotonin.

From the description of the monoaminergic pathways it is apparent that the majority of the ascending nonoamine fibres converge in the medial forebrain bundle (2,13,17,37). Lesion and stimulation studies also indicate the significance of this bundle in the male sex behaviour (13). Hypothalamic neurones, in particular those located anteriorly and in the medial preoptic area, have been identified as a focal point in the regulation of sex behaviour. Medial preoptic area has been shown to possess receptor sites for the action of androgens to elicit male sex behaviour (8,16,18). It is difficult to assess the type of interaction that may be involved between the androgens and the neurotransmitters at these sites which may allow the elaboration of male sex behaviour. Further studies will be required to elucidate these and others aspects of brain mechanisms controlling the male sex behaviour.

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