SIGNIFICANCE OF SPATIAL AND TEMPORAL DYSFUNCTION EXHIBITED BY ENHANCED RUNNING ACTIVITY IN HIPPOCAMPALLY-LESIONED RATS

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Summary : The present work is designed to study the role of Hippocampus in the control of circadian running activity of rats subject to discrete lesions in ventral hippocampus and having free access to the cues namely food, water, male rat and female rat provided in maze-cum-activity cage indigenously prepared for recording open field behavioral activities.

The study was done with 8 male adult albino rats. Those in which lesion was confirmed to be located in antero-ventral hippocampus, exhibited marked increase in running activity with disruption of running activity pattern. There was increase of drive towards socio-sexual cues which were non-rewarding under the present experimental set up. The animals in which lesion was located in posteroventral hippocampal areas showed slight increase in the activity but without disruption of circadian running activity nor was there any significant change in the drive. The functional dissociation observed in present study is believed to be due to involvement of fimbrial/fornical system in the lesion process and therefore responsible for disruption of circadian running activity as well as increase of the running activity in hippocampally-lesioned animals.

The present work emphasises the importance of Hippocampus-septum-hippocampus feedback loop in controlling relative time, functioning as internal "stop watch" thus providing a temporal reference and detecting phase relation during activity. Interruption of this loop in hippocampally-lesioned rat probably leads to failure to inhibit inappropriate responses and failure to discriminate rewarding and non-rewarding cues.

Key words : hippocampally-lesioned rats, stereotypy, circadian running activity, hippocampus-septum-hippocampus loop, spatial and temporal dysfunction

INTRODUCTION

It is known that several body functions namely humoral behavioral and biochemical, repeat with periods close to 24 hours of geophysical day. In lower animals such as rats, these cyclic functions reflect on running activity and as such the running activity in rats follows circadian rhythm. It is now generally accepted that not only photic cues but non-photic cues as well, are capable of entraining circadian rhythms (6,16,20). The

running activity in rats therefore, shifts subject to availibility, visibility etc. of external environmental cues that fulfil instinctual drives at particular period of the day.

There is a tacit assumption growing in recent years that there are multiple endogenous oscillators for controlling biorhythms, located at various levels of Central Nervous System (8). Our previous work leads us to conclude that there are separate endogenous oscillators for food and for water in the control of circadian running activity in rats (6). It is likely that independent endogenous centers exist for other instinctual drives such as socio-sexual behavior.

It was demonstrated by Kluver and Bucy (12) that ablation of temporal lobe (Hippocampal formation and Amygdala) in monkeys produces marked behavioral changes viz. aberration of feeding behavior manifested in hyperphagia and loss of taste discrimination, aberration of socio-sexual behaviour (hypersexuality without discrimination of sex), oral tendencies to identify the objects and enhanced running activity in the cage. Subsequently, work on hippocampus either by ablation technique or by stimulation was carried out and a wide variety of functions has been attributed to the Hippocampus. This paleocortex has been implicated at one time or another in control of emotion, inhibition of inappropriate response, error evaluation, coding of non-reward, orientation, exploration, habituation, attention, recognition memory and spatial memory, spatial and cognitive mapping, information processing and link between internal and external environment (21). It is also documented that hippocampus by itself participates in the control of socio-sexual behaviour (9, 11, 14, 18). There are few remarks in the literature to point out the putative role of hippocampus in the mechanism of remembering *time count* (17).

In most of the works so far reported, the rats with hippocampal lesions have shown enhanced running activity (1, 10, 13, 19) and are even sleepless at night as compared to control animals (10). However, the exact significance of the enhancement of the activity observed in hippocampally-lesioned animals is not clearly understood.

The available studies are mostly concerned with lesion in dorsal hippocampus (22). Our previous studies on correlates of visceral and behavioral patterns induced on stimulation of ventral hippocampus in cats and monkeys revealed that there is functional dissociation within hippocampus (3, 4) and that hippocampal responses are frequency dependent (3). The motivational circumstances under which the animals are tested appear to be of crucial importance for open field behaviour (10). This work will help in disclosing the putative role of hippocampus in the control of the circadian running activity of the rats subject to discrete lesions in ventral hippocampus having free access to the cues namely food, water, male rat and female rat provided in maze-cum-activity cage indigenously made (5).

MATERIAL AND METHODS

The work was carried out with eight adult male albino rats weighing between 250-300 *gms*. The circadian running activity was studied with the help of maze-cum-activity cage with automatic recording system indigenously made for evaluation of circadian incentive drives in rats. The detail of the apparatus is described in a separate communication (5). To describe in brief, the animal was provided with free access to four goal compartments, two on the right side and two on the left, through doors with guillotine shutters. The food and water were provided in compartments placed diagonally opposite to each other; male rat and female rat were kept in remaining goal compartments. The experimental animal could have direct contact with water and food trays in the respective compartments but the male and female cue rats present in other compartments are separated with a grid so that these cue rats cannot enter the maze box.

Experimental schedule : The animals were allowed to get adapted to the instrumental environment for 15 days. The cage was opened once daily at 9 A.M. to clean the chambers and replenish the food and water. The food intake and water intake were determined daily at the time of replenishment. The cue animals were also exchanged every 24 hours by a fresh batch which was well fed prior to their placement in the instrument.

The running activity recorded from the start box was an index of the movements registered during the activity of the animal on central platform through the maze. The records from the goal compartments were compiled and studied separately to evaluate the activity of the animal towards each one of these non-photic entrainers on the running activity. 24 hour activity of each rat was recorded continuously for 15 days. Usually, after about eight days the running activity was observed to be stabilized. So this activity was considered as rats' own control. This procedure was followed by bilateral hippocampal lesions extended from coordinates A_1 to A_4, L_4 to L_5 and H_0 to H_2 (De Groot's Stereotaxic Coordinates). The lesion was made by passing cathodal current of 1.5 mA for 30 sec. through 28 gauge stainless steel insulated electrode except at the tip. After 2-5 days of recovery from surgical truama, rat's activity was subsequently recorded for further period of 15 days.

Four animals were sham operated by passing electrodes in ventral hippocampus but without making electrolytic lesions. The sites of lesions were confirmed histologically by hematoxylin-eosin staining techniques.

RESULTS

The disruption of activity pattern with marked increase in running activity was

seen in three rats in which the lesion was confirmed to be located in anteroventral hippocampus. In remaining five animals in which the lesions were confirmed to be placed in postero-ventral areas, slight increase in the activity was observed instead.

Figure 1 displays marked increase of general running activity of the animals with antero-ventral hippocampal lesion as compared to that in animals with postero-ventral lesion.

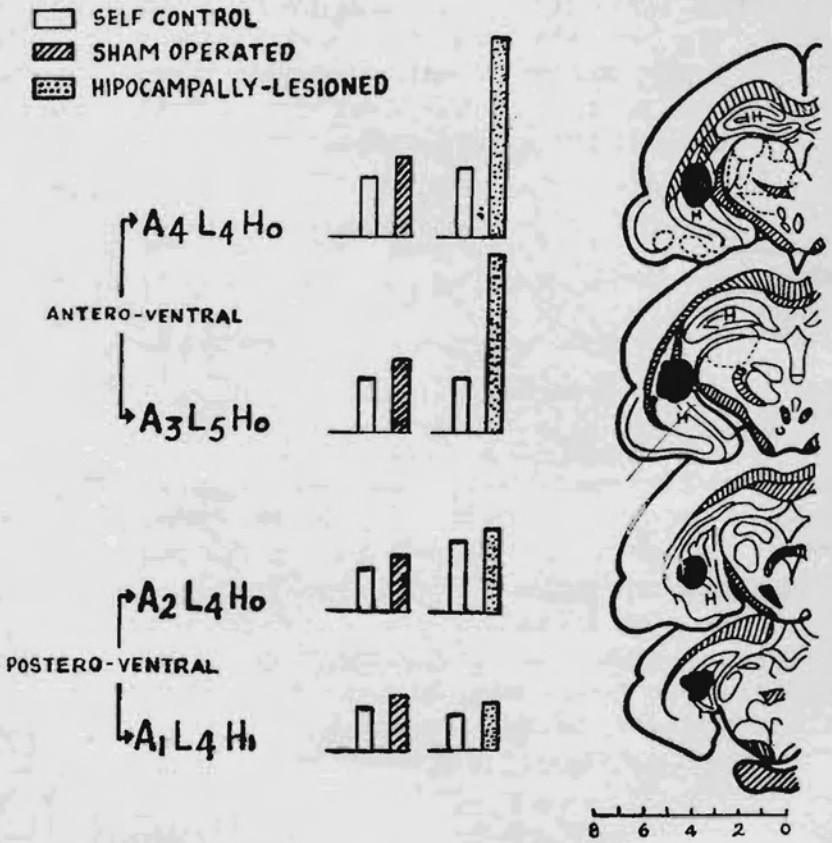

Fig. 1 : Histograms of activity in hippocampally-lesioned rats.

On right side of the diagram, is indicated the extension of lesion made in ventral hippocampus. The activity of the rats with Antero-ventral lesion is shown to be markedly increase as compared to the activity of the rats with lesion in postero-ventral hippocampal areas.

It was further noticed that in the antero-ventral hippocampally lesioned series, the increase of activity was observed even during night period with complete disruption of normal circadian diurnal pattern of running activity as represented in channel III

of Fig. 2. It is also obvious from this record that the activity in some goal compartments was markedly increased as compared to that in other compartments (Fig. 1).

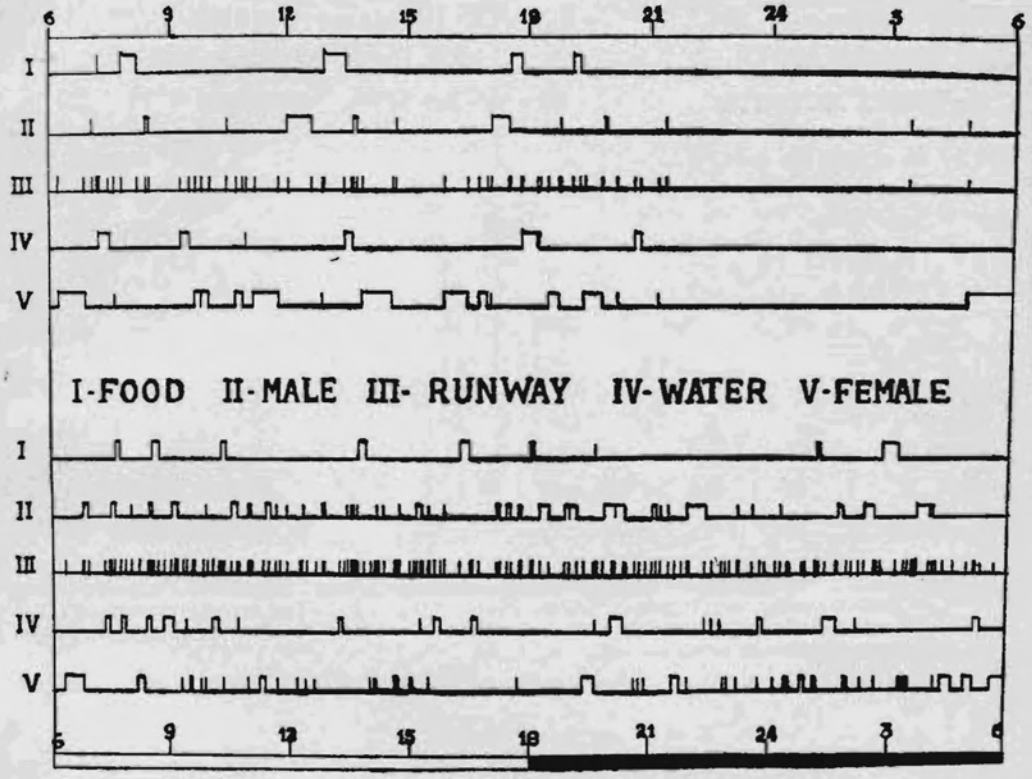

Fig. 2 : Activity record displaying simultaneously the activity in 5 channels of the rat No. 6 before and after antero-ventral hippocampal lesion. The activities are indicated by upward deflections. Site of lesion : A_3 L_5 H_0.

Channel I - food ; Channel II - male rat; Channel III - central platform of start box (total activity) ; Channel IV - water; Channel V - female rat.

When the activity in each chamber was measured and compared with sham operated series, it was found that the activity was more towards the male and female compartments in antero-ventrally lesioned animals (Fig. 3). As a matter of fact, male as well as female cues are non-consumatory drives and are also non-rewarding in those compartments because the animal cannot have direct contact with these cue animals.

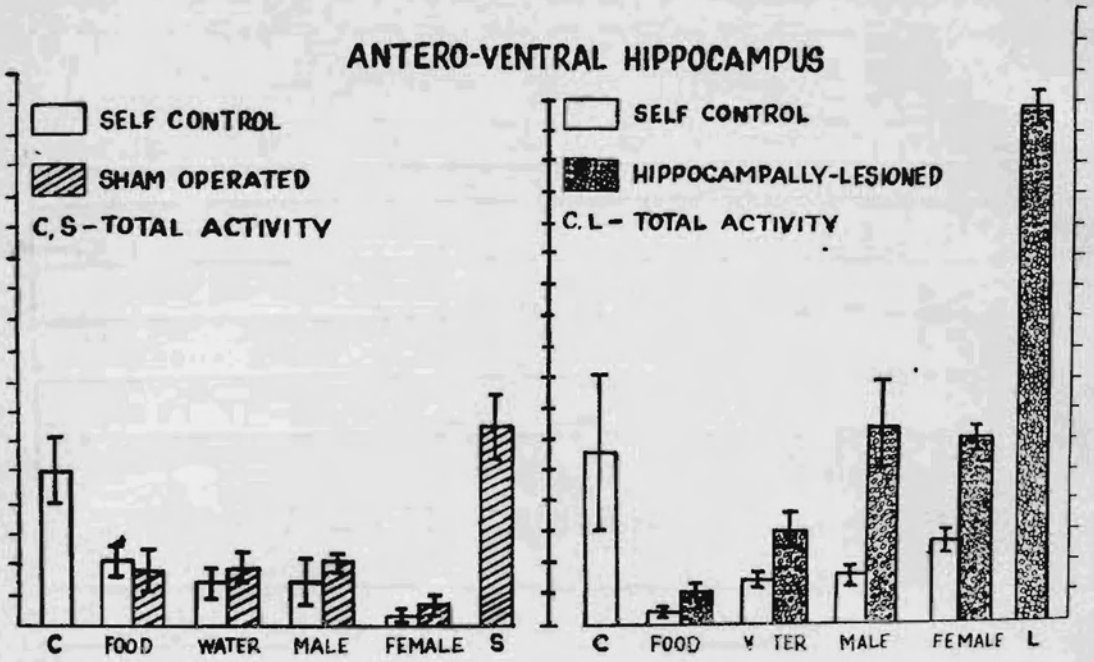

Fig. 3 : Histograms of activity recorded in each goal compartment of rat No. 2 with lesion in Antero-ventral Hippocampus. Site of lesion : $A_4\ L_5\ H_0$. The marked increase of total activity is found to correlate increased activity in male and female compartments as compared to sham operated rats.

DISCUSSION

The motivational circumstances under which the animals were tested in this work, indicate that there is functional dissociation within ventral hippocampus and that behavioral effects differ in two groups of the lesioned rats. Disruption of circadian pattern as well as marked increase of running activity was observed in rats in which lesion was located in antero-ventral hippocampus. It was also noted that animals of this group showed marked increase in activity-shifts towards non-consumatory cues (males and female rats) as compared to consumatory cues (water and food) inspite of the fact that both these non-consumatory cues were non-rewarding. Though the shift of activity was slightly increased towards food and water compartments in these animals, the actual food and water consumption for 24 hours was not altered significantly as compared to its control period. It is to be noted that the number of activity shifts was increased, not only because of extension of activity span throughout 24 hours but also by means of curtailing the duration of stay in each compartment as compared to the duration spent by the animal in each compartment prior to lesion. Probably, "shortening of

satiety period" of instinctual drives may be the reason behind the short lasting shifts of running activity in each chamber revealed by hippocampally-lesioned rats.

On careful observation of the areas represented in Fig. 1 it is noted that in the process of lesions made in antero-ventral hippocampal areas (A_3 to A_4) there is an involvement of a large portion of fimbria and fornix, whereas, lesions made in postero-ventral hippocampal areas did not involve fornix. This leads to think of the possibility that the increase of activity as well as disruption of its circadian pattern could be related to interruption of fimbrial output-input pathway to the other important areas of Limbic system.

It is generally accepted now that the main hippocampal efferents (CA_1 and CA_3) travel along the alveus and fimbria to be distributed by the pre- and post-commissural fornical system to several areas of the forebrain and mid-brain. The axons of CA_1 and CA_3 have two projection areas, one being lateral septal nucleus and another being subicular complex. Reports on septo-hippocampal connections in the rat indicate that hippocampus receives projections from Medial Septal Nucleus through fornical and fimbrial system (13). Thus it is believed that hippocampus-septum-hippocampus forms a closed circuit that works as functional entity (7,17).

The earlier reports as well as the present findings of this work suggest that hippocampus-septum-hippocampus feedback loop plays a role in controlling relative time, functioning as an internal "stop watch" thus providing a temporal reference and detecting phase relation during activity. Interruption of this loop leads to persistent repetition of senseless acts (stereotypy) reflecting the failure to inhibit inappropriate responses and failure to discriminate rewarding and non-rewarding cues.

It is therefore, concluded that disruption of circadian activity manifested by hippocampally lesioned rats is due to lack of control for detecting phase relation during activity for instinctual drives in which there is involvement of fimbria-fornix pathways. The motivational circumstances under which the present work was done might also point to the importance of the hippocampus as an endogenous oscillator for biorhythmic control of instinctual drives in which hippocampus-septum-hippocampus loop plays an important role and as such should be a pointer for further investigation in this direction.

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