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THE MEDIAL SEPTUM ACTS THROUGH THE MEDIAL PREOPTIC AREA FOR THERMOREGULATION AND WORKS WITH IT FOR SLEEP REGULATION

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Abstract : The chronic changes in sleep-wakefulness (S-W), body temperature (T_b), locomotor activity (LMA) and thermal preference were studied in male Wistar rats after the destruction of neurons in both the medial preoptic area (mPOA) and the medial septum (MS) by intracerebral injection of N-methyl-D-aspartic acid.

An increase in the T_b, and a preference for higher ambient temperature (T_{amb}) of 30°C were observed after the combined lesion of the mPOA and the MS. Similar changes were reported to occur after the lesion that was restricted to the mPOA. But these alterations were in contrast to the decrease in T_b and preference for lower T_{amb}, observed after the MS lesion. The thermostat of the brain would have been reset at a higher level after the combined lesion, as there was an increase in T_b, along with a preference for a higher T_{amb}, and an increase in LMA. There was a reduction in the frequency and the duration of the slow wave sleep (SWS) episodes, and a reduction in the frequency of the paradoxical sleep (PS) episodes after the combined lesion. The destruction of the MS neurons was probably responsible for the reduction in the frequency of SWS, whereas the loss of mPOA neurons was responsible for the decrease in the duration of SWS and frequency of PS.

It can be suggested that the MS exerts its influence on thermoregulation through the mPOA. However, the MS and the mPOA seem to play independent, but complementary roles in sleep promotion.

Key words : preoptic area sleep medial septum wakefulness telemetry ambient temperature thermoregulation

INTRODUCTION

The medial preoptic area (mPOA) and the medial septum (MS) are two adjoining basal forebrain structures that play important roles in the regulation of sleep and body

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temperature (T_b) (1, 2, 3, 4). However, neurotoxic lesion studies have shown that these structures may play different roles in the regulation of sleep and T_b. Lesion of the mPOA with the cell specific neurotoxin N-methyl-D-aspartic acid (NMDA) produced a deficiency in the maintenance of slow wave sleep (SWS) (1, 4, 5, 6), while the lesion of the MS produced a deficiency in the initiation of SWS (3, 7). Lesion of the mPOA caused a reduction in the ability of the rats to defend their body temperature in a low ambient temperature (T_{amb}) (2, 4), while lesion of the MS produced a deficit in their heat defence ability (8). It was also reported that the brain temperature of the rats were reset at a higher level after the mPOA lesion, while it was reset at a lower level after the MS lesion (2, 3, 4, 8). There was a shift in the thermal preference for a higher T_{amb} after the mPOA lesion (6), while there was a shift in the thermal preference for a lower T_{amb} after the MS lesion (3). Moreover, it has been reported that that the sleep deficits were attenuated when the lesioned rats were given freedom to select their preferred T_{amb} (3, 6).

The mPOA and the MS might be regulating these physiological functions through independent neuronal circuits. On the other hand, it could also be possible that one area influences the other to achieve a homeostatic balance, as per requirement. This could become evident when the observations from a combined lesion of two adjoining brain regions are interpreted in the light of existing information on isolated lesion of the MS and the mPOA. The changes in physiological parameters, monitored after both the areas are lesioned, can give information about the interaction between the two areas (9, 10).

There is no report in which changes in T_b, sleep-wakefulness (S-W), locomotor activity (LMA) and thermal preference were studied after the destruction of both the MS and the mPOA, though these parameters were studied after isolated lesions of these two areas. So, in this study, S-W and T_b were recorded, using a telemetric system, along with LMA, when they were given freedom to select their preferred T_{amb}, in the rats whose MS and mPOA were lesioned. These parameters were also studied when the same rats were not given freedom to select their preferred T_{amb}.

METHODS

The study was conducted on six adult male Wistar rats weighing between 200 and 250g. The rats were housed in separate cages in an animal room having lights on from 6:00 to 20:00 h (14:10 light: dark cycle) and controlled T_{amb} of 26 ± 1°C. Food and water were provided *ad libitum*. All procedures were conducted in accordance with the rules of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and were approved by the Institutional Animal Ethics Committee, AIIMS, New Delhi, India. All the rats were chronically implanted with electroencephalogram (EEG), electromyogram (EMG) and electrooculogram (EOG) electrodes for the assessment of S-W, under pentobarbital sodium anesthesia (40 mg/kg body weight, i.p.). The electrodes were soldered to a plug that was fixed to the skull with dental cement. In order to assess the intraperitoneal temperature, a temperature-sensing transmitter (Data Sciences, USA, TA10TA-F40, 7.15 g and 3 × 1.3 × 0.8 cm) was

surgically implanted in the abdomen. The rats were then allowed six days for recovery from surgical trauma.

The rats, with chronically implanted electrodes and transmitter, were placed in an environmental chamber, which consisted of three interconnected compartments. The three compartments in which the rats could move freely were maintained at three different T_{amb} of 24°, 27° and 30°C (11). These temperatures were selected on the basis of the earlier findings of the thermal preference of adult male Wistar rats (11, 12). A three channel telemetric transmitter (Data Sciences, TL10M3F50-EEE) was used for recording EEG, EOG and EMG. Before the actual recordings of S-W and other parameters, the rats were accustomed to the environmental chamber and trained to pass through the openings in the partition separating the three compartments. Those rats that did not move from one compartment to another were discarded. The rats were put in the chamber one day prior to the recording, to habituate them to the surroundings. The telemetric system, which was used in this study, did not permit simultaneous recordings from two transmitters. So, using the triple channel telemetric system, EEG, EMG, and EOG were recorded along with LMA and thermal preference for 24h on three days to have pre-lesion control data. Using the other telemetric system, T_b along with LMA and thermal preference, were recorded for 24h, for another three days. These days alternated with those of EEG, EOG and EMG recordings. Thermal preference and LMA were assessed by activity monitor systems (Coulbourn Instruments, Allentown, PA, USA) placed on the floor of the chambers. This system, assessed the number of movements made by the animal (i.e. LMA), in addition to the time spent by the animal in each compartment (i.e. the thermal preference). Telemetric receivers (RPC-1) were kept in each of the compartments of the chamber. These receivers were attached to a computerized data acquisition system (Dataquest, Data Sciences International, USA) and the EEG, EOG and EMG records were displayed and stored on the computer, as described earlier (11). The transmitters were activated using a magnet, and the signals were received by the RPC-1 receivers.

After the six pre-lesion recordings in which the rats selected their own preferred T_{amb}, one more recording of S-W and T_b, along with LMA was done with all the three compartments maintained at 27±0.5°C to assess S-W and T_b when the rats were not given the freedom to choose their preferred T_{amb}. This temperature was selected on the basis of earlier studies in which the normal rats preferred to stay at 27°C (11, 12). After all these pre-lesion recordings, the rats were anaesthetised using sodium pentobarbitone (40 mg/kg, i.p.) and the mPOA and the MS neurons were destroyed by intracerebral injection of 5 µg NMDA (Sigma, St. Louis, USA) in 0.2 µl distilled water. The mPOA was initially destroyed by intracerebral injection of 0.2 µl NMDA at A 7.8, H–1.5 and L 0.6 mm as per DeGroots atlas (13). After a period of 30 min, the needle was lifted to the MS (H 0.5) and this area was destroyed by an injection of 0.2 µl NMDA. The same procedure was repeated on the other side after an interval of 30 min. S-W, thermal preference and LMA were recorded on the 7th, 14th and 21st days, after the lesion. On the other hand, T_b, thermal preference

and LMA were recorded on the 8th, 15th and 22nd days after the lesion. S-W and LMA were recorded on the 24th day, while T_b was recorded on the 25th day, with the temperature of all the three compartments maintained at 27 ± 0.5°C. At the end of the experiment, the rats were anaesthetised with sodium pentobarbitone (45 mg/kg, i.p.) and perfused with 10% formalin. The brains were then removed and 10 µm thin sections were processed for histological examination of the lesion site, with cresyl violet stain (14). The neural damage due to the NMDA injection was ascertained as described in the literature (15).

The time spent (in 24h) in each of the compartments was calculated to find out the thermal preference. The 24h S-W records were split into 30 sec epochs and visually scored. The wakeful period was classified into two stages namely, active wakefulness (W1) and quiet wakefulness (W2). The sleep period was classified into three stages, light slow wave sleep (S1), deep slow wave sleep (S2) and paradoxical sleep (PS) as described earlier (1, 4, 5).

Friedman's two-way analysis of variance (ANOVA) was done in order to find out the variation in thermal preference, T_b, LMA and S-W between the rats as well as between the days of pre-lesion recordings. The pre-lesion recordings of each parameter were pooled together and considered as the pre-lesion average, after finding that there was no significant variation. These average values were used for comparison with the values of the respective parameter of each post-lesion day using the same ANOVA. Duncan's multiple comparison tests were done in those cases in which there was a significant difference in two-way ANOVA. The pre-lesion values and the post-lesion values, when the rats were not given freedom to choose the $T_{amb,}$ were also similarly treated. Durations of S-W stages, when the rats were in the different compartments during the light period (14h), dark period (10h), and during 24h, were assessed. Total sleep time (TST) during the 14h light and 10h dark periods, in addition to 24h, were expressed as the percentage of the recording time. Two-hourly average values of each of the four parameters, and the values during dark (10h) and light (14h) periods were calculated from the 24h recordings and plotted. The percentage of the light period sleep was divided by that of the dark period to calculate the light/dark ratio of sleep. After scoring the different stages of sleep as mentioned above, the number of times of the different stages of S-W (W1, W2, S1, S2 and PS) occurred per h in the light, dark and the total period were calculated. This was taken to be the frequency. The duration of each stage (in min) was noted down and the mean of the duration of the episodes in the light, dark and total periods were calculated. Friedman's ANOVA was done in order to find out the variation between the pre-lesion and the post-lesion values of these parameters. The values of various parameters obtained when the rats were given the choice of three $T_{amb,}$ were compared with the values obtained when they were not given the choice of T_{amb}, using two way ANOVA. All the statistical analysis was done by System Analysis Software (SAS version 8).

RESULTS

Histological confirmation of lesion

All the rats had extensive destruction of the MS and the mPOA. The neurons were replaced by the glial cells at the site of NMDA injection (Fig. 1). An area of moderate destruction surrounded the region of severe lesion. The destroyed areas were generally restricted to the MS and the mPOA, except for a very thin area of mechanical destruction along the needle tracts. The lesions did not extend to the lateral preoptic area or the lateral septum, in any of these rats.

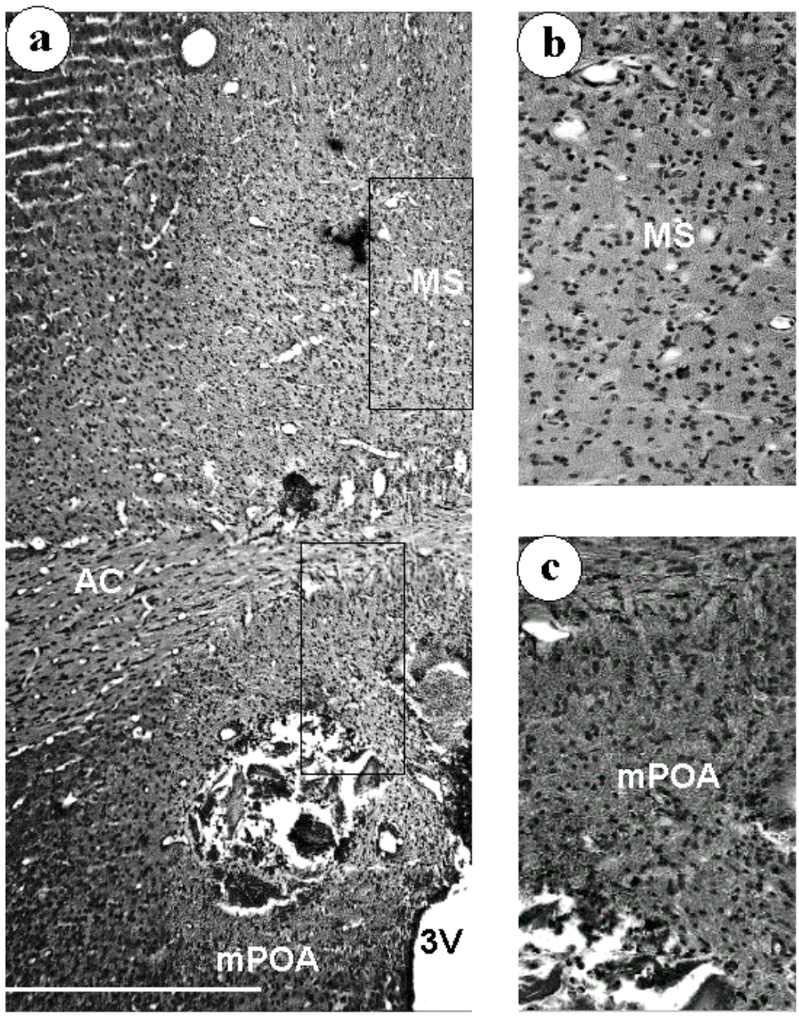

Fig. 1 : Photomicrographs of a 10 µm thin coronal section of the brain passing through the MS and the mPOA, stained with cresyl violet. The rectangular areas in the photomicrograph Fig. 1.a are magnified and shown in Fig. 1.b and Fig. 1.c. Neural damage in the MS due to the intracerebral injection of NMDA is shown in Fig. 1.b, while Fig. 1.c shows the neural damage in the mPOA. AC – Anterior commissure, mPOA – medial preoptic area, MS – medial septum, 3V – Third ventricle. Scale bar : 1 mm.

Pre-lesion control recording of S-W, LMA, T_b and thermal preference

There were no significant differences (P>0.05) in thermal preference, S-W, LMA and T_b between the animals, and the days of recording, before the lesion. The recording of thermal preference for 24h, for six days, showed that the rats had spent the maximum time in the chamber maintained at 27°C when given a choice of three temperatures, i.e. 24, 27 and 30°C (Fig. 2). They preferred a cooler T_{amb} of 24°C in the dark period, than during the light period. In addition to thermal preference, LMA and T_b, also showed circadian variation with more LMA and T_b during the dark period than during the light period. The amount of sleep was more during the light period (Fig. 2). W1 formed the major

Fig. 2 : The left panel shows the mean ± SD of total sleep time (TST), locomotor activity (LMA) and thermal preference on the pre-lesion (PRE-LESION) and post-lesion (POST-LESION) days 7, 14 and 21. The right panel shows the body temperature (T_b), LMA and thermal preference on the pre-lesion (PRE-LESION) and post-lesion (POST-LESION) days 8, 15 and 22. The TST (%) and T_b (°C) are expressed as the average value of 14h light period, 10 h dark period and 24 h total period recordings. The LMA (Counts/hour) during light, dark and total periods are shown in the middle row. The thermal preference during 24 h of recording, when given a choice between 24°, 27° and 30°C, is shown in the lower row. The average three days of pre-lesion recording in the left panel are different from the three days average shown on the right panel. Data are expressed as mean ± S.D. *P<.05, **P<.01.

component of wakefulness, and S1 formed the major component of sleep (Table I).

The S-W, T_b and LMA showed no significant difference, when the rats were kept at 27 ± 0.5°C, as compared to the values of these parameters, when the same rats were allowed free selection of T_{amb} (Fig. 3). The durations and frequencies of all the S-W stages, under restricted and non-restricted T_{amb} conditions also did not show any significant difference (Table II).

TABLE I: Time (min/h) spent in different stages of S-W (Mean±SD) when rats selected their preferred ambient temperature (unrestricted), and when they were kept at a constant ambient temperature (restricted) of 27°C before (PRE-LESION) and after MS and mPOA lesion (POST-LESION).

	Pre-lesion		*Post-lesion*			
	Unrestricted	*Restricted (27°C)*	*Unrestricted*			*Restricted (27°C)*
			Day 7	*Day 14*	*Day 21*	*Day 24*
W1	22.9±1	23.5±2	30.9±2**	28.5±2*	24.7±1*--	36.5±3***
W2	3±0.5	2.6±0.5	4.3±0.5*	4.1±0.5*	5.8±1**++	3.2±1
S1	23.2±1	22.6±1	16.6±1**	18.3±1**	20.7±1*++	13.9±2**
S2	6.9±1	6.5±0.5	4.6±0.8**	5.1±1**	4.8±1**++	4.3±1**
PS	4.9±0.5	4.8±0.5	3.6±0.5*	4±0.4*	5.0±0.6++	2.1±0.6**

Data are expressed as mean ± S.D.
*P<0.05, **P<0.01, ***P<0.001 (compared to pre-lesion),
++P<0.01, (significant increase compared to the restricted conditions),
--P<0.01, (significant decrease compared to the restricted conditions)
L = Light period (14h), D = Dark period (10h), T = Total time (24h)

TABLE II: Duration of episodes (in min) and frequency (per hour) of S-W episodes (Mean±SD) before (PRE-LESION) and after the lesion (POST-LESION) of the MS and the mPOA, with NMDA when rats selected their preferred ambient temperature (unrestricted), and when they were kept at a constant ambient temperature (restricted) of 27°C.

		Pre-lesion		*Post-lesion*			
		Unrestricted	*Restricted (27°C)*	*Unrestricted*			*Restricted (27°C)*
				Day 7	*Day 14*	*Day 21*	*Day 24*
W1	DUR	7.1±0.5	7.2±0.4	8.5±0.4**	8.1±0.4*	8.2±0.2*-	9.2±0.3**
	FREQ	3.1±0.5	3.3±0.4	3.7±0.5*	3.7±0.5*	3±0.5--	4±0.4*
W2	DUR	1.3±0.3	1.2±0.2	1.1±0.4	1.1±0.4	1.3±0.5	1.1±0.2
	FREQ	2.3±0.5	2.2±0.5	3.9±0.5**	3.7±0.5**	4.4±0.3**+	2.8±0.5
S1	DUR	2.3±0.5	2.2±0.2	1.8±0.5*	1.9±0.4*	2.3±0.5++	1.5±0.3**
	FREQ	10.4±0.2	10.3±0.2	9.2±0.2**	9.5±0.2**	9.5±0.2*+	9±0.2**
S2	DUR	1.6±0.2	1.5±0.2	1.1±0.2*	1.3±0.2	1.5±0.2+	1.1±0.2**
	FREQ	4.4±0.2	4.4±0.3	4±0.3*	3.9±0.3*	3.6±0.3*	3.6±0.4**
PS	DUR	3.3±0.3	3.2±0.3	3.5±0.3	3.5±0.3	3.6±0.3	3.4±0.3
	FREQ	1.6±0.3	1.6±0.5	1±0.4**	1.1±0.3*	1.4±0.3++	0.6±0.4***

Data are expressed as mean ± S.D.
*P<0.05, **P<0.01 (compared to pre-lesion).
+P<0.05, ++P<0.01, (significant increase compared to the restricted conditions),
-P<0.05, --P<0.01, (significant decrease compared to the restricted conditions)
L=Light period (14h), D=Dark period (10h), T=Total time (24h)

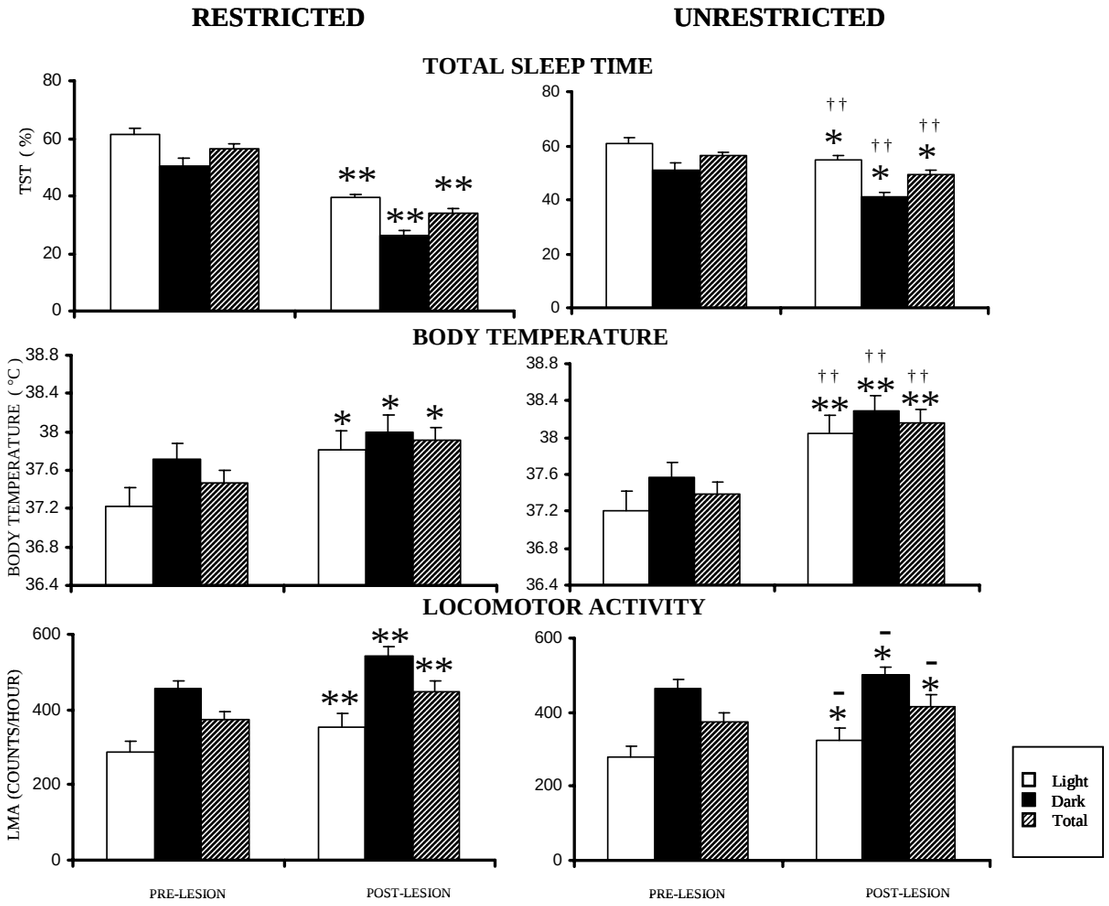

Fig. 3: The left panel shows the mean ± SD of total sleep time (TST) in %, locomotor activity (LMA) in counts/hour and body temperature (T_b) in °C in the rats that were kept at a restricted temperature of 27 ± 1°C before (PRE-LESION) and on the 25th day after MS lesion (POST-LESION). The right panel shows the TST, LMA and T_b when the rats were given a choice between 24°, 27° and 30°C before (PRE-LESION) and on the 22nd day after the MS lesion (POST-LESION). The TST, LMA and T_b during light (14h), dark (10h) and total periods (24h) are shown separately. The post-lesion values in the restricted and the unrestricted conditions were compared with their respective pre-lesion values and also with each other. *P<0.05, **P<0.01, (compared to the pre-lesion recordings), ††P<0.01, –P<0.05 (significant change compared to the restricted conditions).

S-W, T_b and LMA in the lesioned rats when they were allowed to select their own preferred T_{amb}

The rats preferred to stay at a higher T_{amb} after the lesion (Fig. 2). SWS and PS were decreased after the lesion, but the sleep parameters, showed a tendency to get back to the pre-lesion values with the passage of time. It was the S1 of the SWS, and W1 of wakefulness, which showed the maximum recovery (Table I). Though the durations and frequencies of S1 and S2 were decreased after the lesion, it was the durations that

showed greater recovery (Table II). A decrease in the frequency of episodes was responsible for the decrease in PS, and it regained the pre-lesion level by the 21st day after the lesion (Table II). Increase in the T_b and LMA were significant on all the days after the lesion during both the light and dark periods (Fig 2).

S-W, T_b and LMA after the lesion when the rats were kept at 27±0.5°C

Though there was considerable improvement in sleep, when the animals were allowed to select their own preferred T_{amb}, there was a reduction in all the sleep parameters, even on the 24th day, when the lesioned rats were kept in a T_{amb} of 27 ± 0.5°C (Fig. 3). There was an increase in W1 and a decrease in W2 and SWS (S1 and S2), as compared to the recording on the 21st day (Table I). The PS showed marked reduction (Table I), primarily due to a reduction in the frequency of the episodes (Table II). The drastic reduction in PS resulted in a decrease in the PS/TST from 0.14 before the lesion to 0.1 ($P<0.05$) after the lesion. There was no significant change in the light/dark ratio of TST. Though there was increase in T_b and LMA, the T_b change was less, and LMA more, when the animals were kept at a restricted temperature after the lesion (Fig. 3). The light-dark difference in T_b was increased ($P<0.001$) when the animals were kept at a restricted $T_{amb.}$

DISCUSSION

Large lesions using NMDA, which destroyed the neurons of both the mPOA and the MS, produced a decrease in SWS and PS. A reduction in the frequency and the durations of the episodes contributed towards the decrease in SWS, whereas a reduction in frequency was responsible for the PS reduction. There was an increase in the T_b, LMA and a preference for higher T_{amb} after the lesion. Preference for higher T_{amb} resulted in considerable recovery of SWS, PS and the PS/TST ratio.

Changes in SWS after the MS and mPOA lesion

The combined lesion of the mPOA and the MS produced a reduction in SWS though these effects were less pronounced when the lesioned rats were allowed to choose their own preferred T_{amb}. The reduction in SWS produced by the combined lesion of the mPOA and the MS was similar to the deficits observed after the lesions of either the mPOA (4, 6) or the MS (3, 7). However, the mPOA lesion produced a decrease in the SWS during the light period (1, 4, 6) whereas the MS lesion produced a decrease in sleep during the dark period (3, 7). The combined lesion of the MS and the mPOA in the present study produced a decrease in SWS both during the light and dark periods. Similarly, the MS lesion produced a decrease in the number of the SWS episodes (3, 7), while the lesion of the mPOA produced a decrease in the duration of the SWS episodes (1, 4, 6). The combined lesion of the MS and the mPOA produced a decrease in both the number and the durations of the SWS episodes.

Though the destruction of both the mPOA and the MS produced a reduction in both the frequency and the durations of the SWS episodes, the selection of a warm T_{amb} resulted in an increase in the durations of the episodes of SWS. This was similar to the trend observed after the MS lesion (3). On the other hand, the increase in the number of episodes was responsible for the recovery in the SWS in the mPOA lesioned rats, when they were allowed to choose the appropriate T_{amb} (6). Some brain areas other than the mPOA and the MS, or the small

portion of the mPOA that was not destroyed, might have played a role in increasing the duration of SWS, when the rats had access to a warm T_{amb}. At the same time, the present observation supports the earlier observation regarding the role of the MS in sleep genesis (7). A decrease in the number of SWS episodes after the lesion indicates a failure in the sleep genesis mechanism.

Changes in the PS after the lesion

The decrease in PS after the lesion, when the rats were restricted at a constant T_{amb} in the present study, is similar to that found after the mPOA lesion (4, 6). But this is in contrast to what was observed after the MS lesion (3, 7). So, it is reasonable to assume that the decrease in PS in this study was due to the destruction of the mPOA. It was previously suggested that the mPOA is involved in the initiation of PS, as the lesion of the mPOA caused a decrease in the frequency of the PS episodes (1, 16, 17). It is also possible that the decrease in PS was due to a decrease in the durations of the SWS (4). PS usually occurs after SWS and continues for some time. There was an increase in the durations of SWS episodes, when the lesioned rats were given freedom to select their T_{amb}. This probably increased the possibility of occurrence of PS, resulting in its recovery when the rats were given freedom to select their T_{amb}.

It could be argued that the recovery in the PS when the rats were given freedom to select their own preferred T_{amb} of 30°C was due to the elimination of thermal stress, which they faced when they were kept at a constant T_{amb} of 27 ± 05°C. The selection of appropriate T_{amb} probably helped to reduce the stress, which in turn helped in increasing the number of PS episodes. It had been reported that the PS is maximal at the thermoneutral zone (18). It was also reported earlier that there was a recovery in both the PS and the PS/TST ratio in the basal forebrain lesioned animals, when they were exposed to a higher T_{amb} of 30°C (6, 19, 20).

Changes in circadian variation in S-W and T_b after the lesion

After the combined lesion of the MS and the mPOA, there was a reduction in sleep during both the light and the dark periods. Hence there was no significant change in the light/dark ratio of TST. But there was a significant increase in the light-dark difference in T_b when these rats were maintained at 27 ± 0.5°C. However, the light-dark difference of T_b was significantly attenuated when the rats were allowed free selection of T_{amb}. An increase in the light-dark difference in the T_b was seen after the mPOA lesion (4, 21) and after the MS lesion (8). There was attenuation in the light-dark difference in the T_b when the rats of the present study (and the earlier reports on the mPOA and the MS lesions) were allowed free selection of T_{amb}, though the mPOA lesioned rats selected a higher temperature (6) and the MS lesioned animals selected a lower temperature (8). The exaggeration of light/dark difference in T_b in all these studies, when these rats were in 27 ± 0.5°C, probably resulted from maintaining them in an uncomfortable T_{amb}. The T_{amb} chosen by the rats might have reduced the circadian fluctuations in T_b when they had the opportunity to select their preferred $T_{amb.}$ However, circadian rhythms of S-W, T_b and LMA were still present after the combined mPOA and the MS lesions, even when the rats selected their T_{amb}.

Changes in T_b and resetting of thermostat

The increase in T_b, after the combined

lesion of the mPOA and the MS, is similar to the increase in T_b found after the mPOA lesion (6, 16, 18, 21, 22). But, this is in contrast to the decrease in T_b observed after the MS lesion (8, 23). It was proposed previously that there is an increase in the setpoint of T_b after the mPOA lesion (2, 4, 6) and a decrease in the setpoint of T_b after the MS lesion (8). However in the present study, when both the mPOA and the MS were lesioned, the setpoint of the animal shifted towards a higher T_b. This could be explained in terms of hierarchy in the interaction between the MS and the mPOA. It was proposed that the mPOA is placed at the topmost level in the hierarchy of brain structures for T_b regulation (21). Lesion of the mPOA produced an increase in the setpoint of the T_b that was defended by the body by appropriate heat loss/heat gain mechanisms (2). If the MS exerts its influence on thermoregulation through the mPOA, the combined lesion can produce changes, which are similar to the changes produced by the mPOA lesion. Therefore, it is possible that the thermoregulatory zone of these rats had shifted towards a higher T_{amb} after combined lesion of the MS and the mPOA.

It was suggested that the decrease in T_b after the MS lesions was due to the hyperactivity of the “heat loss” center (24). It was earlier thought that the POA is a “heat loss center” as electrolytic lesion of this area produced a failure of the heat loss mechanism (25–28). On the basis of this observation, it was proposed that there is a mechanism in the mPOA which is tonically active to bring the T_b to a lower level. Destruction of the mPOA caused the T_b to be set at a higher level after the mPOA lesion. This mechanism in the mPOA is probably under the tonic inhibitory influence of the MS. Therefore, lesion of the MS caused the release of the mPOA from the inhibition, producing an overreactivity of the mPOA resulting in lowering of the T_b. Evidences provided by the neurotoxic lesion studies have slightly changed this concept (2, 4). Though there was an increase in T_b after the mPOA lesion, there was no failure of the heat loss mechanism. At the same time, there was a shift in the thermostat setting towards a higher level (2). A shift in the thermal preference of the rats for a warmer environment further supports the theory that the thermostat was set at a higher level after the mPOA lesion (4, 6).

Changes in the thermal preference after the lesion

When the lesioned rats of the present study were allowed to choose their own preferred T_{amb}, they chose a higher temperature of 30°C, showing that the thermoneutral zone was shifted to a higher temperature. This, by and large, is similar to the T_{amb} chosen by the mPOA lesioned rats (6). Again this was opposite to what was observed after the MS lesion (3). This further supports the earlier assumption that the setpoint of the T_b was increased in the lesioned animals of the present study, similar to the mPOA lesioned animals. The explanation that the MS has an influence on the mPOA, whose tonic action makes the rats select a lower T_{amb}, is supported by this observation also. The behavioral thermoregulatory ability of the rats was not abolished after the destruction of the MS or the mPOA neurons (6, 29). In the present study, by choosing a higher T_{amb} (i.e. by behavioral thermoregulation), the lesioned rats attained a higher T_b (higher than the levels when they were in restricted to a T_{amb}) of 27°C which was the T_{amb} preferred the rats before the lesion.

Changes in the LMA after the lesion

The increase in LMA observed in this study after the combined lesion of the MS and the mPOA, is similar to those reported in earlier studies after lesion of the mPOA (1, 5, 6, 30, 31) but not after the MS lesion (3). This could be attributed to the increase in the setpoint of T_b after the combined lesion of the MS and the mPOA. As the increased LMA would result in increased heat production, it would be helpful in maintaining the T_b at a higher level (6). As the thermostat was reset at a higher level after the combined lesion of the MS and the mPOA, the increase in LMA may be described as the animals' efforts to maintain hyperthermia. The observed decrease in LMA when the animals chose their own preferred temperature of 30°C (in comparison to the situation where the animals maintained were at a constant T_{amb} of 27°C), may be attributed to the lesser requirement of heat production by LMA, as the higher T_{amb} itself have contributed towards increasing the T_b. Increase in the LMA might have also resulted in an increase in the W1 in the animals that were kept at a constant T_{amb} of 27°C after the MS and the mPOA lesion.

The hypothesis

The MS and the mPOA are important forebrain structures that can influence the thermostat setting. Results from the combined lesion suggest the possibility that the MS may have an inhibitory influence on the mPOA for thermoregulation. The MS inputs to the mPOA help in raising the thermostat setting to a higher level. Increase in the LMA and selection of a higher T_{amb} by the rat are some of the measures that are initiated by the MS to increase T_b, by acting on the mPOA. On the other hand, the activity of the mPOA results in the lowering of the thermostat (and lowering of T_b). This is facilitated by decreased LMA, and a preference for lower T_{amb}. So, the normal thermostat setting and T_b are dependent on the activity of the mPOA, which is under the influence of the MS. Though the influence of the MS on thermoregulation is mediated through the mPOA, the same is not true for sleep regulation. The MS and the mPOA have separate roles for sleep regulation. Though both the structures play a sleep-promoting role, the former is important for SWS initiation and the latter is important for SWS maintenance.

The results from the present study indicate that the neuronal circuits involved in thermoregulation and sleep regulation are largely independent, though there is an anatomical overlap of these circuits at the basal forebrain. At the same time, there are evidences to suggest that the mPOA do play a role in interlinking sleep regulation and thermoregulation (32).

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