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SHORT TERM REM SLEEP DEPRIVATION EFFECT ON TEMPERATURE RHYTHM OF RATS

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Abstract : Circadian rhythm of body temperature (CRT) is altered in endogenous depression and many psychiatric disorders. Even the sleep pattern is disrupted. Sleep deprivation alleviates symptoms in depression. The present study was conducted to find the role of noradrenergic innervation to the pineal gland in bringing about the effect of REM sleep deprivation (REMSD) on the CRT. Adult male Wistar rats (n=12) divided into 2 groups were used for the study. The group I rats (n=6) underwent superior cervical ganglionectomy and the group II rats (n=6) were sham ganglionectomised. After recovery rats were given REMSD for 48 hours. The CRT was measured in three periods of the study ie basal, post operative and post REMSD. The results indicated REMSD increased the Amplitude and Mesor of the CRT in both the groups which was shortlasting and reversible thus suggesting non sympathetic mediation of the pineal in bringing about the circadian rhythm alteration due to REMSD.

Key words : sleep deprivation, superior cervical ganglionectomy, temperature rhythm, rats

INTRODUCTION

There are numerous indications that sleep pattern is impaired in mental disorders, especially in endogenous depressives (1, 2). Alterations of diurnal variations of circadian rhythm of temperature (CRT) have been reported in maniac depressives and abnormalities in the phase and amplitude of CRT reported in case depressives (3, 4). In view of the sleep disturbances associated with depression, it is paradoxical that sleep deprivation can exert a therapeutic effect (5, 6). Various hypothesis have been put forward to explain this relationship. They have generally centered on the concept of internal desynchronization, postulating that biological rhythms vary in their mutual phase relationship. One is the phase-advance hypothesis, developed by Wehr and co workers (7, 8). Sleep deprivation therapy, as well as advancing bedtime for several hours would prevent sleep from occurring at a wrong (depressogenic) time of circadian phase. There are evidences to suggest that

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the therapies for depression like lithium and antidepressants also act on the circadian system (9). There is also a proposal that the amplitude of circadian rhythms may be more affected than the phase (10). A study on rats, the clomipramine model of depression showed hyperactivity of the hypothalamic pituitary axis (11). In this study it was also found that after a period of REM-SD the corticosterone levels, which were raised in case of the experimental rats reversed back to that of control level. In the past two decades there are many studies conducted of sleep deprivation effect on the circadian rhythms of body function on animals and human. Yamaguchi *et al.* (12) have studied the circadian rhythm of plasma cortisol levels in depressive patients, after sleep deprivation as antidepressive therapy and they have reported the disrupted rhythm was normalised after the therapy. In a study on healthy human beings it was found that after a period of 36 h of sleep deprivation the level of melatonin increased but of cortisol remained same, suggesting the role of melatonin in resetting the rhythms. (13). The study of Peder *et al* (14), conducted on the castrated Wistar rats has shown that REM-SD elevates the pineal content of melatonin. This mechanism might also be involved in the alleviation of human depression after REM-SD. Also, melatonin secretion is dependent upon the noradrenergic pathway via the superior cervical ganglion (15)

The present study was designed to investigate the role of pineal in bringing about the changes in the temperature rhythm after REM sleep deprivation. This was studied by denervating the sympathetic innervation of pineal gland in rats.

METHODS

The study was conducted on 12 adult male wistar rats in the weight range of 200–250 grams. The animals were divided into 2 groups, one with superior cervical ganglionectomy (n=6) and the other sham ganglionectomised (n=6). All throughout the study the rats were maintained under 12 : 12 light-dark cycle and ad libitum food and water was given. Three days of basal CRT was recorded by measuring rectal temperature 4 hours. A digital thermometer (OMRON Corpn.. Japan) was used which has a dependable accuracy of ± 0.1 °F. On the 4th day one group was superior cervical ganglionectomised (16, 17) while the other underwent sham operation. After post - operative recovery period of 4 days the CRT was again recorded for three more days. After this the rats were subjected to 48 hours of selective REM sleep deprivation by using a modified version of flower pot procedure also known as platform pedestal or water tank procedure (18). The REM-SD was started at 2000 hours and continued for 48 hours to end at 2000 hours on the 3rd day. Immediately after the REM-SD the rectal temperature rhythm recording was repeated for 3 days.

Statistical analysis

In the present study, the circadian rhythm analysis was done by using the cosinar analysis (19). From this analysis the phase (ACR), amplitude (AMP) and mesor (ME) of the circadian rhythm was determined. The values obtained for individual rats on total 9 days were grouped into control and experimental period and the mean of 3 days of recording period was

taken for comparison. Intra group comparisons for unpaired observations were made by one way ANOVA. Inter group paired comparisons were made by two sample 't' test.

RESULTS

The basal 1st, 2nd and 3rd day values of ACR, AMP & ME did not differ significantly in both the groups of rats. Therefore the average of the 3 days was taken for comparison. Similarly, the average of the 3 post SCGx/sham SCGx days were considered. (Table I shows the values in sham operated rats while Table II shows the same for SCGx rats). The mean ACR, AMP and ME of 3 post REM sleep deprivation days were individually compared with the average basal and average post operative values of the control and the experimental groups.

TABLE I: Shows the values of Amplitude. Acrophase and Mesor of the temperature rhythm in the non ganglionectomised rats. (Group 1). The 3 days of basal and 3 days of post operative values are given with their average values.

	Control							
	Basal				*Post operative*			
	Day 1 Mean (SD)	*Day 2 Mean (SD)*	*Day 3 Mean (SD)*	*Avg. Mean (SD)*	*Day 1 Mean (SD)*	*Day 2 Mean (SD)*	*Day 3 Mean (SD)*	*Avg. Mean (SD)*
AMP (°C)	0.54 (0.29)	0.36 (0.1)	0.52 (0.14)	0.47 (0.12)	0.43 (0.09)	0.47 (0.14)	0.35 (0.18)	0.41 (0.11)
ACR (hrs)	21.64 (1.14)	20.74 (1.7)	21.80 (1.02)	21.39 (1.16)	21.98 (0.81)	21.25 (1.56)	21.77 (1.05)	21.66 (0.74)
ME (°C)	37.35 (0.19)	37.21 (0.1)	37.15 (0.06)	37.24 (0.09)	37.33 (0.19)	37.33 (0.14)	37.34 (0.20)	37.33 (0.12)

TABLE II: Shows the values of Amplitude. Acrophase and Mesor of the temperature rhythm in the non ganglionectomised rats. (Group II). The 3 days of basal and 3 days of post operative values are given with their average values.

	Experimental							
	Basal				*Post operative*			
	Day 1 Mean (SD)	*Day 2 Mean (SD)*	*Day 3 Mean (SD)*	*Avg. Mean (SD)*	*Day 1 Mean (SD)*	*Day 2 Mean (SD)*	*Day 3 Mean (SD)*	*Avg. Mean (SD)*
AMP (°C)	0.58 (0.29)	0.39 (0.11)	0.49 (0.12)	0.49 (0.12)	0.31 (0.07)	0.33 (0.21)	0.34 (0.14)	0.33 (0.09)
ACR (hrs)	20.76 (1.41)	20.79 (1.03)	19.98 (1.15)	20.51 (0.87)	17.48 (2.77)	22.21 (2.43)	20.19 (5.94)	19.96 (3.48)
ME (°C)	37.28 (0.24)	37.4 (0.19)	37.37 (0.15)	37.35 (0.13)	37.46 (0.24)	37.41 (0.29)	37.46 (0.22)	37.44 (0.2)

Both the control and the experimental groups showed significant increase in the AMP on the day 1 of REM-SD as compared to the basal value. The day 1 AMP of the control group (0.85 ± 0.23) was significantly higher than the basal AMP and the post operative AMP (P<0.01). The day 2 and day 3 AMP did not differ from the basal or the post operative value. In the experimental group the AMP of the post REM-SD day 1 (0.76 ± 0.23) was significantly higher than the basal (P<0.05) and average post operative AMP (P<0.01). The day 2 and day 3 AMP did not differ from the basal and post operative values (Fig. I).

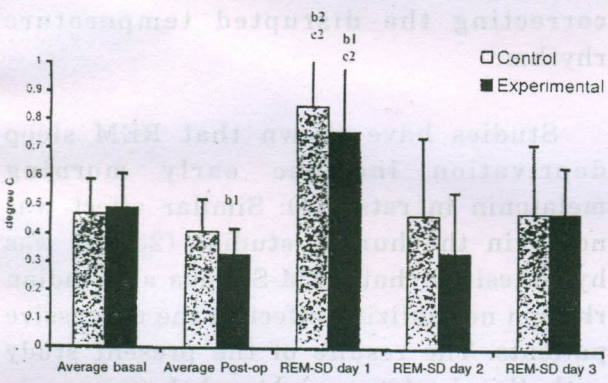

Fig. 1 : Shows comparison of basal and Post ganglionectomy AMP of temperature rhythm with the Post REMSD AMP in both the groups. There is significant increase in the AMP on the day 1 post REMSD.

a = Control Vs Experimental,

b = Basal Vs Post operative SCGx/Sham or post REMSD

c = REMSD Vs post SCGx/sham.

1 = P<0.05; 2 = P<0.01 and 3 = P<0.001

The day 1 ME of the control group (37.74 ± 0.18) was significantly higher than the basal ME (P<0.001) and the post operative ME (P<0.01). The day 2 and day 3 ME did not differ from the basal or the post operative values. In the experimental group the ME of the post REM-SD day 1 (37.72 ± 0.13) was significantly higher than the basal (P<0.001) and average post operative ME (P<0.05). The day 2 and day 3 ME did not differ from the basal and post operative values (Fig. 2). The acrophase values in both the experimental and the control groups did not show significant changes as compared to the average basal and the average postoperative values. Statistical analysis however failed to show any significant changes (Fig. 3).

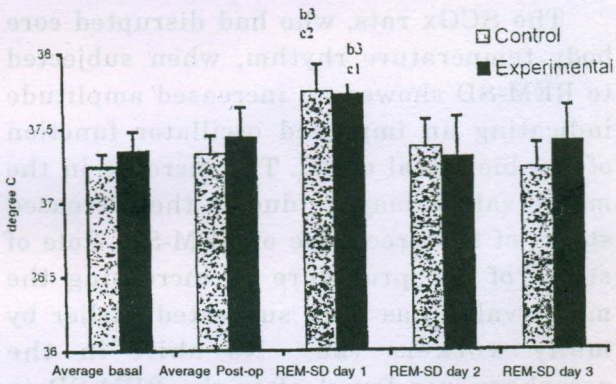

Fig. 2 : Comparison of basal and Post ganglionectomy ME of temperature rhythm with the Post REMSD AMP in both the groups. There is significant increase in the ME on the day 1 post REMSD and this is seen in both the groups.

a = Control Vs Experimental,

b = Basal Vs Post operative SCGx/Sham or post REMSD

c = REMSD Vs post SCGx/sham.

1 = P<0.05; 2 = P<0.01 and 3 = P<0.001

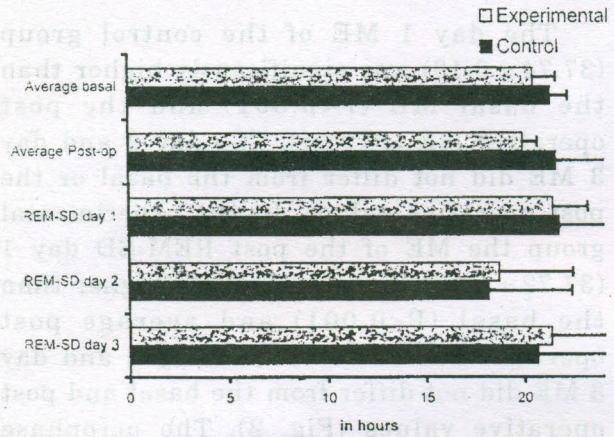

Fig. 3 : Shows comparison of basal and Post ganglionectomy AMP of temperature rhythm with the Post REMSD ACR in both the groups. There was no significant change in the ACR in both the groups.

DISCUSSION

The SCGx rats, who had disrupted core body temperature rhythm, when subjected to REM-SD showed an increased amplitude indicating an improved oscillator function of the biological clock.. The increase in the mesor values may be due to the increased stress of the procedure of REM-SD. Role of stress of the procedure in increasing the mesor value has been suggested earlier by many workers (20). No shift in the acrophase was found after the REM-SD in both the groups. The reason for this may be the 12:12 Light dark cycle which was maintained during REMSD and thus indicating that photoperiod has primary effect on the phase pattern of rhythm which was unaltered in our animals. Amplitude blunting of temperature rhythm is the most consistent change seen among the depressives and it is known that electroconvulsive therapy increase the amplitude of temperature rhythm and the mood of depressive patients (21). REM-SD is effective in improving the mood of the depressives (5 & 6). The increased AMP seen in the present study points at the circadian rhythm correcting effect of REM-SD. Here the increased AMP has taken place in the absence of main neural supply of the pineal i.e. postganglionic fibers from the superior cervical ganglion (15). Here the possibility of direct effect on the suprachiasmatic nucleus (SCN) by the other areas of brain cannot be ruled out, keeping in mind that there are many cholinergic and serotonergic afferents to the SCN (22). Cholinergic and adrenergic neurons are involved in the modulation of REM sleep (23), and the cholinergic activity seen after REM-SD (24) suggests a direct effect of REM-SD on the SCN in correcting the disrupted temperature rhythm.

Studies have shown that REM sleep deprivation increase early morning melatonin in rats (14). Similar effect was noted in the human studies (25). It was hypothesized that REM-SD has a circadian rhythm normalizing effect in the depressive patients. The results of the present study with this background knowledge supports the role of pineal melatonin in rhythm correcting effect of REM-SD. The pre tectal fibers connecting the pineal (26) and the serotonergic pathway from the dorsal raphe nucleus to the pineal (27, 22) suggest a possibility that nonsympathetic neural connections may also be involved in the regulation of melatonin secretion. The involvement of dorsal raphe nucleus in the REM sleep process (23) and their connections to the pineal suggests its role

in the effect of REM-SD. Increased pineal melatonin through the above mentioned neural connections, resulting in resetting the clock, through the actions of melatonin on the SCN cannot be ruled out. The conclusive evidence for such a role of melatonin can only be tested by studying the melatonin rhythm in a similar experimental setup.

The improvement seen in the rhythm of the SCGx rats is short lived and the rhythm gets disrupted on the 2nd day post REM-SD. Depressive patients treated by REM-SD show an improvement in mood, but there is a relapse of symptoms after a period of sleep (28). The short-lived improvement in the temperature rhythm in the present study are consistent with the observations in depressive patients treated with REM-SD.

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