

REM SLEEP DEPRIVATION AND FOOD INTAKE

J. L. BHANOT*

Department of Human Biology,
Punjabi University, Patiala - 147 002

AND

G. S. CHHINA, B. SINGH, U. SACHDEVA AND V. MOHAN KUMAR

Department of Physiology,
All India Institute of Medical Sciences,
New Delhi - 110 029

(Received on June 2, 1989)

Abstract : The effect of REM-sleep deprivation (REM-SD) on diet preference was studied in rats. REM-SD for a period of 72 hrs produced an increase in day, night and 24 hrs (day plus night) intakes of Carbohydrate Rich diet (CRD) and Total diet (TD). Body weight (BWt) was also increased. The maximum increase in the above parameters were recorded on the 2nd day of REM-SD. During recovery period the intakes of TD fully recovered, but the BWt and consumption of CRD remained high. Intakes of Balanced diet (BD) remained significantly on the lower side when compared to the pre REM-SD mean values. During REM-SD, the rats preferred CRD than BD. The body temperature did not show any change. The increase in TD intake and BWt could be the result of an increase in insulin level and the change appears to be mediated by the activation of hypothalamic feeding centre.

Key words : REM sleep deprivation (REM-SD)
carbohydrate rich diet (CRD)

food intake (FI) total diet (TD)
balanced diet (BD) body weight (BWt)

INTRODUCTION

Extensive information exists on several aspects of the influence of sleep on body functions (1, 2, 3, 4, 5, 6, 7, 8). These relate to cardio-respiratory, metabolic, endocrinal, visceral and autonomic activities of the body. However, very little is known about the effect of partial sleep deprivation on food preference. In modern day living exigencies of job requirements like night-shifts, intercontinental travel, and diverse forms of social living may lead to partial sleep deprivation. Dement has reported an increase

in BWt and appetite in human subjects after REM-SD (9). Rats and cats deprived of sleep showed an enhanced drive and motivation to obtain food (10, 11, 12). It was only the REM-sleep deprivation which was found to have any correlation with the altered FI (12). In contrast, Bowersox *et al* (13) have shown that the amount of REM sleep during the phase of a 12:12 hr illumination cycle does not significantly correlate with FI during the same or adjacent phases.

The majority of available evidence is indicative of

*Corresponding Author

an increase in FI as a result of REM-SD. However, there is no study showing the effect of REM-SD on the consumption of different type of food. The study was, therefore, undertaken to determine the quantitative changes in the FI as well as the changes in the preference for different types of diets when the rats are on REM-SD. It was also aimed at seeing whether these alterations are reflected on the body weight, and body temperature of the rats.

METHODS

Twelve 60 days old normophagic, normothermic adult male albino rats with body weight 200 to 250 g were used for the present study. The animals were housed in individual cages kept in an air conditioned room. A controlled illumination for dark and light period was maintained by means of an electric timer (lights off 1700-0500 hrs). The room temperature varied between 23°C and 25°C.

To determine the dietary intake and preferences for different foods under REM-SD conditions, the rats were supplied with 30 g each of three different diets viz balanced diet (BD) (Table I), carbohydrate rich diet (CRD) and protein rich diet (PRD) (Table II, III and IV) placed in three different spill proof containers. The cages were checked after every 6 hrs. to see if any of the food containers required an additional supply. The left over food in each container was weighed 12 hourly (8.00 to 8.30 am/pm) to determine day, night and 24 hrs intakes of different diets. The body weight (BWt) and rectal temperature (T_{rec}) were also recorded (8.00-8.30 am) daily.

TABLE I : Composition of balanced diet.

Crude protein (minimum)	24.0%
Ether extract (minimum)	4.0%
Crude fibre (maximum)	4.0%
Ash (maximum)	8.0%
Calcium (minimum)	1.0%
Phosphorous (minimum)	0.6%
Nitrogen free extract	50.0%

TABLE II : Composition of protein rich diet and carbohydrate rich diet.

Ingredients	Carbohydrate rich diet	Protein rich diet
Casein	15%	90%
Dextrose	78%	3%
Corn oil	3%	3%
Salt mixture	4%	4%
Vitamin mixture	2.2 gms added to 100 gms of each diet	

TABLE III : Composition of salt mixture

Calcium Carbonate (CaCO ₃)	390.0 gms
Calcium hydrogen phosphate (CaHPO ₄ ·2H ₂ O)	682.0 gms
Sodium hydrogen phosphate (Na ₂ HPO ₄ ·2H ₂ O)	375.0 gms
Potassium chloride (KCl)	392.0 gms
Magnesium sulphate (MgSO ₄ ·7H ₂ O)	121.0 gms
Ferric amonium citrate	34.0 gms
Mangnese sulphate (MnSO ₄ ·4H ₂ O)	1.8 gms
Copper sulphate (CuSO ₄ ·5H ₂ O)	2.5 gms
Zinc sulphate (ZnSO ₄)	0.1 gm
Sodium fluoride (NaF)	1.0 gm
Potassium aluminium sulphide (KAl(SO ₄) ₃ ·12H ₂ O)	0.2 gm
Potassium iodide (KI)	0.1 gm

TABLE IV : Composition of vitamin mixture.

Thiamin	0.15 gm
Riboflavin	0.25 gm
Pyridoxin	0.15 gm
Biotin	0.005 gm
Inositol	5.00 gm
Nicotinic acid	0.50 gm
Calcium pantothenate	0.50 gm
Ascorbic acid	0.10 gm
Vit. K ₃	0.05 gm
Folic acid	0.05 gm
Vit. B ₁₂	0.005 gm
PABA	1.00 gm
Sucrose to make 1000 gm.	

The above mentioned parameters in the rats were studied daily for a period of ten days. The pre-exposure period values of all these parameters did not show much variations. Therefore, every third day (i.e. 1st, 4th, 7th and 10th) value of the parameters were taken for calculation of pre-exposure readings.

The animals were deprived of REM phase of sleep for a period of 72 hrs from 8 am on the 11th day to 8.00 am on the 14th day of the study. REM-SD was achieved by using a modified version of the flower pot procedure also known as the platform pedestal or water tank procedure (14, 15, 16, 17, 18). This procedure has been validated against appropriate electro-physiological measures of sleep (2). This technique consisted of a water filled plastic truf with 25.0 cm diameter and 30.0 cm height with a heavy platform of 5.0 cm. diameter and 18.0 cm height placed in the middle of the truf. The animals rested on the platform placed in the middle, with its top just protruding above the surface of the surrounding water. The experimental platform permitted wakefulness and non REM sleep but not REM sleep. The platform was so small that the animal was awakened as it falls towards water with the loss of postural muscle tone at the onset of each REM period.

All the parameters were measured daily during the period of REM-SD. The parameters were again recorded on every 3rd day (i.e. 14th, 17th 20th and 23rd days) for determining the manner of recovery of different parameters in the rats.

Since the animals did not consume PRD, therefore the same was not processed for statistical calculations.

To find out the significant pairs of means among the pre-exposure means of each parameter on different days Newman Keuls Multiple range test (19) was applied. No significant differences between

these pairs of means were found and therefore, the means and standard deviations of each parameter recorded on the last day of the pre-exposure period was taken for further applying Newman Keuls Multiple range test to see the level of significance of the effects of the experimental procedure (REM-SD) as well as the pattern of recovery.

Range of percentage changes in each parameter during REM-SED was found out by calculating the percentage change in each parameter on each day of REM-SD in all the animals. The mean percentage change during the whole period of REM-SD was also calculated for each parameter.

RESULTS

TD intake showed on enhancement during REM-SD, details of which is given below :

Effect of REM-SD on 24 hrs TD intake : The values of 24 hrs TD intake ranged from 24.41 ± 3.15 g to 29.67 ± 1.83 g with a mean value of 27.55 ± 2.78 g. REM-SD for 3 days (72 hrs) produced a significant increase in 24 hrs TD intake which ranged from 16.12% to 41.22% with a mean value of 31.13%. The maximum increase in 24 hrs TD intake was seen on the 2nd day of REM-SD. On the very first day of the recovery period, was noticed a significantly reduced 24 hrs TD intake than pre REM-SD 24 hrs TD intake which with a progressive increase recovered by 10th day of the recovery period (Fig. 1). The variation in 24 hrs TD intake was uniformly distributed in day and night intakes of TD, the details of which are given below :

Effect of REM-SD on day TD intake : The mean values of day TD intake ranged from 8.50 ± 1.44 g to 10.42 ± 1.31 g with a mean value of 9.50 ± 0.96 g. REM-SD produced a significant increase in day TD intake which ranged from 20.06% to 46.97% with a mean value of 33.99%. The maximum increase in day TD intake was observed on the 2nd day of

REM-SD. Like 24 hrs TD intake there was a significant reduction in day TD intake on the first day of recovery which subsequently recovered to pre REM-SD intake by 4th day (Fig. 1).

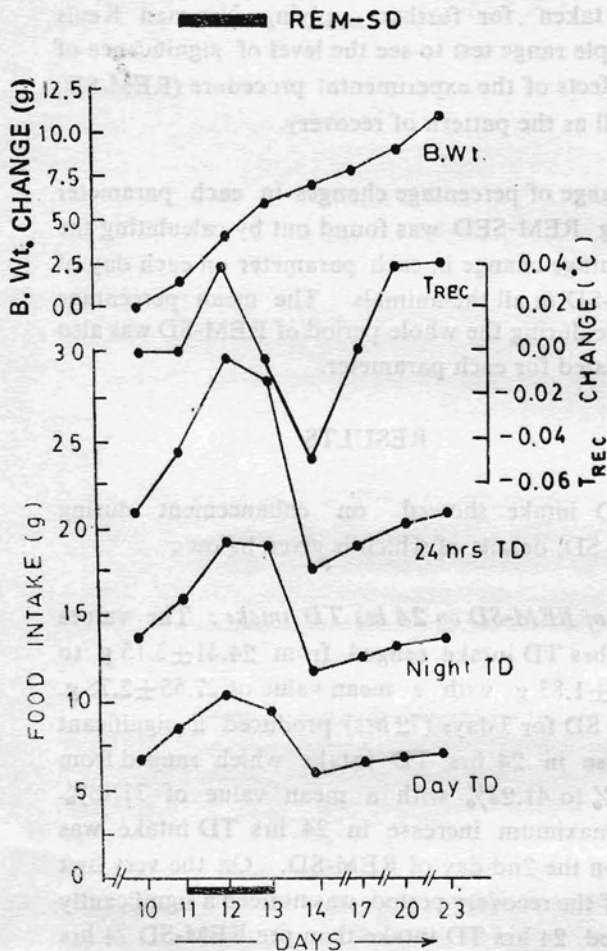


Fig. 1. Graph showing effect of REM-SD on 24 hrs, day and night TD intakes in g and changes in B.Wt. in g and Body Temperature (Trec) in °C in rats.

Effect of REM-SD on night TD intake : The mean values of night TD intake ranged from 15.91 ± 2.39 g to 19.25 ± 1.42 g with a mean value of 18.06 ± 1.86 g. A significant increase in night TD intake ranging between 14.30% and 38.29% with a mean value of 29.67% was noticed during REM-SD. The maximum increase in night TD intake was seen on the 2nd day of REM-SD. Like 24 hrs and day TD intakes, a significant decrease in night TD intake was observed on the first day of the recovery which with a progressive increase recovered to the pre REM-SD intake by 7th day (Fig. 1).

Effect of REM-SD on Dietary preferences : During REM-SD the animals showed a preference for CRD intake in comparison to BD intake, details of which is given below :

Effect of REM-SD on 24 hrs CRD : A significant increase in 24 hrs CRD intake was seen during REM-SD which ranged from 60.93% to 114.79% with a mean value of 92.25%, whereas the mean values ranged from 15.16 ± 1.80 g to 20.25 ± 0.96 g with a mean value of 18.11 ± 2.64 g. The increase in 24 hrs CRD intake was maximum on 2nd day of REM-SD. During the period subsequent to REM-SD, though a steep fall in 24 hrs CRD intake was noticed on the first day of the recovery but it remained significantly higher than the pre REM-SD mean value throughout recovery period (Fig. 2).

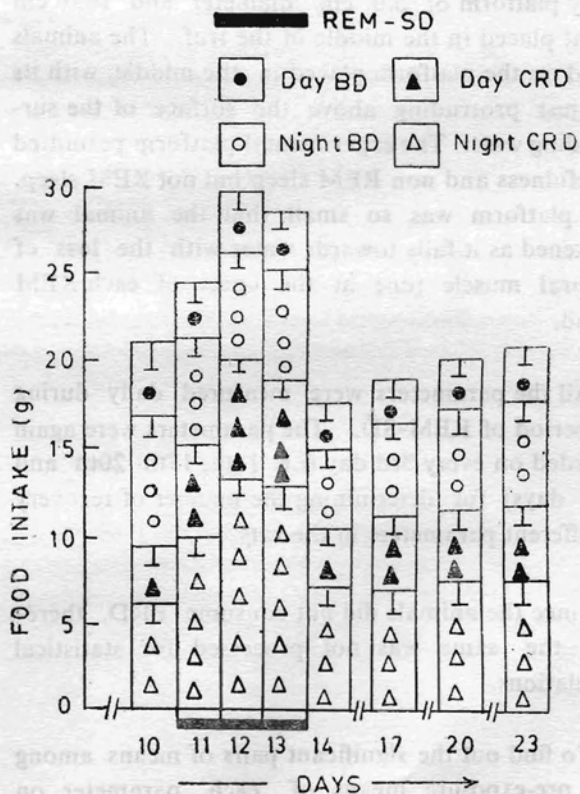


Fig. 2. Histogram showing effect of REM-SD on day and night CRD and BD intakes in g in rats.

Effect of REM-SD on day CRD intake : A significant increase in day CRD intake ranging from 60.25% to 118.30% with a mean value of 91.80% was observed during REM-SD and the mean values ranged from 5.08 ± 0.99 g to 6.92 ± 0.66 g with a mean value of 6.08 ± 0.93 g. The increase in day CRD intake was maximum on 2nd day of REM-SD. Like 24 hrs CRD, day CRD intake also showed a steep fall on the first day of the recovery period but the intake remained significantly higher, throughout the recovery period, than the pre REM-SD level (Fig. 2).

Effect of REM-SD on night CRD intake : REM-SD produced a significant increase in night CRD intake which ranged from 61.28% to 113.28% with a mean value of 92.48% and the mean values ranged from 10.08 ± 1.15 g to 13.33 ± 0.98 g with a mean value of 12.03 ± 1.72 g. The maximum increase in night CRD intake was seen on 2nd day of REM-SD. During recovery period, night CRD intake showed recovery on the very first day while the same again increased significantly by 7th day (Fig. 2).

Effect of REM-SD on 24 hrs BD intake : REM SD did not produce any change in 24 hrs BD intake, whereas throughout the recovery period a significant decrease than the pre REM-SD intake of 24 hrs BD was noticed (Fig. 2).

Effect of REM-SD on day BD intake : REM-SD did not produce any change in day BD intake and throughout the recovery period remained significantly on the lower side when compared to the pre REM-SD value (Fig. 2).

Effect of REM-SD on night BD intake : The mean values of night BD intake ranged from 5.83 ± 1.70 g to 6.33 ± 1.55 g with a mean value of 6.02 ± 0.26 g. A significant decrease in night BD intake was produced by REM-SD which ranged between 17.47% and 23.98% with a mean value of 21.51%. The maximum decrease noticed was on the first day of REM-SD. During recovery period night BD intake

remained significantly decreased as compared to the pre REM-SD mean value (Fig. 2).

Effect of REM-SD on Body Weight : The mean values of BWt ranged from 228.25 ± 11.54 g to 233.00 ± 11.46 g with a mean value of 230.72 ± 2.38 g. REM-SD produced a significant increase in BWt which ranged from 0.59% to 2.68% with a mean value of 1.67%. The maximum increase in BWt was observed on 3rd day of REM-SD. Subsequent to REM-SD the BWt did not recover but remained significantly increased (Fig. 1).

Effect of REM-SD on Body Temperature : REM-SD did not produce any effect on body temperature (Fig. 1).

Thus it has been found that REM-SD produced significant increase in TD and CRD intakes both during day and night. The animals preferred CRD than BD. During recovery period the intakes of CRD and BD remained significantly on the higher and lower sides respectively, while the TD intake recovered to the pre REM-SD level. The BWt also showed a significant rise during REM-SD which did not return during the subsequent period. REM-SD did not effect the body temperature.

DISCUSSION

Increase in FI was demonstrated by Dement *et al* (10) in starved animals with REM-SD. Within a short duration of REM-SD, in the present study an increase in BWt accompanied by an increase in FI both during day and night is observed. The increase is primarily because of a higher intake of CRD. The preference for CRD and its higher intake during night as compared to day suggest that the normal rhythm of eating in dark periods in rats is not changed by REM-SD. The continued change in the preference for CRD and increase in BWt even when the TD intake has recovered suggests the triggering of mechanisms in the body for long lasting

positive energy balance and enhanced CRD intake for meeting the immediate energy requirements. The finding not only confirm the observations of Dement (9) in human subjects, who had demonstrated an increase in BWt but also provide explanation for the basis of this increase. The reduced amount of T4 produced by SD (20) tends to lower the metabolic rate, while the availability of GH may facilitate the anabolic processes leading to weight gain.

This trend of BWt gain by SD is also supported by Vondera *et al* (21) who reported that enzymatic activity in the skeletal muscle is more in favour of storage than mobilisation.

It is quite likely that higher intake of carbohydrate which is known to stimulate insulin release (22, 23, 24, 25, 26) and thus anabolic processes in the body (27, 28) may be involved in bringing about weight gain. This is supported by the fact that small amount of insulin injected daily produces an increase in BWt and FI (29). Thus increase in FI and BWt which accompanies the REM-SD could be the result of an increase in insulin level. The change appears to be mediated by the activation of the hypothalamic feeding centre.

REFERENCES

- Baust W, Weidinger H, Kirchner F. Sympathetic activity during natural sleep and arousal. *Arch Ital Biol* 1968; 106 : 379-84.
- Bulow K. Respiration and wakefulness in man. *Acta Physiol Scand* 1963; 59 : Suppl. 209 : 1-110.
- Bulow K, Ingvar DH. Respiration and state of wakefulness in normals, studied by spirography, capnography and EEG. *Acta Physiol Scand* 1961; 51 : 230-38.
- Dement W, Klaitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility and dreaming. *Electroencephalogr. Clin Neurophysiol* 1957; 9 : 673-90.
- Iwamura Y, Okuno A, Nakamoto Y, Suzuki J. Blood pressure and REM sleep in normotensive and spontaneously hypertensive rats (SHR). *Jpn Heart J* 1979; 20 : (Suppl. I) 126-8.
- Parker DC, Rossman LG, Kripke DF, Gibson W, Wilson K. Rhythmicities in human growth hormone concentrations in plasma. In "Endocrine Rhythms" edited by D. T. Krieger, *New York : Raven Press*, 1979b; 143-73.
- Phillipson EA, Read DJSC, Murphy E, Kozar LF. Ventilatory and waking responses to hypoxia in sleeping dogs. *J Appl Physiol Respir Environ Exercise Physiol* 1978a; 44 : 512-20.
- Van Den Noort S, Brine K. Effect of sleep on brain labile phosphates and metabolic rate. *Am J Physiol* 1970; 218 : 1434-9.
- Dement W. The effect of dream deprivation. *Science* 1960; 131 : 1705-7.
- Dement W, Henry P, Cohen H, Ferguson J. Studies on the effect of REM deprivation in humans and in animals. In "Sleep and altered states of consciousness". edited by S. S. Kety, E. V. Everts and H. L. William. Baltimore; pp 456-69, 1967.
- Froham LA, Goldman JK, Schnatz JD, Bernardis LL. Hypothalamic obesity in the weanling rat : effect of diet upon hormonal and metabolic alterations. *Metabolism* 1971; 20 : 501-12.
- Siegel JM. REM sleep predicts subsequent food intake. *Physiol Behav* 1975; 15 : 399-403.
- Bowersox SS, Baker TL, Dement WC. Rapid eye movement sleep and its relationship to feeding behaviour in the adult cat. *Physiol Behav* 1984; 32 : 907-9.
- Hicks RA, Moore JD, Hayes C, Phillips N, Hawkins J. Rem sleep deprivation increases aggressiveness in male rats. *Physiol Behav* 1979; 22 : 1097-1100.
- Hicks RA, Pettey B, Okuda A, Thomson D. The effects of REM sleep deprivation on age and locomotor activity in rats. *Psychol Rec* 1979; 29 : 355-60.
- Jouvet-Monnier D, Vimont P, Delorme F, Jouvet M. Etude de la privation selective de la phase paradoxale de Bommeil Chez la Chat. *CR Soc Biol* 1964; 158 : 756-9.
- Morden B, Mitchell G, Doment W. Selective REM sleep deprivation and compensation phenomena in the rat. *Brain Res* 1967; 5 : 339-49.

18. Vimont-Vicary P, Jouvett D, Delorme JF. Effect of EEG at comportementaux des privation de Sommeil paradoxal chez le Chat. *Electroenceph Clin Neurophysiol* 1966; 20 : 439-49.
19. Newman D. *Biometrics* 1939; 5 : 250. Quoted in "Statistical methods" by G W. Snedecor and W. G. Cochran, VIth edition, Oxford and IBH Publishing Co., New Delhi. 1967; pp 273-5.
20. Opstad PK, Aakvaag A. The effect of sleep deprivation on the plasma levels of hormones during prolonged physical strain and caloric deficiency. *Eur J Appl Physiol* 1983; 51 : 97-107.
21. Vondera K, Brodan V, Bass A, Kuhn E, Teisinger J, Andelm A, Veselkova A. Effects of sleep deprivation on the activity of the selected metabolic enzymes in the selected muscle. *Eur J Appl Physiol* 1981; 47 : 41-6.
22. Curry DL, Benett LL, Grodsky GM. Dynamics of insulin secretion by the perfused rat pancreas. *Endocrinology* 1968; 83 : 572-84.
23. Elomaa E, Johansson GG. Rapid eye movement stage of sleep participates in the generation of the nocturnal meal pattern in the rat. 1980; 24 : 331-6.
24. Gerich JE, Charles MA, Grodsky GM. Characterization of the effect of arginine and glucose on glucagon and insulin release from the in-vivo perfused rat pancreas. *J Clin Invest* 1974; 54 : 833-41.
25. Grodsky GM. A threshold distribution hypothesis for packet storage of insulin and its mathematical modeling. *J Clin Invest* 1972; 51 : 2047-59.
26. Grodsky GM, Curry D, Landahl H, Benett LL. Further studies on the dynamic aspects of insulin release *in vitro* with evidence for a two compartmental storage system. *Acta Diabet Lat* 1969; 6 (Suppl) : 554-79.
27. Dangvir J, Nicoladis S. Dependence of sleep on nutrients availability. *Physiol and Behav* 1979; 22 : 735-40.
28. Mendelson WB, Guthrie RD, Guynn R, Harris RL, Wyatt RJ. Rapid eye movement (REM) sleep deprivation; stress and intermediary metabolism. *J Neurochem* 1974; 22 : 1157-9.
29. Le Magnen J, Devos M, Gaudilliers JD, Loise-Sylvestre J, Tallon S. Role of lipostatic mechanism in regulation by feeding of energy balance in rats. *J Comp Psychol* 1973; 84 : 1-23.

Indapamide has been shown to be a potent stimulator of vasopressin (AVP) release (1, 2). LeBlond et al. (3) have reported in 11 of 19 patients with essential hypertension that indapamide (2.5 mg daily for 6 weeks) increased urinary PGE₂ excretion probably via stimulation of renal production; however there was no correlation between the percentage difference in PGE₂ excretion and the mean changes in blood pressure, plasma renin activity or plasma aldosterone concentration. The present study was undertaken to study the antihypertensive effect of indapamide and modification of the same after chronic treatment with indomethacin (PG antagonist) in DOCA-salt hypertensive rats.

INTRODUCTION
 Indapamide is a new antihypertensive agent which has been shown to exert effective control of hypertension in animals (1) and in man (2). The nature of the antihypertensive effect of indapamide is still debatable. Chemically it is analogous with chlorothalidone (3). Several studies on hypertensive patients have shown indapamide to be unique among diuretics with regards to its ability to induce a significant reduction in arterial pressure at doses which produce little or no diuresis (4, 5). Therefore, it has been hypothesized that the antihypertensive action of indapamide may be due to some alternative mechanism.

*Present address: K. M. Kundann College of Pharmacy, 100 No. 1, Dr. K. O. T. Reddam, Marol Nagar, Bangalore - 560 018.
 **Medical Director and Dean, K. M. Kundann College and O.M. Hospital, Kundann Nagar, Bangalore.
 Corresponding Author.