

Differential Circadian Eating Patterns in Two Psychogenetically Selected Strains of Rats Fed Low-, Medium-, and High-Fat Diets

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Spontaneous eating patterns in male, inbred Roman high- and low-avoidance rats (RHA/Verh, RLA/Verh) were continuously recorded while animals were successively offered three isocaloric (≈ 16.5 -kJ/g) diets: a low-fat, high-carbohydrate diet (LF; 3.3% fat), a medium-fat diet (MF; 18% fat), and a high-fat diet (HF; 40% fat), the latter being followed once again by the LF diet. Under the conditions of this experiment, overall 24-h food intake did not differ significantly between RHA/Verh and RLA/Verh rats, but was significantly higher for both rat strains on the MF and HF diets than on the LF diet. Despite the similar 24h-food intake, RHA/Verh rats ate transiently less than RLA/Verh rats during the third quarter of the dark phase under all dietary conditions. These differences were due to the RHA/Verh rats' longer intermeal intervals (with all diets) and smaller meals (with the MF and HF diets) and were compensated for during the last 3 h of the dark phase. On the LF diet, dark-phase meal frequency was higher and both nocturnal meal size and mean eating rate within meals were lower in RLA/Verh rats than in RHA/Verh rats. With the MF and HF diets, mean nocturnal meal size and meal duration were higher and mean eating rate was lower in RLA/Verh rats than in RHA/Verh rats. For both strains, nocturnal meal size was significantly higher with the MF and HF diets than with the LF diet, and nocturnal meal frequency was lower with the HF diet than with the other two diets. Although body weights were similar at the start of the study, RLA/Verh rats gained significantly more weight than did RHA/Verh rats by the end. As has often been the case with other aspects of behavior studied, differences in neuromodulatory systems (e.g., serotonergic and dopaminergic) between RHA/Verh and RLA/Verh rats may directly or indirectly contribute to the subtle differences in eating patterns observed here.

KEY WORDS: RHA/Verh and RLA/Verh rats; serotonin; dopamine; regulation of food intake.

INTRODUCTION

The Swiss sublines of Roman high- and low-avoidance rats (RHA/Verh and RLA/Verh) are selected

and bred for the rapid versus nonacquisition of two-way, active avoidance behavior. Compared to RHA/Verh rats, RLA/Verh rats react more negatively to repeated handling and injections and show greater increases in plasma corticosterone, ACTH and prolactin in various novel situations (Gentsch *et al.*, 1982; Walker *et al.*, 1989), and more pronounced heart rate changes in response to nonconditioned and conditioned stressful stimuli (D'Angio *et al.*, 1988; Roozendaal *et al.*, 1992). RHA/Verh rats are also more active than RLA/Verh rats at

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Table I. Composition of Diets (%)

	LF	MF	HF
Casein ^a	13.00	13.00	13.00
Corn starch	76.67	46.00	0
Soybean oil	3.33	3.41	3.54
Beef tallow	0	9.42	23.54
Lard	0	5.17	12.92
Mineral mixture ^b	4.00	4.00	4.00
Vitamin mixture ^c	3.00	3.00	3.00
Diluent ^d	0	16.00	40.00
Total	100.00	100.00	100.00

^a Säurecasein (UFAG Sursee), crude protein content 89%, supplemented with 1% DL-methionine.

^b One kilogram of mineral mixture contained 162.14 g Ca, 80.75 g P, 66.31 g Na, 90.88 g K, 38.99 g Mg, 102.0 g Cl, 2.92 g Fe, 665 mg Mn, 174 mg Cu, 411 mg Zn, 27 mg I, 63 mg F, 13 mg Co, 9 mg Se.

^c One kilogram of vitamin mixture contained 700,000 IU A, 70,000 IU D₃, 4.91 g E, 1.80 g C, 1.00 g B₁, 0.60 g B₂, 0.45 g B₆, 1.20 mg B₁₂, 1.80 g nicotinic acid, 1.50 g pantothenate, 100 mg folic acid, 3 mg biotin, 18.75 g choline.

^d Polyethylene powder (Lupolen; BASF, Ludwigshafen, Germany).

various times during the light/dark cycle, with three distinct locomotion peaks, at the beginning, in the middle, and at the end of the dark phase. Locomotor activity of RLA/Verh rats does not show such peaks and decreases gradually during the dark phase (Gentsch *et al.*, 1991).

Marked differences between RHA/Verh and RLA/Verh rats have been found in serotonergic (Driscoll *et al.*, 1983; Driscoll, 1988; Charnay *et al.*, 1995) and dopaminergic (D'Angio *et al.*, 1988; Driscoll *et al.*, 1990; Giorgi *et al.*, 1994) pathways. Basal dopaminergic activity in the nigrostriatal system (Driscoll *et al.*, 1990) and the density of D₁ dopamine (DA) receptors in the nucleus accumbens are higher in RHA/Verh rats than in RLA/Verh rats (Giorgi *et al.*, 1994), and these differences may be responsible for the two rat lines' differences in locomotor activity. There is also a greater dopaminergic stress response in the prefrontal cortex of RHA/Verh rats, which has been associated with the heightened attention and the attempt of that rat line to actively (rather than passively) cope with the environment (D'Angio *et al.*, 1988). In addition, RHA/Verh rats have a higher basal turnover rate of serotonin (5-HT) in the hypothalamus (Driscoll, 1988) than RLA/Verh rats.

Hypothalamic serotonergic and dopaminergic pathways are implicated in satiety (for re-

views see Leibowitz, 1986; Blundell, 1991), and a nucleus accumbens dopaminergic pathway seems to be involved in the initiation and reinforcement of behavior (Hoebel, 1985; Hoebel *et al.*, 1990). Extrahypothalamic DA, specifically in the striatum, stimulates eating (Stricker and Zigmond, 1984), and the olfactory stimulation associated with food presentation has been shown to be sufficient to activate the mesocortical dopaminergic system in hungry rats (Bertolucci-D'Angio *et al.*, 1990). Given the putative involvement of DA and 5-HT in the control of food intake, the differences between the two Roman sublines in these neurochemical pathways may translate into differences in eating behavior. This prompted us to record the circadian free eating pattern and cumulative food intake of RHA/Verh and RLA/Verh rats. As the effects of DA and 5-HT on eating may depend on the macronutrient composition of the food, isocaloric diets with varying fat contents were offered successively.

METHOD

Animals and Housing Conditions

In contrast to all previous studies published with the Swiss sublines of RHA/Verh and RLA/Verh rats (outbred within a closed colony since 1972), the present experiments were performed with 12 inbred (fifth-generation) male rats of each strain, derived from the outbred stock. All rats came from different litters, weighed 351 ± 6 g (RHA/Verh) and 360 ± 5 g (RLA/Verh) at the beginning of the experiment, and had not been used in previous research. The rats were individually housed in Plexiglas cages with floors of stainless-steel rods, in an isolated, temperature-controlled ($22 \pm 1^\circ\text{C}$) room, kept on a 12/12-h dark-light cycle (lights off at 1900). After being acclimatized to the cages for several weeks, they were successively fed three isocaloric (≈ 16.5 -kJ/g) diets with different carbohydrate and fat contents: a low-fat, high-carbohydrate diet (LF; 3.3% fat), a medium-fat diet (MF; 18% fat), and a high-fat diet (HF; 40% fat) (Table I). Each diet was presented for at least 14 days, all diet switches being conducted between 1830 and 1900, and the rats were weighed at each switch in diet. Tap water was always available ad lib.

Data Acquisition and Analysis

Cumulative food intake and meal patterns were continuously recorded by a computerized device. The cages were constructed so that the rats were forced to eat out of spill-resistant cups which were fixed on scales (Mettler, PE 300). The actual weight of the cups was automatically checked every minute by a computer (Olivetti M240). Meals were defined as food removals exceeding 0.3 g, with the time between any two removals not exceeding 15 min (Langhans and Scharrer, 1987). Using this meal definition, the recorded meals accounted for approximately 99% of the cumulative food intake. After each 24 h of data collection, the data were saved on a disk and the computer was restarted. For meal pattern analysis, all meal parameters were computed for each rat separately. Consequently, all tables and figures show the means of the 12 individual values for each rat strain. Statistical analysis was performed using unpaired *t* tests or one-way ANOVA with post hoc Bonferroni multiple comparisons. *p* values <.05 were considered significant.

RESULTS

Twenty-four-hour daily food intake did not differ significantly between RLA/Verh and RHA/Verh rats at any time during the experiment (Fig. 1). The mean daily food intake during the initial 16 days on the LF diet was 17.8 ± 0.3 g ($X \pm SE$) and 18.4 ± 0.4 g for RHA/Verh and RLA/Verh rats, respectively. The switch to the MF diet caused an immediate increase in food intake (Fig. 1). After the initial surge, the daily MF diet intake stabilized around 21 g (14-day mean: RHA/Verh rats, 20.3 ± 0.4 g; RLA/Verh rats, 21.4 ± 0.5 g), which was significantly ($p < .001$) higher than the previous LF diet intake (Fig. 1). The switch from the MF to the HF diet caused a transient, insignificant decrease in daily food intake in both strains before it stabilized again around 21 g (RHA/Verh rats, 21.3 ± 0.4 g; RLA/Verh rats, 21.6 ± 0.4 g) [significantly ($p < .001$) higher than LF diet intake]. Finally, switching the rats from the HF diet back to the LF diet caused a dramatic reduction of food intake (Fig. 1). LF diet intake during the final days of the experiment was not significantly different from LF diet intake in the beginning (days 1–16). Despite the absence of any

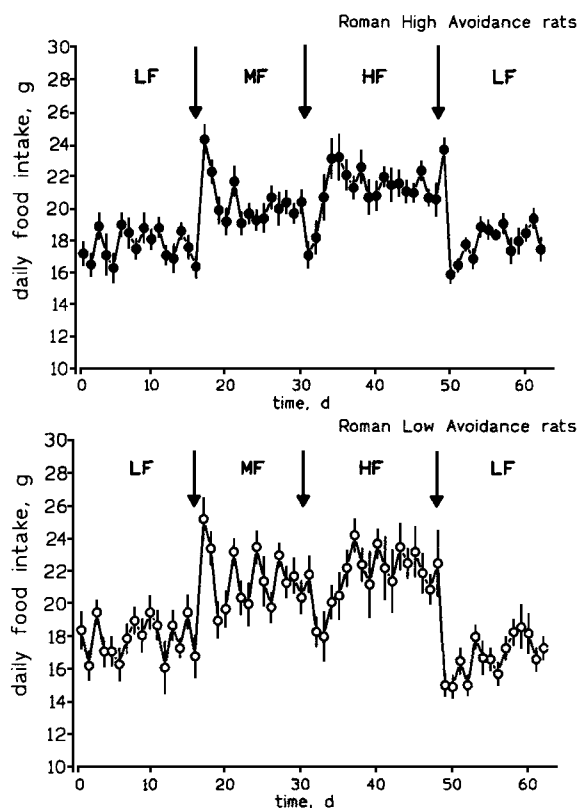


Fig. 1. Mean daily food intake of Roman high-avoidance and Roman low-avoidance rats, successively fed equicaloric low-fat (LF; 3.3% fat), medium-fat (MF; 18% fat), and high-fat (HF; 40% fat) diets. Arrows indicate the diet switches. Each value represents the mean \pm SE of 12 rats. See text for further details.

difference between RHA/Verh and RLA/Verh rats' 24-h food intake, RLA/Verh rats consistently ate significantly more than RHA/Verh rats during the third quarter of the dark phase under all dietary conditions (Fig. 2). This difference reached a maximum of about 3.5 g (LF diet) or 5 g (MF and HF diets) and disappeared toward the end of the dark phase.

The overall mean dark-phase meal patterns of RHA/Verh and RLA/Verh rats were also different (Table II). When calculated over the initial 16 days on the LF diet, the dark-phase meal frequency was higher and the nocturnal meal size, as well as the mean eating rate (meal size/meal duration) within nocturnal meals, was lower in RLA/Verh rats than in RHA/Verh rats. With the MF diet (days 18–31), overall nocturnal meal size and meal duration were higher, and eating rate was lower, in RLA/Verh rats

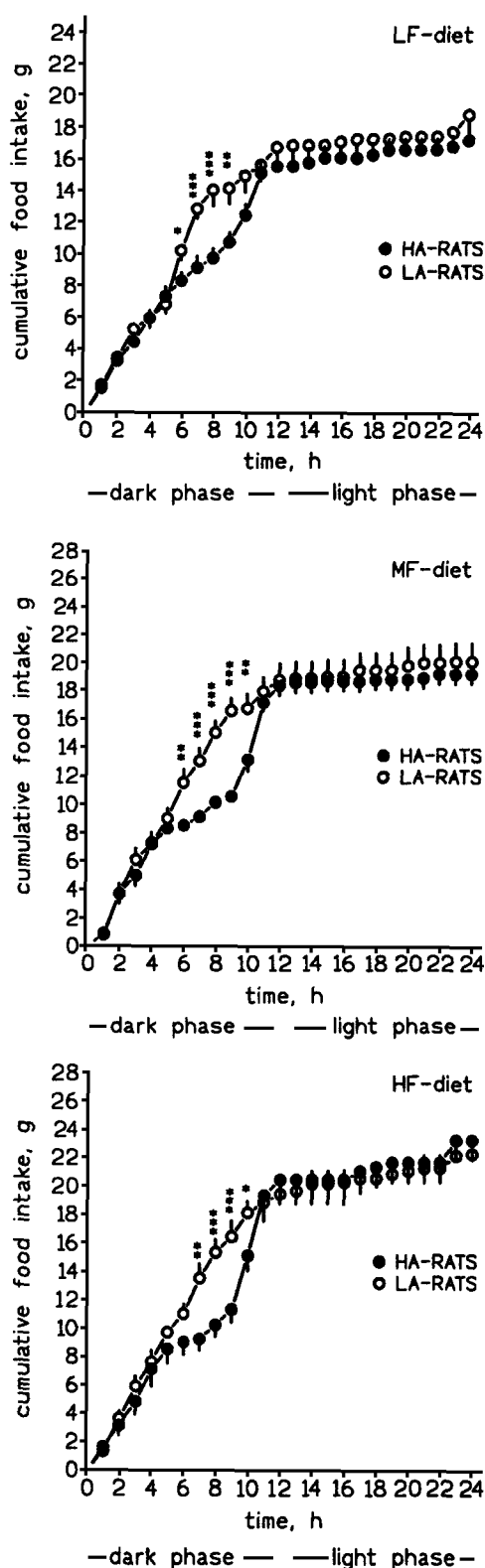


Fig. 2. Cumulative food intake of Roman high-avoidance and Roman low-avoidance rats on typical days with low-fat (LF), medium-fat (MF), and high-fat (HF) diet. Significantly different from the corresponding RHA/Verh value: * $p < .05$; ** $p < .01$; *** $p < .001$.

Table II. Overall Dark-Phase Eating Pattern of Roman High ($n = 12$)- and Low ($n = 12$)-Avoidance Rats Fed Three Diets^a

	RHA/Verh rats	RLA/Verh rats
Low-fat diet		
Meal frequency	6.2 ± 0.1	6.9 ± 0.2*** ^b
Meal size (g)	2.7 ± 0.1 ^b	2.5 ± 0.1 ^b
Meal duration (min)	20.3 ± 1.0 ^b	20.8 ± 1.0
Eating rate (g/min) ^b	0.14 ± 0.01	0.12 ± 0.01*
Satiety ratio (min/g) ^c	35.1 ± 1.1	33.8 ± 1.6 ^b
Medium-fat diet		
Meal frequency	6.2 ± 0.2	5.8 ± 0.3
Meal size (g)	3.2 ± 0.1	3.7 ± 0.1***
Meal duration (min)	15.0 ± 1.1	21.6 ± 1.5**
Eating rate (g/min)	0.23 ± 0.01	0.18 ± 0.01***
Satiety ratio (min/g)	32.6 ± 0.73	25.6 ± 0.54***
High-fat diet		
Meal frequency	5.5 ± 0.1 ^a	5.2 ± 0.2
Meal size (g)	3.8 ± 0.04	4.3 ± 0.2*
Meal duration (min)	13.9 ± 1.0	21.4 ± 2.0**
Eating rate (g/min)	0.28 ± 0.02	0.20 ± 0.01***
Satiety ratio (min/g)	31.6 ± 0.66 ^c	25.5 ± 0.95***

^a The rats were fed each diet for at least 14 days. Values are means ± SE of 12 high- and 12 low-avoidance rats' individual means calculated over the 14-day test periods. Significantly different from the corresponding high-avoidance value: * $p < .05$; ** $p < .01$; *** $p < .001$. ^bSignificantly different from high-fat diet and medium-fat diet value, $p < .05$. ^cSignificantly different from medium- and high-fat diet value, $p < .01$. ^dSignificantly different from low-fat diet value, $p < .05$.

^b Meal size/meal duration.

^c Duration of intermeal interval/size of subsequent meal.

than in RHA/Verh rats. The picture was basically the same during the first day on the MF diet, when rats of both strains ate larger amounts. This transient hyperphagia was due to insignificant increases in both meal size and meal frequency (data not shown). With the HF diet (days 32–45), overall nocturnal meal size and meal duration were also greater, and eating rate was lower, in RLA/Verh rats than in RHA/Verh rats. As the RLA/Verh rats' greater MF and HF meals were generally not accompanied by longer intermeal intervals, the satiety ratio of nocturnal MF and HF meals was lower in RLA/Verh than in RHA/Verh rats. The pronounced hypophagia in response to the final switch from the HF to the LF diet was due to a marked reduction in meal size. Average nocturnal meal size was reduced from $4.4 ± 0.8$ g ($X ± SE$) on the last HF day to $2.3 ± 0.2$ g on the first LF day in RLA/Verh rats and from $3.6 ± 0.4$ to $2.3 ± 0.2$ g in RHA/Verh rats, respectively. Meal patterns gener-

Table III. Successive Nocturnal Meals of Roman High (RHA/Verh)- and Low (RLA/Verh)-Avoidance Rats Fed Three Diets^a

	Low-fat diet		Medium-fat diet		High-fat diet	
	RHA/Verh rats	RLA/Verh rats	RHA/Verh rats	RLA/Verh rats	RHA/Verh rats	RLA/Verh rats
1. Meal size (g)	2.92 ± 0.09	2.43 ± 0.16**	3.22 ± 0.18	3.39 ± 0.19	3.77 ± 0.11	3.84 ± 0.12
Meal duration (min)	21.3 ± 1.4	21.1 ± 1.6	13.6 ± 1.4	16.1 ± 1.1	13.0 ± 1.6	20.4 ± 2.3**
IMI ^b (min)	83.7 ± 4.5	66.4 ± 3.3**	90.0 ± 7.2	78.1 ± 5.8	100 ± 4.7	81.6 ± 4.9**
2. Meal size (g)	2.82 ± 0.14	2.45 ± 0.11	2.98 ± 0.13	4.12 ± 0.22***	3.96 ± 0.11	4.71 ± 0.21**
Meal duration (min)	19.6 ± 1.1	20.0 ± 1.2	12.1 ± 0.7	22.6 ± 1.8***	11.2 ± 0.8	24.4 ± 1.2***
IMI (min)	104 ± 6.2	75.7 ± 4.5***	118 ± 8.4	72.7 ± 6.2***	175 ± 6.7	109 ± 5.1***
3. Meal size (g)	2.57 ± 0.10	2.45 ± 0.14	2.72 ± 0.07	3.69 ± 0.10***	3.31 ± 0.13	3.89 ± 0.3
Meal duration (min)	19.0 ± 1.2	20.9 ± 1.4	11.9 ± 0.6	21.2 ± 1.6***	10.4 ± 1.0	18.6 ± 2.9**
IMI (min)	123 ± 9.1	81.6 ± 5.6***	133 ± 11	93.6 ± 5.9**	133 ± 6.0	104 ± 6.8**
4. Meal size (g)	2.45 ± 0.19	2.62 ± 0.16	2.98 ± 0.12	3.39 ± 0.20	3.85 ± 0.16	3.71 ± 0.09
Meal duration (min)	16.2 ± 1.5	23.6 ± 1.9**	13.2 ± 1.0	19.5 ± 1.5**	15.6 ± 2.7	16.8 ± 0.7
IMI (min)	87.0 ± 5.1	61.3 ± 5.6**	95.4 ± 5.6	83.1 ± 7.2	89.0 ± 6.5	99.2 ± 8.0
5. Meal size (g)	2.70 ± 0.15	2.45 ± 0.10	2.97 ± 0.13	3.00 ± 0.17	3.57 ± 0.2	3.87 ± 0.30
Meal duration (min)	20.4 ± 1.9	19.9 ± 1.1	15.4 ± 1.9	16.0 ± 1.6	13.6 ± 1.0	16.9 ± 2.0
IMI (min)	64.3 ± 3.7	88.2 ± 5.8**	74.1 ± 9.3	103 ± 10*	47.0 ± 7.2	100 ± 10***
6. Meal size (g)	2.73 ± 0.27	2.36 ± 0.10	3.34 ± 0.18	2.85 ± 0.24	3.50 ± 0.23	3.31 ± 0.21
Meal duration (min)	18.4 ± 2.1	19.1 ± 0.5	15.1 ± 1.3	15.6 ± 1.9	12.3 ± 1.8	15.0 ± 1.7
IMI (min)	67.8 ± 5.2	70.4 ± 8.5	37.7 ± 2.9	96.9 ± 12**	44.6 ± 4.6	134 ± 14***
7. Meal size (g)	2.81 ± 0.20	2.20 ± 0.19*	2.92 ± 0.16	2.45 ± 0.18	3.50 ± 0.26	3.22 ± 0.24
Meal duration (min)	20.5 ± 2.3	18.1 ± 2.1	12.8 ± 1.6	8.4 ± 0.9*	11.2 ± 1.5	12.9 ± 1.9
IMI (min)	40.1 ± 4.8	73.3 ± 8.8**	65.4 ± 15	139 ± 23**	29.1 ± 3.1	42.0 ± 15

^a Only the first seven successive meals are shown. Based on the average number of meals during the dark phase (see Table II) and the average meal and intermeal interval durations, these seven meals cover the vast majority of all meals that occurred. Significantly different from the RHA/Verh value: * $p < .05$; ** $p < .01$; *** $p < .001$.

^b Intermeal interval.

ally differed between dietary conditions (Table II). Thus, the nocturnal meal size of both rat strains was significantly higher with the MF and HF diets than with the LF diet. In addition, nocturnal meal frequency of both strains was significantly lower with the HF diet than with the other two diets. LF meal duration was longer than MF or HF meal duration in RHA/Verh but not RLA/Verh rats. Perhaps as a result, the satiety ratio was nearly the same under all three dietary conditions in RHA/Verh rats, whereas in RLA/Verh rats satiety ratio was lower with the MF and HF diet.

Closer analysis of successive nocturnal meals and intermeal intervals (Table III) revealed that RHA/Verh rats ate transiently less than RLA/Verh rats during the third quarter of the dark phase because of longer intermeal intervals when rats were eating the LF diet (Table III). With the MF and HF diets, this difference was due to longer intermeal intervals and smaller meals.

At the onset of the experiment, body weights of the RLA/Verh and RHA/Verh rats were 360 ± 5 and 351 ± 6 g, respectively. At the switch from

the LF to the MF diet, only the body weight of RLA/Verh rats had increased significantly (to 380 ± 5 g), and it was significantly higher than the body weight of RHA/Verh rats at that time (359 ± 8 g). At the switch from the MF to the HF diet, the body weight of RLA/Verh rats had further increased to 397 ± 4 g, vs. 370 ± 7 g in RHA/Verh rats ($p < .01$). Body weight at the switch from the HF back to the LF diet was 397 ± 4 and 377 ± 7 g for RLA/Verh and RHA/Verh rats, respectively. This difference was still significant ($p < .05$). After the final 14 days on the LF diet, body weights were 405 ± 4 g (RLA/Verh rats) and 386 ± 7 g (RHA/Verh rats) ($p < .05$).

DISCUSSION

The lack of a difference in overall food intake between singly caged, inbred RHA/Verh and RLA/Verh rats in the present experiment demonstrates that both rat strains are able to regulate food intake similarly and do not respond differently to variations in the level of dietary fat. Despite the

similar overall food intake, however, body weight gain differed between the two strains. RLA/Verh rats gained significantly more weight than RHA/Verh rats did. This is presumably due to the well-known differences between the two lines in motor activity (Gentsch *et al.*, 1991; Bättig *et al.*, 1976; Driscoll and Bättig, 1982) and thermogenesis (Waldvogel, 1977), although the relative contribution of these two mechanisms to the differences in body weight gain cannot be judged from the present experiment. Also, it should be remarked that group-housed, outbred RHA/Verh rats have been observed to eat more over 24-h periods than their RLA/Verh counterparts (unpublished results), as have singly caged, outbred rats of these lines as well (Meerlo *et al.*, 1997).

Increasing the fat content of the diet led to an increase in 24-h food intake in both strains of rats. This increase was seen mainly when the rats were switched from the LF to the MF diet, i.e., when the fat content was increased from 3 to 18% (by weight). The switch from the MF to the HF diet (18 to 40% fat) did not further increase daily food intake. Hyperphagia is typically seen in laboratory animals and humans consuming high-fat diets (see Warwick, 1996). The mechanisms of high-fat diet hyperphagia are not completely understood. High-fat diets have a reputation of being highly palatable, and orosensory influences have often been implicated in high-fat diet hyperphagia (see Warwick 1996). A preference for the orosensory properties of the MF diet may contribute to the peak in daily food intake immediately after the switch from the LF to the MF diet. However, it is unlikely that orosensory factors alone account for the continuing hyperphagia during MF diet consumption, because differences in palatability usually do not lead to permanent changes in daily food intake (Scharrer and Geary, 1982). Given the well-established differences in emotionality between RHA/Verh and RLA/Verh rats (e.g., Ferré *et al.*, 1995; Steimer *et al.*, 1997), one might also expect that the reaction of both rat strains to hedonic factors and, hence, food intake would be different in this case. Moreover, high-fat diets are often also overconsumed when the high- or low-fat diets are offered alone for several days, and when the sensory properties of the high-fat diet are less attractive than those of the low-fat diet (Warwick, 1996). This indicates that postingestive effects play an important role in high-fat diet hyperphagia. Postingestive effects pre-

sumably also contribute to the high level of MF intake in RHA/Verh and RLA/Verh rats between day 19 and day 30 in the present study, but the nature of these postingestive effects needs to be identified. Food intake increased when rats were switched from the LF to the MF diet, although the diets were isocaloric. This is interesting because high-fat diets that are overeaten typically have a higher energy density than low-fat diets (see Warwick, 1996), and in the few studies that controlled for energy density, rats usually did not increase energy intake with the high-fat diet when this diet was isocaloric to the low-fat diet (Geary *et al.*, 1979, Warwick 1996). The reason(s) why RHA/Verh and RLA/Verh overate on the isocaloric MF diet is unknown and requires further investigation.

Shifting the rats from the HF diet back to the LF diet caused a marked decrease in daily food intake in both strains, i.e., this shift essentially reversed the high-fat hyperphagia because the daily food intake returned to the baseline levels recorded at the onset of the experiment. The decrease in food intake was due to a reduction in meal size, which is in line with a recent report by Del Prete and Scharrer (1995). However, unlike the Sprague-Dawley rats in the experiment described by those authors, RHA/Verh and RLA/Verh rats in the present study already significantly reduced the size of their very first LF meal. Therefore, conditioning effects which may contribute to the decline in meal size after the HF-LF switch in Sprague-Dawley rats (Del Prete and Scharrer, 1995) do not seem to be involved. The suppression of food intake upon the introduction of a low-fat, high-carbohydrate diet in subjects previously kept on a high-fat diet may be a consequence of the reduced glucose tolerance and the changes in glucose metabolism brought about by high fat intake (Lundbaek and Stevenson, 1947; Mayer and Thomas, 1967; Geary *et al.*, 1979). Yet, whatever regulatory mechanisms are responsible for this change in food intake, they are obviously functional and do not differ between RHA/Verh and RLA/Verh rats, because both strains similarly decreased their food intake in response to the HF-LF diet shift. Whereas a contribution of orosensory factors to the rapid decline in food intake after the switch from the HF to the LF diet cannot be excluded, it appears again unlikely that such differences would account for the lasting differences in food intake.

Comparison of overall meal patterns revealed some interesting differences. Eating rate was higher in RHA/Verh than in RLA/Verh rats under all dietary conditions, i.e., RHA/Verh rats were able to eat more in less time. This fits the observation that (outbred) RHA/Verh rats which were allowed to eat for only 1 h per day ingested significantly more food than (outbred) RLA/Verh rats did during the same time period (P. Ferré and R. M. Escorihuela, personal communication). Despite their lower eating rate, RLA/Verh rats consumed larger meals than RHA/Verh rats when eating the MF and HF diet. Meal duration decreased in RHA/Verh rats but did not change in RLA/Verh rats when dietary fat increased. Together, these findings indicate that RHA/Verh rats are highly motivated to eat but become satiated more quickly than RLA/Verh rats. Further studies are necessary to determine whether these differences are related to the well-known differences between the two strains (lines) in neurochemical pathways. Access to food has been shown to increase dopaminergic activity in the nucleus accumbens, hypothalamus, and amygdala (Heffner *et al.*, 1980), and dopaminergic activity in the nigrostriatal pathway (Driscoll *et al.*, 1990) as well as the density of D₁-DA receptors in the nucleus accumbens, is higher in RHA/Verh rats than in RLA/Verh rats (Giorgi *et al.*, 1994). The nucleus accumbens dopaminergic system that is implicated in the initiation and reinforcement of behavior might therefore contribute to the higher eating rate of RHA/Verh rats. On the other hand, hypothalamic 5-HT turnover is higher in RHA/Verh rats than in RLA/Verh rats (Driscoll, 1988), and this difference might contribute to the RHA/Verh rats' smaller MF and HF meals. Medial hypothalamic 5-HT turnover has long been implicated in satiety (see Leibowitz, 1986, 1988, Simansky, 1996), and it has recently been hypothesized that 5-HT has a strong effect on fat consumption (Blundell *et al.*, 1995). Certain 5-HT receptor types, in particular, have been implicated in the serotonergic control of appetite and food intake (Pan and Gilbert, 1993; Tecott *et al.*, 1995).

A closer look at the circadian distribution of food intake and meal patterns revealed that, despite the similar 24-h food intake, and irrespective of diet, cumulative food intake between 6 and 9 h of the dark phase was significantly lower in RHA/Verh than in RLA/Verh rats. With the LF diet this difference appeared to originate from an ac-

cumulation of longer intermeal intervals (IMIs) observed in RHA/Verh rats during the first 6 h of the dark phase. This was compensated for by a shortening of IMIs for the meals taken subsequently (meals 5 to 7; Table III). Thus, LF meals seemed to satiate RHA/Verh rats more than RLA/Verh rats during the first part, and less so during the second part, of the dark phase. Whether these variations are somehow related to differences in their metabolism or locomotor activity is unknown. Indirect support for a contribution of locomotor activity is derived from the finding that food-deprived RHA/Verh rats obtained less food than RLA/Verh rats in a DRL-20 operant conditioning test, due to their incapability of suppressing nonrelevant activity in that test (Zeier *et al.*, 1978). As no rats were food-deprived in the present study, the possibility exists that the urge to locomote was often stronger in RHA/Verh rats than the urge to eat and that this tendency particularly expressed itself after initial eating bouts had been concluded, lasting until energy requirements and hunger once again predominated toward the end of the dark phase (see Gentsch *et al.*, 1991). With the MF and HF diets RHA/Verh rats had longer IMIs but also ate smaller meals than RLA/Verh rats during the first part of the dark phase, whereas the opposite was observed thereafter. Further studies are necessary to clarify whether there are also differences in the circadian variations of neurochemical pathways between the two rat strains which might account for these subtle circadian variations in eating behavior.

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