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Kurzmitteilung

Influence of age and hepatic branch vagotomy on the night/day distribution of food intake in rats

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Einfluß des Alters und der hepatischen Vagotomie auf die Nacht/Tag-Verteilung der Futteraufnahme bei der Ratte

Summary: The aim of the present study was to investigate the influence of age and hepatic branch vagotomy on the night/day distribution of food intake in male rats. Food intake of young (age: 2 months) and aged (age: 13.5 months) hepatic branch vagotomized (HBV) and sham-vagotomized (SV) rats was measured at intervals of 6 h during the 12 h dark and the 12 h light phase.

The results show that in rats the night/day ratio of food intake decreases with age and is not affected by hepatic branch vagotomy. However, the time-course of spontaneous diurnal food intake was influenced by hepatic branch vagotomy. The change in the night/day distribution of food intake might be due to age-related changes in the nucleus suprachiasmaticus of the hypothalamus.

Zusammenfassung: Ziel der Untersuchung war es, den Einfluß des Alters und der hepatischen Vagotomie auf die Nacht/Tag-Verteilung der Futteraufnahme bei der Ratte zu untersuchen. Es wurde die Futteraufnahme von jungen (Alter: 2 Monate) und alten (Alter: 13.5 Monate) Ratten, deren hepatischer Vagusast durchtrennt worden war oder die scheinvagotomiert worden waren, alle 6 Stunden in der jeweils 12 h dauernden Dunkel- bzw. Hellphase gemessen.

Die Ergebnisse zeigen, daß das Nacht/Tag-Verhältnis der Futteraufnahme mit dem Alter abnimmt und daß die hepatische Vagotomie die Nacht/Tag-Verteilung der Futteraufnahme nicht beeinflußt. Dagegen wurde der Verlauf der spontanen Futteraufnahme in der Hellphase durch den hepatischen Vagusast beeinflußt. Die altersabhängigen Veränderungen der Nacht/Tag-Verteilung der Futteraufnahme könnten auf altersbedingten Veränderungen im Nucleus suprachiasmaticus im Hypothalamus zurückzuführen sein.

Key words: Age – night/day distribution of food intake – hepatic branch vagotomy – rat

Schlüsselwörter: Alter – Nacht/Tag-Verhältnis der Futteraufnahme – hepatische Vagotomie – Ratte

Introduction

Many kinds of behavior and physiological functions show rhythmic variations synchronous with the natural alternation of night and day (1). This also applies to feeding and drinking behavior (5, 6, 11). For instance, rats ingest about 70–80 % of their food during the dark phase of the light/dark cycle (11).

Some studies in laboratory animals suggest age-related changes in circadian rhythms. For instance, the amplitude of the circadian temperature rhythm and the amplitude of several hormonal rhythms are reduced in old rats (17). Peng and Kang (14) reported among other findings a complete loss of circadian rhythmicity for feeding-associated behavior in six out of 10 aged rats (age: 22–24 months). The night/day distribution of food intake was however not quantified in this study. We therefore measured food

intake separately during the dark and light phase in young (age: 2 months) and aged (age: 13.5 months) rats. Since there is some evidence that the liver and the hepatic vagus branch play an important role in control of feeding (2, 4, 7–10, 15, 16) the experiments were performed with hepatic branch vagotomized and sham-vagotomized rats. Food intake was determined every 6 h during the 12 h dark and 12 h light period. The animals were fed a diet with about 40 % of the metabolizable energy in the form of fat, in order to simulate fat intake in man in highly developed countries.

Methods

The experiments were performed with young (age: 2 months) and old (age: 13.5 months) male ZUR:SIV hepatic branch vagotomized (HBV) and sham-vagotomized (SV) rats. The ZUR:SIV strain is an outbred strain which belongs to the Sprague-Dawley group. The method for hepatic branch vagotomy has been described in detail elsewhere (7). Briefly, after rats were anesthetized a midline incision was made from the xyphoid process to about 1 cm behind the umbilicus. In order to expose the upper abdominal organs, a self-retaining retractor was inserted and the xyphoid process was bent towards the head with a hemostatic forceps. The stomach and lower esophagus were gently retracted and the lobes of the liver were laid to the animal's right side. The hepatic branch of the vagus was identified with a binocular microscope and sectioned between two 3–0 silk sutures placed 5–10 mm apart. For sham-vagotomy the nerve was exposed but not sutured nor cut. Wounds were closed with sutures. An antibiotic and analgesic were administered after surgery. Surgery was performed on 1.5 months old rats 2 weeks (young rats) or 12 months (old rats) before the experiments were started. It was shown previously that a functional reinnervation does not occur during this interval (3, 15). Rats were individually housed in a temperature-controlled (21 ± 1 °C) room on a 12 h light 12 h dark cycle. The rats were fed a medium-fat (MF, 18 % fat) diet. Diet composition is shown in Table 1. Body weight of rats is presented in Table 2. Body weight of the old rats was stable, when the experiment was performed. However, the young rats were still gaining weight. Food intake during the dark and light phases was

Table 1. Composition of the MF diet (g)

Casein[a])	13.00
Corn starch	46.00
Soybean oil	3.41
Beef tallow	9.42
Lard	5.17
Mineral mixture[b])	4.00
Vitamin mixture[c])	3.00
Diluent[d])	16.00
Total	100.00

[a]) Säurekasein (UFAG, Sursee), crude protein content 89.0 %, supplemented with 1 % D,L-methionine

[b]) 1 kg mineral mixture contained 162.14 g Ca, 80.75 g P, 66.31 g Na, 90.88 g K, 38.99 g Mg, 102.00 g Cl, 2.92 g Fe, 665 mg Mn, 174 mg Cu, 411 mg Zn, 27 mg J, 63 mg F, 13 mg Co, 9 mg Se

[c]) 1 kg vitamin mixture contained 700 000 IU A, 70 000 IU D_3, 4.91 g E, 1.80 g C, 1.00 g B_1, 0.60 g B_2, 0.45 g B_6, 1.20 mg B_{12}, 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, FRG)

measured by weighing the food cups every 6 h (± 0.1 g). Values are presented as means ± SEM. The significance of differences between values was tested with the unpaired (Table 2) or paired (Table 3) *t*-test and *p* values less than 5 % were considered significant.

Table 2. Body weight, daily and nocturnal food intake of young and old HBV rats and SV rats

		Body wt. (g)	Intake/day (g)	Nocturnal intake (%)
Young rats (age: 2 months)				
HBV	(n = 16)	246 ± 5	24.1 ± 0.9	82.0 ± 2.3
SV	(n = 16)	248 ± 4	22.8 ± 0.8	81.6 ± 2.8
Old rats (age: 13.5 months)				
HBV	(n = 17)	789 ± 21	23.9 ± 0.7	60.1 ± 2.3***
SV	(n = 14)	788 ± 19	24.2 ± 0.6	55.1 ± 2.2***

Values are means ± SEM
*** Significantly different ($p < 0.001$) from corresponding value in young rats

Table 3. Diurnal and nocturnal food intake (g) of young and old HBV rats and SV rats

		0–6 h	6–12 h	0–12 h
Diurnal				
young HBV	(n = 16)	0.9 ± 0.3***	3.2 ± 0.5	4.2 ± 0.5
young SV	(n = 16)	1.5 ± 0.5	2.8 ± 0.4	4.1 ± 0.7
old HBV	(n = 17)	4.0 ± 0.5*	5.3 ± 0.4	9.3 ± 0.7
old SV	(n = 14)	5.6 ± 0.4	5.2 ± 0.4	10.8 ± 0.5
Nocturnal				
young HBV	(n = 16)	11.1 ± 0.7*	8.8 ± 0.8	19.7 ± 1.1
young SV	(n = 16)	10.9 ± 0.6**	7.7 ± 0.6	18.7 ± 0.7
old HBV	(n = 17)	8.6 ± 0.6**	6.0 ± 0.3	14.6 ± 0.6
old SV	(n = 14)	7.5 ± 0.6	6.0 ± 0.6	13.4 ± 0.7

Values are means ± SEM
*, **, *** Significantly different from corresponding value in the second half of the light or dark phase (paired t-test, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$)

Results

Total 24 h food intake was similar in young and old rats and was not influenced by hepatic branch vagotomy (Table 2). The percentage of nocturnal food intake was significantly lower ($p < 0.001$) in old rats than in young rats and did not differ between HBV and SV rats (Table 2). Both the young and the old rats ate more in the first than in the second half of the dark phase (Table 3). During the light phase the young and the old HBV rats ate significantly more in the second half than in the first half. This does not apply to the SV rats. The food intake during the first and the second halves of the light phase was similar in the old SV rats, whereas in young SV rats it appeared to be somewhat higher in the second half. This difference was, however, not statistically significant.

In the old rats results very similar to those reported were obtained in an experiment performed 4 weeks earlier.

Discussion

The results clearly show that in rats the night/day distribution of food intake is affected by age. Aged rats (age: 13.5 months) ate only about 55–60 % and young adult rats (age: 2 months) over 80 % of their food during the dark phase. These observations are not in accord with the observations of Peng et al. (13). These authors did not find a change in the night/day distribution of food intake in Long Evans rats between 4 months and 12 months of age. There was also no significant difference between 8–12 and 24–30 months old Long Evans rats (13). Thus, strain differences might be important with regard to the age-dependent decrease in the night/day distribution of food intake. Although old rats considerably differed in body weight from young rats (Table 1), body weight was not significantly correlated with the night-to-day ratio of food intake, neither in young (SV rats: $r = 0.17$; HBV rats: $r = 0.02$) nor in old rats (SV rats: $r = 0.32$; HBV rats: $r = 0.09$). Thus, an effect of body weight and obesity on the age-dependent decrease in the night/day distribution of food intake is unlikely. The decrease in the night/day distribution with age also seems not to depend on feeding the fat-enriched diet, because similar findings were recently obtained in rats fed a commercial high carbohydrate diet (15).

Neither in the young nor in the old rats did hepatic branch vagotomy (HBV) affect the night/day distribution of food intake. Others have reported that diurnal food intake is increased following HBV in Charles River rats fed Purina laboratory chow (4). Interestingly HBV produced a significantly greater food intake in the second half of the light phase as compared to the first half (Table 3). In intact rats this difference in diurnal feeding behavior did not occur, suggesting that the time-course of spontaneous diurnal food intake is influenced by the hepatic vagus branch. There is indeed some evidence that hunger is partly signaled to the brain via the hepatic vagus branch (2, 8, 9, 16). Unlike diurnal feeding behavior, nocturnal feeding behavior was not markedly affected by HBV.

Since the circadian rhythm of food intake depends on the nucleus suprachiasmaticus in the hypothalamus (12), the change in the night/day distribution of spontaneous food intake with advancing age might be due to age-related changes in this pacemaker. Evidence of age-related alterations within this nucleus has been provided by Wise et al. (18, 19) who found that aging alters the circadian rhythm of its glucose utilization.

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