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Food Preference and Length of Life

Abstract. *When random-bred rats were given freedom of dietary choice throughout postweaning life, their life-span correlated with the dietary practices before midlife, particularly those exhibited during early life.*

The relationship between diet and longevity was established when it was demonstrated experimentally that a regimen of caloric restriction imposed throughout postweaning life increased the length of life (*1*). Under natural conditions, however, the quantity or composition (or both) of the diet consumed may change with age and differ from individual to individual. Thus it is important to determine whether, and to what extent, self-determined dietary practices correlate with life-span.

We reported that when rats were given freedom of choice, the composition of the diet selected varied from rat to rat in a manner that maximized the risk to the individual of developing a neoplasm and other diseases associated with aging (*2*). The longevity data presented here were obtained from the same animals.

The self-selection regimen of the 121 individually housed male Charles River COBS rats, which are genetically relatively heterogeneous, was begun at 21 days of age and maintained throughout life. Each rat was provided with three complete isocaloric purified diets in separate containers. Inasmuch as these diets differed in protein (casein) and carbohydrate (sucrose) content only (*3*), the number of dietary variables was limited to the quantity of food consumed and the relative and absolute intakes of protein and carbohydrate. The amounts of each of the three diets consumed and the preference data derived from these values were determined daily. Mean values for successive weekly, 50-day, and 100-day periods were used for actuarial (*4*) and statistical (*5*) analyses.

Without exception, the rats consumed some food daily from each container, but no two rats had the same feeding habits. After an initial period of adjustment, the quantity and composition of the composite diet selected by an individual usually stabilized within narrow limits. The durations of the adjustment period and of the stable peroid differed from rat to rat.

The stable phase for amount of food consumed persisted as long as 300 days. At any time during this period, the food intake values nearly fit a normal distribution curve (*6*). The time required for the protein/carbohydrate ratio of the diet selected (*6*) to stabilize was more variable than that for either component separately. Some rats attained a stable ratio as early as the second week of feeding; approximately 50 percent reached it by the fifth week. Once the ratio was established, it was maintained by some rats throughout most of life. However, a number of rats failed to establish a stable ratio, and from the beginning exhibited a slow and progressive change in the protein/carbohydrate ratio of the preferred diet.

If the dietary preferences of the animals are not considered, their life expectancy at time of weaning was age 630 days. The largest number of deaths per 100-day age period, 32 percent, occurred between ages 600 and 699 days. The death ages were nearly normally distributed, ranging from 317 to 1026 days.

Data presented below show that (i) longevity was related to the dietary habits of the animal, (ii) the correlations were limited to age periods before midlife, and (iii) the age when a correlation was first found, as well as the duration and direction of the correlation, differed for each dietary variable.

Actuarial analyses demonstrated that rats that chose to consume large amounts of food were more likely to be short-lived than rats whose intake was smaller (Table 1). The earliest indication of an association between appetite and life-span was found when the rats had been on the self-selection regimen for only 5 weeks. During the period of relatively constant intake, a 10 percent difference in intake was associated with an 8 percent difference in the probable length of life.

For a more critical appraisal, ungrouped data were used (simple correlation values in Table 2). Inasmuch as a strong association of life-span with one variable may mask an association with another, or may interact to give rise to an apparent but invalid correlation, partial correlation coefficients were computed (Table 2). This method of analysis permits singling out the character of a correlation between two variables while another or other variables are held constant. To assess the combined effects of two or more dietary variables, multiple correlation values were also derived (Table 2).

Simple correlations. In agreement with the actuarial analyses, simple correlations indicated that length of life was inversely related to the amount of food consumed. However, the magnitude of the food intake effect, as determined from the regression equations, changed with age. It was maximal during age period 100 to 199 days (26-day loss in life-span for a 1-g daily difference in food intake), and by midlife it was negligible. If the level of food intake still later in life related to life-span, it was not detected in this study.

If the amount of food consumed is not considered, low-protein diets early in life were more likely to be associated with

Table 1. Life-span of rats permitted freedom of dietary choice: relationship to food intake. Rats are classified according to the mean daily food intake during age period 100 to 199 days. The age for 50 percent survival was estimated from survival curves. The mortality ratio reflects the relative death risk at all ages. It is computed as 100 times the actual number of deaths divided by the expected number of deaths. Values < 100 indicate the extent of reduction in risk relative to "standard" population; those > 100 indicate the extent of increase in relative risk. Age-specific mortality rates for all rats (N = 121) were used as standard rates in deriving the expected number of deaths at consecutive age periods for each of the subclasses.

Food intake (g/day)		N	Life-span (days, mean ± S.E.)	Age for 50% survival (days)	Mortality ratio
Mean ± S.E.	Range				
18.3 ± 0.8	16.2 to 19.2	20	733 ± 117	690	62
19.8 ± 0.3	19.4 to 20.2	20	653 ± 126	650	97
20.7 ± 0.3	20.3 to 21.1	20	630 ± 111	630	103
21.6 ± 0.2	21.2 to 21.9	20	612 ± 115	610	108
22.4 ± 0.4	22.0 to 22.9	20	600 ± 113	580	121
24.1 ± 1.0	23.0 to 26.6	21	556 ± 106	540	162

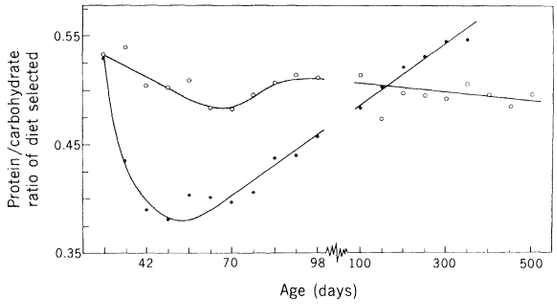

Fig. 1. Protein/carbohydrate ratio of diet selected by 30 of the shortest-lived rats (●) and 30 of the longest-lived rats (○). Each class represents 25 percent of the total population. Mean life-span was 473 days for short-lived rats and 787 days for long-lived rats. The protein/carbohydrate ratio of the diet selected by the short-lived rats was significantly different from that selected by long-lived rats ($P < .05$ for weeks 7 to 13).

short life-spans than high-protein diets. Later in life this pattern reversed, so that rats choosing low-protein diets lived longer.

For carbohydrate intake, the age when a significant negative correlation with life-span was first seen was the same as for total food intake, but significant correlations were obtained only through age period 200 to 299 days. For protein, the rats attained levels of intake that correlated with life-span in only 4 weeks. At this age the correlation was direct, but at later ages it was inverse. After approximately 200 days of age, the level of protein intake was associated with a greater change in life-span than was the level of carbohydrate. Individual regression equations for age period 200 to 299 days indicated that 1-g increases in daily intakes of carbohydrate and protein decreased the probable life-span by 15 and 24 days, respectively.

Partial and multiple correlations. Even when the composition of the chosen diet was statistically held constant, length of life was an inverse function of the amount of food consumed. Life-span also correlated with the composition of the diet when food intake was held constant. Before age 50 days the protein content was the determining factor; between ages 50 and 300 days food intake was the determining factor. After age 300 days, both factors exerted their influences individually and, in combination, correlated more closely with life-span than did either independently. Thus, the association of life-span with food intake was either strengthened or weakened, depending on the type of diet chosen.

Both carbohydrate and protein intakes correlated with life-span more closely, and for a longer period, than was evident from the simple correlation values. Removal of the effect of carbohydrate intake invalidated the positive simple correlation for protein intake early in life. On the other hand, partial correlation analysis exposed, as early as age 10 weeks, an independent, highly significant inverse relationship between protein intake and longevity. Correlations of life-span with carbohydrate intake and with protein intake diminished with age, more so for carbohydrate than for protein. These age-related changes were also evident when the effects of the two components were considered together. As determined from the multiple regression equation for age period 100 to 199 days, an intake difference of 1 g of carbohydrate and 1 g of protein was associated with a change in probable life-span of 64 days (30 and 34 days, respectively). For age period 300 to 399 days, a similar difference in intake was associated with a change in life-span of only 36 days (11 and 25 days, respectively).

Although the correlations were computed for discrete age periods, the progression of dietary changes associated with long life can be inferred. It appears that rats that elected to consume, in limited amounts, a relatively high-protein diet early in life and a relatively low-protein diet later in life had a greater probability for long life than rats with different dietary preferences. This interpretation was tested by a sequential analysis of the dietary history of rats classified according to life-span. Retrospective examinations also permitted assessment of whether long-lived individuals selected a high-protein diet early in life as well as a low-protein diet later, or whether either condition alone was sufficient.

In the retrospective analyses, the dietary preferences of short- and long-lived rats were found to differ quantitatively and qualitatively. During the first 4 weeks, there were no significant differences in the food intake of rats that died between 317 and 551 days and those that died between 714 and 1026 days. Beyond this time, the daily intake of the short-lived rats was greater by at least 10 percent ($P < .00001$) than the intake of the long-lived rats.

The protein content of the diet selected by the long-lived rats remained relatively uniform throughout the greater part of life (Fig. 1). This was contrary to our expectations based on the prospective analyses. By contrast, short-lived rats showed a progression of changes in preferences. This

Table 2. Relationships between dietary choice and life-span.

Variable correlated with life-span	Correlation coefficient (r) by age period								
	35–41 days ($N=121$)	42–48 days ($N=121$)	49–56 days ($N=121$)	63–69 days ($N=121$)	70–76 days ($N=121$)	100–199 days ($N=121$)	200–299 days ($N=121$)	300–399 days ($N=116$)	400–499 days ($N=101$)
Simple									
Food intake (g)	+.11	+.02	−.19*	−.29‡	−.37‖	−.40¶	−.40¶	−.29‡	−.22*
Protein content of diet (%)	+.15	+.18*	+.15	+.10	+.11	−.02	−.14	−.17	−.21*
Carbohydrate intake (g)	−.01	−.14	−.25†	−.28‡	−.36‖	−.25†	−.19*	−.11	−.05
Protein intake (g)	+.16	+.18*	+.10	+.002	+.001	−.15	−.27†	−.27†	−.27†
Partial									
Total food intake (g) (% of protein constant)	+.10	+.02	−.19*	−.31§	−.36‖	−.40¶	−.39‖	−.30‡	−.22*
Protein content of diet (%), food intake constant	+.14	+.18*	+.15	+.14	+.16	+.04	−.10	−.19*	−.22*
Carbohydrate intake (g), protein intake constant	+.06	−.06	−.25†	−.31§	−.43¶	−.38‖	−.31§	−.19*	−.09
Protein intake (g), carbohydrate intake constant	+.17	+.13	−.08	−.14	−.24†	−.33§	−.36‖	−.31§	−.28†
Multiple									
Food intake (g) and protein content (%)								−.42¶	−.30†
Carbohydrate and protein intake (g)					−.43¶	−.41¶	−.41¶	−.32§	

*$P < .05$. †$P < .005$. ‡$P < .001$. §$P < .0005$. ‖$P < .00005$. ¶$P < .000005$.

difference between the two classes was well defined by the third week of feeding. Initially, the short-lived rats preferred diets significantly lower in protein content than those selected by the long-lived rats. At approximately 7 weeks of age, the tendency to select diets of lower protein/carbohydrate ratio was reversed. Beyond age 200 days they selected diets containing even higher levels of protein than those chosen by the long-lived rats.

The diets chosen by young animals not subjected to bias appear to have a physiological basis (*7*), but with regard to longevity, the selections confer an advantage for only some of the rats; for others the selections are associated with short lifespans. Regardless of the quantity or composition of the diet selected, the frequency of several age-related diseases is uniformly high (*2*). Individual appetite specificity notwithstanding, there are dietary regimens that are conducive to an extension of life-span (*1, 3, 8*) and reduction in suseptibility to some age-related diseases (*2, 3, 9*). However, there seem to be limits to the age period during which dietary manipulation will evoke such responses (*10*). Some imposed regimens that exert an appreciable life-prolonging influence when begun at an early age may drastically curtail duration of life if delayed until midlife. There are also temporal limitations under free choice conditions in that there are distinct time differences with regard to when and to what degree a dietary factor correlates with length of life.

The number of dietary choices open to the rat was limited in this study. Even so, a substantial proportion of the variation in life-span among animals has been explained solely by the appetite for carbohydrate and protein. It is likely that an even larger proportion of the variance would have been accounted for had the rats been permitted to express their choice for other essential nutrients. If such choices also contribute to an extension or curtailment of life, dietary practices early in life may provide a critical measure for estimating the life-span of an individual.

M. H. Ross
Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111

G. Bras
Pathologisch Instituut, Faculty of Medicine, Rijksuniversiteit, Utrecht, Netherlands

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Satiety: A Graded Behavioral Phenomenon Regulating Caloric Intake

Abstract. *Rhesus monkeys inhibited their feeding in response to intragastric nutrient preloads, so as to maintain a constant caloric intake. There is a definite dose-response relationship to calories which does not depend on the volume, caloric concentration, or nature of the nutrient. This accurate control is accomplished even though some of the preload remains in the stomach throughout the feeding period.*

The concept of satiety has been the subject of much theoretical consideration in feeding control, but until recently only modest experimental study has been directed toward it. Thus, a disturbance in satiety has long been proposed as an explanation for hypothalamic hyperphagia (*1*), and the ventromedial hypothalamic (VMH) region has been proposed as the "satiety center." However, recent experimental results have challenged these proposals by showing that hyperphagic animals with VMH lesions seem just as capable as normal animals of inhibiting feeding in response to nutrient. Studies in the rat have employed intragastric (*2*), intravenous (*3*), and intraperitoneal (*4*) nutrient preloads to demonstrate this capacity. We

Table 1. The effect of intragastric nutrient preloads on caloric consumption. The total column under the experimental condition is calculated by adding the caloric value of the preload to the meal calories. All results are expressed as mean ± standard error of the mean. *N*, number of experiments; glu, glucose; B.N., balanced nutrient; sta, starch; cas, casein. Numbers of groups of experiments, total number of experiments, and means (± S.E.M.) of groups of experiments and of the total are printed in italics.

N	Control condition	Experimental condition			
	Meal (kcal)	Preload (kcal)	Meal (kcal)	Reduction from control (kcal)	Total (kcal)
5	489 ± 10	75 (glu)	422 ± 15	68.5 ± 6	497 ± 17
6	451 ± 14	150 (glu)	305 ± 21	148 ± 15	454 ± 21
8	437 ± 15	150 (B.N.)	273 ± 22	164 ± 13	423 ± 22
6	454 ± 24	150 (sta)	305 ± 23	150 ± 7	455 ± 23
6	438 ± 26	150 (MCT)	282 ± 25	156 ± 16	432 ± 25
6	418 ± 8	150 (cas)	251 ± 24	167 ± 17	401 ± 24
32	*439 ± 7*			*157 ± 4*	*432 ± 11*
7	442 ± 13	300 (B.N.)	134 ± 15	306 ± 18	434 ± 14
6	447 ± 19	300 (sta)	156 ± 21	291 ± 19	456 ± 21
6	461 ± 16	300 (MCT)	156 ± 29	304 ± 17	456 ± 29
6	461 ± 15	300 (cas)	159 ± 14	302 ± 20	459 ± 14
25	*452 ± 5*			*301 ± 3*	*451 ± 6*
5	446 ± 22	450 (B.N.)	38 ± 12	408 ± 25	488 ± 12
67	*449 ± 2*				*448 ± 3*