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HOW RATS ECONOMIZE—ENERGY LOSS IN STARVATION¹

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Adaptation of energy expenditure to partial or complete food deprivation was studied in the laboratory rat. Energy expenditure was measured by means of a material balance technique and with indirect calorimetry. Increasing the temporal resolution of the latter method and combining it with other techniques allowed a detailed analysis of expenditure into its components. All experiments were done at a temperature of 30 C. Total expenditure during food deprivation went down by nearly three-fifths of its ad lib. value. Of the total decrease of 59%, 12%–13% was due to cessation of food processing, 12% to reduction of activity, and 34%–35% to a drop of fasting resting metabolic rate. Finally the consequences of the expenditure changes for the regulation of body temperature were studied. The mean core temperature fell by 1 C while the animals reduced their thermal conductance. The adaptive significance of the findings is discussed.

Adult animals, living in an adequate environment, maintain a balance between energy uptake and expenditure. The energy store of the body does not fluctuate much, as the constancy of body mass and body composition shows, although the store is small in comparison to the daily energy turnover, especially in small animals. This can be achieved by control of either the uptake or the expenditure of energy. The latter possibility is often called into question; recently Le Magnen (1974) even stated that the control of energy expenditure is contrary to what body mass would require, in view of hyperactivity in food deprivation and hypoactivity in obesity. Published studies on this point involved either partial (Keys et al. 1950; Grande, Anderson, and Keys 1958; Meyer and

Clawson 1964; Walker and Garrett 1970) or complete (Cumming and Morrison 1960; Kleiber 1961; Morrison 1968) food deprivation or, in man only, raising of intake by overfeeding (Miller and Mumford 1967). I shall discuss only the case of underfeeding, since this was the only condition used in my experiments. In these experiments, body mass did not remain at the equilibrium level for ad lib. conditions, a new balance between intake and expenditure was reached only occasionally (Keys et al. 1950; Walker and Garrett 1970). It is hard to decide, therefore, whether adaptation of expenditure to uptake occurred. Some metabolic savings will result from the mere fact that the underfed subject has to handle and digest less food. Moreover, during partial or complete deprivation body mass will decrease, and this is bound to cause a drop in metabolism. However, following Cumming and Morrison (1960), I shall not call these decreases "adaptive." Rather, I will restrict this term to the case where the underfed animal spends less free energy on a given function (e.g., protein turnover or muscular effort for a given

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behavior) than an ad lib. fed conspecific of the same mass and body composition would do (see also final discussion). If so, it is a plausible assumption that evolution has provided the individual with an ability to conserve its stores so that it can survive a temporary food scarcity, an occurrence common in the natural habitat of many species. At a later stage I shall discuss the operational difficulties of this definition of adaptive reduction of expenditure. For the moment it will suffice to state that the literature is not unanimous as to whether or not changes in metabolism caused by deprivation are due exclusively to changed body mass and cessation of food processing. Cumming and Morrison (1960) state, "The total energy expenditure of the rats fell during the 48 hr fast and rose during refeeding. When the changes in body weight and food intake were allowed for, the metabolic rate was found to remain constant throughout the whole experimental period" (p. 241). In contrast, Walker and Garrett (1970) conclude that even after correction for body size reduction "the energy expenditure declined markedly as the period of undernutrition was prolonged" (p. 186).

The present study is a contribution to the further analysis of these problems. Clearly, not only total metabolic rate, but also the various components that make up this total must be studied. Customarily four such components are distinguished in homeotherms (Gessaman 1973): basal metabolism, metabolism above the basal level which is used for thermoregulation, metabolism associated with activity, and metabolism for the processing of food. I shall use the same division. However, it should be pointed out that what I measured in my experiments was not energy expenditure, e.g., on muscular activity, but only the difference in metabolic rate between the

period with and without muscular activity. This difference equals the cost of activity only if the "resting" components of energy expenditure proceed at the same rate irrespective of the occurrence of muscular activity. This seems highly doubtful, e.g., in view of the effects of sympathetic discharge and adrenomedullary secretion causing splanchnic vascular constriction, inhibition of lipogenesis, etc. In principle therefore I know only the difference in metabolic rate between the following conditions: (1) animal resting in the postabsorptive state, (2) animal resting and processing food, (3) animal engaging in activity. For brevity, however, I shall speak of a resting, a food-processing, and an activity component of metabolism (see also below). The possible influence of the demands of thermoregulation on metabolic rate could be studied in principle by observing the effect of varying ambient temperatures on the three components just mentioned. Such observations, however, fell outside the scope of the present study.

The laboratory rat (*Rattus norvegicus*) was chosen as the subject of my experiments because it is commonly used in studies on caloric regulation. Intake was changed in one direction only, namely, reduction. All experiments were done at the same temperature, in the thermoneutral zone of the rats, for two reasons. First, I wished to avoid the complication of special (and not directly measurable) heat production for thermoregulation. Second, food-deprived animals survive longer at temperatures in or near the thermoneutral zone, as they can mobilize more of their energy stores (Kendeigh 1945; Kleiber 1945). Consequently in my experiments, notwithstanding long periods of food deprivation, only two out of more than 100 animals died.

The energy expenditure was measured by two methods: (1) a material balance

technique, calculating expenditure from food intake, feces production, and changes in body reserves; and (2) indirect calorimetry calculating expenditure from the gas exchange of the animals. By increasing the temporal resolution of the latter method and combining it with other techniques, a detailed analysis of total expenditure into its components was made possible.

I first determined the change in total expenditure during food deprivation. This change was further analyzed in terms of the energetic consequences of: (1) the cessation of food processing; (2) changes of activity; and (3) changes of fasting resting metabolic rate. Finally, the consequences of the expenditure changes for regulation of body temperature were studied. The energy expenditure on feeding behavior could not be separated from that on other behavior. Therefore my estimate of the energy expenditure associated with food processing included only the costs of internal processing, while, for instance, food handling was measured together with the costs of nonfeeding behavior.

GENERAL MATERIAL AND METHODS

The investigation comprises four experiments: experiment I, energy loss during total food deprivation (material balance technique); experiment II, energy expenditure on food processing (indirect calorimetry); experiment III, energy expenditure during total food deprivation (indirect calorimetry); experiment IV, body temperature and thermal insulation during total food deprivation. This paragraph describes material and methods of my investigation, except for points that apply to only one experiment which will be described in the paragraph concerned.

Definitions and abbreviations.—As the present investigation asks “what hap-

pens to expenditure of the animal as a whole during underfeeding?” rather than “how does expenditure per unit (metabolic) body mass change?” I shall present only data on overall expenditure and its components for whole individuals.

The following concepts underlie the analysis of the flow of energy through the animal body to be presented. There are two supplies of energy to the blood: intestinal absorption, and mobilization of reserves. Intestinal absorption equals the rate of intake of food (IE) minus that of fecal waste (FE). Energy is removed from the blood by three processes: (1) combustion of fuel for energy release (rate = E_{rel}), (2) storage in the reserves (RE), and (3) elimination by the kidney in urine (UE), which, in practice, is of importance only in the case of protein breakdown. As regards the reserves, the net rate of retention of energy (RE) is the difference between the rates of storage and mobilization. RE is positive in a growing animal but negative during deprivation. The cost of storing reserves, as judged by increase in body mass, even under ad lib. conditions amounted to less than 1% of total metabolism and will therefore be disregarded. The cost of mobilizing reserves is negligible. As regards energy release, part of this energy flow is channeled into energy-rich phosphates that provide free energy for vital processes (and via this route eventually degenerates into heat), another part is inevitably dissipated as heat in the course of the synthesis of these energy-rich compounds.

Energy loss (rate = E_{loss}) as measured by the material balance technique equals the difference between intestinal absorption and energy retention. Energy release as measured by indirect calorimetry is identical to total metabolic rate (M_{tot}). This comprises an activity component (M_{act}) and a resting compo-

nent (M_{rest}) and the latter consists of a food processing component (M_{foodp}) and a maintenance component (M_{maint}). These components will be regarded as additive (however, see the introductory section above). For the present study it is convenient to consider the metabolism for the processing of food as a fraction (C_{foodp} = costs of food processing) of the intake of metabolizable energy ($\text{ME} = \text{IE} - \text{FE} - \text{UE}$).

The following equations summarize those implications of these concepts that are especially relevant to the subsequent investigation (for the case in which all processes mentioned proceed at constant rates):³

$$E_{\text{loss}} = \text{IE} - \text{FE} - \text{RE} = E_{\text{rel}} + \text{UE}$$

$$E_{\text{rel}} \equiv M_{\text{tot}}$$

$$M_{\text{tot}} = M_{\text{act}} + M_{\text{rest}} = M_{\text{act}} + M_{\text{foodp}} + M_{\text{maint}}$$

$$C_{\text{foodp}} = \frac{M_{\text{foodp}}}{\text{ME}}.$$

For brevity the symbols $\text{dep}_1, \text{dep}_2, \dots, \text{dep}_n$ will be used to denote the first, second, . . . , n th day of food deprivation.

Subjects.—The animals were male albino rats of the Wistar strain, reared in the laboratory. They were used in the first weeks after they had reached adult body mass (at least 200 g), that is at an age of 7–14 wk.

Feeding.—The food was powdered chow (Trouw, Putten, Netherlands) suitable for small rodents. Gross energy was 18.9 kJ⁴ per gram and the weight ratios for digestible carbohydrate, fat, and protein were 70:6:24.

³ Throughout the paper all symbols for metabolic processes ($\text{ME}, \text{IE}, \text{FE}, \text{UE}, \text{RE}, E_{\text{loss}}, E_{\text{rel}}, M_{\text{tot}}, M_{\text{foodp}}, M_{\text{act}}$) denote rates and should be read as ME , etc., unless otherwise stated.

⁴ I shall conform to the use of SI units as recommended by Gagge, Hardy, and Rapp (1969). Whenever necessary figures taken from the earlier literature will be recalculated. The conversion for calories is: 1 cal = 4.187 J (J/s^{-1} = watt).

Climate.—The experiments were done in a temperature room at 30 ± 0.5 C, i.e., in the lower part of the thermoneutral zone of postabsorptive resting laboratory rats. Lower and upper critical temperature depend on the temperature the animal is adapted to; according to Gelineo (1934) in the rat they range, under the same conditions, respectively, from 29 to 32 C, and from 31 to 34 C. The relative humidity was 60%. A 12/12 h light-dark cycle was used.

Housing.—The animals were housed individually in Plexiglas cylinders, 20 cm diameter and 20 cm height, mounted on a funnel, with a wire mesh floor. Feces and urine were separately collected as shown in figure 1. The cages were airtight except for an inlet and outlet for ventilation and measurement of the gas exchange. The ventilating airstream was 2 liters $\cdot$ min⁻¹.

Habituation.—Before an experiment was started the animals, which so far had been living in groups of six to eight in larger cages with wood shavings at a temperature of 19–23 C, were habituated to the new situation for at least 14 days. This was deemed sufficient because the change in metabolism induced by moving rats from 18 C to the thermoneutral zone is completed in 8 days (Gelineo 1934) and the effects of a change of cage on drinking (and other) behavior last no longer than 14 days (Grant et al. 1971).

Maintenance.—The animals were weighed and data were collected on food intake and feces production daily, 2–3 h before light out. At that moment the disturbance will be minimal. The animals have just awakened and have not yet started their nightly activity, as reflected also in the daily rhythm of food intake (fig. 2). The period of disturbance is indicated in this figure with a shaded zone.

For calculation of energy expenditure data the body mass of fed animals must be corrected for the amount of non-metabolizing food and feces in the gut. However, at the time of day used for data collection, the gut content of my animals was very small, namely, about 2.5 g dry weight, i.e., only one-sixth of daily food intake or little more than one meal for an animal of this size. So body mass comes very close to postabsorptive body mass at this time of day. After 1 day without food there was only about $\frac{1}{2}$ g left in the cecum.

Indirect calorimetry.—Indirect calorimetry was used in experiments II and III, and the general formula for the calculation of energy release, derived from the figures from Carpenter (1948), is $E_{rel} = 16.20 O_2 + 5.00 CO_2 - 0.95 P$ (Brouwer 1957), where

E_{rel} = energy released (kJ),

O_2 = oxygen consumed (liters),

CO_2 = carbon dioxide produced (liters),

P = protein oxidized (grams).

The contribution of P to E_{rel} is small. In case of oxidation of the diet used in

FIG. 1.—The metabolic cage

this study it is 1.2%. During food deprivation it is even closer to zero until the terminal stage, 2–3 days before death, when oxidation of structural protein suddenly rises (table 1). However, in my indirect calorimetry experiments the contribution of protein to E_{rel} never exceeded the ad lib. value. In view of this I did not undertake the laborious determination of urine nitrogen to obtain a separate estimate of P.

Determination of the gas exchange.—Oxygen consumption and carbon dioxide production were derived from the changes in composition of a measured flow of air through the cage of the animal (fig. 1). Air was sucked through the respira-

tion chamber and dried with calcium chloride before determining flow and composition.

Flow was measured with a mass flowmeter and an oil gasmeter. The mass flowmeter gave a continuous measure of the flow rate (which proved quite satisfactorily constant in all cases). The oil gasmeter gave the total volume of air that passed through the cage for calculation of the mean flow over longer periods. After flow measurement, part of the air went through the gas analyzers.

Carbon dioxide was determined with an infrared analyzer (Grubb Parsons, model SB2). Changes in the oxygen concentration do not influence this car-

FIG. 2.—Upper graph, day-night cycle of body mass (daily mean of body mass is 100%). Lower graph, day-night cycle of food intake (expressed as percentage of total daily intake per hour). The shaded zone indicates the time of disturbance for data collection (means and SE of 16 animals, each observed 1 day).

TABLE 1
DATA ON MEAN BODY MASS, $\bar{I}\bar{E}$, $\bar{F}\bar{E}$, GUT CONTENT, FAT CONTENT, PROTEIN CONTENT, AND
ENERGY CONTENT WITH THE CALCULATED $\bar{E}_{\text{loss}}$ PER ANIMAL,
BEFORE AND DURING FOOD DEPRIVATION

SURVIVING ANIMALS					SACRIFICED ANIMALS							
TIME (Days)	<i>N</i>	Body Mass (g)	$\bar{I}\bar{E}$ (W)	$\bar{F}\bar{E}$ (W)	<i>N</i>	Body Weight (g)	Gut Fresh (g)	Content Dry (g)	Fat Content (kJ)	Protein Content (kJ)	Energy Content (kJ) ¹	$\bar{E}_{\text{loss}}$ (W)
- 10	48	279.8	2.56	.62								
	48	277.5			2.98	.68						
	48	279.4	2.87	.62								
- 5	48	283.7			2.81	.66						
	48	286.6	2.94	.63								
	0	48			288.9	6	288.8	9.9	2.5	995	1,346	2,420
	42	272.0	...	.15	6	272.6	1.8	.6	838	1,373	2,254	
	36	261.3	...	.00								1.65
	36	253.5	...	.00	6	252.0	1.0	.4	586	1,352	1,969	
	30	247.0	...	.00								1.38
5	30	240.2	...	.00	6	240.3	...	...	414	1,285	1,731	
	24	232.9	...	.00								1.00
	24	225.0	...	.00	6	226.3	...	...	291	1,259	1,558	
	18	215.8	...	.00								.94
	18	207.2	...	.00	6	208.3	...	...	183	1,178	1,397	
10	12	198.3	...	.00								0.76
	12	190.6	...	.00	6	190.3	...	...	136	1,095	1,255	

NOTE.—N = number of animals.

bon dioxide analysis. Disturbance by methane (which may be produced by bacteria in the digestive tract) was prevented by passing the radiation through filtering tubes containing 50% methane, so that the wavelength absorbed by methane was removed. Oxygen was determined with a paramagnetic analyzer (Taylor Servomex, type OA 184). This method is specific for oxygen apart from a few other gases which do not occur in respiration air.

Both analyzers consisted of two separate units for simultaneous measurement of the composition of inlet and outlet air. The concentration difference of these two was recorded directly, so that corrections for changes in oxygen and carbon dioxide concentration of inlet air were automatically made. The pressure in both channels proved to be the same (of particular importance as the analyzers measure partial pressures), because the flow systems through the analyzers were identical and had an open outlet.

The output voltages of the analyzers were continuously recorded by means of a multipoint recorder (Philips, PR 3500). A difference in partial pressure of oxygen or carbon dioxide of 0.5% of an atmosphere gave full-scale deflection (25 cm). Mean difference in composition between inlet and outlet air over a given time interval was determined from these recordings by means of a planimeter. The relative error amounted to about 2% in the case of short-term measurement, e.g., estimates of resting metabolic rate. In the case of longer records, the accuracy was even better.

Response time.—Metabolism sometimes fluctuates rapidly so that measurements must be made within 10–15 min. Two problems arise here. First, there may be a time lag between changes in cell metabolism and the corresponding

alteration of pulmonary gas exchange with the environment. However, certainly in the case of oxygen this lag is short, whereas it can be seen from Brouwer's formula that a possible error in CO₂ measurement has a relatively small effect on the estimate of E_{rel} . Second, the response time of the measuring system should be reduced as far as possible by using a small respiration chamber and a high ventilation rate. These considerations resulted in cages of 20 cm diameter and 20 cm height (the minimum in which the animal could turn and stand on its hind legs), with a volume of 8 liters including the funnel (fig. 1). Given these measures, the ventilation rate usually recommended (10× per hour) would result in a flow of 1.5 liters/min.

When a steplike change occurs in O₂ consumption or CO₂ production in the respiration chamber, the rates at which these gases leave the chamber will move asymptotically toward new equilibrium values (Christensen 1947). This process follows the equation

$$\left| \frac{\Delta q}{\Delta p} \right| = 1 - e^{-\frac{Ft}{V}},$$

where

Δq = change of amount of O₂ or CO₂ carried off (liters·min⁻¹),

Δp = change of O₂ consumption or CO₂ production (liters·min⁻¹),

F = ventilation rate (liters·min⁻¹),

V = cage volume (liters),

t = time after start of a change (min);

$\Delta q/\Delta p$ is termed the fractional response of the system after t min (Rf_t). Under the above-mentioned conditions Rf_{12} amounts to only 90%. Rf_{12} was raised to 95% by raising the ventilation rate to 2 liters/min. Since the relative error of the gas analysis is proportional to F , and still higher F might have

disturbed the animals, I contented myself with $Rf_{12} = 0.95$.

Analysis of total expenditure.— M_{rest} was determined during periods of inactivity. M_{act} was calculated by subtracting M_{rest} from M_{tot} . M_{foodp} was determined by measuring M_{rest} at different rations.

Detection of activity.—I used two systems to record automatically the movements of the animals, one with photocells and the other with radar. For the photocell system a horizontal row of lamps was mounted on one side of the cage at 1 cm intervals, behind an infrared filter so that the light beams were invisible to the animal. On the other side of the cage there was a row of photocells. The beams were $\frac{1}{2}$ cm above the animal when it lay down sleeping, i.e., 5–7 cm above the cage floor, depending on the size of the individual rat, to prevent recording of breathing movements. The radar system consisted of an oscillator with a wavelength of approximately 3 cm, transmitted by a horn antenna. Reflections from the moving animal were detected with the same antenna. Reflections from the surroundings were prevented with asbestos plates. Small movements like breathing were not recorded because of a built-in threshold in the output of the system. The reliability of this system will be considered in a later section.

Measurement of M_{rest} .—Rats have only short resting periods, especially during the night. Yet it is necessary to measure M_{rest} in all phases of the 24 h cycle because of the diurnal rhythm (Heusner 1956). In principle, there are two ways to determine M_{rest} . The direct way is simply to measure metabolic rate during resting periods. The indirect way is to calculate M_{rest} from the relation between the fraction of time spent on activity and the metabolic rate over the

same interval. The indirect method does not require prolonged resting periods, the bottleneck of the direct method, but it does require a number of observations, all made in the same phase of the diurnal cycle, covering a broad range of activity levels.

A pilot experiment was done to compare both methods. Metabolic rate and activity (photocell data) were recorded for 24 h in each of five animals. I obtained at least one direct measurement of M_{rest} of each animal in every 2 h period. The M_{rest} during the night was $17 \pm 0.5\%$ higher than that during the day, changes in M_{rest} within either night or day were small. This allows us to pool all data for the night, or the day, in the indirect determination of M_{rest} , which will now be presented.

In the indirect determination, observations lasting at least 1 h were used in order to avoid response time problems. Moreover, different types of activity might require different amounts of energy, and longer observations are more likely to contain a fair sample of all types. Only one of the five animals used showed a sufficient activity range for the indirect method. In figure 3, $\bar{M}_{tot}$ (over 1 h) for this animal is plotted against the time spent on activity in the same hour, with the calculated regression lines extrapolated to zero activity.

The indirect method and the direct method resulted in the same animal on the same day in M_{rest} values of, respectively, 1.30 and 1.35 W (night) and 1.20 and 1.21 W (day). As these figures agree well and only one out of five animals could be used for the indirect method, I selected the direct method.

EXPERIMENT I: E_{loss}

M_{tot} fell after intake reduction, as shown previously by Tigerstedt's (1910) review. However, the extent of M_{tot}

FIG. 3.—Relation between the percentage of time spent on activity (T_{act}) and $\bar{M}_{tot}$ during nighttime (○) and daytime (●) with the calculated linear regression lines (daytime: $\bar{M}_{tot} = 0.0084 T_{act} + 1.20$; nighttime: $\bar{M}_{tot} = 0.0092 T_{act} + 1.30$).

changes caused by deprivation has not been sufficiently described so far. Kleiber (1961) reported a reduction of expenditure per unit metabolic body size, i.e., the three-fourths power of body mass, up to 60% in rats during starvation. As body mass goes down, the reduction per animal should be even greater. However, it is not clear if all components of M_{tot} were included. Recently Walker and Garrett (1970) studied E_{loss} in rats during food restriction. Their only conclusion was that this declined *markedly*. Since Tigerstedt's review, a few statements have appeared that metabolic rate did not decrease during starvation, but all of these were based on constancy of metabolism per unit (metabolic) mass (e.g., Cumming and Morrison 1960; Meyer and Clawson 1964). In other words, they confirm that metabolism of the individual as a whole decreases during starvation.

Experiment I was undertaken to determine more precisely the magnitude of expenditure reduction. Therefore I measured E_{loss} in the ad lib. food situation and at different stages of complete food deprivation.

Method.—The material balance technique consisted of measurement of: (a) energy uptake, and (b) energy content of the body. The former was determined from the weight and heat of combustion of food and feces, measured in a ballistic bomb calorimeter. For the latter, animals were sacrificed and the cadavers homogenized after removal of the gut content. Samples of the homogenate were analyzed for fat, protein, and energy content. Fat was determined by ether extraction in a Soxhlet apparatus, protein by the Kjeldahl method, and energy again by means of the ballistic bomb calorimeter. The gut content was weighed separately to know the con-

tribution of this metabolically inert mass to gross body mass. Its estimated energy content was added afterward to the energy content of the animals. The balance method allows only measurements over periods of at least 24 h.

The experiment began with 48 animals. During a habituation period of 2 wk, food intake, body weight, and feces production were measured. After eight groups were formed of six animals each, such that mean body weight for all eight groups was the same, all rats were deprived of food. The weight range within groups was considerable (about 50 g), but the groups were closely similar in that, if one ranked the animals within each group according to increasing weight, the weight range (across groups) of animals with the same rank number never exceeded 6 g. Because I adopted this procedure only group means, but no standard errors, are presented in table 1.

At the start, and after 1, 3, 5, 7, 9, 11, and 13 days of deprivation, one group was sacrificed for body analysis. The last group consisted on dep_{13} of only four animals, two having died on dep_{12} . The data for this group were not used because these two animals, being the lightest, formed a nonrandom sample.

Results.—Data on mean body mass (grams) and IE and FE (watts) of all surviving animals are presented on the left in table 1. On the right are the data for the sacrificed animals on mean body mass (grams), mean gut content (grams), and mean fat, protein, and energy contents (kJ), at the time of death.

The low food intake and decrease of body mass over the first 3 days indicate that the change in environment required some adjustment by the rats. Over the 3-day periods (−7 to −4 and −4 to −1), however, mean growth rates and rates of food intake are similar. This

indicates that by day zero adjustment was complete. Unfortunately this day is marked by an unexpectedly high rate of food intake and gain of body mass, the latter no doubt due to increased intestinal content. Whatever the cause of this may be, it is in any case better to base an estimate of ad lib. E_{loss} on days −4 to −1. Over this period body mass increased by 2.9 g. The composition, and hence energy content, of this added body mass is not precisely known. If it were pure fat tissue, the energy content would have been 76.8 kJ (Miller and Mumford 1967); if it were average body mass, only 24.3 kJ (table 1). The real growth rate therefore will have been somewhere between 76.8 and 24.3 kJ per 3 days, or 0.30 and 0.09 W. From the relation $E_{\text{loss}} = \text{IE} - \text{FE} - \text{RE}$ it follows that the mean rate of E_{loss} over this ad lib. period must have been $\bar{E}_{\text{loss}} = 2.81 - 0.66 - (0.09 \text{ to } 0.30) = 1.85 \text{ to } 2.06 \text{ W}$. Energy loss during deprivation decreased at an approximately constant rate of 0.11 W per day, from the ad lib. value of approximately 2 W to 0.76 W after 11 days of deprivation (table 1).

Discussion.—From the reduction of fat and protein contents it appears that in the first days of food deprivation the animals used almost only fat as energy substrate, but then utilization of fat was reduced at the cost of protein. The fat of the last group, 136 kJ or 3.5 g per animal, probably did not represent mobilizable energy but structural lipids. The contribution of protein had increased from zero to two-thirds of E_{loss} . Benedict and Fox (1934) found values for protein combustion up to 62% of total expenditure on the day of death in albino rats during prolonged fasting. The low fat content with the high protein combustion in the last deprivation stage meant that my animals had depleted their energy stores completely.

Daily energy loss as calculated from food minus feces, corrected for changes in body reserves, is not completely equal to M_{tot} . If protein contributes to the energy substrate, part of the energy derived from protein, about one seventh, is lost as urea with the urine. The energy contribution of protein under ad lib. food conditions, when net protein storage or mobilization can be neglected, was 29% of uptake, according to the weight ratio of digestible nutrients of the food and their caloric values. So E_{loss} exceeds M_{tot} by about 4% (one-seventh part of this fraction) of uptake, which results in $M_{\text{tot}} = 1.78$ to 1.98 W. In the last deprivation stage, when protein contributed 62% to the energy substrate, the correction was 9%, resulting in $M_{\text{tot}} = 0.69$ W. To conclude, during 11 days food deprivation M_{tot} went down by 61%–65% of its value under ad lib. conditions (fig. 4).

EXPERIMENT II: M_{foodp}

Rats are periodic eaters and continuous metabolizers. They store part of the food energy before use, partly in the stomach and gut, partly in glycogen and fat stores. It may be cheaper to get

FIG. 4.— M_{tot} during deprivation, expressed as a percentage of its ad lib. value in the same animal(s) ($\blacktriangle$, experiment I, mean of six animals; $\circ$, experiment III, individual data). In the case of experiment I, upper and lower estimates for each observation are plotted.

energy out of these reserves than from food consumed, but this view disregards the fact that storage of reserves is a costly process. This paragraph analyzes what reduction of M_{tot} during food deprivation is due to the cessation of food processing.

Food processing, as here defined, consists of digestion, intestinal absorption, possible conversions of absorbed dietary metabolites into stored reserve fuel, and finally the mobilization of these stores.⁵ Feeding behavior could not be separated from other behavior and is included in M_{act} .

Food deprivation abolishes digestion, absorption, and conversion. The consequences for energy expenditure can be evaluated with the aid of theoretical estimates (Armstrong 1969; Baldwin 1968, 1970). Synthesis of digestive enzymes costs about 4% of the energy content of the food supplied. The costs of bond breakage during digestion are small, 0.6%, 0.1%, and 0.5% of the energy content for breakage of the glucoside bond, the glyceride fatty acid bond, and the peptide bond, respectively. Absorption of hexoses costs 2.6% of the energy content. Absorption of at least some amino acids is also active and may take as much energy as that of hexoses. Absorption of fatty acids and monoglycerides, mainly as micelles that penetrate the cell membrane, is an energy independent process (Johnston 1968). The costs of conversion for storage depend on the metabolite, form of storage, and amount stored. Storage of hexoses as glycogen costs about 5%, as fat 20%–25%, and conversion of dietary tri-

⁵ In the case of amino acids, the cost of urea synthesis is part of the cost of processing. However, in experiments II and III this plays a negligible role both in fed and deprived rats, for in the former the protein content of the diet was moderate and in the latter breakdown of structural protein became important only in the terminal stages.

glycerides to reserve fat costs about 5% of the energy content. The amount of energy stored is more difficult to estimate because under ad lib. conditions an unknown fraction of the dietary metabolites passes through temporary storage before being oxidized. In rats there is a nocturnal net fat synthesis and diurnal net fat mobilization. At night the animals eat nearly 80% of their daily total but metabolize only 55%. Part of the nocturnal excess intake, 12% of the 24 h energy turnover, is temporarily stored as fat, and mobilized in the following day period (Le Magnen and Devos 1970; Le Magnen et al. 1973). This figure of 12% is a minimum estimate of temporary energy storage, as it includes only that nocturnal fat storage directly linked with energy needs during daylight. It does not include possible short-term storage as fat during the night or the day or storage in the form of glycogen. To sum up, the main determinants of energy costs associated with food processing will be composition of the diet and amount of storage. The latter depends on the pattern of food intake.

Method.—The normal procedure for measuring the costs of food processing (C_{foodp}) is to measure the increase of M_{rest} over the basal level after a test meal, resulting in the so-called specific dynamic action (Glickman et al. 1948; Charlet-Lery 1961, 1975; Garrow 1973). The criterion used for the completion of food processing is the return of M_{rest} to the premeal fasting level. This took 6–7 h in the experiments with man of Glickman et al. and 10–11 h in the pigs of Charlet-Lery. However, such long intervals are lacking in the free feeding pattern of rats. This is characterized by some eight to 10 meals per day, separated by intervals lasting about 4 h during day and about $1\frac{1}{2}$ h during night (Le Magnen and Tallon 1966). Therefore, I had to

use another method for determining C_{foodp} . I measured resting metabolic rate over prolonged periods at different rations (full, half, and zero) and attributed the differences in the observed values to the decrease of M_{foodp} . Of course the data from experiment II also provide estimates of M_{act} and M_{maint} .

The measurements of M_{rest} were made over 24 h periods in order to avoid the influence of diurnal changes in processing costs caused by such things as the daily cycle of fat storage and of diurnal fluctuations in basal metabolic rate which, although disregarded in traditional SDA measurements, are large (e.g., 24% in birds [Aschoff and Pohl 1970] or up to 20% in the rat [Kayser 1970]) and may vitiate SDA measurements lasting 6–11 h.

When an animal, accustomed to ad lib. conditions, is suddenly put on a lower ration, its intestinal processes will move only gradually toward a new steady state, for some food from the preceding ration is always stored in the digestive tract. For our present purpose we must allow the rat time for this adjustment, but not more than the necessary minimum, for (partial) starvation will not only reduce M_{foodp} , but also M_{maint} . This is the reason why I made a separate experiment on M_{foodp} , experiment II. In experiment III, where total deprivation was imposed in one step, the rate of change of M_{maint} presumably was maximal. I hoped to reduce the uncertainty this entails by depriving the rats more gradually in experiment II.

When does food processing first reach the new steady state after the start of rationing? In order to obviate the problem of diurnal rhythmicity, I shall discuss only 24 h averages of the relevant measures. Further, I shall assume that the rat's glycogen stores reach a new equilibrium earlier than M_{foodp} . In gen-

eral, then, the following two equations hold:

$$\bar{C}_t(t) = \bar{x}(t) \cdot C_d + \bar{y}(t) \cdot C_f,$$

and

$$\bar{O}_t(t) = \bar{x}(t) \cdot O_d + \bar{y}(t) \cdot O_f,$$

where

$\bar{C}_t(t), \bar{O}_t(t)$ = the mean rate (ml·sec⁻¹) of CO₂ production or O₂ consumption, respectively, by the rat over a 24 h interval ending at time *t*,

C_d, *C_f* = the amount (ml·J⁻¹) of CO₂ liberated by the combustion of diet (0.0446) or of body fat (0.0360), respectively,

O_d, *O_f* = the amount (ml·J⁻¹) of O₂ needed for combustion of diet (0.0487) or of body fat (0.0507), respectively,

$\bar{x}(t)$ = the mean rate (watt) of utilization of dietary nutrients (for energy release or storage), over a 24 h interval ending at time *t*,

$\bar{y}(t)$ = the mean rate (watt) of decrease of body fat stores over a 24 h interval ending at time *t* (under ad lib. conditions when there is net storage of fat, *y* is negative).

It is obvious that these equations hold under (partial) deprivation, when body fat is lost. That they are equally applicable under ad lib. conditions is due to the fact that then the rate of fat storage is lower than that at which triglycerides are ingested with the food. Using these equations $\bar{x}(t)$ can be calculated from the observed gas exchange. Now if $\overline{ME}_{adl}$ stands for the mean rate of food utilization under ad lib. conditions, a new steady state of food processing after a change to, e.g., half ration will have been reached as soon as $\bar{x}(t) = \frac{1}{2} \overline{ME}_{adl}$, or even somewhat earlier, because some time may elapse between the (energy consuming) processes needed for making

dietary nutrients available for use and their actual use by the body. In the case of zero ration, of course, food processing has come to a stop when $\bar{x}(t) = 0$, i.e., when the respiratory quotient has reached a value corresponding to the combustion of pure fat (the rat uses practically only fat in the early stages of deprivation).

An observation consisted of 2 days full ration, then 2 days half ration, and finally 2 days without food. Five observations were done, each with a different animal (body masses, see table 2).

To reduce variation of temporary storage of metabolites by animals due to differences in food intake pattern, I fed them even at full ration in a fixed pattern that closely matched the average free feeding pattern. This pattern was as follows: 10 meals a day, all of the same size, three in the light period and seven in the dark. Meal intervals were 240 min in daytime and 103 min in nighttime. To accentuate low uptake in the early part of day and the high peak at the start of the night (fig. 2), the first day meal was served 3 h after light went on and the first night meal 15 min after light went off. The amount of food offered at full ration was such that the amount consumed was equal to that ingested under free feeding ad lib.

TABLE 2
INITIAL BODY MASS, THE DAILY MEAN OF TOTAL METABOLIC RATE ($\overline{M}_{tot}$) AND ME-INTAKE AT FULL AND HALF RATION

Rat	Body Mass (g)	$\overline{M}_{tot}$ (W)	$\overline{ME}$ Full Ration (W)	$\overline{ME}$ Half Ration (W)
73.....	220	1.51	1.60	.73
74.....	281	1.86	2.08	1.00
75.....	229	1.58	1.58	.71
76.....	353	2.17	2.13	.97
78.....	359	2.26	2.32	1.11
Mean...	288	1.88	1.94	.90

conditions. Half ration was offered by halving meal size at the same meal number of 10 a day in the same pattern. The animals did not quite eat this ration, so that their intake was reduced to about 47%.

Results.—Table 2 presents initial body masses, $\bar{M}_{\text{tot}}$, and ME intake of the animals at full and half ration. Figure 5 presents the mean rates of food utilization ($\bar{x}$), calculated as running averages over six consecutive 4 h periods (further details can be seen from the figure). At full ration $\bar{x}$ was constant at a value of 1.92 W, which agrees closely with the mean uptake rate of 1.94 W. After 12 h on half ration a new plateau was reached at a value of 0.90 W, equal to the mean uptake of 0.90 W, and after 8 h on zero ration food utilization had declined to the negligible value of 0.02 W.

$\bar{M}_{\text{rest}}$ of the animals in the steady intestinal state at the successive rations is presented in table 3. For each ration $\bar{M}_{\text{rest}}$ was measured twice. The first observation period started as soon as $\bar{x}$ had reached the steady value. The

second one began exactly 12 h later. The change in M_{foodp} was determined from the difference in resting metabolic rate between the two measurements directly preceding and following a given transition. Finally C_{foodp} was determined. However, the calculation of M_{foodp} and C_{foodp} involved a problem that we must now consider.

The constancy of resting metabolic rate at full ration was good; the mean values over the two intervals were practically the same in all animals. At half ration the value over the second 24 h period was on the average lower than that over the first ones, and at zero ration there was even a much greater difference. This change of M_{rest} in a steady state of food processing indicates that the basal expenditure (M_{maint}) was influenced by the ration. Therefore our present method will tend to overestimate C_{foodp} . If we attempt to correct for this error by extrapolating the change in M_{maint} back to the moment at which the ration was lowered we probably arrive at an underestimate of C_{foodp} because

FIG. 5.—Mean rate of food utilization ($\bar{x}$) in the course of time (— running average over one 24 h period). Arrows indicate transitions from full to half, and from half to zero ration. Shaded areas denote periods over which $\bar{x}$ remained constant for a given ration.

FIG. 8.—Change of daily activity score (a) and M_{act} (b), during food deprivation, individual data of six animals.

FIG. 9.—Activity distribution within the 24 h cycle, score per 2 h (mean of six animals) on different days with respect to the start of food deprivation. The bars within a group of six represent from left to right, respectively, sixth and last day before the start of the deprivation period (open), dep₁, and dep₂ (hatched), dep₇ (black), and dep₁₂ (dotted).

running; costs of other activities are estimated. In this way McNab (1963) and Grodziński and Górecki (1967) estimated the activity component of total metabolic rate in free-living small rodents at 9%–20%. One might expect that caged animals would spend less on activity, being restricted in their movements. Yet in the laboratory rat kept in cages with a diameter of 21.5 cm and a height of 11.5 cm, Morrison (1968) came to a value of 25% for M_{act} .

This paragraph concentrates on changes in M_{act} during complete food deprivation. Can part of the decrease of M_{tot} be attributed to a drop of activity?

Activity changes during food deprivation have often been subject to motivational studies, but it is difficult to use their results for our present purpose. Particularly when automatic recorders were used, only part of the behavior was recorded (sometimes even only a specially induced activity like wheel running), which is not necessarily representative for behavior as a whole (Weasner, Finger, and Reid 1969). Second, the variety of instrumentation used makes quantitative comparison of results almost impossible. Therefore only results of motivational studies with direct observation will be mentioned here. In these studies a marked increase in activity was found during food deprivation. The animals showed less resting and more energy-consuming behavior such as running (Bolles 1965; Mathews and Finger 1966).

Nevertheless Morrison (1968), observing rats during 24 h of food deprivation, found no change in the share of M_{act} in M_{tot} and concluded that only the distribution of activity between feeding and nonfeeding was changed. However, as M_{tot} went down by nearly 10%, the absolute value of M_{act} was in fact reduced.

That more activity is performed at

less metabolic cost indicates a reduction of energy costs per unit of exertion during food deprivation. To get more information on these points I studied activity and its energetic consequences during prolonged food deprivation.

Method.—Activity is difficult to quantify. Time spent moving as recorded with photocells (or, more detailed, by direct observation) is no ideal index, for it does not include the rate of moving, and observations in semistarved man indicate that food deprivation induces slowness (Taylor and Keys 1950). Therefore I used a radar system which is sensitive to both duration and rate of movements. The frequency shift in the radar echo of moving targets was amplified and operated a relay. The number of closures of this relay, subsequently referred to as activity units, was the index of activity. This index is suitable in so far that there is a direct proportionality between activity score and the energy costs of this activity (fig. 6).

Yet this activity index has two limitations. First, changes in the repertoire of movements are not detected, although they may have energetic consequences. Second, comparisons are only valid within an individual experimental situation because the number of units depends on

FIG. 6.—Relation between activity score (N_{act}) and $\bar{M}_{act}$, when both are measured over the same 2 h period, for one animal over one day ($\bar{M}_{act} = 0.00056 N_{act}$).

the oscillator-detector-amplifier system, the position of the antenna with respect to the cage, and the absorption of waves by the cage wall. These factors were kept the same throughout the experiment.

Each of six animals was used once. The observations started with an ad lib. food period, followed by 12 days of complete food deprivation. Records of activity and gas exchange were taken over periods of 24 h two times in the ad lib. situation (6 days and 1 day before the start of food deprivation) and four times during deprivation, namely, on dep₁, dep₂, dep₇, and dep₁₂. It will be shown later that Brouwer's formula for the calculation of energy release was applicable throughout this experiment.

Results.—Figure 7 presents the body mass values (the change of M_{tot} is presented in fig. 4). Comparison with table 1 shows that they were similar to those in experiment I. Figure 8a shows the data on total daily activity. The variation

was quite high under ad lib. conditions. Between animals within a day it ranged up to 35% and between days within an animal up to 30%. On dep₁ and dep₂ two animals had a higher and three a lower activity level than on the foregoing days with food. All animals showed reduced activity in the later stage of deprivation. Figure 8b shows that all animals spent less energy on activity on dep₁ than under ad lib. conditions. On subsequent deprivation days a further decrease took place. M_{act} amounted to $15.9 \pm 0.5\%$ of M_{tot} on both days with food, but this declined successively on days without food to $15.4 \pm 1.0\%$, $14.0 \pm 0.5\%$, $13.3 \pm 0.8\%$, and $11.0 \pm 1.0\%$.

The reduction of activity was further analyzed by studying the diurnal rhythm (fig. 9), which, as expected, shows a low level in daytime and a high level in nighttime. Deprivation affected mainly nocturnal activity. On dep₁ and dep₂ the animals were as much or more active

FIG. 7.—Change of body mass during food deprivation, individual data of six animals

FIG. 8.—Change of daily activity score (a) and M_{act} (b), during food deprivation, individual data of six animals.

FIG. 9.—Activity distribution within the 24 h cycle, score per 2 h (mean of six animals) on different days with respect to the start of food deprivation. The bars within a group of six represent from left to right, respectively, sixth and last day before the start of the deprivation period (open), dep₁ and dep₂ (hatched), dep₇ (black), and dep₁₂ (dotted).

in the beginning of the night but less active at the end. On dep₇ and dep₁₂ activity was reduced during the whole night. Combination of figure 8a and 8b shows that the costs per activity unit (calculated by dividing the activity component of total daily metabolism by the activity score) also went down: from 4.5 ± 0.2 J per unit in the ad lib. situation to 3.5 ± 0.2 , 3.3 ± 0.2 , 3.5 ± 0.2 , and 2.7 ± 0.2 , respectively, on dep₁, dep₂, dep₇, and dep₁₂.

Discussion.—The significant decrease of M_{act} on dep₁ shows that the savings on costs of eating are not, or not completely, compensated by an increase of expenditure on other activity. The fraction of M_{tot} spent on activity, in my data about 16% under ad lib. conditions, is within the estimated range for free-living small rodents (9%–20% [Grodziński and Górecki 1967]) but much lower than the 25% measured by Morrison in caged rats. This can probably be explained from differences in the way of partitioning M_{tot} . Morrison used resting periods of at least 60 min instead of 12 min as I did, and therefore had no opportunity to measure the elevated M_{rest} during the night. Recalculating these data on the basis of my results, which indicate that M_{rest} during day is only 91.5% of the 24 h mean of M_{rest} , I find that M_{act} in Morrison's rats must have been 18% of M_{tot} , a figure close to the 16% I measured.

The fact that on dep₁ the activity level was not reduced, not even at the start of the night when feeding normally peaks (fig. 2), indicates that at this stage feeding was exchanged for other activity which, however, was cheaper per unit. (Indeed, Morrison found that energy expenditure during activity bouts is positively correlated with the fraction of the bout spent on feeding).

The tendency to a further decrease of

energy expenditure per unit activity during deprivation, indicated by the low figure on dep₁₂, can be explained in at least two ways. First, the costs per unit will decrease due to loss of body mass. Second, the costs per unit may go down because the animals move more slowly, for in rats the costs of running a fixed distance become less when running speed decreases (Taylor, Schmidt-Nielsen, and Raab 1970). The fractional reduction of M_{tot} that can be ascribed to savings on activity amounted to 0.12 ± 0.01 .

M_{maint}

Introduction.—The energy expenditure of a resting animal in the postabsorptive state in the region of thermoneutrality is usually called basal metabolic rate (BMR), indicating that this is the irreducible minimum of metabolism. The BMR, of course, depends on body size. The following general equation holds: $BMR = a \cdot M^b$ in which BMR = basal metabolic rate (watts), M = body mass (kilograms), and a and b are constants. Across all homeotherms, a quite satisfactory approximation is obtained with $a = 3.4$ and $b = 0.75$ (Kleiber 1961). As BMR has diurnal rhythmicity (Aschoff and Pohl 1970), so that the time factor should be taken into account, it is advisable to use the 24 h average of BMR (Kayser 1970).

BMR subserves processes such as breathing, circulating blood, maintaining muscle tone, preserving electrochemical gradients, and replacing proteins and other macromolecules. According to Passmore (1971), the last two items make up over 80% of total maintenance costs.

This paragraph considers whether BMR, as defined above, is indeed the irreducible minimum of metabolic rate. Milligan (1971) suggested already that

the animal may economize on the upkeep of electrochemical gradients and on the turnover of macromolecules. Indeed the turnover rate of muscle protein may go down by as much as 50% in rats on restricted diets (Waterlow and Stephen 1968). In view of this I shall use maintenance metabolism (M_{maint}) instead of BMR.

If M_{maint} decreases during deprivation this will be due at least in part to decreasing body mass. For another part, it may be due to the fact that the constants a and/or b in the above equation are reduced. Such a reduction may stem from two different causes: (1) for some or all types of tissue the metabolic rate (per unit of mass) may fall during deprivation, (2) during starvation the relative proportion of tissues with lower metabolic rate may rise (those with higher metabolism giving a relatively large contribution to mass loss). Hence, when body mass goes down during deprivation, the corresponding change of maintenance costs does not necessarily obey the above equation, as assumed in most studies so far (Kleiber 1961). For that reason, it is not enough to give only data per unit body mass. I shall present data on M_{maint} , measured over periods of 24 h, for whole animals, also stating

the body mass of each individual at the time of measurement.

Method.—Data on $\bar{M}_{\text{maint}}$ were obtained from M_{rest} as measured in experiment III. Indicator for the postabsorptive state, after the withdrawal of food, was the respiratory quotient. The M_{maint} was calculated over four 24 h periods: from 12–36 h after the start of deprivation (dep_{14}), 24–48 h (dep_2), 144–168 h (dep_7), and 264–288 h (dep_{12}), respectively. Body mass over the same intervals was calculated as the mean of initial and final values.

Results.—Figure 10 shows that under ad lib. conditions the mean RQ ranged from 0.86 to 0.99 but that from 12 h after food withdrawal onward it had gone down to an average of about 0.71, indicating complete fat oxidation. At that time the animals had certainly reached the postabsorptive state. Note that in experiment III even on dep_{12} there is no rise of RQ indicating an increase of protein combustion.

M_{maint} is presented in figure 11. M_{maint} on dep_{14} is the best estimate available of M_{maint} under ad lib. conditions (normal M_{maint}). This was $69 \pm 0.5\%$ of ad lib. M_{tot} . On dep_{12} $\bar{M}_{\text{maint}}$ had gone down to about half ($52 \pm 1\%$) the normal value, body mass to about three fourths ($73 \pm 5\%$; fig. 7).

FIG. 10.—Change of RQ during food deprivation, mean of six animals, shaded zone indicates postabsorptive period.

FIG. 11.—Change of M_{maint} during food deprivation, individual data of six animals

Discussion.—The M_{rest} of the non-deprived animal in the postabsorptive state in the zone of thermoneutrality (normal M_{maint}) cannot be called basal metabolic rate if this term stands for an irreducible rest of total metabolic rate. Food deprivation causes a reduction, especially in the beginning. The drop from dep_7 to dep_{12} was only half as large as that from dep_2 to dep_7 .

The daily mean of normal M_{maint} amounted to 1.21–1.47 W per animal. Body masses of these animals ranged from 289–315 g. For the sake of comparison with data in the literature, this may be recalculated per unit metabolic body size. The daily mean of normal M_{maint} then amounted to $3.3 \pm 0.1 \text{ W} \cdot \text{kg}^{-3/4}$, a value that agrees with the interspecific mean of BMR, $3.4 \text{ W} \cdot \text{kg}^{-3/4}$ (Kleiber 1961). The fractional reduction of M_{tot} that can be ascribed to savings

on maintenance amounted to 0.33 ± 0.01 (fig. 4).

The fact that even toward the end of deprivation RQ remains at the level for complete fat oxidation indicates that the terminal increase of protein combustion seen in experiment I did not occur in experiment III, presumably due to the higher starting mass of the animals in the latter. However that may be, it has two fortunate consequences. First, Brouwer's formula can be used for calculation of E_{rel} over the entire experimental period. Second, we can get some impression of how far the metabolic rate (per unit mass) of some or all tissues declines during deprivation.

Keys et al. (1950) and later Grande et al. (1958) suggested that the contribution of fat to M_{maint} is negligible. Schieman (1958), however, concluded from measurements in cattle before and

after fattening that fat tissue has a maintenance cost per unit mass comparable to that of the body as a whole. In vitro experiments by Ball (1965) with fat tissue of rats gave metabolic rate values up to $5.8 \text{ W} \cdot \text{kg}^{-1}$, a value even higher than normal M_{maint} of total body mass of my animals ($4.5 \text{ W} \cdot \text{kg}^{-1}$; figs. 7, 11). Depending on which of these views as to the costs of maintenance of fat is correct, the contribution of the loss of fat tissue to the reduction of M_{maint} in the present experiment must have been somewhere in between 0% and 70%. Hence, in any case at least 30% of the reduction of M_{maint} must stem from a decrease in metabolic rate of some or all tissues.

EXPERIMENT IV: BODY TEMPERATURE

Introduction.—During deprivation heat production decreases due to the cessation of food processing and the lowering of activity and maintenance. When discussing the thermoregulatory aspects of this, two possibilities must be distinguished: (1) Temperature is regulated at the normal level. If so, the rat will attempt to compensate its decreased heat production by improving its insulation (by vasomotion, curling up, etc.). If this is not enough it will restrict the deprivation-imposed reduction of total metabolic rate for thermoregulatory reasons. Temperature of the body core will remain at the ad lib. level (possibility 1a) unless acute lack of fuel prevents metabolism from obeying the commands of the thermoregulatory system (possibility 1b). (2) Temperature is regulated at a lower level during food deprivation. Less heat will then be lost, and this (possibly together with improved insulation) may make thermoregulatory heat production unnecessary.

Lower body temperatures in relation to restricted food have been reported in

mammals. Some of these reports regard species with pronounced rhythms, either seasonal (e.g., hibernators) or diurnal (e.g., bats). There are similar data, however, on strictly homeothermic species. Taylor and Keys (1950) measured a lowering of body temperature of 0.75 C in man during food restriction. McCance and Mount (1969), found body temperatures over 2 degrees below normal values in undernourished pigs.

In rats, starvation caused a fall in body temperature when activity was severely restricted but not when it was allowed (Stevenson and Rixon 1957). Neither Campbell (1964) nor Hamilton (1969) observed any change of body temperature in freely moving rats. To my knowledge no studies on changes in insulation during food deprivation have been published.

The subjects of the experiments referred to had to be handled for insertion of a sensor, with the risk of abnormal values caused by disturbance. Further the measurements were done during only one period of the day while body temperature has a diurnal rhythm that amounts to above 1.5 C in mammals (Irving 1964). I therefore supplemented these studies by chronic measurements of core temperature during food deprivation, in freely moving animals without disturbance.

Method.—I measured core temperature in the blood in the right atrium, with a permanently implanted copper-constantan thermocouple, the output of which was recorded at 24 s intervals on a micrograph (Kipp, model BD5, paper speed $2 \text{ mm} \cdot \text{min}^{-1}$). The connecting leads, 0.1 mm diameter, were spiralized for flexibility. The entire implanted length was put inside a silicon tubing sleeve, 0.5 mm internal diameter and 1.0 mm external diameter, closed with silicon paste to prevent infection. Ex-

ternal connections were housed in a small plastic box attached to the skull with stainless steel screws and dental cement. Undue slack in the external leads was taken up by attaching them to the ceiling of the room by means of a long rubber band. This left the animals practically complete freedom of movement in their cages. Implantation of the sensor in the right atrium was performed via the vena jugularis according to a method of Steffens (1969).

Observations were done on seven animals. After operation they were allowed at least 7 days for complete recovery. Four animals were deprived of food for 7 days and the other three for 14 days. Temperatures were measured on 2 days in the ad lib. situation and throughout the immediately succeeding deprivation period.

Results.—Figure 12*a* shows a representative 24 h record of core temperature in the ad lib. situation (rat 121). Core

temperature showed a clear diurnal rhythm. Daily averages were very reproducible. Differences within animals were a little smaller than those between animals. One animal (rat 96) had an exceptionally low daily average of 37.5 C, while those in the other animals varied from 37.8–38.1 C; this animal will be treated separately. Overall mean core temperature of the other six animals under ad lib. conditions was 37.9 ± 0.05 C (range 36.8 ± 0.04 – 39.0 ± 0.06).

The effects of deprivation are summarized in figure 13. For each individual this figure presents the difference between (*a*) the temperature measured in that individual on a given deprivation day, and (*b*) the mean value of the temperature, measured in the same animal, on the 2 ad lib. days. The daily average of core temperature (fig. 13*b*) decreased during deprivation in all animals including rat 96. It went down by

FIG. 12.—24 h records of core temperature of rat 121, *a*, under ad lib. conditions; and *b*, on the last deprivation day (dep₁₄).

FIG. 13.—The change of core temperature during food deprivation, *a*, daily maximum, *b*, average, and *c*, minimum. Results of rat 96 are indicated with open circles instead of points (further explanation in text).

about 0.3 C on dep_1 , and afterward the decrease was approximately linear at a rate of 0.1 C per day. The extremes changed in the same direction though the drop of the daily minimum (fig. 13*c*) was greater than that of the daily maximum (fig. 13*a*), resulting in a higher daily amplitude. This is also shown in the 24 h record of core temperature of rat 121 on the last deprivation day (fig. 12*b*).

Discussion.—In interpreting the data on core temperature it should be realized that the daily range of core temperature measured is not the daily range of set point of the thermoregulatory system. The highest core temperatures were seen during activity, when body temperature is considerably above the norm. It is doubtful therefore whether under ad lib. conditions the set point of rat 96 differed from those of the others. The daily minima, which presumably give a fair indication of the set point in the inactive period, were closely similar in all seven rats. Core temperature tended to decline and the daily temperature cycle attained a greater amplitude during food deprivation. This indicates that the animals

lowered the norm of the thermoregulatory system (see Introduction, possibility 2).

The next question is whether the animals reduced their heat loss by improving insulation. A rough impression can be gained by using the formula $\bar{H}l = h(T_c - T_a)$, where $\bar{H}l$ = mean heat loss rate (W), h = heat transfer coefficient ($\text{W} \cdot ^\circ\text{C}^{-1}$), T_c = core temperature ($^\circ\text{C}$), T_a = ambient temperature ($^\circ\text{C}$). Daily heat gain equals heat loss, both under ad lib. conditions and on dep_{12} . Using the subscripts adl and dep_{12} , respectively, to indicate these two conditions, and bearing in mind that

$$\bar{H}l_{\text{dep}_{12}} = 0.4 \bar{H}l_{\text{adl}} \text{ and } T_{c\text{adl}} = T_{c\text{dep}_{12}} + 1.0 \text{ C,}$$

we find that

$$\frac{h_{\text{dep}_{12}}}{h_{\text{adl}}} = \frac{\bar{H}l_{\text{dep}_{12}} \cdot (T_{c\text{adl}} - T_a)}{\bar{H}l_{\text{adl}} \cdot (T_{c\text{dep}_{12}} - T_a)} = 0.46.$$

The decrease of core temperature and rise of insulation during deprivation mean that the drop of heat production is not, or is only partly, constrained by

expenditure specifically for thermoregulatory reasons. To what extent such a constraint does occur can only be verified by increasing the ambient temperature. If this does not cause energy expenditure to go down still further, the reduction by the cessation of food processing and the curtailing of activity and maintenance was not constrained at all. This fell outside the scope of this study.

GENERAL DISCUSSION

Total energy expenditure.—Figure 14 presents the individual measurements of M_{tot} under ad lib. food conditions plotted against body mass. This figure gives no reason to think that there is heterogeneity between experiments. This permits comparison of the data from experiments I and III on the change of M_{tot} under complete deprivation. Figure 4 presents M_{tot} on a given deprivation day as a percentage of its ad lib. value in the same animal. Here again, the different sets of data agree well. The M_{tot} decreased at an overall rate of about 6% per day. However, at the start of the deprivation period, it decreased somewhat more

rapidly and at the end the decrease tended to slow down.

Experiments I and III differed in one respect. Only in the former had the rats completely exhausted their fat stores in the terminal stages of deprivation and begun to burn protein. This means that the yield of free energy for maintaining vital processes was even lower in these animals at that time than in the rats of experiment III after an equally long fast. This may be so because starting body masses were lower in experiment I than those in experiment III.

In any case, the results of experiment III justify the conclusion that energy expenditure of the adult rat after a 12 days' fast is 40% of that under ad lib. conditions and that the animals can survive this extreme reduction of their metabolism!

The components of energy expenditure.—Before we attempt to interpret the data in terms of an analysis of M_{tot} into components, the limitations of this analysis should be pointed out. These are partly practical, partly of a more

FIG. 14.— M_{tot} of individual rats under ad lib. food conditions, plotted against body mass ($\blacktriangle$, experiment I; $\bullet$, experiment II; and $\circ$, experiment III). The regression equation is: $M_{\text{tot}} = 0.0053 \text{ mass} + 0.30$. In the case of experiment I, upper and lower estimates of M_{tot} for each individual have been plotted.

fundamental nature. With regard to the latter, we have already seen that there are probably interactions between, for example, M_{act} and M_{rest} , but that during activity the processes making up M_{rest} proceed at a lower rate. However, having no operational means for taking this into account, I shall assume that the components of M_{tot} are mutually independent and additive, although further work may well prove this to be a crude approximation. The practical problems stem from the response time of the apparatus, which were discussed in

Material and Methods. Particularly during the night, when resting periods are brief, I often had to content myself with a fractional response of 0.95 in 12 min.

Because M_{act} is calculated by subtracting M_{rest} from M_{tot} and because the objections just mentioned will result in an overestimate of M_{rest} , the values obtained for M_{act} will be systemically too low. Figure 15 presents the individual measurements of M_{act} , M_{foodp} , and M_{maint} under ad lib. food conditions, plotted against body mass. Comparing the results of experiments II and III, we can

FIG. 15.— M_{act} (a), M_{foodp} (b), and M_{maint} (c) of individual rats under ad lib. food conditions, plotted against body mass (●, experiment II; and ○, experiment III). In the case of M_{foodp} and M_{maint} upper and lower estimates for each individual have been plotted (see text).

make the following comments: (1) There is a suggestion that M_{act} was higher in experiment II than in experiment III. The reason for this probably was that the animals in experiment II were disturbed by the imposed feeding pattern. (2) Data on M_{foodp} and M_{maint} should not be compared before pointing out the difference in method between the two experiments. In experiment II the ration was reduced to zero in two steps, whereas in experiment III the change from ad lib. to total deprivation was instantaneous. Now changes in M_{maint} during the interval between the two M_{rest} measurements (before and after the change in ration) might result in an overestimate of M_{foodp} (see the discussion under Experiment II). This interval was inevitable, because it took time for the digestive system to reach a new steady state. Attempts to correct for this error are likely to result in an underestimate of M_{foodp} . However, the range between upper and lower estimate of M_{foodp} , and hence our uncertainty as to its real value, will be larger in experiment III than in experiment II, because in the latter the changes in M_{maint} accompanying the change in ration are less marked. This difference in accuracy between the two experiments is visible in figure 15b and 15c. There is no reason to think that the two experiments gave contradictory results, but clearly the more precise estimates of M_{foodp} and M_{maint} are those from experiment II.

Under ad lib. food conditions the rat spent 16% of M_{tot} on activity, 12%–13% on the internal processing of food, and thus 72% or 71% on maintenance. Experiment III revealed that during long-term deprivation M_{act} is reduced by 75% and M_{maint} by nearly 50%.

Adaptive changes of energy expenditure.—I will call a change of energy expenditure during food deprivation adaptive if (1) this change is not a

direct consequence either of the cessation of feeding or the drop of body mass, and (2) it raises the chances of survival under these adverse conditions.

Adult rats at a body mass of about 290 g have a mobilizable energy reserve of 1,100 kJ (table 1). In the ad lib. food situation under the present experimental conditions, their daily $\bar{M}_{\text{tot}}$ amounted to nearly 1.9 W. Consequently at this rate they could survive a little less than 7 days without food. However, they prolonged their survival to up to 11 days. Figure 16 compares ad lib. M_{tot} with M_{tot} values during long-term food deprivation, plotted against body mass. Toward the end M_{tot} of the deprived animals was about half the normal level. Part of this difference, of course, is due to cessation of M_{foodp} , but if we take this into account (by raising the regression line for the M_{tot} values of the deprived rats by an amount equal to the mean M_{foodp} for ad lib. animals of the same mass) the corrected regression line is still well below that for ad lib. conditions.

To what extent is the remaining difference adaptive? As regards activity, the decrease of M_{act} from the ad lib. situation to the first deprivation day is hard to interpret in the absence of information on the costs per unit of eating and other activities. In the further course of deprivation, the decrease of M_{act} continues, eventually to 25% of the ad lib. value. This is accompanied by a smaller drop of the daily number of activity units (N_{act}), which reaches about half the ad lib. value. In other words, the costs per unit are also halved in the course of deprivation.

The decrease of N_{act} means that the deprived rat engages less in some or all kinds of activities. In terms of savings this may be called adaptive. The reduced costs per unit may have several different causes. First, lower body mass will

FIG. 16.— M_{tot} during long-term food deprivation, plotted against body mass ($\blacktriangle$, experiment I, mean of six animals; $\circ$, experiment III, individual data with the number of deprivation days). —, M_{tot} under ad lib. food conditions (taken from fig. 14). - - - : M_{tot} during total deprivation; $M_{\text{tot}} = 0.0093 \text{ mass} - 1.21$ (only data from experiment III). - - - - M_{tot} during total deprivation but raised by an amount corresponding to ad lib. M_{foodp} at the corresponding body mass, $M_{\text{tot}} = 0.0105 \text{ mass} - 1.36$. Further explanation in text. Data from experiment I, although plotted, have not been included in the regression calculation because the two experiments are clearly heterogeneous.

result in less energy expenditure on a given amount of behavior. Second, the fasting rat may tend to engage only in behaviors that are energetically inexpensive. To check this would require direct observations of behavior, which were not feasible in my experiment. Third, for a given body mass, the costs per unit may decrease for some or all kinds of behavior. This might be due on the one hand to purely "passive" inability of the motor system to obtain energy from the reserves at the normal rate during deprivation. The fact that animals in the cold die of starvation before they have depleted their fuel reserves (Kendeigh 1945) proves that rate of mobilization of energy may be a limiting factor. On the other hand we might be dealing with some more active form of economizing. In principle it seems possible to choose between these alternatives by observing energy ex-

penditure of deprived rats during forced exercise. In the absence of further data, however, I will not try to answer the question whether the decrease of costs per unit activity is adaptive.

As regards M_{maint} the question is whether this has the same value during deprivation as it would have in an ad lib. fed animal of the same mass and body composition. The answer depends on our estimate of the costs of maintenance of fat tissue, since the reduction of body mass during deprivation goes largely at the expense of this tissue. However, I have argued earlier that even if we assume that M_{maint} of fat tissue equals (or slightly exceeds) the mean M_{maint} of all tissues, loss of fat tissue can explain only part of the decrease of overall M_{maint} . Another part is due to a decrease of M_{maint} of the other tissues. As the mass of the latter does not change much, their maintenance metabolic rate

per unit mass goes down. Since in general (in the absence of deprivation) M_{maint} per unit mass is inversely correlated with body mass, it is certain that the decrease I find is adaptive under the above definition.

Needs of thermoregulation.—I did my experiments at a temperature in the thermoneutral zone of postabsorptive resting animals, to avoid the complication of special heat production for thermoregulation. This does not preclude that the rat, when digesting food and performing various activities in the ad lib. situation, may have to take special measures for dissipating the heat generated thereby. However, as the ambient temperature of 30 C was in the lower part of the thermoneutral zone, it is unlikely that in my experiments the animals ever had to cope with this problem. The other possible criticism of my working temperature is that during deprivation the thermoneutral zone may have shifted to higher temperatures, so that in fact my rats were below the lower critical temperature. I cannot completely refute this, but I believe that owing to improved insulation and decreased core temperature the (adaptive) reduction of M_{tot} has not been greatly hampered by the demands of thermoregulation.

The results of the temperature observations can be summarized as follows. Mean core temperature after about 12 days deprivation was decreased by about 1 C. It seems justified to regard this as a change in set point of the thermoregulatory system. Overall thermal conductance had dropped to less than half the starting value.

In conclusion it can be stated that the thermoregulatory system has tolerated a considerable reduction of heat production during deprivation.

Ecological implications.—At the close of a study of laboratory rats under laboratory conditions, one may ask to

what extent the conclusions reached can be generalized to the case of wild animals in a natural environment.

Let us first consider M_{act} . It is typical of my experimental arrangements that during deprivation the rats had no chance of finding food, however much exploration occurred. This may not necessarily be so in a natural environment. In the latter, exploratory behavior is a gamble in which the animals' energy reserves are staked against the chance of finding new food, and reduction of activity is a wise move only if the odds against winning are heavy. It is of interest in this context that Richter and Rice (1954), measuring activity of wild and domesticated Norway rats with a running wheel, found that in the wild form deprivation caused a quadrupling of activity.

Similarly, with respect to the reduction of M_{maint} the possibility arises that the animal, by saving energy reserves, risks an increased susceptibility to other environmental stresses such as exposure to cold or disease. It is true that at least for rats under laboratory conditions drastic long term restriction of caloric intake greatly enhances longevity (Berg and Simms 1960). It seems likely that M_{maint} in these animals was reduced. Further work, however, will be needed to decide whether this finding is applicable to animals outside the laboratory.

To conclude, then, the laboratory rat has a surprisingly great capacity for reducing its energy expenditure when deprived of food. Decreases in activity and maintenance metabolism contribute much to this effect. There are good grounds for ascribing adaptive significance to this increased economy, at least under laboratory conditions. To what extent these conclusions can be generalized to wild animals in nature can only be resolved by future ecological studies.

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