Regulation of food intake during growth in fatty and lean female Zucker rats given diets of different protein content

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1. Food intake, and the rates of protein, lipid and energy deposition during growth were measured for lean and congenitally obese (fatty) female Zucker rats given diets of different protein content *ad lib.* Six semi-synthetic diets were used, which contained 40, 100, 150, 300, 500 and 700 g casein/kg (diets 40C, 100C, 150C, 300C, 500C and 700C).

2. Dietary treatments began when the rats were 34 or 35 d old. Collections of urine and faeces were analysed for energy content. The total carcasses of all the rats were analysed individually for protein, lipid and energy.

3. In the first experiment, twelve rats of each phenotype were given diets 150C or 300C. Four fatty and four lean rats were killed at 50, 66 and 98 d of age. In the second experiment groups of four fatty and four lean rats were given diets 40C, 100C, 500C and 700C *ad lib.* until they were killed at 66 d of age. Other groups of fatty rats were pair-fed from 35 to 67 d of age on diets 100C and 500C. Rats were also killed at 24 and 34 d of age to provide initial samples for the comparative slaughter procedure.

4. When given food *ad lib.*, fatty and lean rats had identical rates of protein deposition at all ages and for all diets, but lipid and energy deposition were always much greater in the fatty rats. Food intake was also much greater for the fatty rats (except on diet 40C). Differences in food intake and growth rate attributable to diet were most pronounced for the range of diets 40C–150C.

5. Fatty rats pair-fed to lean rats deposited less protein but about twice as much energy and lipid as lean rats on the same diets.

6. The results are discussed in relation to existing theories of appetite control. It appears that food intake is precisely regulated in the congenitally obese Zucker rat. This regulation is intimately linked with the impetus for protein deposition and the rates of retention of lipid and energy appear to be of no importance in relation to appetite control.

Zucker & Zucker (1961) described a strain of rats in which obesity is inherited as a simple, autosomal, recessive gene. Homozygous recessive individuals (fafa, fatty rats) are noticeably fatter than their lean litter-mates by about 3 weeks of age. Individuals carrying one or two normal alleles (Fafa or FaFa, lean rats) are normal in appearance and body composition.

Given free access to a diet adequate in all nutrients, the fatty rat has a much higher rate of lipid deposition than a lean rat of the same sex. This is not, however, due to hyperphagia alone. When fatty rats were restricted to a food intake equal to that of lean rats the rate of lipid deposition was 50% greater in the fatty rats (Bray, York & Swerloff, 1973).

The influence of food intake on the rate of protein deposition during growth in fatty and lean Zucker rats is less clear. The rate of protein deposition is undoubtedly much lower in fatty rats when given comparable amounts of food to lean rats. The extent of the difference has been reported to be 67% (Bray *et al.* 1973) or 56% (Pullar & Webster, 1974). The results of Bray *et al.* (1973) also suggested that protein deposition was lower in female fatty rats than in lean females when both were given food to

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appetite. Pullar & Webster (1974) claimed, however, on the rather insecure basis of nitrogen balance studies, that the rate of protein deposition was very similar in fatty and lean rats if they had free access to food, and they suggested that hyperphagia in the immature fatty rat may be directed towards the maintenance of a normal rate of skeletal and muscle growth.

This paper describes a study designed to provide systematic information on relative rates of protein and lipid deposition during growth in fatty and lean female Zucker rats offered to appetite diets differing in protein content.

A preliminary report of some of this work has been published (Radcliffe, Webster, Dewey & Atkinson, 1975).

EXPERIMENTAL

Animals and diets

A total of fifty-six fatty (congenitally obese) and forty-eight lean female Zucker rats were used. These rats were taken at 24 d of age from a breeding colony maintained at the Rowett Research Institute. Families of rats in the breeding colony received a commercial, pelleted diet (Oxoid; H. C. Styles (Bewdley) Ltd, Bewdley, Worcs.) having (g/kg dry matter) 228 crude protein (N × 6·25), 44 fat, 31 crude fibre, and a gross energy value of 18·5 MJ (4·43 Mcal)/kg dry matter. Four fatty and four lean rats were killed at weaning (24 d of age) for carcass analysis. The rest received Oxoid *ad lib.* until 34 d of age, when another four fatty and four lean rats were killed. The remainder were kept individually in cages with suspended, stainless-steel floors, at an air temperature of 20°. A 12 h (09.00–22.00 h) light–dark cycle was operated. Animals were given one of six semi-synthetic diets, the composition of which is given in Table 1. The diets were formulated by substitution of casein for sucrose to produce mixtures ranging in casein content from 40 to 700 g/kg, and in energy from 19·9 to 23·6 MJ/kg.

Unless stated otherwise, all diets were offered *ad lib.* In Expt 1 twelve fatty and twelve lean rats were given, beginning at 34 d of age, diets containing either 150 or 300 g casein/kg, and four fat and four lean rats fed on each diet were killed at 50, 66 and 98 d of age.

In Expt 2 four rats from each phenotype were given diets containing 40, 100, 500 or 700 g casein/kg from 34 d of age until they were killed at 66 d of age. In addition one fatty rat was given the same amount of food as that consumed the previous day by each of the lean rats fed on diets 100C and 500C. These pair-fed fatty rats were killed at 67 d of age.

Any uneaten and spilled food was weighed at the end of each day and a record was kept of food intake. Spillage was recorded for the pair-fed fatty rats and an allowance made for this so that spillage-corrected food intake was the same as that of lean animals. Fresh tap-water was available to the rats at all times.

Balance trials

Collections of urine and faeces were made using individual stainless-steel metabolism cages (North Kent Plastic Cages Ltd, Dartford, Kent). Urine was collected into a 50 ml conical flask containing 1 ml 2 M-H_2SO_4 as preservative. Daily collections were

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Table 1. *The composition of the six diets given to rats and their determined gross energy, crude protein (nitrogen × 6·25) and lipid contents*

	Diet					
Ingredients (g/kg)	40C	100C	150C	300C	500C	700C
Casein	40	100	150	300	500	700
Cooking fat*	150	150	150	150	150	150
Maize oil	50	50	50	50	50	50
Mineral mix†	37	37	37	37	37	37
Trace element mix‡	2	2	2	2	2	2
Vitamin mix§	50	50	50	50	50	50
Sucrose	671	611	561	411	211	11
Gross energy (MJ(MCal)/kg)	19·9 (4·75)	20·4 (4·78)	20·5 (4·90)	21·3 (5·09)	22·5 (5·37)	23·6 (5·64)
Crude protein (g/kg)	37·3	93·4	135	269	443	627
Lipid (g/kg)	193	195	197	202	207	212

* White Cap; Van den Burgh and Jurgens Ltd, Burgess Hill, West Sussex RH15 9AW, England.

† Contained (g): $CaCO_3$ 12·4, Na_2HPO_4 8·6, KH_2PO_4 8·2, KCl 6·0, $MgCl_2.6H_2O$ 3·4.

‡ Contained (mg): KI 32, $MnSO_4.4H_2O$ 210, $ZnSO_4.7H_2O$ 176, $FeSO_4.7H_2O$ 260, $CuSO_4.5H_2O$ 98. This mixture was made up to 2 g with sucrose.

§ Contained (mg): thiamin 10, riboflavin 20, nicotinic acid 40, pyridoxine 10, pteroylmonoglutamic acid 10, cyanocobalamin 0·05, calcium pantothenate 160, biotin 20, *myo*-inositol 800, *p*-aminobenzoic acid 20, choline chloride 2000, ascorbic acid 150, DL-α-tocopheryl acetate 400, retinyl acetate 8·4, cholecalciferol 0·4, menaphthone sodium bisulphite 1·0. This mixture was made up to 50 g with sucrose.

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stored at −20°. Each balance trial lasted 4 d; at the end of this time the four collections of faeces and of urine from the four rats in each group (sixteen samples each of faeces and urine) were pooled for subsequent analysis.

Each rat took part in a balance trial at intervals of 16 d. The rats given food *ad lib.* were 40 d of age when the first trial was started; pair-fed animals were 1 d older. Three subsequent trials were done for those animals used in Expt 1 that were killed at 98 d of age. In Expt 2 two trials were done for each rat.

Preparations of samples for analysis

Excreta. Samples of faeces and urine were freeze-dried.

Carcasses. Rats were killed by carbon dioxide inhalation. The abdomen was opened, the gut removed and its contents flushed out with water. The washed intestine was replaced and the carcasses frozen at −20°. While frozen they were chopped into small pieces, sealed in a Kilner jar and autoclaved at 124° and 103 kN/m² for 15 min. This facilitated the next stage, which was to mince the carcass, which was then freeze-dried.

Analytical techniques

All determinations were carried out in triplicate. The gross energy content of all samples was determined by adiabatic bomb calorimetry, the N content of faeces, carcasses and diets by the macro-Kjeldahl method (Davidson, Mathieson & Boyne, 1970) and the lipid content of carcasses and diets by the method of Atkinson, Fowler, Garton & Lough (1972).

Statistical analysis

All analyses except where indicated to the contrary were done by the analysis of variance.

RESULTS

Results given in Table 2 indicate that fatty and lean rats already differed markedly in body composition at weaning, 24 d of age, and even more so at the start of the feeding trials at 34 d, at which time the fatty rats had more than four times as much carcass lipid as lean rats. Body protein was, however, the same for both phenotypes at both ages.

The apparent digestibility of the energy content of all diets was at least 0·90. The apparent digestibility of N was greater than 0·90 for all groups except those fed on diet 40C, for which it was only about 0·50 (Table 3). The low values for the animals fed on this very-low-protein diet are probably due to a relatively larger contribution of endogenous faecal N to total faecal N, although it is not possible to say whether absolute values for endogenous faecal N were different from those for other rats fed on diets higher in protein content.

The apparent metabolizability of all diets, with the exception of those with the lowest and highest protein contents (diets 40C and 700C respectively), was greater than 0·87. The lower values for diet 40C were probably, in part, due to the relatively larger contribution of endogenous urinary energy losses to total urinary energy. The relatively greater loss of absorbed energy into the urine as end-products of dietary

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Table 2. *Body weight and body composition of fatty and lean female Zucker rats fed on stock diet† and killed at 24 and 34 d of age*

(Mean values with their standard errors for four rats/group)

Age (d)	Phenotype	Body-wt (g)	Body composition: Protein (g)	Lipid (g)	Energy (MJ)
24	Fatty	52·7 ± 0·75	7·57 ± 0·09	7·84 ± 0·45	0·487 ± 0·01
24	Lean	52·0 ± 0·22	7·70 ± 0·06	3·74 ± 0·21	0·321 ± 0·01
Statistical significance of difference		NS	NS	**	**
34	Fatty	97·0 ± 3·9	14·2 ± 0·84	20·7 ± 0·68	1·10 ± 0·03
34	Lean	78·4 ± 5·2	13·4 ± 0·93	4·67 ± 0·26	0·477 ± 0·02
Statistical significance of difference		*	NS	**	**

NS, not significant.
* $P < 0.05$, ** $P < 0.01$.
† Oxoid; H. C. Styles (Bewdley) Ltd, Bewdley, Worcs.

Table 3. *Mean values for apparent digestibility of energy and nitrogen, and metabolizability of diets containing 40, 100, 500 or 700 g casein/kg (40C, 100C, 500C and 700C) respectively by fatty and lean female Zucker rats*

	Diet*	Phenotype	Digestibility: N	Digestibility: Energy	Meta-bolizability
Expt 1†	150C	Fatty	0·94	0·94	0·90
	150C	Lean	0·94	0·93	0·89
	300C	Fatty	0·96	0·96	0·90
	300C	Lean	0·96	0·94	0·90
Expt 2‡	40C	Fatty	0·49	0·90	0·84
	40C	Lean	0·52	0·90	0·82
	100C	Fatty	0·92	0·93	0·90
	100C	Lean	0·90	0·90	0·87
	500C	Fatty	0·97	0·97	0·90
	500C	Lean	0·97	0·97	0·88
	700C	Fatty	0·95	0·95	0·81
	700C	Lean	0·95	0·94	0·77
	100C	Fatty (pair fed)§	0·94	0·94	0·91
	500C	Fatty (pair-fed)§	0·97	0·97	0·88

* For details, see Table 1.
† Means of four determinations.
‡ Means of two determinations.
§ Given the same amount of food as that consumed the previous day by each of the lean rats fed on diets 100C and 500C.

protein catabolism in comparison with other diets probably accounted for the lower metabolizability of diet 700C.

On the whole, fatty and lean rats metabolized food energy and digested N with equal efficiency at all ages and for all diets. This was due to a slightly higher digestibility of dietary energy by the fatty rat and a relatively smaller proportion of the digestible

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Table 4. *Expt* 1. *Metabolizable energy* (ME) *intake and body composition of fatty and lean female Zucker rats offered to appetite diets containing* 150 *or* 300 *g casein/kg* (150*C and* 300*C respectively*) *from* 34 *d of age to* 50, 66 *or* 98 *d of age*

(Mean values for four rats/group)

Age (d)	Diet†	Phenotype	ME intake (MJ)	Body-wt (g)	Body composition: Protein (g)	Body composition: Lipid (g)	Body composition: Energy (MJ)
50	150C	Fatty	6·33	215	25·8	89·6	3·97
		Lean	3·83	140	23·9	12·1	1·25
	300C	Fatty	6·94	238	25·6	101	4·41
		Lean	3·92	150	26·0	18·9	1·31
SE of difference			0·17	6·68	2·11	3·66	0·10
Statistical significance of:							
Phenotype			**	**	NS	**	**
Diet			**	**	NS	*	**
66	150C	Fatty	13·1	366	39·1	184	8·05
		Lean	7·8	213	38·1	44·0	2·55
	300C	Fatty	14·6	402	40·1	213	9·07
		Lean	8·4	223	41·6	41·8	2·53
SE of difference			0·48	14·8	1·65	10·4	0·38
Statistical significance of:							
Phenotype			**	**	NS	**	**
Diet			*	*	NS	NS	NS
98	150C	Fatty	25·0	503	46·5	274	11·6
		Lean	15·0	245	42·7	57·1	3·13
	300C	Fatty	26·0	526	47·8	296	12·5
		Lean	16·4	269	46·8	69·9	3·72
SE of difference			1·13	26·0	3·02	17·3	0·72
Statistical significance of:							
Phenotype			**	**	NS	**	**
Diet			NS	NS	NS	NS	NS

† For details, see Table 1.
NS, not significant
* $P < 0.05$; ** $P < 0.01$

energy intake being lost into the urine. The absolute loss of urinary energy was 30% greater in the fatty than in the lean rats. The absolute loss of urinary N was estimated to be 54% greater in the fatty rats. This suggests that urinary N in the fatty rats was in a relatively simpler form.

The results of Expt 1 are given in Table 4. Metabolizable energy (ME) intakes and body-weights were both significantly higher for the fatty rats at all ages ($P < 0.01$). Daily intake of ME in both phenotypes was remarkably constant from 34 to 98 d of age (Fig. 1). The effect of diet was significant for ME intake and body-weight for the rats killed at 50 and 66 d of age (the values being higher in the rats fed on diet 300C) but this significant difference had disappeared by 98 d. As expected, the fatty rats deposited far more energy and lipid than the corresponding lean rats but protein deposition was the same for both phenotypes. Changes in body composition occurring during growth in fatty and lean rats given diet 150C are shown in Fig. 2.

Table 5 summarizes the results of Expt 2. With the exception of the values for ME

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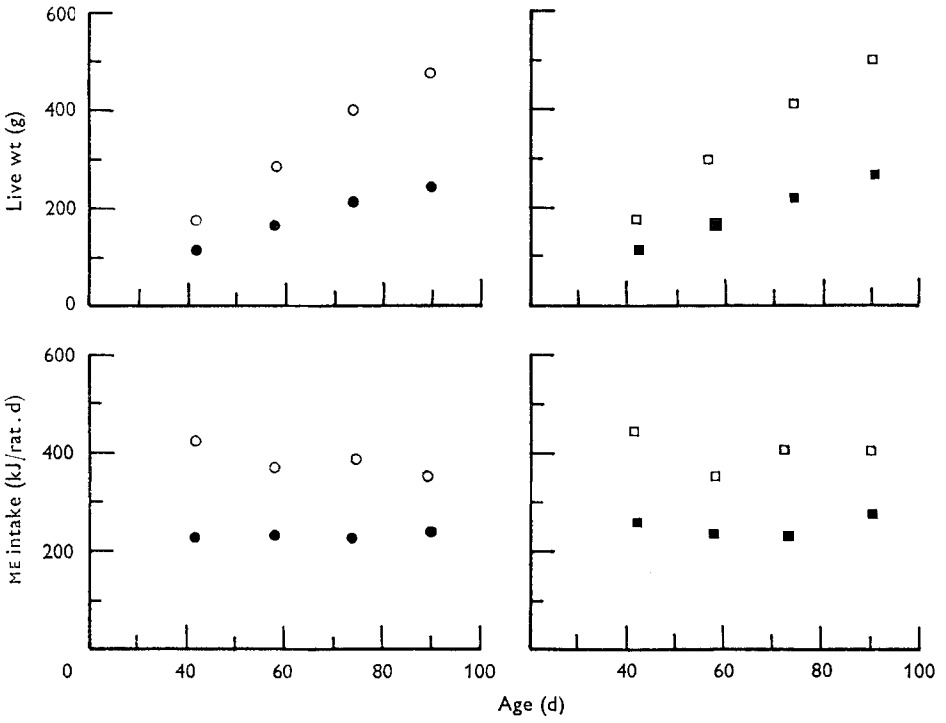

Fig. 1. Expt 1. Changes in live weight (g) and metabolizable energy (ME) intake (kJ/rat per d) during growth in fatty and lean female Zucker rats offered to appetite diets containing 150 or 300 g casein/kg (150C and 300C respectively) (for details, see Table 1) from 34 to 98 d of age. (○), fatty, diet 150C; (●), lean, diet 150C; (□), fatty, diet 300C; (■), lean, diet 300C.

intake and body-weight increase for the rats fed on diet 40C (where there were no statistically significant differences between the phenotypes) ME intake, body-weight and weight gain, the content and deposition of lipid and energy were all significantly higher ($P < 0{\cdot}001$) in the fatty rats than in age-matched lean rats fed on the same diet in all instances.

There were significant differences between diets for all measurements. This was largely due to lower rates of ME intake and body-weight gain for the rats fed on diet 40C.

The effect of varying dietary protein content on ME intake and body-weight gain is shown in Fig. 3, which indicates gains from 34 to 66 d of age using results from Expts 1 and 2. Gains in body-weight and lipid closely reflected differences between phenotypes in ME intake. In the lean rats ME intake increased to a maximum for diet 150C and remained roughly constant at higher protein concentrations. ME intake for the fatty rats fed on diet 40C was only slightly greater than in the lean rats, when appetite in both was abnormally low. Increasing the protein concentration of the diet increased ME intake in the fatty rats to a peak for diet 300C, above which it decreased so that differences in ME intake between fat and lean rats decreased as casein content increased from 300 to 700 g/kg diet.

Rates of protein deposition were identical for both phenotypes, being about 0 for

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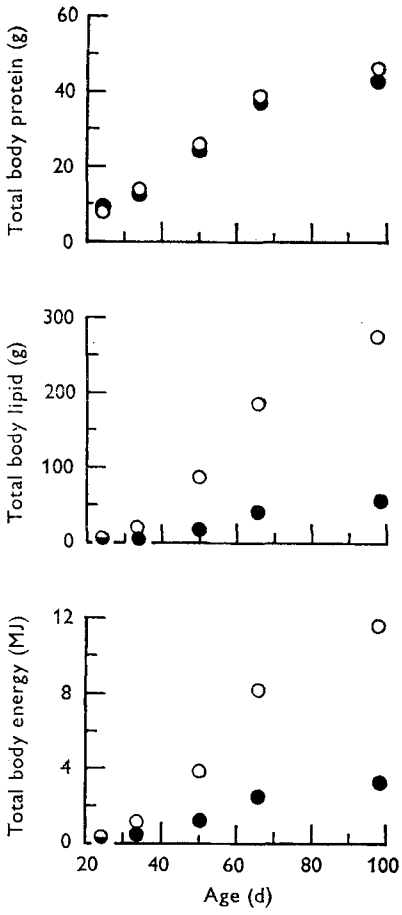

Fig. 2

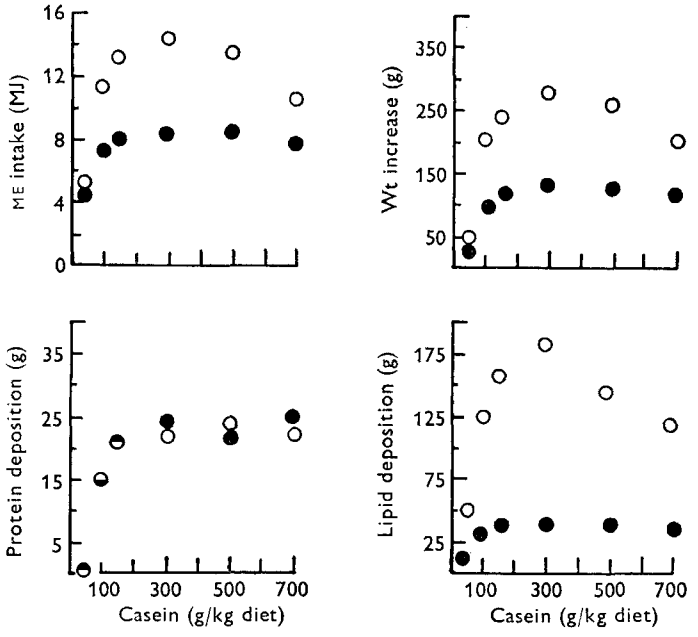

Fig. 3

Fig. 2. Expt 1. Changes in total body protein (g), lipid (g) and energy (MJ) during growth in fatty (○) and lean (●) female Zucker rats. The rats killed at 24 and 34 d of age were given the stock diet (Oxoid; H. C. Styles (Bewdley) Ltd, Bewdley, Worcs.), those killed at 50, 66 and 98 d of age were offered to appetite a diet containing 150 g casein/kg (for details, see Table 1).

Fig. 3. Expts 1 and 2. Metabolizable energy (ME) intake (MJ) and changes in body composition during growth in fatty (○) and lean (●) female Zucker rats offered to appetite diets containing various amounts of casein (for details, see Table 1) from 34 to 66 d of age.

diet 40C, increasing to a maximum for diet 150C, and remaining the same at higher protein concentrations.

The gross efficiency of retention of apparently digestible N for each diet is given in Table 6, which also indicates that the gross efficiency of retention of ME was much higher for the fatty than for the lean rats and supports the findings of Pullar & Webster (1974) that the heat production of fatty rats is much lower than that of lean rats when both are eating the same amount of food but that the two phenotypes have similar heat production when eating *ad lib.* and retaining protein at similar rates.

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Table 5. *Expt 2. Metabolizable energy* (ME) *intake and body composition of fatty and lean female Zucker rats offered to appetite diets containing* 40, 100, 500, *or* 700 *g casein/kg* (40*C*, 100*C*, 600*C and* 700*C respectively*) *from* 34 *to* 66 *d of age*

(Mean values for four rats/group)

Diet†	Phenotype	ME intake (MJ)	Body-wt (g)	Body composition		
				Protein (g)	Lipid (g)	Energy (MJ)
40C	Fatty	5·6	161	17·1	75·9	3·27
	Lean	4·9	103	18·0	16·6	1·04
100C	Fatty	11·7	316	33·8	150	6·70
	Lean	7·5	187	31·5	41·1	2·30
	Fatty (pair-fed)§	7·5	243	27·4	99·8	4·42
500C	Fatty	13·9	358	40·8	169	7·60
	Lean	8·5	215	38·2	42·1	2·51
	Fatty (pair-fed)§	8·8	271	31·5	107	4·87
700C	Fatty	10·9	306	38·9	154	6·70
	Lean	7·9	207	44·4	38·9	2·48
SE of difference‡		0·56	14·4	2·18	8·40	0·36
Statistical significance‡ of:						
Phenotype		**	**	NS	**	**
Diet		**	**	**	**	**

NS, not significant.
** $P < 0.01$.
† For details, see Table 1.
‡ Excluding results for pair-fed rats.
§ Given the same amount of food as that consumed the previous day by each of the lean rats fed on diets 100C and 500C from 35 to 67 d of age.

DISCUSSION

Values for the body composition of the fatty and lean Zucker rats used in these experiments were similar to those of Bray *et al.* (1973) and Zucker (1975). The present study gives a more complete picture than was hitherto available of the extent to which body composition in the female Zucker rat is determined by phenotype, stage of maturity and the quantity and quality of food eaten. Recent unpublished work indicates that these factors interact to affect body composition slightly differently in the male Zucker rat.

This study also confirms that obesity in the Zucker fatty rat is not simply a result of hyperphagia. When fatty rats were restricted to a food intake equal to the normal amount eaten by their lean litter-mates, their rate of protein deposition was abnormally low but they still had a much higher rate of lipid deposition (Table 7). When food was available to appetite, both fat and lean rats achieved identical rates of protein deposition, even when given diets of low protein content which restricted growth. Although both phenotypes deposited protein at the same rate, the distribution of protein between different organs may not have been the same. The fatty rats, for example, probably contained more skin protein and thus less muscle protein than lean rats of

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Table 6. *Expts* 1 *and* 2. *Gross efficiencies of utilization of apparently digestible nitrogen and metabolizable energy* (ME) *and calculated total heat production by fatty and lean female Zucker rats offered to appetite diets containing* 40, 100, 150, 300, 500 *or* 700 *g casein/kg* (40*C*, 100*C*, 150*C*, 300*C*, 500*C and* 700*C respectively) from* 34 *to* 66 *d of age*

(Mean values for four rats/group)

Diet*	Phenotype	N retention / Intake of apparently digestible N	Energy retention / ME intake	Heat production† (MJ)
40C	Fatty	−0·011	0·343	3·65
100C		0·314	0·464	6·27
150C		0·234	0·508	6·45
300C		0·114	0·527	6·91
500C		0·085	0·456	7·50
700C		0·066	0·498	5·47
		Mean (diets 100C–700C)	0·491	6·52
100C	Fatty (pair-fed)‡	0·322	0·432	4·30
500C		0·082	0·400	5·26
	Mean		0·415	4·78
40C	Lean	−0·0123	0·087	4·47
100C		0·438	0·233	5·75
150C		0·398	0·243	5·97
300C		0·234	0·232	6·37
500C		0·122	0·228	6·60
700C		0·098	0·230	6·11
		Mean diets (100C–700C)	0·233	6·16

* For details, see Table 1.

† Total heat production = ME intake − energy retention.

‡ Given the same amount of food as that consumed the previous day by each of the lean rats fed on diets 100C and 500C from 35 to 67 d of age.

comparable age. An analysis of the nature and distribution of the major proteins of fatty and lean Zucker rats is now in progress.

A growing animal regulates its appetite to serve two objectives which are to some extent distinct from one another. First, the intrinsic capacity of the animal for growth determines nutrient requirement at any stage of maturity and thus the long-term strategy for appetite control. Secondly, the animal makes a series of decisions to start or stop eating which are in response to signals from the internal environment and are designed, in the short term, to maintain homoeostasis. To achieve maximum growth rate the animal must be able to reconcile these two demands.

Many studies on appetite control in the rat have indicated the way in which food intake is used to maintain homoeostasis with respect to specific substances in the internal environment such as blood glucose (Mayer, 1955), amino acids (Harper, Benevenga & Wohlhueter, 1970), and body temperature (Brobeck, 1948). The conclusions resulting from these studies are not mutually exclusive. Each simply provides an example of a single factor which can, in certain circumstances, assume prime importance in regulating appetite.

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Table 7. *Expt 2. Changes in body composition of fatty female Zucker rats pair-fed to the intakes of lean female Zucker rats given diets containing* 100 *or* 500 *g casein/kg* (100*C and* 500*C respectively*†) *from* 35 *to* 67 *d of age*

(Mean values with their standard errors for four rats/group)

	Wt increase (g)	Retention of: Protein (g)	Lipid (g)	Energy (MJ)
Fatty, pair-fed diet 100C	140 ± 9·6	11·9 ± 0·92	77·7 ± 12	3·24 ± 0·4
Difference (%) from lean rats	+49	−24	+118	+85
Statistical significance of difference (fatty *v.* lean)‡	**	*	**	**
Fatty, pair-fed diet 500C	162 ± 8·9	15·2 ± 0·44	84·1 ± 5·71	3·55 ± 0·25
Difference (%) from lean rats	+31	−33	+130	+82
Statistical significance of difference (fatty *v.* lean)‡	**	**	**	**

* $P < 0{\cdot}05$, ** $P < 0{\cdot}01$.
† For details, see Table 1.
‡ Determined by the analysis of variance.

In seeking an explanation for hyperphagia in the congenitally obese Zucker rat, there is no need to look outside these concepts of appetite control in relation to homoeostasis. The results of the present experiments indicate that when offered food *ad lib.* both fatty and lean rats had an identical, normal capacity for protein deposition which imposed the long-term strategy, the size of the demand for nutrients from the internal environment. Since as a result of an inborn error of metabolism the fatty rats used food less efficiently to promote protein deposition, they ate more to achieve the same short-term objective, the maintenance of homoeostasis in the face of these demands.

Rats of both phenotypes, given diets 300C, 500C and 700C, deposited protein at the same maximum rate. The lean rats ate the same amount of diets, 300C, 500C and 700C, but in the fatty rats both food intake and the rate of lipid deposition decreased with increasing dietary protein content from a peak at 300C.

The protein content of these diets imposed no limit on the capacity of either phenotype to deposit protein. Neither phenotype, however, ate more than just enough to satisfy its long-term requirement for protein deposition. Other factors which have been implicated in appetite control, such as the capacity of animals to store energy (Mayer, 1958), the mass of body fat (Kennedy, 1953), or even body-weight (Hoebel & Teitelbaum, 1966) were all of little or no importance, since all these decreased in proportion to decreasing food intake in the fatty rats as the protein content of the diet increased from 300 to 700 g/kg, whereas protein deposition remained constant.

The rate of protein deposition, while still the same for both phenotypes, decreased sharply with dietary casein contents less than 150 g/kg. It is well known that genetically normal rats given diets of low protein content eat less and grow more slowly than when protein content is optimum (e.g. McCance & Widdowson, 1974). Here again, therefore, the response of both Zucker phenotypes was normal. In these

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circumstances the rats were unable to reconcile the long-term strategy for maximum protein deposition with the immediate demands of homoeostasis.

It has been suggested that rats on low-protein diets reduce their food intake because they have a limited capacity to store a relative excess of energy as fat or to dissipate it as heat (Meyer, 1958). In these circumstances an increase in energy requirement induced by exercise or cold stress increases food intake (Meyer & Hargus, 1959). It is possible that both fatty and lean rats in our experiments restricted their food intake on low-protein diets because of a limited metabolic capacity to support the pattern of protein and lipid (by way of lipoprotein) deposition normal to each phenotype. Whether this was because they sensed an excess of some metabolites concerned with energy metabolism or because they sensed a deficiency or imbalance of amino acids, one cannot say. Perhaps both reasons are valid, because although these rats ate little, they spent much time searching through their food as if for specific nutrients.

In conditions of no protein growth, on the the 40C diet for example, or in absolute zinc deficiency (Chesters, 1975), the food intake of both phenotypes was about the same, which further supports the concept that hyperphagia in the fatty rat is a regulated response to the capacity of the animal for growth of protein.

We can make three major conclusions from this study. First, food intake is precisely regulated in the fatty (congenitally obese) Zucker rat. Thus, in this mutant strain, it is not true to claim, as the joint ARC/MRC Committee (1974) report does, that 'obesity follows from an uncontrolled dietary intake'. Since the single primary defect in the fatty Zucker rat is not a defect of appetite control, a study of the regulation of food intake using this strain is not just an academic pursuit of the cause of a rare genetic freak, but the study of normal appetite control in the face of unusual metabolic demands. For this reason it may be pertinent to certain cases of intractable obesity in man, particularly those of juvenile onset.

Secondly, the regulation of food intake during growth is intimately linked to the impetus for protein deposition whether the protein content of the diet be adequate or not and whether the animals be congenitally predisposed to leanness or to obesity.

Thirdly, during growth, the rate of retention of energy and its storage in lipid are of little or no importance in the regulation of food intake.

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