Effects of dietary fat and energy on body weight and composition after gonadectomy in cats

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Objective—To evaluate the effect of dietary fat and energy density on body weight gain, body composition, and total energy expenditure (TEE) in neutered and sexually intact cats.

Animals—12 male and 12 female cats

Procedure—Male cats were castrated (castrated male [CM]) or underwent no surgical procedure (sexually intact male [IM]). Female cats underwent ovariectomy (spayed female [SF]) or laparotomy and ligation of both uterine tubes without ovary removal (sexually intact female [IF]). Cats were fed either the low-fat (LF) or high-fat (HF) diet for 26 weeks, with the final allocation consisting of 8 groups: IF-LF, IF-HF, SF-LF, SF-HF, IM-LF, IM-HF, CM-LF, and CM-HF. Mean food intake for each group was recorded daily, and body weight was monitored weekly throughout the study. Body composition and TEE were measured before surgery in week 0 and at the end of the study (week 26) by isotope dilution (double-labelled water).

Results—Neutered cats gained significantly more body fat and body weight (53.80 ± 5.79%) than sexually intact cats (27.11 ± 5.79%) during the study. Body weight gain of neutered cats fed the HF diet was greater than those fed the LF diet. Following correction for body composition, TEE was similar in all groups and no pattern towards increased food intake was evident.

Conclusions and Clinical Relevance—Weight gain in neutered cats was decreased by feeding an LF, low energy-dense diet. To prevent weight gain in cats after neutering, a suitable LF diet should be fed in carefully controlled meals rather than ad libitum. (*Am J Vet Res* 2004;65:1708–1713)

Similar to other species, obesity is the most common nutritional problem in cats. The prevalence of obesity in cats has increased from < 10% in 1973[1] to 17% to 52% in recent studies.[2-8] This represents a major health risk, with obese cats at risk for hepatic lipidosis[9] and 3.9 times more likely to develop diabetes mellitus, 4.9 times more likely to develop lameness, and 2.3 times more likely to suffer from nonallergic skin disease[10] than cats that are not obese.

The cause of the increase in obesity in cats is unclear, although several risk factors have been identified, including middle age (3 to 9 years[2] or 4 to 6 years[4]), inactivity and confinement indoors,[2,3,7] certain types of premium or prescribed diets,[3] and unrestricted access to food.[5,11] Results of several studies[2,5,7,12] indicate that neutering is a risk factor for obesity in cats, with neutered cats 3.4 times more likely to become obese than sexually intact cats.[3]

The mechanism by which neutering causes obesity has been investigated, and gonadectomy appears to induce changes in metabolic rate and feeding pattern. Results of 1 study[13] indicate that resting metabolic rate was 28% higher in sexually intact male cats and 33% higher in sexually intact female cats, compared with neutered cats, whereas the metabolic rate after food was withheld was lower in female (but not male) cats after neutering.[14] Food intake in male cats is reportedly 26% higher and food intake in female cats is 17% higher 3 months after neutering, compared with food intake before neutering,[14] whereas neutered female cats consistently eat most or all of the food offered to them[15] and neutered cats of both sexes substantially increase their food intake when fed ad libitum.[16] This increased energy intake, combined with reduced energy expenditure due to a reduction in metabolic rate, may be the cause of obesity after neutering.

The energy requirements of neutered cats are therefore substantially less than sexually intact cats.[15,17] Results of a long-term study[11] of 60 female cats during the 12 months before and 12 months after ovariohysterectomy indicate that cats that were offered carefully controlled portions of food (40 to 45 kcal of **metabolizable energy (ME)**/kg/d) gained only 7.5% of body weight after neutering (with no change in body composition), compared with 3.6% in the previous 12 months.[11] In that study, cats that were fed ad libitum gained approximately 31% of body weight after neutering.

Results of those studies[11,13] indicate that weight gain in neutered cats is not inevitable and may be controlled by restriction of dietary energy. The purpose of the study reported here was to evaluate the effect of dietary fat and energy density on body weight gain, body composition, and **total energy expenditure (TEE)** in neutered and sexually intact cats.

Material and Methods

Cats—Twenty-four (12 male and 12 female) sexually intact European shorthair cats were used in the study. Cats were sourced from an inbred specific pathogen free colony at 6 to 7 months of age. Cats were permitted to adapt to their new environment and a commercially available, nutritionally complete dry cat food[a] for approximately 1 month. Cats were housed in large indoor pens and maintained on a 12-hour light-dark cycle, with room temperature maintained between 20° to 24°C.

At the end of the adaptation period when the mean ± SE age of cats was 9.1 ± 0.5 months, all cats received glycopy-

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rrolate[b] (0.01 mg, SC), and 15 minutes later, cats were anesthetized with tiletamine (10 mg/kg, IV) and zolazepam[c] (10 mg/kg, IV). Six male and 6 female cats were neutered, whereas the remaining cats underwent control procedures. Male cats were castrated (**castrated male [CM]**) or underwent no surgical procedure (sexually **intact male [IM]**). Female cats underwent ovariectomy (**spayed female [SF]**) or laparotomy and ligation of both uterine tubes without ovary removal (sexually **intact female [IF]**). Each group (CM, IM, SF, and IF) of cats was housed separately in large indoor pens (3 cats/pen) and maintained in the same environmental conditions as before surgery. After surgery, all cats were fed one of the experimental diets. All experimental protocols were approved by the Animal Use and Care Advisory Committee of the Nantes Veterinary School and adhered to European Union guidelines.

Diets—Two experimental dry diets were formulated by use of the same ingredients but differed in starch, fiber, and fat content (**Table 1**). The **low-fat (LF)** diet contained 109 g of fat and 14.4 MJ of ME/kg, whereas the **high-fat (HF)** diet contained 206 g of fat and 18.4 MJ of ME/kg. In week 13 of the study, metabolizable energy content was determined by measuring the digestibility of the diets in accordance with the American Association of Feed Control Officials and assuming an energy loss of 3.6 MJ/g of digestible crude protein.[18]

Study design—The study was performed for 26 weeks. Half of the cats were fed the LF diet, and half were fed the HF diet. The final allocation resulted in 8 study groups (n = 3) as follows: IF-LF, IF-HF, SF-LF, SF-HF, IM-LF, IM-HF, CM-LF, and CM-HF.

During the study, each group of 3 cats lived together and were fed together ad libitum with constant access to fresh drinking water, unless otherwise indicated. All food was renewed once daily, and food intake was calculated gravimetrically; the amount of food remaining uneaten was subtracted from the amount of food offered. Mean daily food intake for each group was therefore calculated as total intake for the pen divided by the number of cats in that pen (ie, 3).

Measurements—Body weight of all cats was recorded once weekly, and food intake of each group was recorded daily. Blood samples from each cat were obtained from a jugular vein on day 0 and at the end of week 26 for CBC; to determine concentrations of hemoglobin, urea, creatinine, glucose, total protein, albumin, sodium, potassium, and chloride in plasma; and to determine activities of alkaline phosphatase and alanine aminotransferase in plasma.

Isotope studies—Body composition and TEE were assessed before the surgical procedures were performed and at the end of week 26 by use of the dilution and elimination rate of double-labelled water isotopes.[19] On the day before these measurements were obtained, urine (cystocentesis) or blood (jugular venipuncture) samples were obtained for analysis of background concentration of isotopes.

Table 1—Composition of low-fat (LF) and high-fat (HF) diets fed to neutered and sexually intact male (IM) and female (IF) cats.

Nutrients	LF diet	HF diet
Dry matter (g/kg)	920	923
Crude protein (g/kg)	323	333
Ether extract (fat; g/kg))	109	206
Ash (g/kg)	52	55
Total dietary fiber (g/kg)	113	66
Nitrogen free extract (carbohydrate; g/kg)	403	340
Metabolizable energy (MJ/kg)	14.4	18.4

Diets were formulated in accordance with the American Association of Feed Control Officials recommendations[18] for growth and maintenance in cats.

On the day that measurements were obtained, each cat was individually housed in a metabolism cage and food and water were withheld for 2.5 hours, by which time the cat was assumed to have equilibrated its body water. The 2 isotopes,[d] deuterium oxide (D_2O; 99.9% deuterium-to-hydrogen ratio administered at a dose of 0.190 ± 0.003 g/kg, SC) and **water containing oxygen 18** (^{18}O; 10.5% ^{18}O:O administered at a dose of 0.177 ± 0.003 g/kg, SC), were given to cats separately (time = 0 hours). Blood samples from each cat were obtained from a jugluar vein 2.5 hours after administration of the isotopes (time = 2.5 hours), after which cats were permitted to eat and drink and returned to their groups.

Urine or blood samples were collected 8 and 15 days after administration of isotopes for isotope dilution analysis. On the morning of those days, each cat was individually housed in a metabolism cage for 3 hours for urine collection. Blood samples were obtained from a jugular vein in cats that had not urinated after 3 hours. Blood samples were immediately centrifuged, and plasma and urine were stored at –20°C prior to analysis.

Measurement of isotopes in plasma or urine was performed by use of **isotope ratio mass spectrometry**[e] **(IRMS)**. Oxygen 18 enrichment in biologic fluids was measured by use of in vitro ^{18}O equilibration with **carbon dioxide (CO_2)**, as previously described.[20] Deuterium (^2H) enrichment in biologic fluids was measured following reduction to hydrogen gas on zinc at 550°C.[21]

Total energy expenditure (TEE) was determined by use of the Weir formula[22] as described previously, assuming that the respiratory quotient was identical to the food quotient, which was estimated from food composition and measured digestibility coefficients.[23] **Carbon dioxide production rate (rCO_2)** was calculated from the difference of ^{18}O elimination rate (loss in water and CO_2) and deuterium elimination rate (loss in water) and corrected with factors, taking into account the isotopic fractionation occurring inside the body or between the body and the outside environment. A single homogenous water pool (equivalent to N_o) was assumed.[24] The isotope elimination rate was determined by use of logarithms (K_d for deuterium and K_o for ^{18}O), following transposition of linear regressions of enrichments (atom percent excess). Isotope pools (N_d for deuterium and N_o for ^{18}O) were calculated from the injected doses and enrichments of biologic fluids 2.5 hours after injection of isotopes, assuming the extrapolated values from linear regressions of isotopic enrichment at time zero were similar to the plateau enrichment measured 2.5 hours after injection of isotopes. Body composition was determined as described previously[23]; total body water and **fat-free mass (FFM**; in kg) were calculated from ^{18}O enrichment at time zero and 2.5 hours after injection of isotopes.

Statistical analyses—Statistical comparisons were performed by use of ANOVA; values of $P < 0.05$ were considered significant. Multifactor ANOVA (with diet, sex, and neuter status as factors and absolute and relative changes in body weight, FFM, body fat, and TEE corrected for body weight, metabolic body weight [$BW^{0.75}$], and FFM as variables) was used to identify significant effects and interactions. Although the sample sizes were small (n = 3), a 1-way ANOVA was used to identify differences between the groups after post hoc examination by use of the Student Newman Keuls test. Computer software[f] was used for all statistical comparisons.

Results

There were significant differences in week 0 values for body weight and FFM among groups; therefore, rel-

ative percentage change, calculated as ($Value_{week\ 26}$ – $Value_{week\ 0}$ /$Value_{week\ 0}$) × 100, during the course of the study was analyzed. Body weight increased in all groups during the 26-week study (**Figures 1 and 2**), and this increase was significantly greater in neutered cats (53.8 ± 5.1%) than sexually intact cats (27.1 ± 5.9%). There was no significant effect of diet or sex on body weight. There was no significant difference in relative percentage change in body weight among the 8 groups of cats during the study, although within a group, relative percentage change in body weight was numerically greater in all cats fed the HF diet, compared with cats fed the LF diet (**Table 2**).

Similar to the observed increase in body weight, FFM (kg) increased numerically in all groups during the study. There was no significant effect of diet or sex on body composition, and there was no significant difference in the relative percentage change of FFM among the 8 groups.

Similar to body weight, fat mass (kg) increased numerically in all groups during the study, and this increase was significantly greater in neutered cats (168.4 ± 28.2%) than in sexually intact cats (83.9 ± 23.6%) and cats fed the HF diet (176.0 ± 31.8%), compared with the LF diet (76.3 ± 14.7%). There was no significant effect of sex on body composition; however, neutered males fed the HF diet (CM-HF) had a significantly higher increase in fat mass than all other males and females fed the LF diet (IF-LF and SF-LF), but not females fed the HF diet (IF-HF and SF-HF). This increase in body fat in the CM-HF group was similar to that seen in all females fed the HF diet.

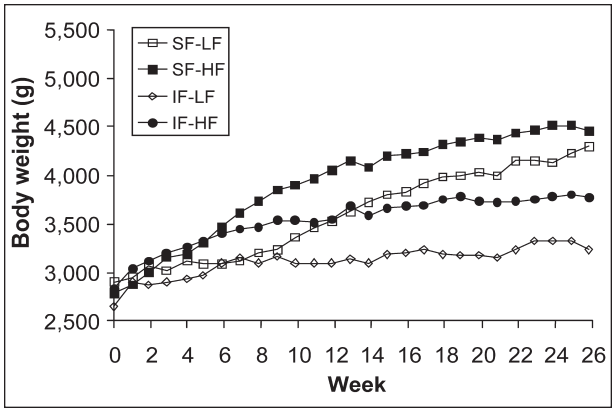

Figure 1—Mean body weight (g) in sexually intact (IF) or spayed female (SF) cats fed a low-fat (LF) or high-fat (HF) diet for 26 weeks. Standard error bars have been omitted for clarity (the mean of the standard errors was 10% of the mean).

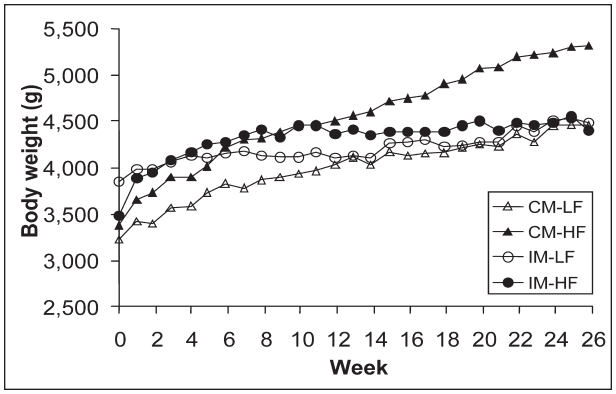

Figure 2—Mean body weight (g) in sexually intact (IM) or castrated male (CM) cats fed an LF or HF diet for 26 weeks. Standard error bars have been omitted for clarity (however, the mean of the standard errors was 5% of the mean).

Table 2—Mean ± SD relative percentage change in body weight (BW), fat-free mass (FFM; kg/cat), and body fat (kg/cat) in IM and IF cats, and neutered male (castrated, CM) and female (spayed, SF) cats fed an LF or HF diet for 26 weeks.

Group	Relative change in BW (%)	Relative change in FFM (%)	Relative change in body fat (%)
IF-HF	36.29 ± 22.72	11.14 ± 11.95	156.86 ± 84.51[a,b]
IF-LF	25.03 ± 9.60	14.34 ± 6.96	65.82 ± 24.82[a]
SF-HF	69.13 ± 11.27	37.09 ± 9.30	178.66 ± 27.53[a,b]
SF-LF	46.70 ± 5.98	32.10 ±3.02	94.63 ± 13.81[a]
IM-HF	28.14 ± 1.02	16.48 ± 2.51	76.31 ± 10.09[a]
IM-LF	18.96 ± 8.52	14.94 ± 5.61	36.55 ± 21.24[a]
CM-HF	55.40 ± 8.58	16.51 ± 6.48	292.23 ± 47.85[b]
CM-LF	43.91 ± 12.41	28.39 ± 13.02	108.06 ± 44.83[a]

[a,b]Within a column, values with different superscript letters are significantly ($P < 0.05$) different.
Relative percentage change was calculated as ($Value_{week\ 26}$ – $Value_{week\ 0}$/ $Value_{week\ 0}$) × 100.

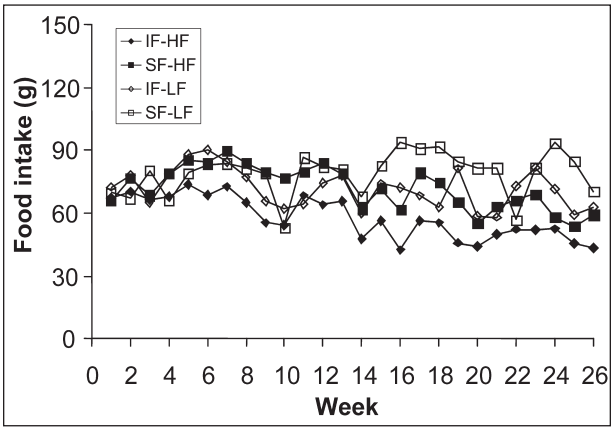

Figure 3—Mean food intake in IF or SF cats fed an LF or HF diet for 26 weeks. Standard error bars have been omitted for clarity (standard error of daily food intake ranged from 1 to 11 g with a mean value of 6 g).

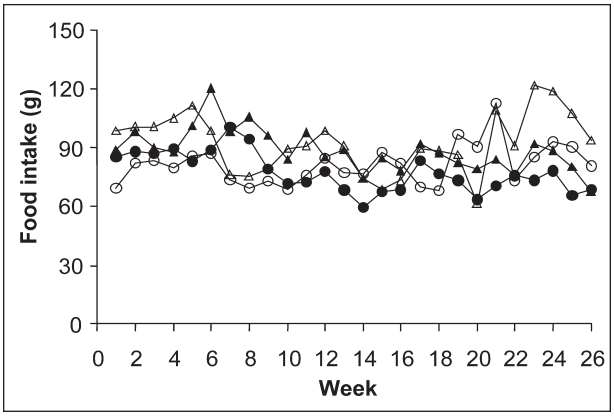

Figure 4—Mean food intake in IM or CM cats fed an LF or HF diet for 26 weeks. Standard error bars have been omitted for clarity (standard error of daily intake ranged from 3 to 10 g with a mean value of 6 g). *See* Figure 2 for key.

Table 3—Mean ± SD total energy expenditure (TEE) corrected for BW, metabolic body weight ($BW^{0.75}$), and FFM in sexually IM and IF cats and neutered male (CM) and female (SF) cats fed an LF or HF diet measured at the beginning (week 0) and end (week 26) of the study.

	Week 0			Week 26		
Group	TEE corrected for BW (kJ/kg of BW/d)	TEE corrected for $BW^{0.75}$ (kJ/kg of $BW^{0.75}$/d)	TEE corrected for FFM (kJ/kg of FFM/d)	TEE corrected for BW (kJ/kg of BW/d)	TEE corrected for $BW^{0.75}$ (kJ/kg of $BW^{0.75}$/d)	TEE corrected for FFM (kJ/kg of FFM/d)
IF-HF	221 ± 15	288 ± 17	271 ± 13	213 ± 8	298 ± 5	316 ± 10
IF-LF	263 ± 53	339 ± 67	336 ± 68	261 ± 12	339 ± 8	346 ± 8
SF-HF	242 ± 7	312 ±16	316 ± 13	211 ± 21	310 ± 24	340 ± 26
SF-LF	288 ± 22	380 ± 30	378 ± 33	231 ± 5	321 ± 3	321 ± 5
IM-HF	205 ± 18	284 ± 25	259 ± 25	242 ± 13	358 ± 20	336 ± 12
IM-LF	229 ± 10	323 ± 12	287 ± 10	254 ± 20	358 ± 28	314 ± 21
CM-HF	248 ± 40	338 ± 49	292 ± 45	222 ± 9	341 ± 10	351 ± 19
CM-LF	171 ± 17	232 ± 17	221 ± 28	236 ± 20	338 ± 28	325 ± 12

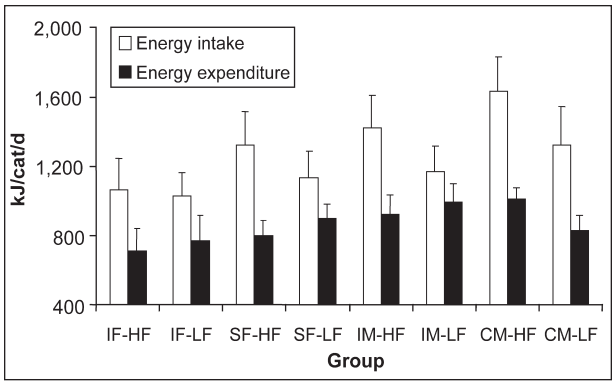

Figure 5—Comparison of mean ± SD daily energy intake and total energy expenditure in IM and IF cats and CM and SF cats fed an LF or HF diet for 26 weeks. Daily energy intake was calculated as the mean value for each group for 26 weeks. Total energy expenditure was calculated as the mean of the values for week 0 and week 26 for each group.

Mean daily food intake of all groups varied during the course of the study, which precluded meaningful statistical analyses (**Figures 3 and 4**). In absolute terms, TEE (kJ/d/cat) increased in all groups during the study. There was a significant interaction between diet and sex; therefore, although both male and female neutered cats fed the HF diet had similar increases in TEE, male cats fed the LF diet had a higher increase in TEE than female cats fed the LF diet. This interaction was not detected in sexually intact cats. There were few differences among the 8 groups, although neutered male cats fed the LF diet (CM-LF) had a significantly higher relative percentage increase in absolute TEE, compared with most other groups.

These differences in TEE may have been caused by changes in body composition because there was no significant effect of diet, sex, or neuter status even after correction of TEE for body weight, metabolic body weight, or FFM and there were no differences among the 8 groups (**Table 3**). Interestingly, at week 26, the TEE decreased in SF-LF cats after correcting for metabolic body weight or FFM, compared with all other groups. Although not directly comparable because of methods of data collection, a comparison of mean daily energy intake and expenditure indicated that intake was greater than expenditure in all cats, particularly in neutered cats fed the HF diet (**Figure 5**).

For all cats, results of CBC; concentrations of hemoglobin, urea, creatinine, glucose, total protein, albumin, sodium, potassium, and chloride in plasma; and activities of alkaline phosphatase and alanine aminotransferase in plasma were within reference intervals at weeks 0 and 26.

Discussion

All cats gained weight during the 26-week study. Because cats were immature (9 months of age) at the beginning of the study, part of this weight gain was attributed to growth. In addition, cats were fed ad libitum during the study, which is a feeding practice that has been identified as a risk factor for obesity.[5] Additionally, cats were inactive, which also predisposes cats to weight gain.[2,3,7]

With only 24 cats and 8 treatment groups, the sample size in each group was small; therefore, the power of the statistical tests was limited. Another limitation of the study was that mean daily food intake for groups of cats rather than individual cats, was measured and recorded.

Similar to results of other studies,[11,14,25] neutered cats gained more body weight during the study than sexually intact cats and this weight gain was comprised mostly of fat mass. Relative percentage change in body weight gain was numerically greater in female than male cats and this finding is supported by results of 1 study[14] but is not supported by results of other studies.[3,26] Differences among studies may be a reflection of differences in methodology, animals sampled, and geographic location.

Weight gain was lowest in neutered cats fed the LF diet, compared with those fed the HF diet, indicating that feeding an LF, low energy-dense diet may be a practical way to prevent obesity in neutered cats. Obesity develops when energy intake is greater than energy expenditure; therefore, an LF diet has been promoted as a means to reduce overall energy intake in humans.[27,28] Controversy exists as to the influence of dietary fat on the prevalence of obesity and the efficacy of an LF diet in reducing obesity[29,30]; however, this may be an issue that is specific to humans. Other species are not influenced by the same social or lifestyle-bound factors, and it may be argued that when an LF diet is the only available food, this dietary approach is likely to be successful in controlling body weight. Consequently, consumption of HF diets results

in a higher risk for obesity.[3] Thus, LF, low energy-dense diets are commercially available and are recommended for treatment and prevention of obesity in companion animals.[31] However, providing an LF diet alone may not be sufficient to completely prevent weight gain in neutered cats. This is evident from the increased body weight in neutered cats in the study reported here and is supported by results of a study[32] indicating that ad libitum access to an LF or HF diet results in similar overall energy intakes. Results of other studies[5,11] indicate that feeding regimen is likely to be important, suggesting that optimal body weight control in cats susceptible to obesity would be achieved by a combination of an LF diet and carefully controlled rations.[33]

There was no effect of either sex or food on TEE, especially when it was corrected for FFM. At the end of our study, values were more homogenous than they were at the beginning, which may have been caused by a constant expenditure per kilogram of FFM and a stabilization of activity levels because of the limited area that was available and because cats were no longer immature. All groups except for 1 had a higher TEE after correction for FFM at the end than at the beginning of the study. At the beginning of the study, cats were growing and it was likely that their energy intake was greater than their energy requirements, compared with later in the study when growth was complete. Excessive energy intake results in an increase in diet-induced thermogenesis and therefore in TEE. In 1 group of cats, TEE corrected for FFM was higher at the beginning than at the end of the study. Numerically, this group had the highest TEE during the initial evaluation, and we believe that this reflected differences in the level of activity, which had probably not stabilized yet. In the study reported here, neutering had little effect on TEE of either sex, even though the sample size was small and individual responses varied. This finding is supported by results of 1 study,[34] which indicated that neutering had no effect on metabolic rate in cats, but is not supported by results of other studies.[12-15] Hence, although results of 1 study[13] indicate that the resting metabolic rate (measured by indirect calorimetry) of both neutered female and male cats decreased, results of another study[14] of metabolic rate (indirect calorimetry) after food was withheld only found a neutering-induced change in females and results of 1 study of energy expenditure (by use of double-labelled water) only found differences in male cats.[26] Results of other studies report that there was neither a change in activity levels[15,35] nor decreased roaming[36] with neutering. Reasons for these differences are not clear and may reflect differences in methodology, including activity levels of cats, in various studies.[13,15] In addition, changes in metabolic rate should be considered separately from voluntary energy expenditure such as exercise; cats in the present study had little opportunity to increase their activity levels.

The primary cause of body weight gain after neutering may be increased food intake, which has been reported in other studies[14,15,25,34] and is supported by results of studies in rodents, in which castration or ovariectomy caused hyperphagia that was reversed by administration of testosterone[37] or estradiol.[38] In the study reported here, food intake of cats varied. There was no pattern towards increased intake in neutered cats, although there appeared to be a larger discrepancy between energy intake and expenditure in neutered cats, compared with sexually intact cats of the same sex eating the same diet. However, the effect of diet was clearly indicated; increases in body weight and body fat were greatest in cats fed the HF diet, compared with cats fed the LF diet. The HF diet was higher in energy content, and although increased weight gain in cats fed this diet was likely a consequence of ingestion of extra energy, this was not confirmed by results of the present study. The macronutrient profile, especially the carbohydrate content, of the 2 diets was also different, and an effect of this difference in diet composition cannot be ruled out. Furthermore, compared with the HF diet, the LF diet contained approximately twice the amount of dietary fiber and this may decrease digestion and absorption of nutrients from the LF diet. The amount of dietary fiber may also affect food palatability and therefore energy intake.

Gonadectomy removes estradiol or testosterone, which have multiple effects within the body, including stimulating physical activity and roaming behavior[39] and acting as satiety signals in the CNS.[37,38] Additionally, results of a study[17] in which the body weight of neutered cats was held constant indicate that neutering induces changes in serum concentrations of nonesterified fatty acids and circulating leptin. Results of other studies report changes in plasma insulin[25] and circulating leptin[25,26] after neutering, although weight gain itself can cause glucose intolerance, increased leptinemia,[26] and changes in the serum lipoprotein profile (triglycerides and α-lipoprotein concentrations increase and cholesterol and pre-β and β-lipoprotein concentrations decrease).[16] Therefore, the metabolic milieu of neutered cats is notably different from that of sexually intact cats and this may feasibly affect the partitioning, utilization, and storage of macronutrients, as detected in rodents.[40] Further studies investigating the influence of hormonal and metabolic changes on energy use in neutered cats are warranted.

[a]Kitten 34, Royal Canin, Cedex, France.
[b]Robinul-V (glycopyrrolate 20 mg/100 mL), Vétoquinol, Lure, France.
[c]Zoletil 100 (tiletamine 50 mg/mL and zolazepam 50 mg/mL), Virbac, Carros, France.
[d]Leman, Saint-Quentin-en-Yvelines, France.
[e]Optima, Micromass, Manchester, UK.
[f]SPSS 10.0.5, SPSS Inc, Chicago, Ill.

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