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Improved growth of lipoprotein lipase deficient kittens by feeding a low-fat, highly digestible diet☆

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Abstract

Adult domestic cats homozygous with a naturally occurring Gly412Arg LPL gene mutation are good models for the study of LPL deficiency. Previous studies report that homozygous LPL deficient kittens have reduced growth rates and develop subnormal body fat mass. It was hypothesized in the present study that homozygote kittens would have normal growth if provided a standard low fat, highly digestible diet at weaning and that their body fat would be increased by provision of a diet high in protein. When fed a nutritionally complete, 10% fat, purified or commercial extruded diet, the body weights of homozygous ($n = 24$), heterozygous ($n = 25$) and normal ($n = 16$) kittens were determined at birth, 2, 3, 4, 6, 12 and 18 weeks of age. Male homozygote kittens from homozygote dams had reduced weight gains ($p < 0.05$) compared to normal males at 2, 3 and 4 weeks. Female heterozygotes and homozygotes from homozygote and heterozygote dams had reduced weight gains ($p < 0.05$) compared to normal females at 2, 3, 4 and 6 weeks. By 6 weeks for males and 18 weeks for females, genotype related differences in weight gain were not observed. At 30 weeks, homozygotes and heterozygotes were given either a 60 or 30% (dry matter) protein diet for two months. As indicated by deuterium dilution estimation of body composition, cats eating the 30% protein diet ($n = 12$) tended to have a lower increase in lean body mass ($p = 0.057$) and a greater increase in fat mass ($p = 0.092$) compared to cats eating the 60% protein diet ($n = 12$). Increase in lean body mass among homozygotes tended to be not as great as that observed in heterozygotes ($p = 0.057$). Poor postweaning gains previously reported in homozygotes probably reflected inappropriate selection of diet for this genotype. The high protein diet increased the rate of lean body mass development but not body fat mass.

Keywords: Kitten; Lipoprotein lipase deficiency; Growth; Body fat

1. Introduction

Lipoprotein lipase is an important enzyme involved in the uptake of circulating triglyceride fatty acids into body cells. First identified as the "clearing factor" in plasma that reduced hypertriglyceridemia [1], lipoprotein lipase has been of increasing interest in the field of metabolic research. Present in many tissues, including adipose, heart, skeletal muscle, lung, and mammary gland, lipoprotein lipase is produced in the parenchymal cells and then secreted to the capillary endothelia [2]. The enzyme acts on circulating chylomicrons and very low density lipoproteins (VLDL) to hydrolyze triglycerides, allowing the resulting free fatty acids to enter cells. Cats used in this study were deficient in LPL activity as a result of a G to A transition at nucleotide 1234 in exon 8 of the LPL gene [3]. The nucleotide base change encodes a Gly412Arg substitution which effectively eliminates catalytic activity. Clinical signs, including lipemia retinalis, xathomas, and fasting hyperlipidemia [4], occur in homozygous cats that are fed diets containing more than 10% dietary fat.

Cats with the Gly412Arg LPL mutation potentially serve as unique animal models for study of LPL deficiency and LPL function. Homozygous LPL-deficient cats are viable, healthy, and reproduce, whereas LPL deficient mice die at weaning and humans with primary LPL deficiency are prone to develop a fatal pancreatitis. These attributes of cats with the Gly412Arg mutation are particularly favorable for development of gene therapy strategies that might be used

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for treatment of hyperlipidemias and LPL deficiencies. Although cats with the Gly412Arg LPL mutation are generally healthy, there are two impediments to efficiently producing such animals. One problem is poor reproductive performance in LPL deficient queens, another problem is poor growth of LPL deficient kittens [3].

Ginzinger et al. (1996) [3] reported diminished birth weights and growth rates in a colony of cats homozygous (*ll*) for the Gly412Arg mutation of the lipoprotein lipase (LPL) gene. Kittens in the Ginzinger et al. [3] study were born to *ll* females (queens) and *ll* males (toms). Diets used at weaning in their study may not have been optimal for all life stages and therefore may not have supported maximal growth (Hill's Prescription Diet®—Feline r/d® and Whiskas® with tuna). The canned diet used (Hill's Prescription Diet®) was high in fiber, approximately 30%; therefore digestibility and metabolizable energy intake may have been below requirements for maximal growth. The exact method of feeding and amount fed in this study was not clearly established in the publication. Earlier work by Jones et al. (1986) [5], using cats with the same mutation, reported no difference in growth rates between *ll* cats and cats with normal LPL activity (*LL*). Animals in this study were offspring of a *ll* tom and a queen heterozygous for the LPL deficiency (*Ll*). Together, observations of Ginzinger et al. [3] and Jones et al. [5] indicate LPL deficiency in the queen may influence the growth of their offspring. Kittens born to *Ll* queens, which have 31–70% of normal LPL activity [3,6], may be larger and have better growth performance than those born to *ll* queens, which have no measurable LPL activity.

The possibility that maternal LPL deficiency affects the outcome of kittens is supported by body composition findings. Adult *ll* cats have approximately half the fat body mass of cats with functional LPL, whereas the lean body mass of *ll* cats is not significantly different from normal [7]. The degree of leanness among *ll* cats varies with dam LPL genotype. In adulthood, *ll* cats born to *ll* dams have substantially less body fat than *ll* cats born to *Ll* dams. The mechanism underlying this maternal effect is unknown.

An objective of the present study was to determine if the growth rate and body fat mass of cats with the Gly412Arg LPL mutation could be improved by dietary modification. Because many diets that are commercially formulated for cats are high in fat, containing as much as 35% fat by weight on a dry matter basis, it was hypothesized that *ll* cats would have normal growth if provided at weaning a highly digestible, low fat diet. It was additionally hypothesized that provision of a diet high in protein would improve body weight gain in *ll* cats by promoting development of fat mass. Cats, unlike humans or rats, preferentially utilize acetate rather than glucose, lactate or pyruvate for lipogenesis in adipose tissue [8]. Because leucine is highly ketogenic and other dietary amino acids are partially ketogenic [9], it was hypothesized that a higher level of dietary protein would result in increased production of acetate available for the production of body fat in adipose tissue. A second objective of the present study was evaluation of the effect of maternal LPL deficiency on the growth of offspring by comparisons of body weight gain between *ll* kittens of *Ll* and *ll* queens.

Table 1
Diet compositions for experiment 1 and 2[1]

Ingredient	Weaning diet g/kg diet (DM)	60% protein diet g/kg diet (DM)	30% proein diet g/kg diet (DM)
Lactic casein[2]	200	300	150
Soybean protein[3]	200	300	150
Starch[4]	212.5	112.5	262.5
Sucrose[5]	212.5	112.5	262.5
Animal tallow[6]	80	80	80
Safflower oil[7]	20	20	20
Mineral mix[8]	50	50	50
Vitamin mix[8]	5	5	5
Choline chloride[9]	4.5	4.5	4.5
L-Methionine[10]	4	4	4
Taurine[11]	1.5	1.5	1.5
Sodium propionate[12]	10	10	10
DM sum	1000	1000	1000

[1] Composition of diets used in experiment 1 and 2, g/kg on a dry matter basis. All diets made with 50% water. Weaning diet fed during experiment 1 from weaning to seven months of age. 60% and 30% protein diets fed during experiment two from seven to nine months of age.
[2] Lactic casein, New Zealand Milk Products, Petaluma, CA.
[3] Soybean protein, Ardex F-dispersible, SPI Group, San Leandro, CA.
[4] Starch, Melojel, National Starch and Chemical, Bridgewater, NJ.
[5] Sucrose, Holly Sugar, Colorado Springs, CO.
[6] Animal tallow, Florin Tallow, Dixon, CA.
[7] Safflower oil, Saffola, Ventura Foods, City of Industry, CA.
[8] See [13].
[9] Choline chloride, International Mineral and Chemical, Terre Haute, IN.
[10] Methionine, Ajinomoto Inc., Tokyo, Japan.
[11] Taurine, Taisho Pharmaceutical, Torrance, CA.
[12] Sodium propionate, ICN Pharmaceutical Inc., Costa Mesa, CA.

2. Methods and materials

2.1. Animals

Specific pathogen free domestic short hair weanling kittens were obtained from and housed at the University of California, Davis Feline Nutrition and Pet Care Center. Sixteen *LL* kittens (nine males and seven females), fourteen *Ll* kittens born to *Ll* queens (five males and nine females), eleven *ll* kittens born to *Ll* queens (seven males and four females), and thirteen *ll* kittens born to *ll* queens (*ll* (*ll*)) (eight males and five females) were used. Only *ll* toms (male cats) were used in breeding of the *ll* and *Ll* queens. *Ll*, *ll* and *ll* (*ll*) animals were weaned to a low fat (10% of dry matter) purified diet, complete and balanced for growth according to NRC requirements [10] (Table 1). *LL* animals were weaned to a low fat (9% minimum) expanded dry commercial diet (Whiskas® Original Crave® Recipe). The label indicated that this diet was 34% crude protein, 9% fat, 4.5% fiber, 1% calcium, 0.8% phosphorus, 1.5% salt, 0.1%

taurine on a dry matter basis and met or exceeded the NRC requirements for all vitamins and minerals. All diets were presented for ad libitum consumption. Experimental procedures adhered to the *Guide for the Care and Use of Laboratory Animals* [11] and were approved by the Animal Use and Care Advisory Committee of the University of California at Davis.

2.2. Genotype

The LPL deficient cats were descendants of the colony of Jones et al. (1983) [5] and the colony described by Ginzinger et al. (1996) [3] in Vancouver, B.C. LPL genotypes of the cats were determined using a PCR-based screening protocol [3]. The *Ll* females that produced the *ll* and *Ll* kittens were the result of outbreeding a *ll* male with a *LL* female from the normal genetic strain in the Feline Nutrition and Pet Care Center. Therefore, the *ll* and *Ll* kittens of *Ll* queens had genes in common with kittens having normal LPL activity.

2.3. Experimental design

Experiment 1, Growth Rate Determination. All *Ll*, ll and *ll* (*ll*) kittens were suckled by queens for approximately the first four to six weeks of life then continuously offered a purified diet (Table 1) prior to weaning (six to eight weeks of age), until cats were seven months of age. The purified diet contained 40% protein (~35% crude protein [CP]) and safflower oil and animal tallow served as fat sources. The purified diet was chosen for its similarity in composition to low-fat, commercially prepared diets that meet the nutrient requirements for growth in normal kittens as demonstrated in American Association of Feed Control Officials (AAFCO) feeding trials. Use of a purified diet instead of a low-fat commercial product was chosen because ingredient composition would be precisely known and digestibility of ingredients would be high and therefore not of concern in interpretation of results.

Treatment of *LL* kittens followed the same protocol but they were fed the low-fat (9% minimum), "all stages" AAFCO-tested, dry commercial diet after weaning. Weekly body weights were taken for each cat to follow weight gain for seven months. Average birth weight and body weights at 2, 3, 4, 6, 12 and 18 weeks of age were determined.

Experiment 2, Body Composition Determination. After blocking for gender and genotype, 24 of the *Ll* and *ll* kittens studied in Experiment 1 were placed randomly into one of two diet groups for two months. Group one (n = 12) was fed a 60% (dry matter) protein (~53% CP) diet (Table 1). Group two (n = 12) was fed a 30% (dry matter) protein (~26% CP) diet (Table 1). Body composition analysis was conducted at the beginning and end of Experiment 2. Body fat and lean body masses were estimated by the deuterium oxide (D_2O) isotopic dilution method [12]. Food and water were withheld for 24 hr and jugular venous blood samples (~3 ml) were obtained from each cat before and two hours after deuterium oxide was injected intravenously (0.4 g D_2O/kg body weight). Serum was obtained from the whole blood samples. Water from the serum was collected by distillation and D_2O enrichment of the water determined by FTIR spectroscopy [13]. Group food intake was recorded daily.

2.4. Statistical analysis

The significance of the effect of genotype on birth weight and body weight at 2, 3, 4, 6, 12 and 18 weeks of age was determined for each sex with one-way analyses of variance. A 3 × 2 × 2 factorial analysis of variance was used to determine the significance of the effects of genotype, sex, and diet (respectively) on change in body lean mass, fat mass, and weight. Bonferroni and Fisher's Least Significant Difference Tests were used in means comparisons. A P-value of less than 0.05 was considered significantly different. A P-value of greater than 0.05 and less than 0.10 was considered a trend.

3. Results

3.1. Experiment 1

No significant differences were found among the birth weights of *ll* (*ll*) (103.1 g ± 4.5 g), *ll* (106.0 g ± 5.1 g), and *Ll* (106.8 g ± 5.9 g) males. However, the birth weight of the *LL* males (120.1 g ± 2.5 g) was significantly higher than *ll* (*ll*) males ($p = 0.043$). The weight gains for all male groups at 2, 3, 4 and 6 weeks of age are shown in Fig. 1. Weight gain in *ll* (*ll*) male kittens was significantly less than the weight gain in *LL* males at 2, 3 and 4 weeks of age ($p = 0.001$, $p = 0.004$, $p = 0.007$ respectively). Weight gain in *ll* (*ll*) males was also significantly less than *Ll* males at 2 weeks of age ($p = 0.020$). No significant differences in weight gains were observed among the male groups at 6, 12, and 18 weeks of age and thereafter until 7 months of age (Table 2).

No significant differences were found among the birth weights of *ll* (*ll*) (97.9 g ± 1.8 g), *ll* (99.2 g ± l.9 g), *Ll* (104.1 g ± 4.8 g), and *LL* (107.0 g ± 4.6 g) females. The weight gains for all female groups at 2, 3, 4 and 6 weeks of age are shown in Fig. 2. Weight gains in *LL* (*ll*), *ll* and *Ll* females were significantly less than *LL* females at 2, 3, 4 and 6 weeks of age ($p < 0.05$). By 18 weeks of age and thereafter, no significant differences in weight gains were observed among any of the female groups (Table 2).

3.2. Experiment 2

During the two-month trial, all kittens gained lean body mass (LBM) regardless of their dietary group. All kittens, except for two, gained in fat mass. Kittens eating the 30%

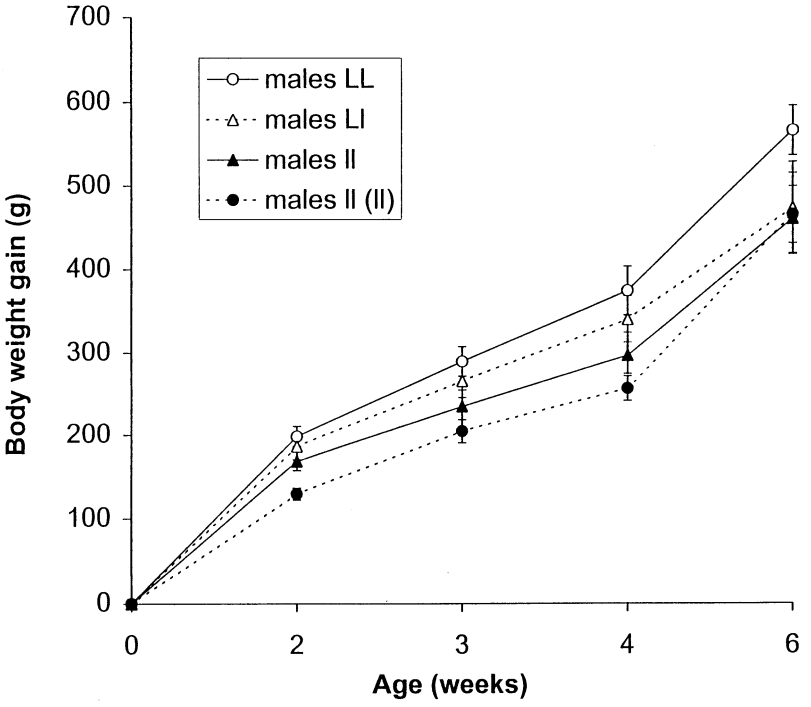

Fig. 1. Body weight gain from birth to 6 weeks of age of male kittens possessing wild-type (*L*) and mutated (*l*) LPL alleles. Plots represent mean ± SEM of body weights of kittens according to LPL genotype. Queens rearing the homozygous (*ll*) or heterozygous (*Ll*) kittens were fed a low fat (10% DM) purified diet. Queens rearing the normal kittens (*LL*) were fed a low fat (9% DM minimum) commercial dry-type (extruded) diet. Allelic symbols listed in parentheses indicate the LPL genotype of queens rearing homozygous kittens. Birth weights of kittens are listed in text reporting results of Experiment 1.

protein diet tended to have a greater increase in percent body fat ($p = 0.092$) compared to kittens eating the 60% protein diet (Fig. 3). Kittens eating the 60% protein diet tended to have a greater increase in LBM ($p = 0.057$) than kittens eating the 30% protein diet during the two-month period (Fig. 4). LPL genotype and gender did not affect increases in percent body fat. Kittens in the 60% protein group consumed an average of 112 g of diet/kitten/day (59 g CP/kitten/day) and kittens in the 30% protein group consumed an average of 129 g of diet/kitten/day (34 g CP/kitten/day). Kittens consuming the 60% protein diet consumed 13% less food during the two-month trial than kittens given the 30% protein diet, whereas kittens eating the 60% protein diet consumed 73% more protein than the 30% protein group.

Table 2
Body weights (mean ± sem) of LPL deficient male and female kittens at 6, 12 and 18 weeks of age

Males	6 week weight (g)	12 week weight (g)	18 week weight (g)
LL	565 ± 30	1334 ± 105	2331 ± 128
Ll	472 ± 55	1225 ± 66	2243 ± 115
ll	459 ± 41	1278 ± 58	2329 ± 66
ll (ll)	464 ± 34	1386 ± 34	2476 ± 88
Female			
LL	571 ± 26*	1062 ± 37	1960 ± 71
Ll	357 ± 30	1080 ± 55	1944 ± 57
ll	403 ± 54	1111 ± 48	1914 ± 60
ll (ll)	408 ± 33	1176 ± 60	1786 ± 122

* At 6 weeks of age body weights of Ll, ll, ll (ll) females were significantly lower ($p < 0.05$) than LL females. By 18 weeks of age, no significant differences in body weight were observed among males at 6, 12 and 18 weeks.

4. Discussion

Cats homozygous with the Gly412Arg mutation (*ll*) are reported to have reduced growth rates and low body fat mass. Although Ginzinger et al. [3], 1996, reported reduced birth weights and impaired growth in *ll* kittens, Jones et al. [5] reported no difference in growth rates between *ll* kittens and *LL* kittens. It is interesting to note here that the normal growth was reported in offspring from a mating between a *Ll* queen and a *ll* male [5], and that subnormal growth was reported in offspring from a mating between two *ll* animals [3]. Thus, maternal genotype may affect the rate of *ll* (*ll*) kitten growth. Indeed, prior to weaning, occurrence of the LPL deficiency in dams did affect the growth performance of *ll* (*ll*) male kittens. Low overall milk production [3] and low total milk fatty acid content [14] among *ll* queens could have contributed to poor growth of *ll* (*ll*) males. Why a similar effect was not observed in the female kittens is not clear. Female kittens didn't come from significantly larger litters than male kittens so litter size does not seem to explain why the growth of female kittens was below that of

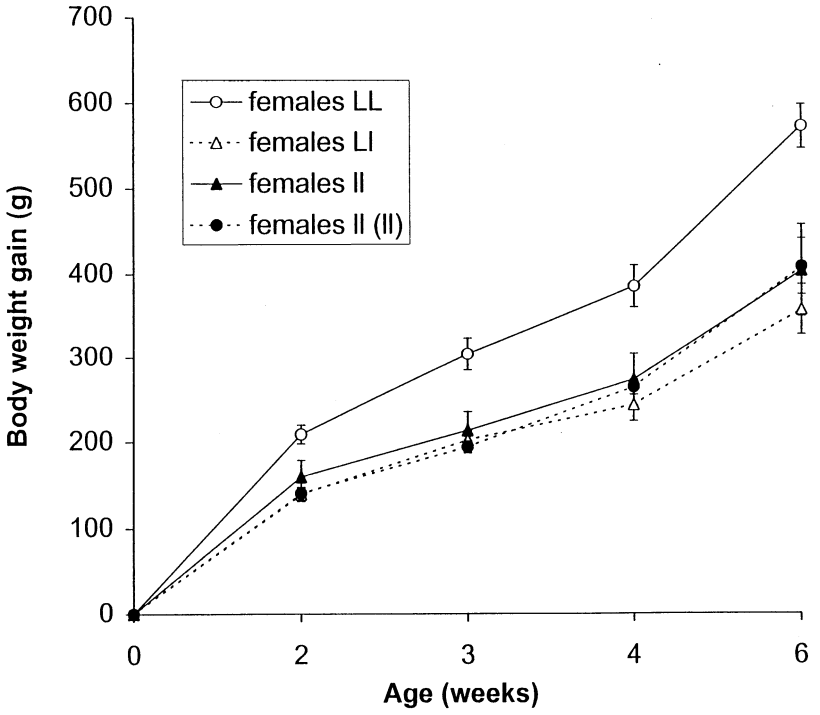

Fig. 2. Body weight gain from birth to 6 weeks of age of female kittens possessing wild-type (*L*) and mutated (*l*) LPL alleles. Plots represent mean ± SEM of body weights of kittens according to LPL genotype. Queens rearing the homozygous (*ll*) or heterozygous (*Ll*) kittens were fed a low fat (10% DM) purified diet. Queens rearing the normal kittens (*LL*) were fed a low fat (9% DM minimum) commercial dry-type (extruded) diet. Allelic symbols listed in parentheses indicate the LPL genotype of queens rearing homozygous kittens. Birth weights of kittens are listed in text reporting results of Experiment 1.

males. Perhaps another factor masked the dam effect in the females. Unlike male kittens, female kittens that possessed a mutated LPL allele, that is, *Ll, ll, ll* (*ll*) females, did not grow as well as normal females (*LL*) during the suckling period. Milk contains much more fat (~50% dry matter) [15] than the low fat purified diet that kittens received at weaning. Males may be more capable than females in processing circulating lipids in the face of a total or partial LPL deficiency. As cats appear to have 20–100% more hepatic lipase activity as humans [16], activity of hepatic lipase may contribute substantially to the clearance of circulating triglycerides in feline LPL deficiency. Hepatic lipase may also release fatty acids from triglyceride into general circulation where they may be used by tissues other than liver. Recently, hepatic lipase activity has been observed to vary with gender [6,17] and testosterone administration has been found to increase hepatic lipase activity in cases of testicular failure [18]. The apparent sex difference presently observed could reflect greater hepatic lipase activity in the male relative to the female kittens.

For both male and female kittens, deficient in lipoprotein lipase activity, weight gain was not reduced below that of normal kittens following weaning (Figs. 1 and 2). Apparently, utilization of the limited quantity of fat provided in the purified diet was not substantially impaired by LPL deficiency. Some other mechanism must permit clearance of plasma triglycerides enough to sustain normal growth. Evidence of increased uptake of lipoprotein remnants in the presence of LPL [19–23] provides a possible explanation for this phenomenon. It has been suggested that LPL functions in the mediation of a non-enzymatic interaction between lipoproteins and heparan sulfate proteoglygans (HSPG) [19,20] and LPL remains associated with lipoprotein remnants following hydrolysis *in vitro* [19]. Recognition of LPL by lipoprotein receptors occurs at both the VLDL receptor [19] and low density lipoprotein (LDL) receptor [20], leading to LPL mediated uptake of these lipoproteins. The importance of these lipase-receptor interactions *in vivo* has yet to be determined. Studies have concluded that lipid and lipoprotein uptake by cells was increased by LPL *in vitro* [22,23]. LPL functions as a link between lipoproteins and HSPG, which then facilitates the incorporation of the lipoproteins into fibroblasts and macrophages. Uptake occurs without the action of a lipoprotein receptor pathway and is said to be receptor independent. Other studies also concluded that LPL-mediated binding of lipoproteins to HSPG facilitated their incorporation into cells but the majority of this uptake occurred in LDL receptor positive cells (receptor dependent) [20,21]. In *ll* cats, LPL is functionally inactive at its active site for fatty acid hydrolysis on the capillary endothelia, but it may remain bound with the circulating lipoprotein forming a bond with HSPG. This bond may then facilitate the uptake of these particles at other body cells, either through receptor dependent or independent pathways. This mechanism plus the hepatic lipase activity may explain why *ll* cats are able to

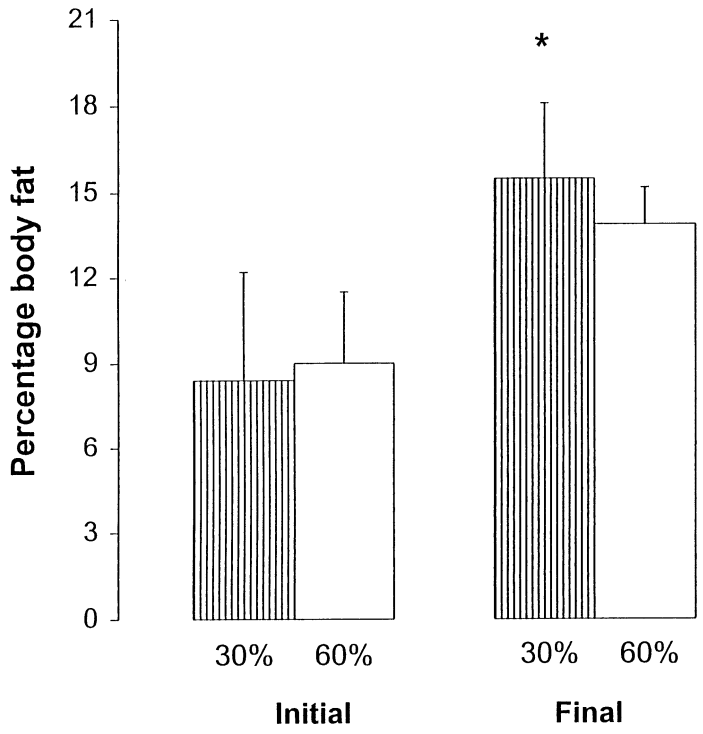

Fig. 3. Effect of dietary protein level on initial and final percent body fat in LPL deficient kittens (*Ll* and *ll*) from seven to nine months of age. LPL deficient kittens eating a 30% protein diet tended to have a higher increase in percent body fat compared to kittens eating a 60% protein diet, regardless of gender or genotype. *Probability result by ANOVA comparing each cats initial percent body fat with final percent body fat ($p = 0.092$).

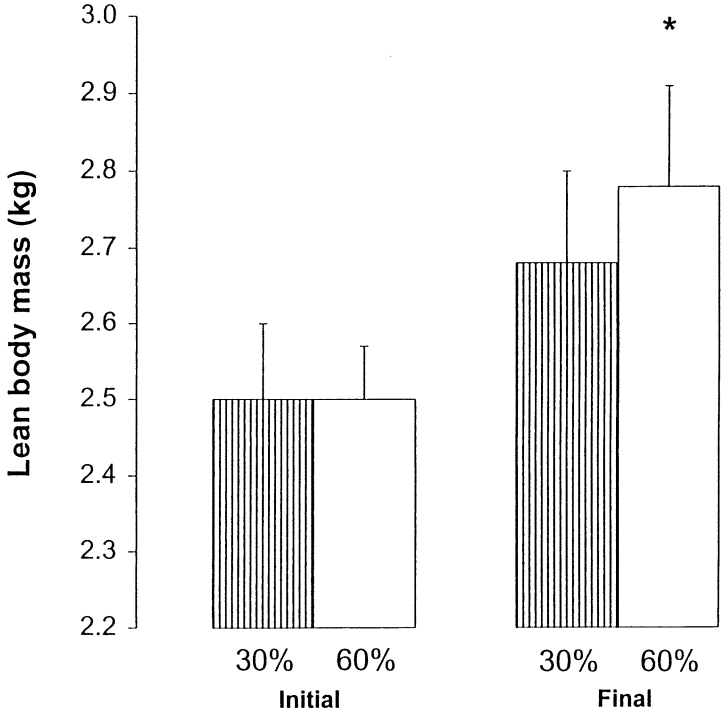

Fig. 4. Effect of dietary protein level on initial and final lean body mass in LPL deficient kittens (*Ll* and *ll*) from seven to nine months of age. LPL deficient kittens eating a 60% protein diet had a trend toward a higher increase in lean body mass compared to kittens eating a 30% protein diet, regardless of gender or genotype. *Probability result by ANOVA comparing each cats initial LBM with final LBM ($p = 0.057$).

absorb and incorporate enough dietary fatty acids to grow at a normal rate.

Relative to many other species, cats have a high dietary protein requirement for maintenance and growth. A high constitutive activity of nitrogen catabolic enzymes in the liver appear to be the cause of the high protein requirement [24]. The purified diet given to the kittens following weaning contained approximately 35% (w/w) crude protein, an amount in excess of the minimum recommended to support normal growth (24% w/w crude protein, NRC 1986). An elevation of dietary protein concentrations from 30 to 60%, did not significantly affect the gain in body weight observed during the seventh to ninth postnatal months. However, the partitioning of gain in body weight between lean and fat mass was affected. Relative to kittens given the high protein diet, a greater increase in fat mass was observed in kittens given the low protein diet. The cause for this result is uncertain. One possible explanation may be the high carbohydrate content of the low protein diet. In formulating the low protein diet, corn starch and sugar were substituted for protein. Insulin release stimulated by the high carbohydrate content (~53% w/w) may have promoted storage rather than oxidation of dietary fat. Because the effect was observed across LPL genotypes, the storage of fat would have to have occurred in the absence of LPL activity in *ll* cats, perhaps by a lipoprotein receptor mediated mechanism or simply by trapping circulating free fatty acids liberated by hepatic lipase activity.

Another possible explanation for the expansion of fat mass in kittens given the lower level of protein is stimulation of *de novo* synthesis of fat in adipose. Despite the report that acetate is used more readily than glucose for lipogenesis in cat adipose and liver tissue slices [6], the high carbohydrate content of the low protein diet might evoke an insulin response that drives fat deposition by providing optimal α-glycerolphoshpate for triacylglycerol synthesis from preformed fatty acids. The abundance of glucose may also provide for fat deposition by serving as substrate for fatty acid synthesis. Thus, the hypothesis that a high protein diet would favor expansion of body fat mass by stimulation of lipogenesis was disproven. Apparently degradation of an excess of dietary amino acids to acetate was not sufficient in adipose tissue to support an increase in lipogenesis. To the contrary, our results indicate that consumption of a high protein diet by cats favors development of lean rather than fat mass.

Whatever the dietary composition, the argument could be made teleologically that the cat, a strict carnivore that normally ingests little carbohydrate, might not be able to synthesize much fat. This would be a deviation from that observed in rats and mice, where as much as 50% of body fat may be acquired from *de novo* synthesis. Humans on a typical western diet do not appear to synthesize much fat; however, under unusual dietary conditions, such as the consumption of a 70% w/w carbohydrate diet, substantial lipogenesis is observed [25]. Adult humans that are LPL deficient have a normal body fat mass, and this fat has been suggested to come from lipogenesis [26]. Unlike humans, cats with LPL deficiency are observed to have a subnormal amount of body fat [7]. This observation would be consistent with cats having a limited capacity to synthesize fat.

The present work shows that a normal growth rate can be achieved in LPL deficient kittens after weaning. Previously reported poor growth rates were probably observed because of inappropriate selection of diet. For the production of LPL deficient kittens, commercially prepared diets with a fat concentration similar to the purified diet presently used (10% by dry matter weight) will probably provide sufficient nutrition for normal growth. Such commercial diets should be labeled as passing an AAFCO feeding trial for growth or "all life stages". The present findings indicate that body fat mass in of LPL deficient cats may be increased by high carbohydrate rather than high protein feeding. This observation may be of use in improving the reproductive performance of LPL deficient queens. Subnormal body fat mass is typically observed in LPL deficient queens, and a diminished fat store is known to reduce reproductive performance [7].

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