Feline Maternal Taurine Deficiency: Effect on Mother and Offspring[1]

JOHN A. STURMAN, ALICE D. GARGANO, JEFFREY M. MESSING AND HUMI IMAKI

Department of Developmental Biochemistry, New York State Office of Mental Retardation and Developmental Disabilities, Institute for Basic Research in Developmental Disabilities, 1050 Forest Hill Road, Staten Island, New York 10314

ABSTRACT Adult female cats were fed a defined purified diet (taurine-free) either alone or supplemented with 0.05% taurine for at least 6 mo prior to breeding. The reproductive performance by the taurine-depleted females was poor, whereas those receiving dietary taurine had normal pregnancies and deliveries. The taurine-depleted females suffered from severe retinal degeneration, including a large loss of photoreceptor outer segments, and degeneration of the tapetum lucidum, and greatly reduced concentrations of taurine in their body tissues and fluids. Surviving offspring from the taurine-depleted mothers exhibited a number of neurological abnormalities and substantially reduced concentrations of taurine in the body tissues and fluids. Except for greater concentrations of cystathionine in neural tissues, other free amino acids in tissues were unaffected. The specific activities of a number of enzymes involved in the biosynthesis of taurine were unchanged in liver and brain. The composition of maternal milk, total protein, protein amino acids and free amino acids was unchanged except for taurine content, suggesting that the abnormalities in the offspring resulted from the diminished dietary taurine. J. Nutr. *116*: 655–667, 1986.

INDEXING KEY WORDS cats • kittens • milk • nutritional taurine • retina • tapetum lucidum • taurine biosynthesis • taurine deficiency

The possible role of taurine in mammals has received much attention in recent years, especially as related to development (see refs. 1–3). Beginning with the observations that brain taurine concentrations in newborn mammals were several-fold greater than in mature mammals of the same species, and that the decrease occurred approximately by the time of weaning, it has been suggested that taurine may have a special role in development. Less attention has been paid to the function of taurine in prenatal development.

Dietary taurine, a constituent of the usual diets of most mammals, has been proven to be essential for cats, and possibly for primates, including humans (4–8). It has been clearly demonstrated that cats receiving little or no taurine in their diet become taurine-depleted and suffer structural degeneration of the retina and tapetum, with consequent adverse effects on visual function (4, 9–18). To date, all investigations of dietary taurine depletion in the cat have been performed with juvenile and adult animals. We have recently been examining the effect of dietary taurine depletion on feline pregnancy and outcome, and have reported that taurine-depleted queens exhibit increased reproductive wastage (19). They frequently resorb or abort their fetuses, and have stillborn or vital low-birth-weight kittens at term. Those kittens born live have a poor

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survival rate, and survivors grow at a substantially smaller rate than kittens from taurine-supplemented mothers. Such kittens also exhibit a variety of neurologic abnormalities, including abnormal hind limb development and a peculiar gait characterized by excessive abduction and paresis, and a grossly apparent thoracic kyphosis. We have also observed severe hydrocephalus in one aborted fetus and in one surviving kitten, and anencephaly in a newborn kitten. The concentration of taurine in the milk from taurine-deprived mothers is substantially lower than that in the milk from taurine-supplemented mothers, and the kittens suckling such mothers have a persistence of cerebellar external granule cell layer cells associated with a reduced cerebellar taurine concentration. We report here in detail the effect of feline maternal taurine deficiency on the taurine concentrations in maternal tissues and those of the offspring, on selected amino acids in tissues, on the protein content and amino acid composition of the milk, and on the activities of several enzymes involved in taurine biosynthesis.

MATERIALS AND METHODS

Four female domestic cats raised in the IBR colony and vaccinated against rhinotracheitis, panleukopenia, calici virus [FVR-C-P (MLV) Pitman-Moore, Washington Crossing, NJ] were fed a completely defined purified diet (taurine-free) (BioServ, Frenchtown, NJ) for at least 6 mo prior to mating. The synthetic diet contained (grams/100 g): casein (vitamin-free), 43.0; chicken fat, 20.0; dextrin, 13.5; sucrose, 13.5; salt mix (see below), 6.4; cellulose, 2.4; vitamin mix (see below), 0.6; L-cystine, 0.3; choline chloride, 0.3. The salt mix contained (in grams/kilogram): potassium phosphate dibasic, 328; calcium carbonate, 290; sodium chloride, 162; magnesium sulfate, 99; calcium phosphate dibasic, 73; magnesium oxide, 32; ferric citrate, 13; manganese sulfate, 1.22; zinc chloride, 0.91; cupric sulfate, 0.29; potassium iodide, 0.077; chromium acetate, 0.044; sodium fluoride, 0.023; sodium selenite, 0.0043. The vitamin mix contained (in grams/kilogram): dextrin, 857; inositol, 100; D,L-α-tocopheryl acetate (500 IU/g), 20; niacin amide, 8.0; calcium pantothenate, 5.0; retinyl acetate (500,000 IU/g), 5.0; riboflavin, 1.60; cholecalciferol (200,000 IU/g), 1.25; thiamin • HCl, 0.80; pyridoxine • HCl, 0.80; folic acid, 0.80; menadione, 0.10; biotin, 0.04; cyanocobalamin, 0.03.

These cats were severely taurine-depleted, plasma taurine concentrations less than 1 μmol/100 ml and with ophthalmoscopically confirmed retinal lesions. Six other females (controls) were fed the same diet supplemented with 0.05% taurine. All were bred as follows: when in estrus they were caged with a male for 1 wk; conception was defined as the middle of this period. Male cats were fed the taurine-supplemented diet, except for the interval of cohabitation with females receiving the taurine-free diet. Pregnancies were confirmed by X-ray 4–6 wk after conception. Fundus photographs were taken with a Kowa RC 2 fundus camera (WCO Ophthalmic Instrument Division, East Rutherford, NJ) using a neutral density filter to reduce the flash intensity.

The birth and semiweekly weights of all kittens were determined. Maternal samples of blood (weekly) and milk (semiweekly) were taken beginning within 48 h of birth.

Kittens were killed at the time of weaning, 8 wk after birth. Half of the brain and one eye were removed rapidly and immersed in cold 0.1 *M* Sorensen's phosphate buffer, pH 7.4, containing 4% glutaraldehyde. Tissues were postfixed with osmium tetroxide for electron microscopy. The remaining brain and eye (along with other body tissues) were dissected, homogenized in five volumes 10% trichloroacetic acid, and centrifuged at 20,000 × *g* for 30 min. The resultant clear supernatant fluid was used for measurement of taurine concentrations (Beckman 120C automatic amino acid analyzer, Beckman Instruments, Irvine, CA). Plasma and milk samples were deproteinized with five volumes of 3% sulfosalicylic acid and centrifuged at 20,000 × *g* for 30 min, and the clear supernatant fluid was retained for measurement of taurine concentrations (20).

The precipitates from the milk samples were retained, and the protein was purified and hydrolyzed as previously described (21). The resulting solutions, and the extracts from selected tissues, were analyzed for amino acids (Beckman 119 CL automatic amino acid analyzer, Beckman Instruments).

Portions of whole milk were retained for measurement of protein concentration by the method of Bradford (22).

Portions of cortex and liver were used for measurement of the activities of several enzymes involved in taurine biosynthesis. Cystathionine synthase was measured as described previously (23), except that the cystathionine formed was measured by using a Beckman 119 CL automatic amino acid analyzer. Cystathionase was measured as described previously (23). Cysteine dioxygenase was measured as described by Yamaguchi et al. (24) as modified by Misra and Olney (25). Cysteinesulfinic acid decarboxylase was measured by collecting the $^{14}CO_2$ produced from [1-^{14}C]cysteinesulfinic acid (obtained from Research Products International Corp., Elk Grove Village, IL) under conditions previously described (26). It has been conclusively demonstrated that cysteinesulfinic acid decarboxylase, which decarboxylates cysteinesulfinic acid but not glutamic acid, in brain is a different protein from glutamic acid decarboxylase (27), although the latter enzyme can utilize cysteinesulfinic acid as substrate. Decarboxylation of cysteinesulfinic acid by glutamic acid decarboxylase can be prevented by saturating this enzyme with unlabeled substrate that will not contribute to the labeled CO_2 produced. Liver does not possess any glutamic acid decarboxylase activity. Measurements of cysteinesulfinic acid decarboxylase activity in brain were, therefore, carried out in the presence of 100 mM unlabeled L-glutamic acid.

Four taurine-depleted adult females, who had each had at least four pregnancies, and four adult females consuming the taurine-supplemented diet, who had each had at least four pregnancies, were killed at least 2 wk after the last kittens were weaned. Tissues were dissected and processed exactly as described for the kittens.

RESULTS

Clinical description. The adult females consuming the taurine-free diet remained in apparently good condition for the duration of the study, which for some was as long as 3 yr. They consumed a similar amount of food to the adult females consuming the taurine-supplemented diet, showed no abnormal changes in weight, and came into estrus regularly. As previously described (19), they did suffer from greatly increased reproductive wastage. The weight gain during pregnancy of both groups was similar; about 30% by the end of full term. They did, however, suffer from severe retinal degeneration, which was easily visible ophthalmoscopically (fig. 1). These lesions, which are

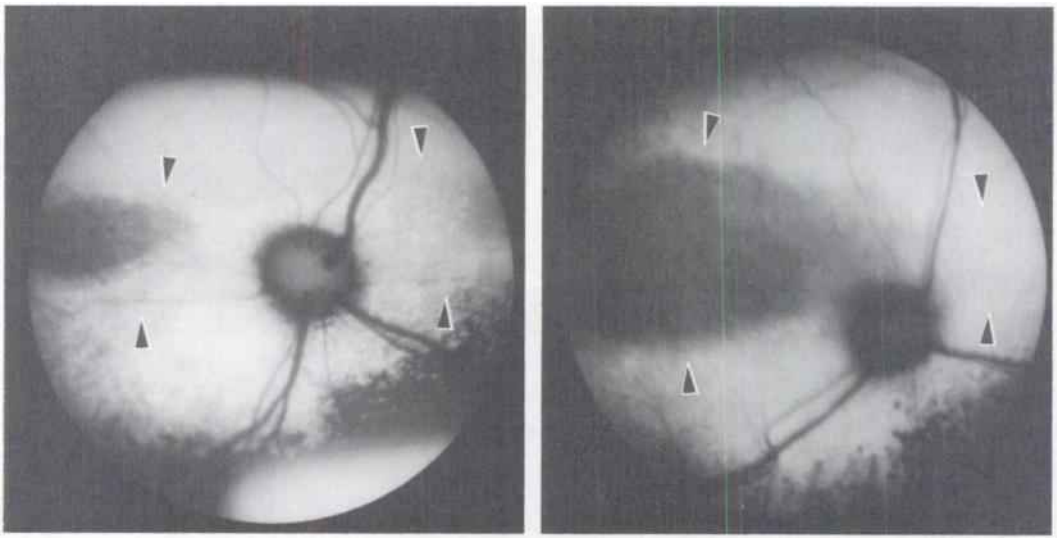

Fig. 1 Fundus photographs of eyes from two of the taurine-deprived queens reported in this study. Note that the hyperreflective lesions extend across the retina from the nasal side to the temporal side. The arrows indicate the margins of the lesions. These lesions are representative of those present in the taurine-depleted breeding females used in this study.

bilaterally symmetrical, were first visible about 6 mo after the initiation of the taurine-free diet (before breeding), and rapidly progressed to the wide band-shaped area reaching from the nasal to the temporal side of the retina on the superior margin of the optic disc. The taurine-depleted females showed a dramatic loss and damage of photoreceptor cell outer segments (fig. 2). These females also had a range of degenerative changes in the tapetum lucidum (fig. 3), many of which have not been observed in previous studies (17, 18), possibly because the duration of the taurine deficiency in this study was longer and the demands of pregnancy and nursing on body taurine pools are greater. In addition to the loss of the regular array of tapetal rods and the presence of electron-dense globules (fig. 3*B*), tapetal cells were seen in which tapetal rods, or pieces of tapetal rods, appeared to be in the process of aggregating (fig. 3*C*). Some cells also contained finger-print-like profiles of membranous debris (fig. 3*C*). Many tapetal cells were observed to contain groups of electron-dense globules of various sizes surrounded by a membrane (fig. 3*D*). This may represent a late stage of degeneration in which the disorganized tapetal rods are being phagocytosed prior to loss of the entire cell.

The data on number of pregnancies and their outcome are summarized in table 1. The clinical description of the kittens has been previously reported in detail (19). Out of 18 pregnancies in the taurine-supplemented queens, all but one came to full-term birth with live-born kittens. The exception was a premature birth, approximately 10 d prior to term, resulting in four live-born, low-birth-weight kittens, which died within 5 d. This was the first pregnancy in this cat and the subsequent pregnancies had a normal outcome. The mean birthweight of live kittens from taurine-depleted mothers was 75 g (mean birthweight of stillborn kittens was 40 g) compared with 107 g for kittens from taurine-supplemented mothers (19). By weaning at 8 wk after birth, mean weights of kittens reported in this study were 592 g and 888 g, respectively.

Taurine concentrations: adult females. The concentration of taurine in all tissues and fluids from adult females consuming the taurine-free diet was substantially smaller than in those consuming the taurine-supplemented diet (table 2). Tapetum and olfactory bulb resisted taurine depletion to the greatest extent, being about two-thirds of control values, followed by optic tract, optic nerve, adrenal and retina, which were about one-third of control. Most brain regions were about 20% of control, and the smallest values were observed in liver and plasma.

Taurine concentrations: kittens. The concentration of taurine in all tissues and fluids from kittens suckling the taurine-depleted mothers was considerably smaller than in those suckling the taurine-supplemented mothers (table 3). The tissues resisting depletion to the greatest extent were olfactory bulb, retina, adrenal, tapetum and optic nerve. Other tissues and fluids were 10–30% of control values.

Free amino acids in kitten tissues. Complete amino acid analyses were performed on the following tissues from 8-wk-old kittens from taurine-depleted and taurine-supplemented mothers (at least six in each group): retina, olfactory bulb, cerebellum, occipital cortex, liver and plasma. The following amino acids were quantified and compared statistically between groups: cystine, methionine, cystathionine, valine, isoleucine, GABA and arginine. Cystathionine concentrations in nervous tissues from taurine-depleted mothers were 40–80% higher than in the same tissues from taurine-supplemented mothers ($P < 0.05$ for retina, olfactory bulb and cerebellum). There were no other significant differences between the groups. The concentration of GABA in olfactory bulb of kittens from taurine-depleted mothers was 25% higher than in olfactory bulb of kittens from taurine-supplemented mothers, but the difference was not statistically significant ($P > 0.05$). Olfactory bulb of adult taurine-deprived cats has previously been reported to have a significantly greater concentration of GABA (28).

Milk: protein. The total protein content was measured in 136 samples from taurine-supplemented mothers and in 70 samples from taurine-depleted mothers, and analyzed statistically (table 4) (29). There was no difference between the groups. Both groups tended to increase slightly as lactation progressed although the slope of the line of best

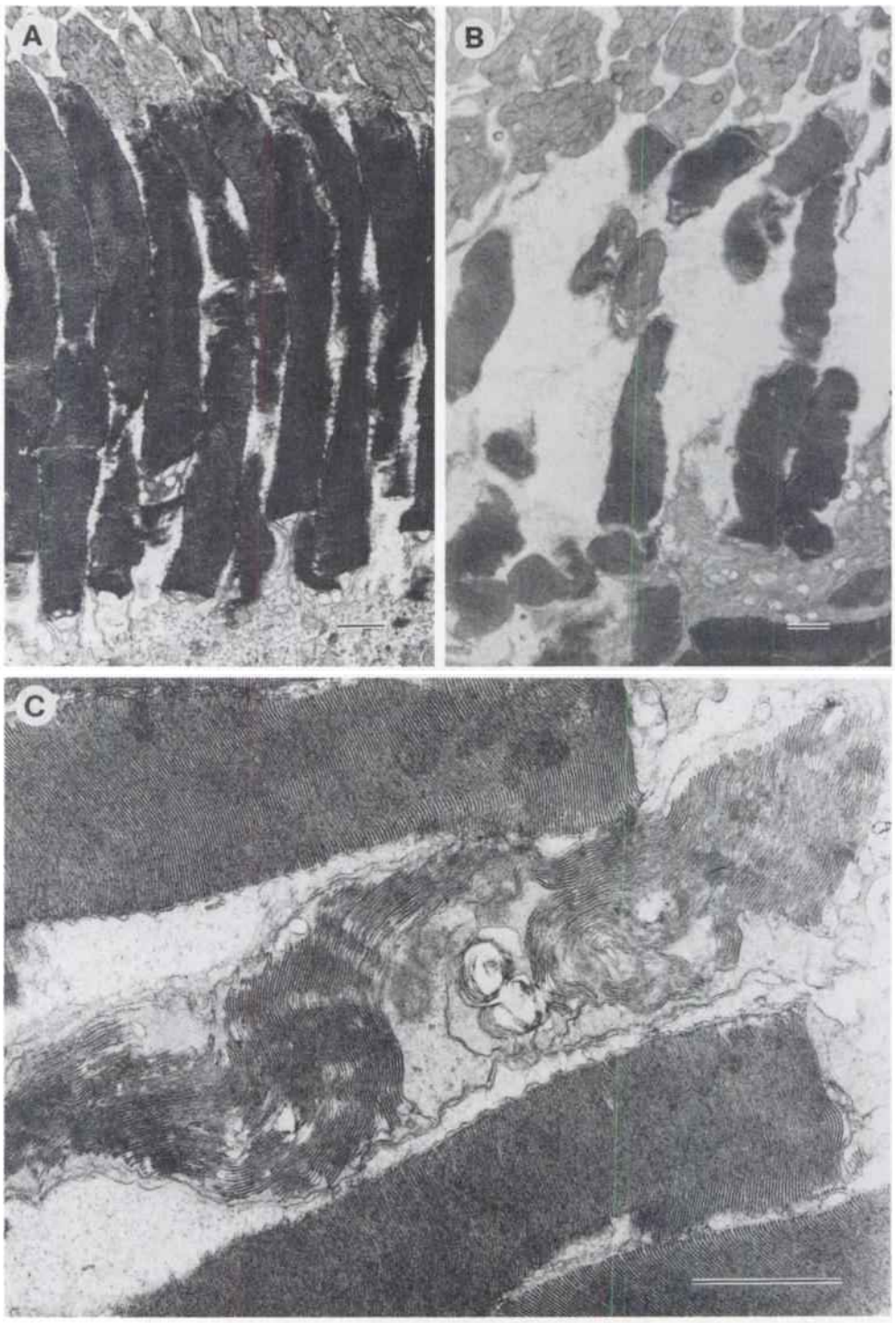

Fig. 2 Electron micrographs of retinal photoreceptor outer segments from adult female cats. 2*A* From cat fed taurine-supplemented diet. 2*B*, 2*C* From cats fed taurine-free formula. Note the large spaces between outer segments and disruption and disorganization of the disk membranes. Scale bars 1 μm.

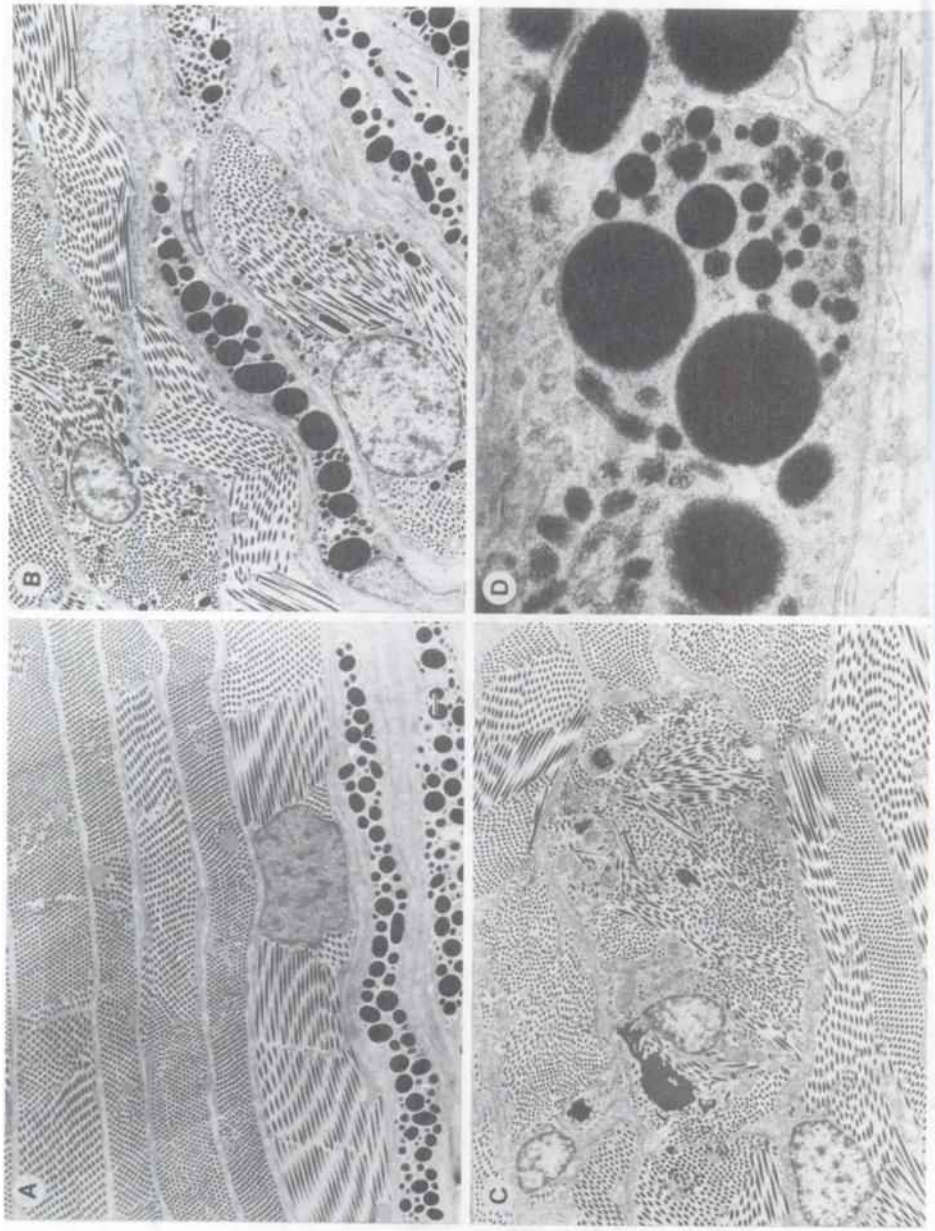

Fig. 3 Electron micrographs of cross-sections of tapetum lucidum from adult female cats. *3A* From cat fed taurine-supplemented diet. *3B*, *3C*, *3D* From cats fed taurine-free diet. Note the loss of the regular shape of the cells and nucleus, the presence of electron-dense globules and loss of the regular array of tapetal rods. There are regions containing membraneous debris and tapetal rods, which appear to be in the process of aggregating (*3C*), and groups of electron-dense globules surrounded by a membrane (*3D*). Scale bars 1 μm.

TABLE 1

Outcome of pregnancies

Parameter	Taurine-supplemented queens	Taurine-deficient queens
Pregnancies	18	18
To full term	17	6
Kittens		
Stillborn	0	6
Live-born	71	18
Survived to weaning	67	8

fit, and the correlation coefficients were small. An increase in milk protein concentration during lactation has previously been noted for the cat (30), the rat (31), and the dog (32). This pattern contrasts to that found for humans (33) and cows (34). When all of the samples in each group were compared directly, there was no difference in the mean protein content.

The milk protein was further analyzed by purification, hydrolysis and amino acid analysis of samples collected at 1 wk and 5 wk after birth (table 5). There were no significant differences in amino acid composition of milk protein from taurine-supplemented mothers and taurine-depleted mothers.

Milk: free amino acids. Apart from taurine, which is reduced in concentration in milk from mothers consuming the taurine-free diet to 10% of that in milk from mothers consuming the taurine-containing diet (19), there were no significant differences in concentrations of free amino acids between taurine-supplemented and taurine-depleted mothers. Taurine concentrations ranged from a mean of 17 μmol/100 ml at birth to 15 μmol/100 ml at weaning at 8 wk after birth for the taurine-depleted mothers compared with values of 288 μmol/100 ml at birth and 280 μmol/ml at weaning for the taurine-supplemented mothers (19). In general, the free amino acids were present in greater concentration at 5 wk after birth than at 1 wk after birth. The major free amino acids in cat milk are glycine, glutamic acid, alanine and serine (also phosphoethanolamine and urea). At 1 wk after birth, small amounts of valine, ornithine, glutamine, lysine, histidine and 3-methylhistidine were detected. At 5 wk after birth, these same amino acids plus cystine, methionine, isoleucine, leucine, tyrosine and phenylalanine were detected. When one makes reasonable assumptions as to the mean molecular weight of the milk proteins, the free amino acids comprised approximately 3% of the protein amino acids.

Enzymes. Cystathionine synthase. Activity of the cystathionine-synthesizing enzyme is high in liver and easily measurable in brain, and was not significantly different in the two groups of kittens (table 6).

Cystathionase. Activity of cystathionase in liver of kittens from taurine-deficient mothers was not significantly different from that of kittens from taurine-supplemented mothers (table 6). As is the case with liver from other mammals this activity is high and not rate-limiting in this metabolic pathway. Cystathionase activity in brain is too low to measure accurately by this method.

Cysteine dioxygenase. Both groups of kittens had easily measurable activity of this enzyme in liver and brain, although the values were not significantly different for the two groups (table 6).

Cysteinesulfinic acid decarboxylase. Decarboxylation of cysteinesulfinic acid by extracts of cat and kitten liver was unaffected by the presence of L-glutamic acid (fig. 4). This was true also for rat liver, which has a much greater activity (data not reported here). Extracts of brain, however, had greatly decreased ability to decarboxylate cysteinesulfinic acid in the presence of L-glutamic acid (fig. 4). The decarboxylation of cysteinesulfinic acid by glutamic acid decarboxylase was eliminated by the presence of 50–100 mM L-glutamic acid, and measurement of cysteinesulfinic acid decarboxylase activity in brain was routinely performed in the presence of 100 mM L-glutamic acid. Neither liver nor brain activity of cysteinesulfinic acid decarboxylase was different in the two groups, although both were low (table 6).

DISCUSSION

The nutritional importance of taurine has been considerably clarified in recent years, and it is generally accepted as an essential nutrient for cats and probably for primates, including humans. Taurine has been added to commercially available human infant

TABLE 2

Concentration of taurine in tissues and fluids of adult female cats fed a synthetic diet alone or supplemented with taurine[1,2]

Tissue	Taurine concentration: Synthetic diet + 0.05% taurine	Taurine concentration: Synthetic diet alone	Deficient–supplemented
	μmol/g wet weight		%
Retina	42.8 ± 4.6	15.0 ± 3.0	35.0
Tapetum	8.92 ± 1.83	5.55 ± 1.10	62.2
Lens	7.74 ± 1.28	1.73 ± 0.68	22.4
Liver	13.1 ± 2.2	0.48 ± 0.33	3.7
Kidney	6.77 ± 1.91	0.90 ± 0.14	13.3
Lung	8.18 ± 2.12	2.10 ± 0.64	25.7
Spleen	7.79 ± 2.24	1.20 ± 0.71	15.4
Adrenal	11.4 ± 3.2	4.30 ± 1.41	37.7
Heart	12.6 ± 3.1	1.40 ± 0.70	11.1
Gastrocnemius	8.66 ± 2.05	1.55 ± 0.77	17.9
Biceps	11.6 ± 3.5	1.43 ± 0.69	12.3
Triceps	9.16 ± 2.80	1.75 ± 1.07	19.1
Diaphragm	7.22 ± 1.95	0.60 ± 0.54	8.3
Plasma[3]	12.6 ± 1.2	0.56 ± 0.31	4.4
Urine[3]	22.5 ± 5.3	3.22 ± 2.44	14.3
Occipital lobe	2.32 ± 0.84	0.35 ± 0.13	15.1
Frontal lobe	1.89 ± 0.51	0.48 ± 0.22	25.4
Temporal lobe	2.14 ± 0.66	0.40 ± 0.08	18.7
Parietal lobe	2.40 ± 0.43	0.45 ± 0.13	18.8
Cerebellum	3.81 ± 0.79	0.65 ± 0.21	17.1
Superior colliculus	1.84 ± 0.62	0.38 ± 0.10	20.7
Inferior colliculus	1.71 ± 0.54	0.30 ± 0.08	17.5
Hippocampus	2.18 ± 0.71	0.55 ± 0.17	25.2
Corpus callosum	3.03 ± 0.70	0.58 ± 0.15	19.1
Thalamus	1.67 ± 0.31	0.40 ± 0.16	24.0
Pons	1.79 ± 0.47	0.33 ± 0.17	18.4
Medulla	1.87 ± 0.66	0.40 ± 0.14	21.4
Olfactory bulb	5.93 ± 1.33	3.80 ± 1.14	64.1
Lateral geniculate nucleus	2.91 ± 0.88	0.40 ± 0.22	13.7
Optic tract	3.07 ± 0.91	1.25 ± 0.59	40.7
Optic nerve	3.84 ± 1.08	1.55 ± 0.42	40.4
Spinal cord	1.33 ± 0.33	0.43 ± 0.22	32.3
Sciatic nerve	1.50 ± 0.41	0.23 ± 0.13	15.3

[1]Each value is the mean ± SD from four cats. The cats were fed the synthetic diet + 0.05% taurine for 24.0 ± 4.3 mo (mean ± SD) and the synthetic diet alone for 28.5 ± 3.4 mo. [2]All values are highly statistically significantly different between groups. [3]Micromoles/100 ml.

formulas in the U.S. since late 1984. The special importance of dietary taurine during development is only now emerging, and this and other reports have documented profound effects of a dietary deficiency of taurine during critical periods of development. The adult female cats consuming the taurine-free diet did not have any reduced food intake, did not suffer any weight loss and came into estrus regularly. Over the period of the study they all developed severe, bilaterally symmetrical, retinal degeneration, which was characterized ultrastructurally by a large loss of photoreceptor cell outer segments, and severe degeneration and disorganization of those remaining. The tapetum lucidum

TABLE 3

Concentration of taurine in tissues and fluids of 8-wk-old kittens from mothers fed a synthetic diet alone or supplemented with taurine[1,2]

Tissue	Taurine concentration: Synthetic diet + 0.05% taurine	Taurine concentration: Synthetic diet alone	Deficient–supplemented
	μmol/g wet weight		%
Retina	50.1 ± 8.0	21.2 ± 5.0	42.3
Tapetum	9.07 ± 2.15	3.42 ± 1.45	37.7
Lens	17.1 ± 4.4	4.96 ± 1.86	29.0
Liver	13.0 ± 4.0	1.89 ± 1.63	14.5
Kidney	6.14 ± 1.33	1.45 ± 0.46	23.6
Lung	9.57 ± 2.60	2.83 ± 1.55	29.6
Spleen	8.18 ± 1.96	1.27 ± 0.82	15.5
Adrenal	8.43 ± 1.27	3.19 ± 1.61	37.8
Heart	17.2 ± 6.7	3.37 ± 1.83	19.6
Gastrocnemius	9.06 ± 2.46	1.62 ± 0.87	17.9
Biceps	12.4 ± 3.9	1.20 ± 0.89	9.7
Triceps	10.5 ± 3.4	1.53 ± 0.69	14.6
Diaphragm	8.82 ± 2.61	1.19 ± 0.58	13.5
Plasma[3]	6.85 ± 2.32	1.01 ± 0.55	14.7
Urine[3]	31.4 ± 7.9	5.50 ± 3.79	17.5
Occipital lobe	5.33 ± 0.87	0.96 ± 0.28	18.0
Frontal lobe	4.85 ± 0.45	0.76 ± 0.41	15.7
Temporal lobe	5.54 ± 0.82	1.08 ± 0.42	19.5
Parietal lobe	4.99 ± 0.47	1.23 ± 0.63	24.6
Cerebellum	5.36 ± 1.00	1.48 ± 0.65	27.6
Superior colliculus	4.47 ± 1.20	0.68 ± 0.17	15.2
Inferior colliculus	3.44 ± 0.52	0.69 ± 0.23	20.1
Hippocampus	5.29 ± 0.93	0.89 ± 0.24	16.8
Corpus callosum	5.52 ± 0.78	0.98 ± 0.42	17.8
Thalamus	3.75 ± 1.08	0.63 ± 0.22	16.8
Pons	2.71 ± 0.76	0.61 ± 0.23	22.5
Medulla	2.67 ± 0.22	0.70 ± 0.31	26.2
Olfactory bulb	8.61 ± 1.14	4.11 ± 1.06	47.7
Lateral geniculate nucleus	4.97 ± 0.90	0.56 ± 0.10	11.3
Optic tract	4.23 ± 1.18	0.98 ± 0.26	23.2
Optic nerve	6.62 ± 1.02	2.47 ± 0.21	37.3
Spinal cord	2.34 ± 0.81	0.38 ± 0.11	16.2
Sciatic nerve	3.32 ± 0.58	0.65 ± 0.26	19.6

[1]Each value represents the mean ± SD from 6 to 12 kittens. [2]All values are highly statistically significantly different between groups. [3]Micromoles/100 ml.

of these cats showed severe degeneration and disorganization of the type previously reported (17, 18), and, in addition, showed some degenerative changes not previously reported, perhaps as a result of the extended period of taurine depletion and a more extreme depletion of taurine resulting from pregnancy and lactation. All female taurine-depleted cats experienced difficulty in completing full-term pregnancies, frequently suffering fetal resorption or abortion (19). Those pregnancies that reached term were often stillborn or liveborn of low birthweight with poor neonatal survival. No such reproductive difficulties were observed with females consuming this same diet supplemented with 0.05% taurine.

Surviving kittens from taurine-depleted mothers had a reduced growth rate and a number of neurological abnormalities (19).

TABLE 4

Total protein content of milk[1]

Measure and analysis	Synthetic diet + 0.05% taurine	Synthetic diet alone
Protein content, *mg/ml*	53.7 ± 14.4 (136)	56.1 ± 20.4 (70)
Slope of best line of fit	0.39	0.22
Correlation coefficient	0.44	0.17
Value at birth (0 d)	43.3	49.9
Value at weaning (8 wk)	64.8	61.6

[1]These data were obtained from the number of samples in parentheses by using a standard computer program for linear regression (29). These samples were evenly distributed between birth (0 d) and weaning (8 wk). The mean value of all samples is presented ± SD.

The central nervous system of these kittens has been shown to be abnormal in the following ways: there is a persistence of cells in the cerebellar external granule cell layer and numerous mitotic figures are evident (19); there are severe abnormalities in the visual cortex in which postmitotic elements have not matured and remain undifferentiated, and many have not migrated normally (35); there is clear ultrastructural degeneration and disorganization in the retina and tapetum lucidum, even though no ophthalmoscopically visible abnormalities are evident (36). Some of these abnormalities, at least, appear to be permanent. For example, in the visual cortex of such kittens there are very few pyramidal and nonpyramidal neurons, and those present have poor arborization with heavily spined dendritic processes, defects that are still present at 12 mo after birth, even after taurine supplementation postweaning.

The data presented in this manuscript suggest that biochemical changes are largely restricted to altered taurine concentrations. No changes in milk composition, other than taurine content, were noted (this, of course, does not preclude the possibility that changes may occur in milk components not measured in this study); no changes in other free amino acids in tissues, with the exception of greater cystathionine concentrations in neural tissue, were found; and no changes were found in the specific activities of several enzymes involved in taurine biosynthesis. This information is important, for it is known that the 10 amino acids that are essential for the growing rat (arginine, lysine, histidine, isoleucine, leucine, methionine, phenylalanine, threonine, tryptophan, valine) are also essential for the growing kitten, and that their

TABLE 5

Amino acid composition of milk protein[1]

Amino acid	Synthetic diet + 0.05% taurine		Synthetic diet alone	
	1 wk	5 wk	1 wk	5 wk
Aspartic acid	5.9 ± 2.0	5.8 ± 0.9	5.9 ± 1.2	6.8 ± 1.0
Threonine	4.5 ± 1.1	5.1 ± 0.8	4.8 ± 1.3	6.1 ± 1.4
Serine	4.2 ± 1.0	3.8 ± 0.6	4.0 ± 1.4	4.5 ± 1.5
Glutamic acid	18.0 ± 4.1	18.2 ± 2.2	18.9 ± 3.5	19.5 ± 2.8
Proline	9.6 ± 2.1	10.1 ± 1.3	10.8 ± 3.0	11.3 ± 1.3
Glycine	2.4 ± 0.6	1.6 ± 0.3	2.0 ± 0.5	2.0 ± 1.0
Alanine	5.8 ± 1.4	4.8 ± 0.8	5.6 ± 1.2	5.5 ± 0.3
Valine	8.6 ± 1.5	7.7 ± 1.2	7.6 ± 1.6	7.6 ± 2.0
Cystine	0.2 ± 0.0	0.2 ± 0.1	0.3 ± 0.1	0.3 ± 0.1
Methionine	2.0 ± 0.7	2.1 ± 0.3	2.3 ± 0.7	1.2 ± 0.7
Isoleucine	3.7 ± 1.5	4.1 ± 1.1	4.2 ± 1.2	4.1 ± 0.9
Leucine	12.4 ± 3.9	13.8 ± 1.7	11.8 ± 3.3	13.4 ± 1.9
Tyrosine	2.9 ± 1.0	3.6 ± 0.4	3.2 ± 0.9	3.6 ± 0.3
Phenylalanine	2.5 ± 0.8	2.6 ± 0.3	2.6 ± 0.7	2.8 ± 0.2
Lysine	6.9 ± 1.4	6.8 ± 1.1	5.6 ± 1.8	6.7 ± 1.4
Histidine	1.9 ± 0.7	2.2 ± 0.5	2.0 ± 0.6	2.5 ± 0.9
Arginine	4.8 ± 1.1	5.1 ± 1.0	4.5 ± 1.6	5.0 ± 0.6

[1]Each value represents the mean ± SD of five samples expressed as percent of total. Note that the values for aspartic acid and glutamic acid include original asparagine and glutamine residues, respectively.

TABLE 6

Activities of some enzymes in kitten liver and brain[1,2]

Enzyme and tissue	Synthetic diet + 0.05% taurine	Synthetic diet alone
	nmol product/(mg protein · h)	
Cystathionine synthase		
Liver	180 ± 19	189 ± 18
Brain	18.7 ± 6.3	25.8 ± 6.3
Cystathionase		
Liver	362 ± 47	268 ± 44
Cysteine dioxygenase		
Liver	123 ± 26	97 ± 22
Brain	336 ± 92	233 ± 32
Cysteinesulfinic acid decarboxylase		
Liver	11.8 ± 1.9	13.7 ± 3.1
Brain	81.0 ± 18.7	70.9 ± 9.7
Brain + 100 mM L-glutamic acid	11.1 ± 1.8	11.1 ± 1.9

[1]Each value represents the mean ± SD of determinations from 6 to 12 kittens. [2]There is no significant difference between the activities of enzymes from kittens suckling mothers fed the diet supplemented with taurine and those suckling mothers fed the taurine-free diet as determined by Student's *t*-test.

absence or a deficiency results in decreased food intake and reduced growth (37–45). Our results indicate that none of these amino acids is altered in the milk of taurine-depleted mothers suggesting that the abnormalities in the kittens are due primarily, if not entirely, to a dietary deficiency of taurine. They show further that such kittens do not show any capability for metabolic adaptation to this deficiency. Other studies indicate that dietary taurine has a direct effect on growth: kittens subjected to a postnatal dietary taurine deficiency have a reduced rate of growth, which is almost entirely corrected by daily taurine feeding (46); infant primates raised on a taurine-free diet have depressed growth compared to similar infants raised on the same diet supplemented with taurine (5). Finally, two female cats in our colony that had been consuming the taurine-free diet for approximately 3 yr and had each had at least six pregnancies, none of which resulted in live-born kittens, were switched to the same diet supplemented with 0.05% taurine. After 6 mo on this diet, the cats were returned to the usual breeding schedule, and, to date, each has produced two litters of live, apparently normal, kittens.

These results establish the importance of taurine in feline maternal nutrition and suggest that some concern is warranted for humans. It has been demonstrated that human infants raised on synthetic formulas containing little or no taurine become taurine depleted (47), and that human infants receiving long-term parenteral nutrition become taurine depleted and suffer retinal changes and visual dysfunction (7, 8, 48). This dietary dependence on taurine probably results from the low hepatic activity of cysteinesulfinic acid decarboxylase in humans, which is smaller even than that in the cat (49). Reports of an increased incidence of pediatric problems in children from strict vegetarian communities (which eat virtually no taurine) suggest that, although usually attributed to malnutrition and deficiencies of currently defined primary nutrients, a taurine deficiency effect cannot be excluded and should be examined in future studies (50, 51).

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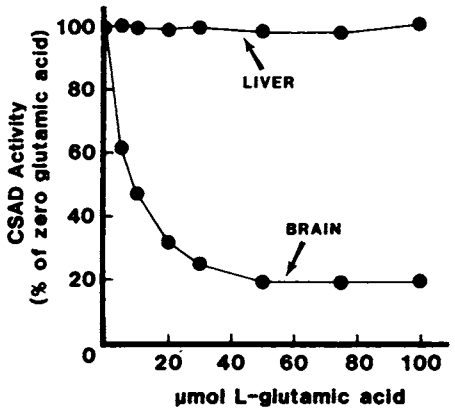

Fig. 4 Activity of cysteinesulfinic acid decarboxylase in kitten liver and brain (occipital cortex) in the presence of increasing amounts of L-glutamic acid. Each point represents the mean of four separate experiments with tissue from different kittens. Standard deviations of data from the separate experiments when expressed as percent were less than 5%.

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