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Retinal Degeneration Associated with Taurine Deficiency in the Cat

Abstract. *A degeneration of the retinal photoreceptor cells develops in cats when casein is the source of dietary protein. Amino acid profiles indicate that the degeneration is associated with a selective decrease in plasma and retinal taurine concentrations. A sulfur amino acid deficit in the casein diet combined with specific amino acid requirements of the cat appear related to this unique expression of taurine deficiency.*

Kittens or adult cats fed casein as the source of dietary protein develop a retinal degeneration within 3 months that is visible with the ophthalmoscope (*1*). The initial fundus change is a hyperreflective granular zone in the area centralis similar in appearance to that reported for feline central retinal degeneration (*2*). A gradual decrease in the amplitudes of the cone and rod components of the electroretinogram and a time delay in the electrical response of the cone have been demonstrated coincident with degeneration of the photoreceptor cells. Ultrastructurally, vesiculation, disorientation, and disintegration of the photoreceptor outer segments occur in the earliest stages in the area centralis (Fig. 1), and are followed by the subsequent degeneration of the entire photoreceptor population (*1*).

Casein appears to be related to the retinal degeneration, since the retinopathy can be prevented or reversed by substituting lactalbumin or egg albumin for the dietary casein (*1*). Since casein is low in sulfur amino acids and because the retinas of several mammalian species have been shown to contain high levels of taurine, an amino sulfonic acid, the concentration of free amino acids in plasma and retina were investigated to determine whether sulfur amino acids were affected in this specific photoreceptor degeneration.

Eleven kittens and seven adult domestic cats were fed a semipurified diet containing casein (16 to 27 percent of the calories as protein) or a commercial chow as previously described (*1*) for periods of 12 to 52 weeks, at which time plasma amino acids were analyzed (*3*). In a subsequent study eight kittens were fed a casein diet (27 percent of the calories as protein) for 4 to 24 weeks, when retinal samples were assayed for amino acid and DNA concentration (*3*).

In the first study all the cats fed the casein diets had evidence of retinal degeneration after 3 to 12 months (*1*). Their plasma amino acid profiles (Table 1) revealed an essential absence of plasma taurine, whereas the concentrations of the other amino acids, including methionine and cystine (taurine precursors), were comparable to control values. As in other species, taurine was the principal free amino acid in the normal cat retina, and the other measured amino acids were also within reported limits (*4*). The retinas of casein-fed kittens revealed a progressive and selective decrease in taurine content beginning with the initial assay at 4 weeks. This decrease in taurine preceded any change in DNA concentration, indicating that taurine depletion preceded cell death. After 24 weeks of the casein diet, retinal taurine was reduced by 80 percent, and a 13 percent decrease in total retinal DNA was observed (Table 2). The DNA decrease correlates with more advanced degeneration where progressive loss of the outer nuclear layer and outer plexiform layer predominates in the area centralis and extends into the peripheral retina (*1*).

Table 1. Plasma amino acid concentrations (in nanomoles per milliliter) in cats fed control (chow) or casein diets (nine animals per group) for three or more months. The results are expressed as the mean ± standard deviation.

Amino acid	Control	Test
Isoleucine	76± 27	60± 14
Leucine	137± 49	108± 34
Lysine	112± 26	119± 42
Methionine	75± 34	92± 35
Phenylalanine	106± 53	71± 9
Threonine	147± 52	113± 36
Valine	161± 55	172± 73
Alanine	472±173	495±171
Arginine	154± 64	118± 43
Asparagine	66± 26	51± 17
Aspartic acid	38± 13	42± 21
Half-cystine	23± 7	28± 9
Cysteic acid	34± 12	23± 11
Glutamic acid	186± 55	211± 84
Glutamine	484±298	468±279
Glycine	385±120	322± 93
Histidine	138± 34	161± 32
Proline	154± 62	194± 86
Serine	255± 84	216± 95
Taurine	54± 24	1± 0
Tyrosine	70± 21	66± 23

The decrease in plasma and retinal taurine is thought to be associated with the retinal degeneration, since this sulfur-containing amino acid is normally present in high concentrations in the retina as well as in muscle and brain (*4*), where it may function directly as a neurotransmitter or indirectly as a regulator of calcium flux influencing membrane potential and the excitability of nerves and muscles. It has also been shown that intravitreal injection of taurine in the chicken depressed the *b*-wave of the electroretinogram and that light stimulation caused the release of taurine in vitro (*5*).

The disappearance of plasma taurine in cats fed casein may have resulted from a combination of factors affecting sulfur amino acid metabolism in cats. Kittens rank among the fastest growing mammals and require approximately 29 percent of their calories from protein for maximum growth. This is also reflected by the high protein content of cat milk (*6*). Adult cats also have high protein requirements, and when protein (from fish and liver origin) comprised less than 21 percent of the diet on a dry weight basis, taurine disappeared from the urine. By contrast, urinary felinine, an isopentanol derivative of cysteine peculiar to feline species (*7*), continued to be excreted during this period of inadequate protein consumption (*8*), suggesting that the biosynthesis of felinine takes precedence over that of taurine when protein is limiting.

Casein is low in total sulfur amino acids, particularly cystine, the precursor for taurine synthesis via oxidation and decarboxylation reactions involving cysteine sulfinic acid, cysteic acid, and hypotaurine (*4*). Comparison of the amino acid composition of casein with the two proteins found to prevent the degeneration—lactalbumin and egg albumin—indicated that these proteins contained 168 and 181 percent more sulfur amino acids than casein.

The cat liver normally contains high levels of taurine, but in comparison to the rat or dog, cannot decarboxylate appreciable

amounts of cysteine sufinic acid to taurine (*9*). This lack of liver decarboxylation may place the cat at a disadvantage under these experimental conditions.

The casein diet also contained little sulfate. This form of sulfur may be required by cats for maximal growth as demonstrated in the chick (*10*). A diversion of cysteine sulfur to sulfate for mucopolysaccharide synthesis may have precluded adequate taurine biosynthesis, even though the plasma concentrations of methionine and cystine remained normal in the casein-fed cats. The ability to fix inorganic sulfur with L-serine to form taurine has been delineated as a possible pathway for taurine biosynthesis in chicks and rats (*11*). Whether this is an important pathway for taurine synthesis in the cat, as suggested by incorporation studies with $^{35}SO_4$ (*12*), remains to be confirmed.

The decrease in retinal taurine content may have resulted from reduced synthesis in the retina or reduced uptake of taurine from the plasma. Both processes may normally regulate retinal taurine concentration, and, in turn, depend on the levels of plasma taurine or precursor or both (*13*). These metabolic interrelationships as well as in situ taurine synthesis are still to be explored.

The obvious control experiment, supplementing the casein diet with taurine or other sulfur amino acids, is currently in progress. Preliminary data based on the funduscopic examination of the retina in growing kittens supplemented with either methionine, cysteine, or taurine suggest that development of the retinal lesion appears to be prevented by taurine, but not by methionine or cysteine (*14*). These observations must be corroborated by electroretinography and electron microscopy, and if substantiated would further suggest that the taurine synthetic pathway from sulfur amino acids may be inadequate or limited in growing kittens.

In any event, the data reported demonstrate that taurine deficiency in the retina is associated with photoreceptor cell degeneration and raises the question of photoreceptor dependence on sulfur amino acid metabolism. Utilization of this model should help delineate the biological role of taurine, which has long remained an enigma.

Table 2. Free amino acid (in nanomoles per milligram, dry weight) and DNA (in micrograms per milligram, dry weight) concentration in retinas of control and test cats after specified time of chow or dietary casein consumption. The results are expressed as the mean ± standard deviation.

Amino acid or DNA	Control	Test		
	8 to 52 weeks	4 to 7 weeks	10 to 14 weeks	24 weeks
Taurine	162±30	97±24	42± 8	25±12
Glutamic acid	22± 3	29± 6	32± 6	22± 2
Glutamine-serine	14± 3	18± 5	27±10	30±10
Aspartic acid	6± 2	6± 3	8± 2	9± 1
Glycine	7± 2	9± 3	9± 2	11± 2
DNA	96±10	91±10		82± 3
Number of animals	5	4	2	2
Number of samples	14	14	8	5

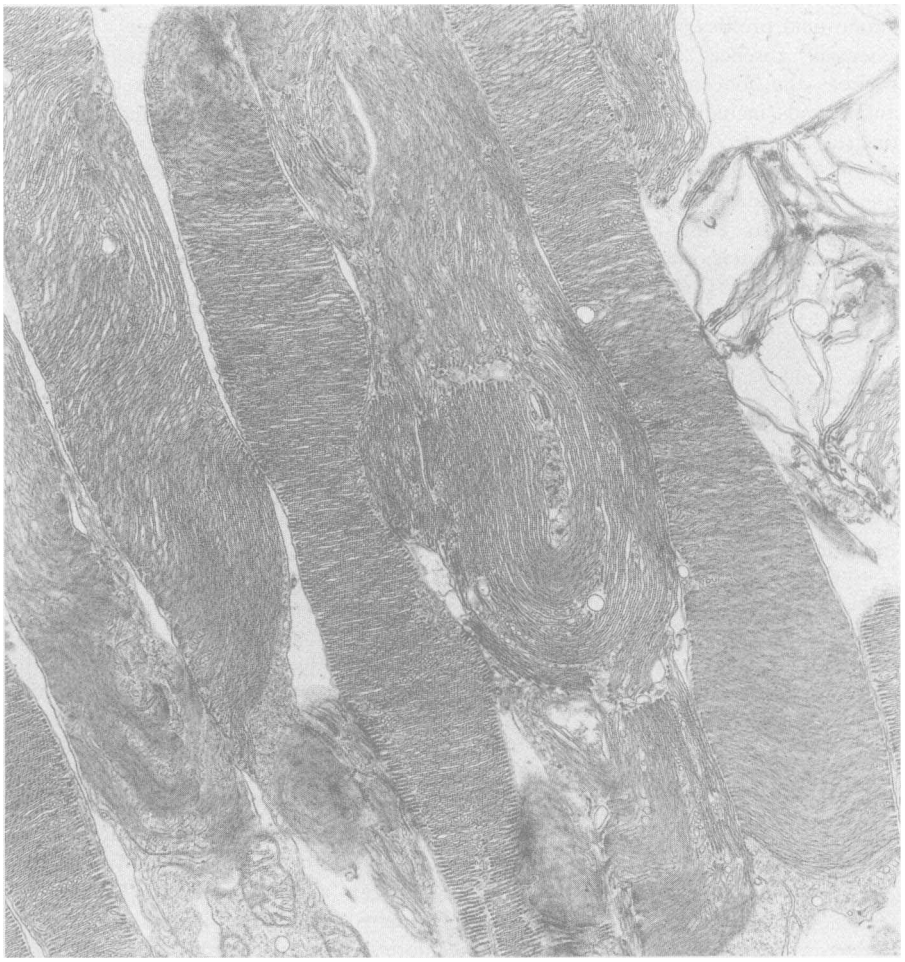

Fig. 1. Extensive disorientation and disintegration of photoreceptor outer segment lamellae from the retina of a cat. These changes are associated with taurine depletion of the plasma and retina in cats fed semipurified diets with casein as the dietary source of protein.

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Moving Visual Phantoms: A New Contour Completion Effect

Abstract. *Moving contours surrounding an empty region make phantoms appear to move through the empty region. The phantoms are contours, dimmer than the inducing contours but of the same pattern, color, speed, and direction of movement. The phantoms originate in the brain and may be related to completion effects most often seen with visual pathology.*

A localized region of blindness often goes unnoticed. Instead of looking like a hole in the visual field, the blind region (scotoma) takes on the appearance of surrounding intact areas of the field. These completion effects may hide the temporary scotomas that accompany migraines (*1*) or the permanent scotomas that result from small lesions of the visual cortex (*2*). Similar processes also render the blind spot (optic disk) in each eye unobtrusive (*3*). We have discovered an entirely new form of completion that operates over large areas in any normal field. This type of completion produces a dramatic change in the appearance of a large empty region surrounded by a field of moving contours: the empty region seems to be filled with phantom versions of the moving surround contours. We have studied this phantom motion under a variety of conditions and report some of the results here.

Standard electronic methods (*4*) were used to make a vertical sinusoidal grating drift across an oscilloscope screen. The spatial frequency of the grating was 0.75 cycle/deg, and it drifted horizontally at about 1 hertz. The grating had a space-average luminance of 60 cd/m^2 and a contrast of 0.25; viewing was in a dimly illuminated room. Observers saw only two sections of this grating, each 1° high, one at the top and one at the bottom of the screen. The sections were separated by several layers of black construction paper 3° high and extending across the entire width of the screen (the total density of black paper was $15D$, where D = density units). A small white fixation mark was painted on the center of the construction paper. Upon staring at the mark in the center of the gap, all observers immediately reported the appearance of a dim grating which seemed to drift across the blank gap in phase with the real pattern flanking the gap. This phantom grating would suddenly disappear when the real grating stopped moving. At this writing, every observer tested has seen the phantom grating (N = 20 observers, from three different laboratories in two countries).

The phantom looked as though a portion of the real grating was being viewed through a neutral density filter. To quantify this appearance, neutral density filters were placed over sections of the real grating to mimic the appearance of the phantoms. Filters between 1.7 and 2.0 density units gave a satisfactory match.

Spatial frequency is an important determinant of the phantom grating and the apparent spatial frequency of the phantoms covaried with that of the real, inducing grating. Under our viewing conditions, the phantoms became less distinct as spatial frequency increased by as little as fourfold (to 3 cycle/deg). Moreover, when the drifting, low-frequency (0.75 cycle/deg) grating had a square-wave luminance profile rather than a sinusoidal one, the phantoms took on a square-wave appearance but were reduced in vividness.

Finally, the angle between the opaque occluder and direction of grating drift is critical. In most of our observations the vertical gratings drifted either leftward or rightward; the occluded section extended across the screen horizontally. When we rotated the occluding material to vertical but kept direction of drift as before, the phantoms were not seen.

We wondered where in the visual system our phantoms originated. To get a rough answer, we arranged two pieces of Polaroid material on the cathode-ray tube. Oppositely oriented Polaroid analyzers produced a dichoptic display: the top section of inducing grating was seen by the right eye only, the bottom section by the left eye only. No phantom gratings were seen when the display was viewed monocularly, but when it was viewed dichoptically, phantoms of normal vividness were seen. This means that the phantom gratings can be produced by mechanisms in the visual system at or beyond the point where information from both eyes is combined (*5*).

Another observation is also consistent with a central origin for our effect. We compared the phantoms seen in two different viewing conditions: in the first condition, the motion of the grating's image across the retina was produced as before, with a stationary fixation located midway between two separate sections of moving grating; in the second condition, equivalent motion of the retinal image was produced by tracking a fixation point that moved across the empty region between two sections of a stationary grating. The fixation point in both conditions was produced on the face of an oscilloscope whose image was combined optically with that of the grating. The speed of the fixation point's movement in condition 2 precisely matched the drift rate of the grating in condition 1. Six observers were tested in both conditions and all reported that the phantoms were very much attenuated or were absent entirely (N = 4) in condition 2. Retinal image motion accompanying movement of the eyes is not sufficient to produce pronounced visual phantoms. This implies that the phantoms are generated somewhere in the nervous system central to the processing of information about the state of the extraocular muscles (*6*).

We wondered what might happen when top and bottom gratings moved in opposite directions. To test this, a Dove prism was set in front of the lower half of one of the observer's eyes and the other eye was occluded. Looking straight ahead, the observer saw the top grating section moving rightward and the bottom section moving leftward. Each section produced a phan-