Effect of diet on the rate of depletion of n–3 fatty acids in the retina of the guinea pig

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Abstract **This study has assessed the influence of maternal n–3 long chain polyunsaturated fatty acid supply and dietary manipulation after weaning on the retinal polyunsaturated fatty acid profile. Infant guinea pigs born of dams fed one of two commercial chow diets (differing in the amount of eicosapentaenoic, docosapentaenoic, and docosahexaenoic acids) were raised in two separate experiments, and subsequently partitioned into two diet groups, one supplied with a high level of alpha-linolenic acid (canola oil supplemented), the other with a very low level of alpha-linolenic acid (safflower oil supplemented). Guinea pigs born of dams supplied with the longer chain n–3 fatty acids in the commercial pellets (experiment 2) showed higher levels of retinal docosahexaenoic acid at weaning compared with those born to dams fed chow containing only alpha-linolenic acid (experiment 1). The rate of depletion of retinal docosahexaenoic acid after weaning onto the safflower oil diet was described by a two-stage exponential decay, possibly reflecting systemic and local conservation mechanisms, in conditions of dietary n–3 fatty acid deprivation. The rate of docosahexaenoic acid depletion in the group with the lower retinal docosahexaenoic acid at weaning was more than double the rate of depletion in the group with the higher weaning docosahexaenoic acid value. The endpoint retinal docosahexaenoic acid level at 16 weeks post-weaning after dietary n–3 fatty acid depletion on the safflower oil diet in the group, which started with the lower retinal docosahexaenoic acid level, was approximately half that compared with the group from the dams fed long chain n–3 fatty acids (experiment 1, 5% (interpolated), experiment 2, 9%). These results suggest that an adequately supplied mother is capable of providing an infant with enough n–3 fatty acids to withstand a longer period of dietary deprivation imposed after weaning.—**Weisinger, H. S., A. J. Vingrys, L. Abedin, and A. J. Sinclair. **Effect of diet on the rate of depletion of n–3 fatty acids in the retina of the guinea pig. *J. Lipid Res.* 1998.** 39: **1274–1279.**

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The mammalian brain is rich in lipid and contains high proportions of essential fatty acid derivatives such as docosahexaenoic acid (DHA) and arachidonic acid (1). Alteration of brain and retinal fatty acid patterns can be achieved by manipulation of the dietary lipid supply, particularly if this is initiated during pregnancy, as major accretion of polyunsaturated fatty acids (PUFA) in the brain occur in utero and in the immediate post-natal period.

In order to assess the role of n–3 PUFA in retinal development, previous reports from this laboratory have shown that guinea pigs deprived of n–3 PUFA over three successive generations have a substantial depletion of DHA in the retina (2–5). In our previous studies, albino guinea pigs fed diets containing safflower oil as the only source of lipid over three generations had 2.5% retinal DHA compared with 22.0% in guinea pigs fed canola oil as the sole source of lipid. Furthermore, these dietary manipulations led to a significantly reduced electroretinographic signal in the n–3-deficient group (3, 4). The guinea pig appears to be a useful model to study the role of n–3 PUFA; however, dietary depletion over successive generations is time-consuming, expensive and is unlikely to be relevant to human nutrition.

In the rat and monkey, dietary deprivation of n–3 PUFA also results in alterations in the retinal and brain PUFA patterns, with significant decreases in DHA (to approximately 40% normal level) (6–8). Ward et al. (9) recently achieved greater depletion of brain DHA levels in rats using a system of artificial rearing. In their first-generation animals, brain DHA levels were 50% of control values by 8 weeks of age whereas in the second generation, the DHA values were only 10% of controls by 8 weeks of age.

The present study sought to determine the effect of dietary n–3 PUFA manipulation on the retinal PUFA profile of the guinea pig over a single generation. As such, the study more adequately simulated the real world situation in which an infant may have an n–3 PUFA change imposed by dietary means. In addition, by chance, we were

Abbreviations: CNO, canola oil; DHA, docosahexaenoic acid; DH, Dunkin Hartley; EPA, eicosapentaenoic acid; ESH, English short-hair; PUFA, polyunsaturated fatty acids; SO, safflower oil.

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able to consider the relevance of maternal dietary n–3 supply on the infant retinal PUFA profile by using two groups of experimental animals, born of dams fed commercial chow either with or without long chain n–3 PUFA (eicosapentaenoic acid (EPA), docosapentaenoic acid and DHA).

MATERIALS AND METHODS

Animals and diets

All procedures involving animals were conducted in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by our Institutional Ethics Committees.

Weanling guinea pigs, born of mothers fed one of two different commercial chow diets, were raised in two separate experiments as indicated in **Table 1**. The first experiment was initiated as a pilot study, to ascertain how long it would take to achieve reductions in retinal DHA after the feeding of an n–3-deficient diet. The second experiment was conducted with a view to determining the effect of retinal DHA depletion in one generation on the electrophysiological responses of the retina. These results will be reported elsewhere. As a result of obtaining the guinea pigs for each experiment from two separate suppliers, we observed differences in retinal DHA levels at weaning and subsequent retinal DHA depletion rates. The reason for this difference was found to be in the composition of the chows being fed to the mothers (see later).

In each experiment, weanling guinea pigs aged 21 days were placed onto one of two semi-synthetic diets (2), containing (g/kg): casein 300, sucrose 100, glucose 70, starch 200, cellulose 100, kaolin 30, l-arginine 3, dl-methionine 2, mineral mix 68 (2), vitamin mix 27 (2). Safflower oil (SO) or canola oil (CNO) were used as the sole source of lipid for each diet (100 g/kg). The diet designed to result in depletion of retinal n–3 polyunsaturated fatty acids utilized SO, as it contains negligible amounts of n–3 and high amounts of n–6 fatty acids (n–6/n–3 = 224; 75.6% linoleic acid, 0.3% alpha-linolenic acid). CNO contains a relatively high level of n–3 fatty acids and served as the n–3-sufficient diet (n–6/n–3 = 2.2; 19.7% linoleic acid, 9.1% alpha-linolenic acid).

In experiment 1, 22 albino Dunkin Hartley (DH) and 21 pigmented English short-hair (ESH) guinea pigs were used. Seven guinea pigs (4 DH and 3 ESH) were killed at weaning and a further 36 guinea pigs (18 DH, 18 ESH) were equally divided by strain and placed onto either the CNO or SO diets (18 per diet group). At 6, 12, and 24 weeks, 6 animals for each group (3 from each strain) were killed for retina tissue lipid analysis (Table 1).

In experiment 2, 43 DH guinea pigs were used. Seven guinea pigs were killed at weaning and a further 36 were placed onto either the SO or CNO diets (18 per diet group). Six animals from each diet group were killed at 6, 11, and 16 weeks post-weaning (Table 1).

Animals were fed once per day and the diets were supplemented with 10 g fresh carrots daily and water containing ascorbic acid (400 mg/L) ad libitum. The light environment was cycled (12 h light; 12 h dark) in the animal housing room, and the temperature was maintained at 21°C.

Retinal fatty acid analysis

Deeply anesthetized (ketamine 0.35 mg/kg, xylazine 0.25 mg/kg) animals were killed by CO_2 asphyxiation. The right eye was immediately removed under room light and the retina was dissected into phosphate-buffered saline. Lipids were extracted from one retina per animal using chloroform–methanol 2:1 (containing 10 mg/L of butylated hydroxy toluene antioxidant) and the phospholipids were separated from the neutral lipids by thin-layer chromatography (10). The methyl esters of the phospholipid fatty acids were formed by a saponification step using KOH followed by transesterification in BF_3 in methanol (10) and the fatty acid methyl esters were separated by capillary gas–liquid chromatography using a 50 m × 0.32 mm (i.d.) fused silica bonded phase column (BPX70, SGE, Melbourne, Australia). In the case of the chow diets fed to the mothers, the total lipids were extracted from the diets using chloroform–methanol (above) and the total lipids were reacted with KOH and BF_3 in methanol so that the total diet fatty acid methyl esters were analyzed by gas–liquid chromatography as described above. Fatty acids were identified by comparison with standard mixtures of fatty acid methyl esters and the results were calculated using response factors derived from chromatographing standards of known composition (NuChek Prep., Elysian, MN). Pooled samples of the fatty acid methyl esters of the retinal phospholipids from each diet group (CNO and SO) and from fatty acid methyl ester standards (above) were separated by silver nitrate thin-layer chromatography and examined by capillary gas–liquid chromatography as described above. Significant differences between proportions of retinal fatty acids were tested using the Student's *t*-test, with an alpha of 0.05.

RESULTS

In experiment 1, animals born to mothers on chow 1 had retinal DHA values of 14% at weaning and this rose to 20% in CNO guinea pigs ($P < 0.05$) by 24 weeks post-

TABLE 1. Outline of the design of experiments 1 and 2

Parameter	Experiment 1	Experiment 2
Guinea pig supplier	Supplier A	Supplier B
Maternal diet	Chow 1	Chow 2
Maternal diet n–3 PUFA	18:3	18:3, 20:5, 22:5, 22:6
Weaning diet lipid	SO or CNO	SO or CNO
Guinea pig strain	DH and ESH	DH
Retina fatty acids analyzed (number of animals)	0 weeks[a] (4 DH, 3 ESH) 6 weeks (3 DH, 3 ESH per diet) 12 weeks (3 DH, 3 ESH per diet) 24 weeks (2 DH[b], 3 ESH per diet)	0 weeks (7 DH) 6 weeks (6 per diet group) 11 weeks (6 per diet group) 16 weeks (6 per diet group)

SO, Safflower oil; CNO, canola oil; DH, Dunkin Hartley; ESH, English short-hair.
[a] Weeks post-weaning.
[b] One animal died in this group.

TABLE 2. Fatty acid composition of retinal phospholipids from guinea pigs born to mothers fed chow 1 and who received diets containing different levels of n–3 PUFA after weaning

Retinal Phospholipid Fatty Acids	Experiment 1			3rd Generation SO Diet
	Weaning	CNO Diet	SO Diet	
	0 wks (7)	24 wks (5)	24 wks (6)	9 wks (12)
16:0	18.1 ± 0.7	18.4 ± 0.5	17.9 ± 0.6	17.6 ± 0.2
18:0	24.3 ± 1.0^a	23.1 ± 0.6^a	22.8 ± 0.5^b	21.7 ± 0.2
18:1n–9	8.7 ± 0.6^a	9.9 ± 0.3^b	8.4 ± 0.6^a	7.4 ± 0.5
18:1n–7	3.0 ± 0.3^a	3.0 ± 0.2^a	2.2 ± 0.1^b	1.8 ± 0.1
n–6 PUFA				
18:2	1.7 ± 0.5^a	1.7 ± 0.3^a	2.4 ± 0.1^b	2.6 ± 0.1
20:4	8.3 ± 0.5^a	8.6 ± 0.5^{a,b}	9.4 ± 0.6^b	9.8 ± 0.1
22:4	3.0 ± 0.4^a	2.0 ± 0.2^b	4.0 ± 0.1^c	4.5 ± 0.1
22:5	8.5 ± 3.4^a	2.8 ± 1.0^b	17.4 ± 1.1^c	23.2 ± 0.5
24:4	1.7 ± 0.3^a	1.3 ± 0.2^a	2.4 ± 0.3^b	2.6 ± 0.1
24:5	0.2 ± 0.0^a	0.1 ± 0.0^b	0.2 ± 0.0^a	0.2 ± 0.0
n–3 PUFA				
22:5	1.0 ± 0.3^a	1.2 ± 0.2^a	0.2 ± 0.0^b	0.2 ± 0.0
22:6	14.0 ± 3.8^a	19.6 ± 1.2^b	4.5 ± 0.8^c	2.5 ± 0.3
24:5	0.4 ± 0.2^a	0.6 ± 0.1^a	0.1 ± 0.0^b	nd
24:6	0.1 ± 0.0^a	0.2 ± 0.0^b	nd	nd

The age post-weaning is given and, in parentheses, the number of retinas analyzed, one per animal. The last column has data from reference 5. Results are expressed as g retinal phospholipid fatty acid /100 g fatty acid (mean ± SD). The n–6/n–3 ratio for the canola oil diet (CNO) was 2.2, and for the safflower oil diet (SO) was 224.

Values with unlike lettered superscripts are different at $P < 0.05$; nd, not detected.

weaning (**Table 2**). The proportion of 22:5n–6 at weaning was 9%, and this fell to 3% ($P < 0.05$) after 24 weeks on the CNO diet. The proportions of arachidonic acid did not change significantly (P = NS) for the CNO group, whereas that of 22:4n–6 and 22:5n–6 fell significantly ($P < 0.05$)between weaning and 24 weeks (Table 2). The retinal DHA level in the SO-fed guinea pigs declined with time ($P < 0.05$) at the rate of 1% per week in the first 6 weeks, 0.4% per week between weeks 6 and 12, and 0.08% per week between weeks 12 and 24 (**Fig. 1**, top). The loss of DHA was associated with significant ($P < 0.05$) increases in 18:2n–6, 20:4n–6, 22:4n–6, 22:5n–6, and 24:4n–6, with particularly large changes occurring in the 22:5n–6 level (from 9% at weaning to 17% after 24 weeks, $P < 0.05$). After 24 weeks on the diet, the DHA value was 4.5% of the retinal fatty acids. By this age the DHA proportion was just under a quarter of that for guinea pigs maintained on the CNO diet, although it was still more than double the value of 9-week-old third generation SO fed guinea pigs (5) (Table 2). There was no significant difference between the DHA values of the DH and ESH strains at any age (P = NS).

The retinal phospholipid fatty acid compositions of the DH strain at the start and finish of experiment 2, from animals born to mothers on chow 2, are shown in **Table 3**. In this experiment, there were no significant changes in the proportions of the main retinal PUFA between weaning and after 16 weeks on the CNO diet. In contrast, on the

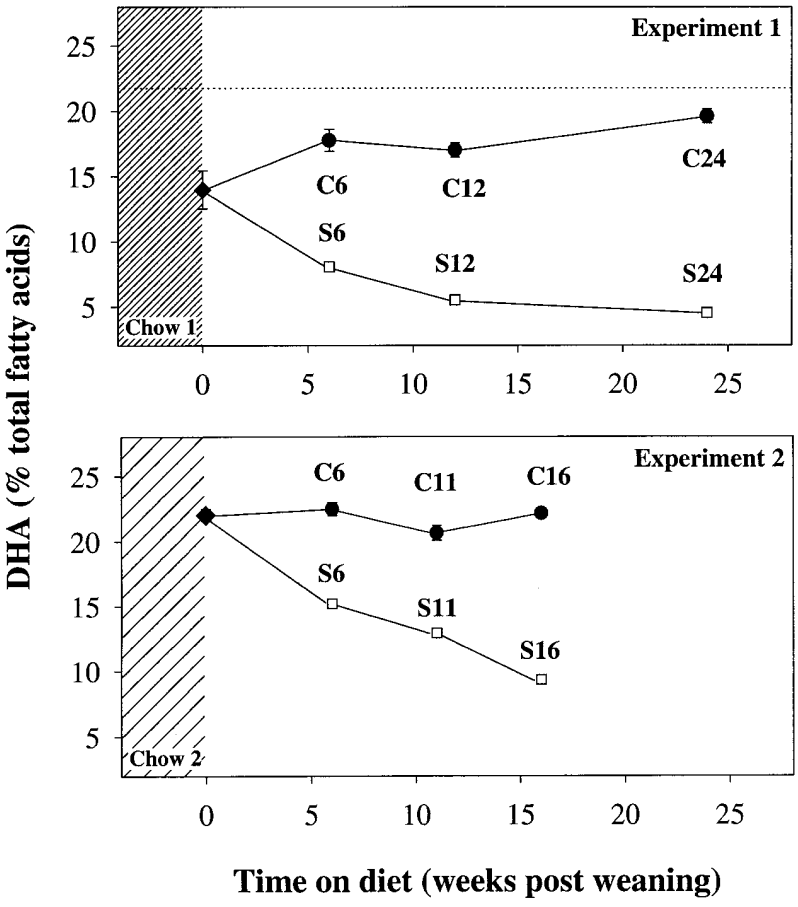

Fig. 1. Manipulation of retinal DHA proportion after post-weaning supply of diets differing in n–3 PUFA. Chow refers to the diet the mothers were fed. In experiment 1: mothers fed commercial chow diet without DHA; experiment 2: mothers fed commercial chow diet 2 including DHA (see Table 4). The retinal DHA value for animals at weaning is indicated as 0 weeks. C*x* refers to animals fed the canola oil diet from weaning with retinal DHA being determined at *x* weeks post-weaning, S*x* refers to animals fed the safflower oil diet. The dotted line in experiment 1 refers to the mean DHA level from the canola oil-fed group in experiment 2.

TABLE 3. Fatty acid composition of retinal phospholipids from guinea pigs born to mothers fed chow 2 and who received diets containing different levels of n–3 PUFA after weaning

Retinal Phospholipid Fatty Acids	Experiment 2		
	Weaning	CNO Diet	SO Diet
	0 wks (n = 7)	16 wks (6)	16 wks (6)
16:0	17.9 ± 0.3	16.5 ± 0.5	17.5 ± 0.8
18:0	23.3 ± 0.5	22.0 ± 1.0	23.4 ± 0.3
18:1n–9	9.0 ± 0.3[a]	8.8 ± 0.3[a]	7.6 ± 0.5[b]
18:1n–7	2.5 ± 0.1[a]	2.8 ± 0.1[b]	2.0 ± 0.2[c]
n–6 PUFA			
18:2	1.4 ± 0.2	1.4 ± 0.2	1.6 ± 0.2
20:4	8.0 ± 0.2[a]	8.2 ± 0.3[a]	9.4 ± 0.5[b]
22:4	1.6 ± 0.0[a]	2.1 ± 0.1[b]	3.6 ± 0.3[c]
22:5	2.2 ± 0.4[a]	2.9 ± 0.8[a]	15.8 ± 1.2[b]
24:4	0.8 ± 0.2[a]	1.3 ± 0.2[b]	2.6 ± 0.5[c]
24:5	0.1 ± 0.0[a]	0.2 ± 0.0[b]	0.2 ± 0.0[b]
n–3 PUFA			
22:5	1.3 ± 0.2[a]	1.2 ± 0.1[a]	0.2 ± 0.1[b]
22:6	22.0 ± 0.9[a]	22.1 ± 0.9[a]	9.3 ± 0.7[b]
24:5	0.7 ± 0.1	0.6 ± 0.1	nd
24:6	0.4 ± 0.2	0.4 ± 0.0	nd

The age post-weaning is given and, in parentheses, the number of retinas analyzed, one per animal. Results are expressed as g retinal phospholipid fatty acid / 100 g fatty acid (mean ± SD). The n–6 / n–3 ratio for the canola oil diet (CNO) was 2.2 and for the safflower oil diet (SO) was 224. Values with unlike lettered superscripts are different at $P < 0.05$; nd, not detected.

TABLE 4. Proportions of fatty acids in the total dietary lipids of commercial chow supplied to mothers in experiment 1 and experiment 2

Fatty Acid	Chow Experiment 1	Chow Experiment 2
16:0	18.1[a]	17.3
18:0	3.8	3.3
18:1	18.9	18.2
20:1	0.6	0.7
24:0	0.3	0.3
18:2 n–6	45.9	44.9
18:3 n–3	4.9	5.1
20:5 n–3	nd	1.0
22:5 n–3	nd	0.2
22:6 n–3	nd	1.0

Values are expressed as g fatty acid / 100 g fatty acid; nd, not detected.

[a] Mean of two determinations.

SO diet there were significant reductions ($P < 0.05$) in the levels of DHA, 22:5n–3, 24:5n–3, and 24:6n–3 and significant increases ($P < 0.05$) in 20:4n–6, 22:4n–6, 22:5n–6, 24:4n–6, and 24:5n–6, with particularly large changes occurring in 22:5n–6 (from 2% at weaning to 16% after 16 weeks, $P < 0.05$). Figure 1, bottom shows the change in DHA values with time in this experiment. In the CNO group, the proportion of DHA was similar between weaning and after 16 weeks on the CNO diet. On the SO diet there was a steady decline in the proportion of DHA in the retina over the 16 weeks (Fig. 1, bottom), equivalent to a loss of 0.8% DHA per week. After 16 weeks, the retinal DHA proportion in the SO group was 9.4% of retinal fatty acids or 42% of that found for CNO fed animals.

It was apparent that the animals born to mothers from the different suppliers (experiment 1 versus experiment 2) had significant differences in their retinal PUFA values at weaning, particularly the proportion of n–6 and n–3 PUFA (Tables 2 and 3). In experiment 1, the total n–3 PUFA level was 15.5% compared with 24.4% in experiment 2 ($P < 0.05$). The n–6 PUFA levels showed an inverse relationship to that of the n–3 PUFA values, with the total level of n–6 PUFA being 23.4% in experiment 1 compared with 14.1% in experiment 2 ($P < 0.05$). The DHA level in experiment 1 was 14% compared with 22.0% in experiment 2. This raised the possibility that perhaps the chow (chow 1 versus chow 2) being fed to the mothers varied. Subsequent analyses showed that the lipid content of the two maternal chow diets was similar (approximately 4%) with the main fatty acids being palmitic, stearic, oleic, linoleic, and alpha-linolenic acids (**Table 4**). Although the chow in experiment 2 had a fatty acid composition very similar to the experiment 1 chow, it also contained a small proportion of EPA and DHA (each about 1.0% of total fatty acids), and (n–3) docosapentaenoic acid (at 0.2% fatty acids).

In both experiments, there was no effect on the ability of animals within either the CNO or SO diet groups to accumulate 22-carbon PUFA (both n–3 and n–6) in the retina, as at the end of each experiment the total proportion of 22-carbon PUFA in SO and CNO groups was similar (26–29% of retinal fatty acids) (Tables 2 and 3).

DISCUSSION

We have shown that the retinal DHA level in the guinea pig can be substantially reduced by feeding diets with a low n–3 PUFA content for up to 24 weeks from weaning. In experiment 1, 24-week-fed SO animals had a mean DHA level 23% of that observed in CNO animals, whereas in experiment 2 the SO group DHA level at 16 week post-weaning was 42% of CNO animals. The first generation change observed in experiment 2 (42%) is consistent with that reported in other species (6, 9). In both experiments reported here, the retinal DHA level in the SO-fed guinea pigs was higher (1.8-fold to 3.7-fold) than that of third generation SO fed guinea pigs reported previously (5).

The results from experiment 1 indicated that the rate of loss of DHA over the first 12 weeks of feeding was greater than that of the second 12 weeks; approximately 90% of the loss occurred in the first 12 weeks. These data reveal that retinal PUFA levels in guinea pigs are readily altered by manipulation of the dietary alpha-linolenic acid supply in the early weeks of life. We have also shown that alpha-linolenic acid (in the CNO diet) can effectively sustain neonatal DHA levels, and in fact, allow for an accumulation in animals with lower values at weaning (experiment 1). This is apparent in the following. Animals born to dams raised on chow 2 (with long chain n–3 PUFA) had similar retinal DHA values after 16 weeks of the CNO diet (22.0% at weaning versus 22.1% after 16 weeks on the CNO diet, P = NS). Furthermore, animals born to dams on chow 1 (no long chain n–3 PUFA) could increase their

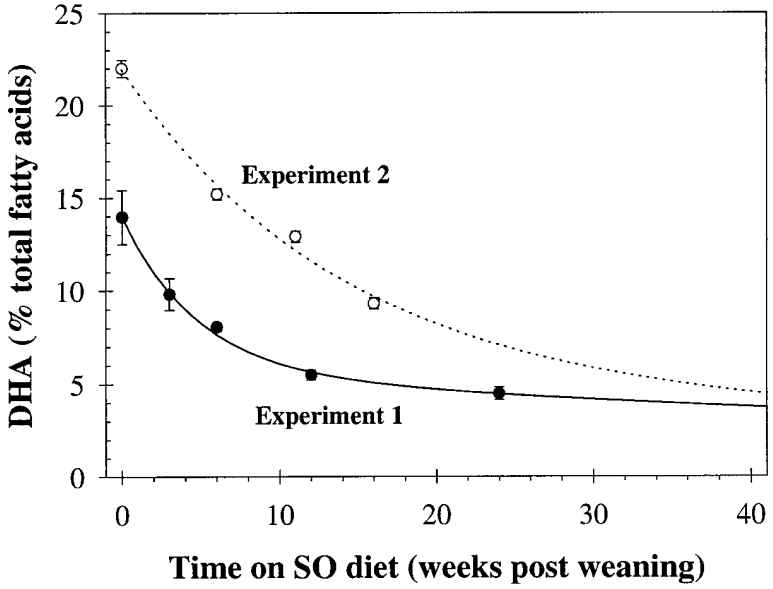

Fig. 2. Comparison of rate of retinal DHA loss in SO-fed guinea pigs from the two experiments. See text for details of modelling procedure (equation 1).

DHA status from 14.0 to 19.6% (Table 2) by 24 weeks post-weaning. It needs to be appreciated that the 19.6% value for these 24-week-fed CNO animals was still significantly removed ($P < 0.05$) from the 22.1% for the 16-week CNO-fed animals (Table 3), which implies that alpha-linolenic acid only allowed a slow rate of DHA accretion in the retina.

As the rates of change of many biological processes show exponential characteristics, we chose to apply an exponential equation to the data of experiment 1. We found that a single exponent failed to fit the data adequately, but the trend was best described by a double exponential decay, as given in equation 1.

$$\text{DHA level} = a.e^{-bt} + c.e^{-dt}, \quad \text{at time t (weeks on diet)} \qquad \textit{Eq. 1}$$

where a is a constant that reflects the proportion of DHA at weaning, b is the time constant that reflects the initial rate of decay, c is a constant that reflects the final DHA level, and d is the time constant that determines both the final rate of decay and the minimum DHA level. Our data have been fit with this model (**Fig. 2**) by floating a, b, c, and d of Equation 1 and using a Levenberg–Marquardt method for minimizing the chi-square statistic (11). This process yielded the following relationship for the data of experiment 1,

$$\text{DHA level} = 8.36e^{-0.21t} + 5.59e^{-0.01t}.$$

As the data set of experiment 2 limited in age samles, it was more difficult to determine the nature of the underlying trend, especially as the maximum age (16 weeks) does not appear to have reached an asymptote. As the data of experiment 1 could be well described by a double exponent, we chose to use the same modelling process for the data of experiment 2. This fitting returned the following equation,

$$\text{DHA level} = 16.35e^{-0.08t} + 5.59e^{-0.01t}.$$

It is useful to reflect on the possible meaning of the two exponents in this relationship. As the first exponent governs the initial rate of decay, this may correspond to the immediate loss of DHA from photoreceptor membranes after cessation of n–3 supply. On the other hand, the second exponent determines both the later rate of DHA loss and the asymptotic value, which probably reflects the balance that is achieved between dietary supply and systemic conservation mechanisms (12).

Applying the model allows an extrapolation for determining when the DHA levels of both neonatal groups will be equal. We found that DHA levels of the two SO diet groups are predicted to be the same at about 50 weeks (Fig. 2). However, the rate of decline varies between experiments. In experiment 2, the time constant (b^{-1}), was 13.3 weeks, compared with 4.8 weeks for experiment 1, revealing a nearly 3-fold increase in the initial rate of depletion in those animals that commenced with a lower DHA content. These data show that animals that commence depletion at higher retinal DHA levels will exhibit a slower rate of loss that may be a consequence of their higher tissue (e.g., liver) stores. However, it appears that there is a plateau for the level of retinal DHA reached and perhaps this reflects both conservation mechanisms and the small amount of alpha-linolenic acid provided by the SO dietary intake. Our data are consistent with those reported by Stinson, Wiegand, and Anderson (13) for the rat retina who found a significantly reduced turnover of n–3 PUFA under conditions of n–3 deficiency.

The influence of maternal diet has been illustrated by this study to be significant. The presence of small amounts of the long chain n–3 PUFA, EPA, and DHA at 1% of the dietary fatty acids in the maternal diet was associated with an approximately 60% increase in the level of DHA in the retina of weanling guinea pigs. We believe that the level of DHA in the retina at weaning reflects maternal nutritional status, as we have found, in an unrelated study, that the DHA level at weaning is similar to the retina DHA level shortly after birth (DHA levels in the retina of DH guinea pigs at 5, 10, 15, and 20 days after birth were 14.6, 16.0,

15.1, and 14.4%, respectively, n = 4/age group). Because the post-weaning rate of loss of DHA in n–3-deprived animals (SO group) was less in those whose mothers had been supplied with long chain n–3 PUFA (experiment 2), it appears that the maternal intake of DHA is important in providing a reservoir of DHA in the neonate. Those animals with small reserves (born to mothers without dietary DHA) lose their DHA over a brief time scale when fed SO diets. On the other hand, dietary alpha-linolenic acid (Fig. 1) is effective in increasing retinal DHA post-natally, although these data do not address whether higher retinal DHA levels would have been reached if DHA, itself, had been fed. Previous studies by our group have indicated that dietary DHA does lead to marked increases in retinal DHA levels in third generation studies with guinea pigs (4).

DHA accretion is influenced by both the ratio of linoleic acid to alpha-linolenic acid (where high levels of linoleic acid inhibit the metabolism of alpha-linolenic acid to DHA) and the direct addition of dietary DHA (4, 14). The present experiment confirms these earlier findings that dietary DHA is an important determinant of DHA accretion in the retina. Indeed, the presence of 1% DHA (of dietary fatty acids) was associated with a 60% increase in the retinal DHA level at weaning.

While these data have been obtained using the guinea pig, they highlight the importance of supplying adequate amounts of essential n–3 PUFA and of the correct balance with the n–6 PUFA for maternal and infant nutrition. The implications of these findings are relevant for maternal nutrition as it may be necessary to supplement a well-balanced n–6/n–3 ratio with small quantities of long chain n–3 PUFA to promote normal DHA accumulation in infants.

Current studies are considering whether the loss of retinal DHA in SO-fed animals over a 16-week period after weaning affects retinal function, as measured by electroretinography, and whether it is possible to recover retinal DHA levels (and function) when these animals are returned to a diet high in n–3 PUFA.

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