Developmental sensitivity of the brain to dietary n-3 fatty acids

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Abstract The developing brain readily incorporates dietary fatty acids, while the adult brain is refractory to changes in fatty acid composition. In order to localize the time in development when this transition occurs, chicks were fed large amounts of n-3 fatty acids from fish oil beginning at 0, 1, 2, or 3 weeks of age. Control chicks were fed a soybean oil-based diet, as were the experimental chicks before introduction of the fish oil diet. Resistance to diet-induced increases in brain n-3 fatty acid levels began at 2 weeks of age, and was substantial at 3 weeks. Docosahexaenoic acid was particularly resistant to change as the brain matured, increasing by 38% when fish oil was fed from time of hatching, but only by 8% when fish oil feeding was delayed until 3 weeks of age. Dietary fish oil caused a compensatory decrease in brain n-6 fatty acids, and this decrease occurred even at later time points when the rise in brain n-3 fatty acids was much less prominent. The liver incorporated high levels of n-3 fatty acids at all ages, and compensated by decreasing monounsaturated fatty acids at early time points and n-6 fatty acids at later time points. These results show that resistance to changes in brain fatty acid composition is evident at a relatively early age, before brain development is complete.—**Anderson, G. J.** Developmental sensitivity of the brain to dietary n-3 fatty acids. *J. Lipid Res.* 1994. **35:** 105–111.

Supplementary key words brain • development • chickens • docosahexaenoic acid • liver

The brain is highly enriched in docosahexaenoic acid [22:6(n-3)], but the biochemical significance of this enrichment is not well understood (1). A functional role for 22:6(n-3), is, however, coming into focus. Animals raised from birth on an n-3 fatty acid-deficient diet have low levels of 22:6(n-3) in the brain and develop behavioral anomalies together with decreased visual acuity and retinal function (2-6). Visual function has now been correlated with 22:6(n-3) status in human infants as well (7, 8). The developing brain can also be seeded with a surplus of n-3 fatty acids from a dietary source such as fish oil (9, 10). This plasticity does not, however, extend to the adult brain, where neither dietary fish oil (11) nor an n-3 fatty acid-deficient diet (12) has much effect on brain fatty acid composition. In a previous experiment (13) we probed the transition between the plastic, developing brain and the adult brain by determining the time at which resistance develops to diet-induced decreases in brain 22:6(n-3). In the present experiment we sought to determine the time at which resistance develops to diet-induced increases in brain 22:6(n-3).

MATERIALS AND METHODS

Design and diets

The study was designed to determine the developmental sensitivity of the brain to dietary n-3 fatty acids. Laying hens were fed a soybean oil-based control diet, and the resulting chicks were fed a similar soybean oil-based control diet, but then switched to a fish oil-based diet at 0, 1, 2, or 3 weeks of age (**Fig. 1**). The fish oil diet was continued for 2 weeks, with chicks killed at 2, 3, 4, or 5 weeks of age. Additional control chicks consumed only the soybean oil diet for 0, 1, 2, 3, 4, or 5 weeks. Four to six chicks were used for each data point.

Single-comb white Leghorn hens and roosters (commercial strain, Skylane Farms, Portland, OR) were housed under controlled temperature and 16 h light/day, as approved by the University Animal Care Committee. Roosters were placed overnight with hens in a 5-day rotation. Hens were fed a soybean oil-based control diet prepared by mixing 900 g of fat-free basal mix with 100 g fat as shown in **Table 1**. The diet supplied > 7% of energy as linoleic acid 18:2(n-6). Chick diets were similarly prepared to contain 5% fat. Basal mixes were obtained from Teklad (Madison, WI). The fish oil diet for chicks used Promega brand fish oil (Parke-Davis) containing approximately 50% n-3 fatty acids. Safflower oil was added to supply 18:2(n-6). This diet, and the control, soybean oil-based diet for chicks, supplied 3% of energy as 18:2(n-6). Hydrogenated coconut oil was used as filler to bring the fat content of all diets to the specified level. The fatty acid composition of the diets is shown in **Table 2.** Diets were handled so as to minimize oxidation of the polyunsatu-

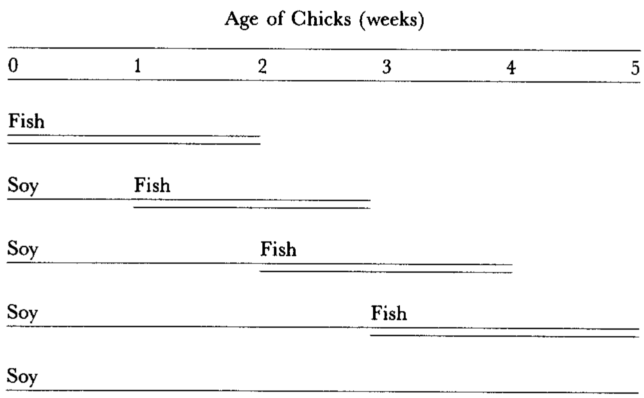

Fig. 1. Design of the fish oil feeding study. Laying hens were fed a soybean oil-based control diet. Chicks were continued on a soybean oil diet and switched to a fish oil diet at 0, 1, 2, or 3 weeks of age for a period of 2 weeks. Chicks were killed at 0 + 2 = 2 weeks, 1 + 2 = 3 weeks, 2 + 2 = 4 weeks, and 3 + 2 = 5 weeks. As a control, additional chicks from the soybean oil-fed hens were fed only the soybean oil diet. These chicks were killed at 0–5 weeks.

rated fatty acids (14). Additional vitamin E was added to the fish oil diet to a level of 259 units/kg because of difficulties observed in a previous study (13).

Chicks were anesthetized with ketamine/xylazine (intraperitoneal), decapitated, and the brain and liver were removed and stored at −20°C until analysis of fatty acids by capillary gas chromatography (14). Fatty acids were identified by comparison with standards run on a daily basis, including a fish oil standard from the Department of Commerce. Fatty acid data were handled with the aid a chromatography workstation running "Omega," a data collection, integration, and reporting program from Perkin-Elmer (Norwalk, CT). Data were then passed electronically to a spreadsheet to minimize data entry and handling errors.

Comparison of the effect of dietary fish oil on tissue fatty acids was done by two-way ANOVA (diet, time), with differences between individual means detected by use of the appropriate t-statistic (15). The Bonferroni inequality (16) was used to control the overall α-level.

TABLE 1. Composition of the diets

	Hen Diet	Chick Diets	
Component	Soy Oil	Fish Oil	Soy Oil
		g/100 g	
Dextrose monohydrate	56.28	59.21	59.21
Fat-free casein	18.70	25.00	25.00
L-Arginine HCl	0.35	1.20	1.20
DL-Methionine	0.35	0.40	0.40
Cellulose	3.00	3.00	3.00
Salt mix	10.98	5.80	5.80
Vitamin mix[a]	0.34	0.39	0.39
Fish oil		3.48	
Safflower oil		1.62	
Soybean oil	5.92		2.39
Hydrogenated coconut oil	4.08		2.61
Total fat	10.00	5.00	5.00

[a]The fish oil diet was supplemented with additional vitamin E (see Methods).

TABLE 2. Fatty acid composition of the diets

Fatty	Hen Diet	Chick Diets	
Acid	Soy Oil	Fish Oil	Soy Oil
		g/100 g	
12:0	16.2		26.2
14:0	10.3	3.6	10.6
16:0	12.2	7.6	10.0
18:0	8.8	1.3	8.0
Total sat.	48.6	12.8	55.0
16:1(n-7)		6.0	
18:1(n-9)/(n-7)	13.8	10.2	11.7
Total mono.	13.8	18.5	11.7
18:2(n-6)	33.5	27.6	28.8
20:4(n-6)		0.7	
Total (n-6)	33.5	29.8	29.5
18:3(n-3)	4.0	0.6	3.1
18:4(n-3)		3.5	
20:4(n-3)		1.0	
20:5(n-3)		18.0	
22:5(n-3)		1.8	
22:6(n-3)		7.7	
Total (n-3)	4.0	32.5	3.1
Total PUFA	38.5	68.4[a]	32.6

[a]The fish oil diet contained 16:2(n-4) (0.9%), 16:3(n-4) (1.3%), and 16:4(n-1) (3.8%).

RESULTS

Newly hatched chicks from hens fed a control (soybean oil-based) diet responded to 2 weeks of dietary fish oil by substantially increasing the proportion of long-chain n-3 fatty acids in the brain (**Table 3**). This effect was also seen in chicks switched from the soybean oil diet to the fish oil diet for 2 weeks beginning at 1 week of age. However, when the switch to a fish oil diet did not begin until 2 weeks of age, the rise in brain total n-3 fatty acids was not as dramatic. Moreover, when the start of the high n-3 fatty acid fish oil diet was delayed until 3 weeks of age there was only a slight rise in brain n-3 fatty acids, with no significant increase in the level of 22:6(n-3). These changes are shown graphically in **Fig. 2.**

The rise in brain n-3 fatty acids that occurred after the feeding of fish oil to chicks beginning at 0–1 week of age was compensated by a drop in n-6 fatty acids, from about 14–15% of total fatty acids in soybean oil-fed chicks to

TABLE 3. Brain fatty acid composition (mol%) of chicks fed a soybean oil diet for 0, 1, 2, or 3 weeks, followed by a fish oil diet for 2 weeks

Fatty Acids	Age (weeks) 0	1	2		3		4		5	
	Soy	Soy	Soy	0 week Soy + 2 weeks Fish	Soy	1 week Soy + 2 weeks Fish	Soy	2 weeks Soy + 2 weeks Fish	Soy	3 weeks Fish + 2 weeks Fish
16:0	36.3 ± 0.4	32.2 ± 1.8	30.8 ± 1.1	31.7 ± 1.7	31.8 ± 1.7	32.1 ± 0.5	30.7 ± 1.4	30.6 ± 1.2	29.4 ± 1.3	29.7 ± 0.8
18:0	15.5 ± 1.2	16.0 ± 0.7	14.3 ± 0.6	15.6 ± 1.3	14.6 ± 0.9*	12.1 ± 0.4	14.4 ± 1.0*	15.8 ± 1.0	13.5 ± 0.8*	14.9 ± 0.6
Total sat.[†]	58.2 ± 1.6	54.7 ± 2.1	51.9 ± 0.8	53.5 ± 1.2	53.1 ± 0.9	51.6 ± 0.5	52.6 ± 0.8*	54.9 ± 1.8	50.7 ± 0.9*	53.4 ± 1.0
16:1(n-7)	1.1 ± 0.8	1.3 ± 0.4	1.4 ± 0.3	1.3 ± 0.1	1.4 ± 0.2	1.6 ± 0.2	1.2 ± 0.1	1.2 ± 0.3	1.2 ± 0.2	1.4 ± 0.1
18:1(n-9)/(n-7)	15.1 ± 0.8	18.8 ± 0.9	18.7 ± 0.6	18.0 ± 0.8	20.1 ± 1.0	19.9 ± 1.0	20.5 ± 0.8	20.0 ± 0.8	21.1 ± 0.7	21.4 ± 0.7
Total mono.	16.8 ± 1.4	20.7 ± 1.3	21.4 ± 1.4	20.1 ± 0.8	22.3 ± 1.1	21.8 ± 0.9	22.5 ± 0.9	22.0 ± 1.1	23.0 ± 0.8	23.5 ± 0.7
18:2(n-6)	1.8 ± 0.1	0.4 ± 0.2	0.8 ± 0.3	1.1 ± 0.2	0.9 ± 0.1	0.9 ± 0.3	0.7 ± 0.1	0.9 ± 0.2	1.0 ± 0.2	0.9 ± 0.1
20:3(n-6)	0.4 ± 0.1	0.6 ± 0.1	0.7 ± 0.1	0.4 ± 0.1	0.6 ± 0.0	0.4 ± 0.1	0.5 ± 0.0	0.4 ± 0.0	0.5 ± 0.1	0.4 ± 0.0
20:4(n-6)	7.7 ± 0.4	7.7 ± 0.7	8.9 ± 0.7*	5.7 ± 0.3	8.6 ± 0.4*	5.8 ± 0.3	8.8 ± 0.8*	5.4 ± 0.3	9.0 ± 0.7*	6.0 ± 0.3
22:4(n-6)	1.7 ± 0.2	1.9 ± 0.5	1.9 ± 0.3*	1.2 ± 0.0	1.9 ± 0.2*	1.2 ± 0.1	1.9 ± 0.4*	1.0 ± 0.6	2.2 ± 0.2*	1.3 ± 0.1
22:5(n-6)	1.1 ± 0.1	1.8 ± 0.2	2.1 ± 0.3*	0.5 ± 0.3	1.8 ± 0.2*	0.8 ± 0.2	1.7 ± 0.2*	0.5 ± 0.3	1.8 ± 0.1*	0.8 ± 0.1
Total (n-6)	13.8 ± 0.7	12.7 ± 1.0	14.7 ± 0.8*	9.5 ± 0.9^{a,b}	13.9 ± 0.5*	9.4 ± 0.3^{a,b}	14.0 ± 1.3*	8.4 ± 1.0^{a}	15.0 ± 1.1*	10.0 ± 1.0^{b}
20:5(n-3)	0.1 ± 0.1	0.0 ± 0.0	0.1 ± 0.1*	1.6 ± 0.1^{a}	0.0 ± 0.1*	1.5 ± 0.3^{a}	0.1 ± 0.1*	1.1 ± 0.1^{b}	0.0 ± 0.1*	0.7 ± 0.1^{c}
22:5(n-3)	0.5 ± 0.1	0.7 ± 0.4	0.6 ± 0.3*	1.7 ± 0.1^{a,b}	0.4 ± 0.0*	1.8 ± 0.1^{a}	0.3 ± 0.1*	1.5 ± 0.1^{b}	0.4 ± 0.1*	1.2 ± 0.0^{c}
22:6(n-3)	10.2 ± 1.2	9.2 ± 1.6	9.3 ± 1.1*	12.3 ± 0.6^{a}	8.4 ± 0.8*	12.2 ± 0.8^{a}	8.5 ± 0.8*	10.3 ± 0.4^{b}	8.5 ± 0.6	9.2 ± 0.2^{b}
Total (n-3)	10.8 ± 1.3	9.9 ± 1.9	9.9 ± 0.9*	15.6 ± 0.8^{a}	8.9 ± 0.7*	16.1 ± 0.6^{a}	9.1 ± 0.8*	13.0 ± 0.4^{b}	8.9 ± 0.6*	11.0 ± 0.2^{c}

Time effect (soy–fish diet only): values with unlike lettered superscripts within a given row are different at $P < 0.037$.
[†]Includes dimethyl acetals.
*$P < 0.037$ (soy vs. soy–fish diet at a given time point).

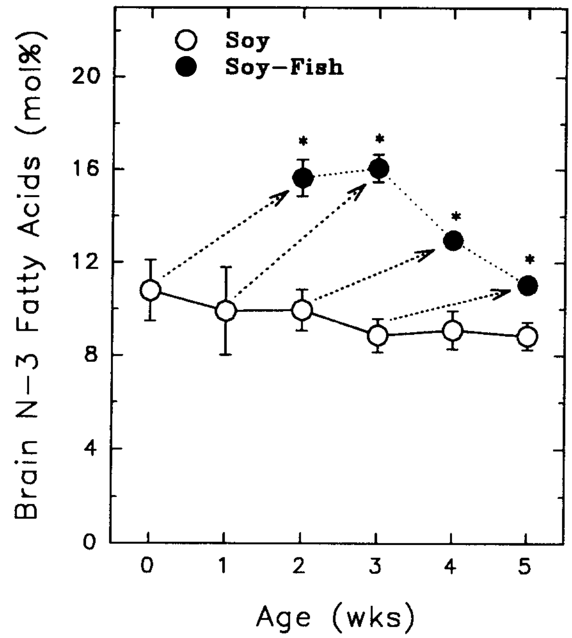

Fig. 2. Response of the developing chick brain to dietary n-3 fatty acids. (O—O, Soy), chicks from soybean oil-fed hens were fed a soybean oil diet. (●--●, Soy-Fish), chicks from soybean oil-fed hens were fed a soybean oil diet for 0, 1, 2, or 3 weeks, followed by a fish oil diet for 2 weeks; these chicks were killed at 0 + 2 = 2 weeks, 1 + 2 = 3 weeks, 2 + 2 = 4 weeks, and 3 + 2 = 5 weeks. Data are from Table 3. *Different from Soy diet at same time point ($P < 0.037$).

9–10% in fish oil-fed chicks. Twenty-two carbon n-6 fatty acids, specifically 22:4(n-6) and 22:5(n-6), were impacted proportionally more than arachidonic acid, 20:4(n-6). Linoleic acid [18:2(n-6)] and 20:3(n-6) were not affected. At later time points, when the fish oil diet was not started until 2-3 weeks of age, the brain n-6 fatty acids declined to the same extent seen at earlier time points, despite there being less increase in n-3 fatty acids in these chicks. Thus, in chicks fed fish oil beginning at 3 weeks of age, there was a substantial drop in n-6 fatty acids accompanied by only a small increase in n-3 fatty acids. This excess decline in n-6 fatty acids was compensated for by a slight increase in saturated fatty acids.

The developing liver responded differently to dietary n-3 fatty acids from fish oil than did the developing brain. At all ages at which fish oil was fed, chick liver incorporated a high level of total n-3 fatty acids compared to control (**Fig. 3**). The individual n-3 fatty acids also responded the same whether fish oil feeding was begun at 0 weeks or at 3 weeks (**Table 4**). Nevertheless, other fatty acids in the liver responded differently to fish oil depending on the age at which fish oil feeding began, with one type of response seen at early points and a different response seen in the oldest chicks. Thus, the liver of 2-week-old chicks that had been fed fish oil from hatching compensated for the increased proportion of n-3 fatty acids by sharply decreasing the proportion of 18-carbon monounsaturated fatty acids, with no change in n-6 fatty acids. Delaying the start of the fish oil feeding to 1 week of age led to an intermediate picture in the liver of the chicks at 3 weeks of age. The increased level of n-3 fatty acids was now accompanied by lower n-6 fatty acids (including 20:3(n-6), which was little affected in the brain) in addition to a lowering of monounsaturates. As in the brain, though, 18:2(n-6) was not affected. Beginning fish oil feeding at 2 weeks of age had a similar effect. However, waiting until 3 weeks of age to start fish oil feeding produced an even larger compensatory decrease in n-6 fatty acids and only a small and statistically insignificant lowering of monounsaturated fatty acids. Arachidonic acid was particularly affected at this point, falling by more than 70% compared to control. Thus, the compensatory response to high levels of n-3 fatty acids in the liver of young chicks was to lower predominantly monounsaturated fatty acids, while the response in older chicks was to lower predominantly n-6 fatty acids.

The liver of control chicks showed dramatic developmental changes in fatty acid composition. The most abrupt of these changes occurred as the chick switched in the first week of life from egg sac yolk to food as its source of nutrition. By 1 week of age liver saturated fatty acids had doubled in proportion (from 20 to 44% of fatty acids), while n-6 fatty acids had declined precipitously.

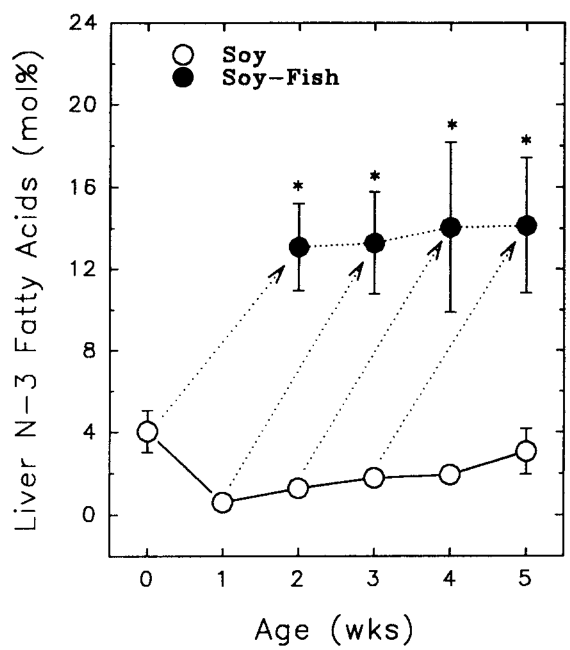

Fig. 3. Response of the chick liver to dietary n-3 fatty acids. (O—O, Soy), chicks from soybean oil-fed hens were fed a soybean oil diet. (●--●, Soy-Fish), chicks from soybean oil-fed hens were fed a soybean oil diet for 0, 1, 2, or 3 weeks, followed by a fish oil diet for 2 weeks; these chicks were killed at 0 + 2 = 2 weeks, 1 + 2 = 3 weeks, 2 + 2 = 4 weeks, and 3 + 2 = 5 weeks. Data are from Table 4. *Different from Soy diet at same time point ($P < 0.01$).

TABLE 4. Liver fatty acid composition (mol%) of chicks fed a soybean oil diet for 0, 1, 2, or 3 weeks, followed by a fish oil diet for 2 weeks

Fatty Acid	Age 0	1	2		3		4		5	
	Soy	Soy	Soy	0 week Soy + 2 weeks Fish	Soy	1 week Soy + 2 weeks Fish	Soy	2 weeks Soy + 2 weeks Fish	Soy	3 weeks Soy + 2 weeks Fish
16:0	10.3 ± 1.5^{a}	33.2 ± 3.4^{b}	29.8 ± 2.3^{b,c}	29.9 ± 2.3	30.6 ± 2.4^{b,c}	30.0 ± 2.6	27.5 ± 2.5^{c,d}	28.8 ± 4.1	25.0 ± 3.8^{d}	26.9 ± 2.5
18:0	9.4 ± 1.2^{a}	9.3 ± 1.6^{a}	13.1 ± 2.6^{b}	16.6 ± 1.6*	14.9 ± 1.4^{b,c}	16.5 ± 2.1	12.9 ± 1.4^{b}	18.0 ± 2.0**	17.4 ± 2.6^{c}	18.4 ± 1.2
Total sat.[†]	20.1 ± 2.0^{a}	44.2 ± 2.5^{b}	45.8 ± 3.0^{b}	47.5 ± 2.7	48.1 ± 3.7^{b}	47.5 ± 2.7	43.5 ± 1.6^{b}	48.0 ± 2.5*	43.8 ± 3.5^{b}	47.2 ± 5.6
16:1(n-7)	1.2 ± 0.4^{a}	9.0 ± 1.0^{b}	6.3 ± 1.2^{c}	4.0 ± 0.8**	5.0 ± 0.7^{c}	4.4 ± 0.8	5.2 ± 0.9^{c}	3.4 ± 0.9**	3.6 ± 1.1^{d}	2.9 ± 0.5
18:1(n-9)/(n-7)	52.0 ± 4.1^{a}	40.1 ± 3.8^{b}	34.6 ± 3.1^{b,c}	23.4 ± 3.3**	28.5 ± 2.8^{d,e}	22.9 ± 3.1*	32.0 ± 1.0^{c,d}	20.9 ± 4.4**	23.6 ± 5.7^{e}	20.9 ± 2.8
Total mono.	53.2 ± 4.4^{a}	49.9 ± 4.1^{a}	41.2 ± 4.2^{b}	27.6 ± 3.7**	33.9 ± 3.4^{c,d}	27.6 ± 3.8*	37.5 ± 1.7^{b,c}	24.7 ± 5.0**	27.6 ± 6.6^{d}	24.1 ± 3.4
18:2(n-6)	14.6 ± 1.1^{a}	3.1 ± 1.6^{e}	6.3 ± 1.9^{d}	6.8 ± 1.1	8.4 ± 0.7^{c,d}	7.8 ± 1.3	9.2 ± 1.1^{b,c}	8.8 ± 2.1	11.0 ± 2.1^{b}	9.7 ± 1.2
20:3(n-6)	0.2 ± 0.1	0.3 ± 0.1	0.5 ± 0.3	0.4 ± 0.1	0.9 ± 0.1	0.4 ± 0.1**	1.0 ± 0.1	0.5 ± 0.2**	1.3 ± 0.4	0.6 ± 0.2**
20:4(n-6)	6.7 ± 0.9^{b}	1.1 ± 0.5^{d}	3.3 ± 1.5^{c}	2.2 ± 0.4	5.2 ± 0.7^{b}	2.0 ± 0.4**	5.1 ± 0.9^{b,c}	2.5 ± 0.7**	9.2 ± 2.5^{a}	2.8 ± 0.7**
22:4(n-6)	0.3 ± 0.1	0.1 ± 0.1	0.2 ± 0.1	0.6 ± 0.9	0.2 ± 0.1	0.1 ± 0.1	0.2 ± 0.0	0.2 ± 0.1	0.5 ± 0.2	0.2 ± 0.1
Total (n-6)	22.5 ± 2.2^{a}	4.9 ± 2.3^{d}	10.7 ± 3.2^{c}	11.2 ± 1.6	15.5 ± 1.5^{b}	10.8 ± 1.5*	16.1 ± 2.1^{b}	12.5 ± 3.1	23.2 ± 5.3^{a}	13.6 ± 2.2**
18:3(n-3)	0.3 ± 0.1	0.1 ± 0.0	0.2 ± 0.0	0.1 ± 0.1**	0.2 ± 0.0	0.1 ± 0.1**	0.3 ± 0.1	0.1 ± 0.0**	0.3 ± 0.0	0.1 ± 0.0**
20:5(n-3)	0.2 ± 0.1	0.2 ± 0.1	0.4 ± 0.2	6.2 ± 1.3**	0.3 ± 0.1	6.2 ± 1.3**	0.3 ± 0.1	6.7 ± 1.8**	0.4 ± 0.3	6.1 ± 1.5**
22:5(n-3)	0.3 ± 0.1	0.1 ± 0.0	0.1 ± 0.1	1.9 ± 0.4**	0.2 ± 0.1	1.9 ± 0.4**	0.2 ± 0.0	1.9 ± 0.5**	0.4 ± 0.2	1.9 ± 0.3**
22:6(n-3)	3.2 ± 0.9^{a}	0.3 ± 0.1^{c}	0.6 ± 0.3^{b,c}	4.3 ± 0.9**	1.0 ± 0.2^{b,c}	4.7 ± 0.7**	1.1 ± 0.3^{b,c}	5.1 ± 1.9**	1.9 ± 0.8^{a,b}	5.8 ± 1.4**
Total (n-3)	4.0 ± 1.0^{a}	0.6 ± 0.2^{b}	1.3 ± 0.4^{a,b}	13.1 ± 2.1**	1.8 ± 0.3^{a,b}	13.3 ± 2.5**	1.9 ± 0.3^{a,b}	14.0 ± 4.1**	3.1 ± 1.1^{a,b}	14.1 ± 3.3**

Time effect (soy diet only): values in a given row with unlike lettered superscripts are different at $P \leq 0.040$.
[†]Includes dimethyl acetals.
*$P \leq 0.05$; **$P < 0.01$ (soy vs. soy–fish diet at a given time point).

Saturated fatty acids remained at this high level, while over time n-6 fatty acids increased at the expense of monounsaturated fatty acids.

DISCUSSION

The adult brain is typically resistant to changes in fatty acid composition (11, 17-23), and even large amounts of dietary n-3 fatty acids have only a modest effect on levels of brain n-3 fatty acids (24, 25). The developing brain, by contrast, is much more plastic. For instance, levels of brain n-3 fatty acids can be raised substantially by the feeding of fish oil to developing animals (10, 14, 26, 27), and levels of brain n-3 fatty acids can be dramatically reduced by feeding an n-3 fatty acid-deficient diet (6, 14). The stark difference between the behavior of the developing brain and the adult brain implies a transition between the two states.

In a previous study, we found that the developing chick brain shows resistance to decreasing the proportion of 22:6(n-3) by 3 weeks of age (13), which is roughly 1 week before the completion of myelination in this species (28, 29). In the present study, we reversed the design of the earlier experiment, and attempted to determine the point at which the developing brain shows resistance to increasing the proportion of 22:6(n-3). The results show clearly that resistance to the effects of dietary fish oil begins by 2 weeks of age and is substantial by 3 weeks of age. That is, chicks not fed fish oil until 3 weeks of age showed only a slight increase in total n-3 fatty acids, and essentially no increase in 22:6(n-3).

As in the previous experiment (13), there was a difference between the behavior of 20:5(n-3) and 22:5(n-3) on the one hand, and 22:6(n-3) on the other. In both the previous and present experiments more liability was shown by 20:5(n-3) and 22:5(n-3) than by 22:6(n-3). In the case of diet-induced lowering of brain n-3 fatty acids, 20:5(n-3) and 22:5(n-3) could be substantially affected at points in brain development at which 22:6(n-3) was no longer labile (13). In the case of diet-induced raising of brain n-3 fatty acids, 20:5(n-3) and 22:5(n-3) could likewise be changed at points in development at which 22:6(n-3) was unaffected.

In conclusion, there is at least a temporal association between the onset of resistance to a diet-induced increase in levels of n-3 fatty acids and the onset of resistance to a diet-induced decrease in levels of n-3 fatty acids in the developing chick brain. Whether these two events are linked to the same biochemical mechanism remains to be determined.

The author thanks Robert C. Leatherman for technical assistance. This work was supported by a First Independent Research Support and Transition Award (DK40935) from the National Institutes of Health.

Manuscript received 11 May 1993 and in revised form 30 July 1993.

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