

Maternal DHA and the Development of Attention in Infancy and Toddlerhood

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Infants were followed longitudinally to document the relationship between docosahexaenoic acid (DHA) levels and the development of attention. Erythrocyte (red-blood cell; RBC) phospholipid DHA (percentage of total fatty acids) was measured from infants and mothers at delivery. Infants were assessed in infant-control habituation at 4, 6, and 8 months augmented with psychophysiological measures, and on free-play attention and distractibility paradigms at 12 and 18 months. Infants whose mothers had high DHA at birth showed an accelerated decline in looking over the 1st year and increases in examining during single-object exploration and less distractibility in the 2nd year. These findings are consistent with evidence suggesting a link between DHA and cognitive development in infancy.

Docosahexaenoic acid (DHA, 22:6n-3) and arachidonic acid (AA, 20:4n-6) are long-chain polyunsaturated fatty acids (LC-PUFAs) that are found in all cell membranes. Both of these LC-PUFAs are especially concentrated in the brain, whereas the retina contains a very high proportion of DHA (e.g., Anderson, Maude, & Zimmerman, 1975). In the brain, DHA is especially concentrated in perisynaptic membranes (Martin & Bazan, 1992), whereas in the retina, DHA is found in both synaptic regions and photoreceptor membranes (Anderson et al., 1975).

Both DHA and AA accumulate rapidly in the central nervous system (CNS) during the last intra-uterine trimester (Clandinin et al., 1980; Martinez, 1991) and during the first 18 postnatal months (Martinez, 1991). Preformed DHA and AA is passed prenatally from the mother to the fetus in utero (Dutta-Roy, 2000), and after birth, these fatty acids are transferred from the mother to the infant through human milk (e.g., Putnam, Carlson, DeVoe, & Barnes, 1982). Infants can also synthesize these fatty acids from their essential fatty acid precursors, α -linolenic acid (18:3n-3) for DHA and linoleic acid (18:2n-6) for AA (e.g., Salem, Wegher, Mena, & Uauy, 1996).

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LC-PUFAs and Development

Because of their roles as structural components in the brain and retina, it has long been suspected that AA and DHA contribute to behavioral function and to the normative course of behavioral development. Research has focused on DHA because it has more consistently been linked to behavioral and neural function (Chalon, Vancassel, Zimmer, Guilloteau, & Durand, 2001; Reisbick, Neuringer, Gohl, Wald, & Anderson, 1997).

A plausible theoretical case can be made for the importance of DHA and AA for the development of the CNS and retina during the prenatal and postnatal periods (Carlson & Neuringer, 1999; Crawford et al., 1993; Gibson, Neumann, & Makrides 1996; Morley, 1998; Neuringer, Reisbick, & Janowsky, 1994; Scrimshaw, 1998; Simopoulos, 1991; Wainwright, 1992). Thus, recent studies have examined the effect of

early manipulations (either supplemented or deprived diets) of DHA and AA on visual and cognitive development.

LC-PUFA and Visual Function

Several studies have examined the effect of LC-PUFA supplementation on infant visual function. This literature is mixed (see Gibson & Makrides, 1999, for a review), with reports of both positive (e.g., Birch, Hoffman, Uauy, Birch, & Prestidge, 1998; Carlson, Werkman, & Tolley, 1996; Carlson, Werkman, Rhodes, & Tolley, 1993; Makrides, Neumann, Simmer, Pater, & Gibson, 1995; Uauy, Birch, Birch, Tyson, & Hoffman, 1990) and null (e.g., Auestad et al., 1997; Bakker, van Houwelingen, & Hornstra, 1999; Innis, Akrabawi, Diersen-Schade, Dobson, & Guy, 1997; Jensen et al., 1997) effects.

LC-PUFA and Standardized Test Performance

Standardized tests of early development have been used in several DHA supplementation studies. Positive outcomes have been observed in many of these (e.g., Agostini et al., 1995, 1997; Birch, Garfield, Hoffman, Uauy, & Birch, 2000; Carlson, Werkman, Peeples, & Wilson, 1994), although null effects predominate in larger scale clinical trials (e.g., Makrides, Neumann, Simmer, & Gibson, 2000; Scott et al., 1998).

LC-PUFA and Laboratory Measures of Infant Cognition

Several studies have employed nonstandardized laboratory tasks with both human and infrahuman samples to evaluate the effects of individual differences or supplementation with LC-PUFAs, particularly DHA. These studies have yielded consistent and positive results in favor of a role for LC-PUFAs in early cognitive function. Werkman and Carlson (1996) administered the Fagan Test of Infant Intelligence to preterm infants fed a DHA-supplemented diet through 9 months of age. Supplemented infants were observed to show shorter looking during some phases of the test, a finding typically interpreted as positive, as briefer looking during the 1st year is generally thought to reflect more rapid or efficient encoding (Colombo, Mitchell, & Horowitz, 1988). Carlson and Werkman (1996) reported the same finding for 12-month-old preterm infants whose supplementation ended 10 months earlier, at 2 months past expected term. These studies provided preterm infants formulas containing alpha-linoleic acid but varied in whether there was a source of

DHA. An analogous test was conducted on primate infants by Reisbick et al. (1997), who depleted infant primates of DHA by feeding an alpha-linolenic acid-deficient diet. The control group was fed a diet with alpha-linolenic acid. The control group had shorter looking during both familiarization and paired-comparison phases of infant recognition testing.

It is worth noting that in both the human and infrahuman studies, dietary supplementation affected look duration but not recognition performance (Carlson & Neuringer, 1999). Finally, Willatts, Forsyth, DiModugno, Varma, and Colvin (1998b; see also Forsyth, Willatts, DiModugno, Varma, & Colvin, 1998) reported that DHA-supplemented infants performed better on means-ends tasks at 10 months of age; such performance suggests differences in the ability to plan and execute a series of actions to achieve a goal.

In line with the expectation that the effects of DHA intake will be manifest in broader cognitive domains, a few studies have examined the effects of DHA on attention in infancy. Willatts et al. (1998a) observed briefer look durations during habituation in DHA-supplemented infants at 4 months of age, but this effect was seen only in infants whose attentional patterns showed nonlinear or nonmonotonic declines in looking. More recently, Willatts, Forsyth, Mires, and Ross (2003) reported negative correlations between look duration measured during habituation at 4 months of age and DHA levels in maternal blood at delivery.

The Current Study

These studies suggest that early DHA intake or levels may be manifest within the domain of attention in infancy. A more comprehensive approach to the study of DHA and its effects on attention might therefore be warranted. Indeed, a recent review of the literature on infant assessment from the point of view of nutrition research (Colombo, 2001b) has argued that such an approach would be characterized by measuring different attentional constructs at several appropriate points in development and by using assessments at several levels of measurement. We report here the results of a study of the association of individual differences in DHA levels and attention across the first 2 years of life. A subset of a sample enrolled in a randomized, double-blind, controlled clinical trial of the effects of prenatal DHA supplementation on pregnancy and gestation (Smuts et al., 2003) was recruited for a follow-up study on measures of visual habituation during the 1st year of

life and on measures of attention span and distractibility during the 2nd year.

Attention is not a monolithic construct, and its developmental course during infancy and early childhood is complex and nonlinear (see Colombo, 2002). Different aspects of attention predominate at different points early in the life span (Colombo, 2001a), and the interpretation of the attentional measures may vary at different ages. For example, the developmental course of look duration in the 1st year features a decline from about 2 months to about 9 months of age. At these ages, the decline in look duration appears to correspond to improved processing efficiency (Colombo & Mitchell, 1990) as well as to improved facility in the disengagement of attention (Frick, Colombo, & Saxon, 1999). Therefore, shorter looking represents the more mature form of attention at these earlier ages. Indeed, several studies (e.g., see Colombo, 1993, for a review) have reported negative correlations between look duration and childhood cognitive and language outcomes.

This contrasts sharply with the inferences from measures of attention later in the 1st year and into the 2nd year, however. At these later ages, looking and examining is more commonly linked to endogenous attentional functions, such as attention span or self-regulation. As such, increased looking (typically measured in free-play or problem-solving situations) is generally interpreted as a reflection of the infant's ability to stay on task, to self-regulate or voluntarily control attention, or to be more highly resistant to distraction. Indeed, laboratories studying distractibility and examining beyond the 1st year and through the preschool years (e.g., Ruff & Capozzoli, 2003; Ruff, Capozzoli, & Saltarelli, 1996; Ruff, Capozzoli, & Weissberg, 1998) typically consider longer examining time and indexes of resistance to distraction to reflect improved attentional function. Finally, the valence of predictive correlations from these ages now shifts to positive; that is, longer looking is related to more positive outcomes (e.g., Ruff & Lawson, 1990; see Ruff & Rothbart, 1996, for a review). If DHA positively affects attention, we would therefore expect shorter look durations during the 1st year but then a tendency toward longer look durations and increased resistance to distraction in the 2nd year.

Method

Participants

Seventy infants were recruited for a longitudinal follow-up study from a total of 350 infants and mothers enrolled in a study of the effects of DHA

supplementation on pregnancy length (Smuts et al., 2003). The follow-up sample was representative of the larger group; it did not vary from the larger sample on any of the demographic or medical variables taken, although the follow-up sample was slightly longer at birth (50.6 cm vs. 49.7 cm), $t(295) = 2.21, p < .05$, than the overall sample. Health and demographic data on the follow-up sample are shown in Table 1. Sample sizes for each of the follow-up episodes are provided in the results sections for each of the assessment tasks. Participants were administered informed consent before each session and were compensated \$50 for each longitudinal visit.

Design

Infants were initially enrolled in a randomized, double-blind, controlled clinical trial (RCT) for the evaluation of the DHA supplementation on pregnancy outcomes. Mothers' DHA intake was manipulated by providing eggs during the last trimester of the pregnancy. All mothers received eggs and recorded the number they ate but were blind to whether they were receiving high-DHA (135 mg DHA per egg) or ordinary (35 mg DHA per egg) eggs

Table 1
Health and Demographic Characteristics of the Follow-up Sample

Continuous variables			
Variable	<i>M</i>	<i>SD</i>	
Gestation length (weeks)	39.29	2.24	
Apgar score (1 min)	7.94	1.62	
Apgar score (5 min)	8.80	0.67	
Birth weight (g)	3248.57	393.02	
Length (cm)	50.60	2.29	
Head circumference (cm)	33.74	1.38	
Mother's education (yr)	11.77	1.18	
Father's education (yr)	11.88	1.37	
Categorical variables			
Variable	Category	<i>N</i>	Percentage
Randomized group	Supplemented	31	55.1
	Nonsupplemented	38	44.9
Infant gender	Female	27	39.1
	Male	42	60.9
Race	African American	54	77.1
	Asian American	0	0.0
	Hispanic	1	1.4
	Caucasian	15	21.4
Prematurity	Gestation \geq 37 weeks	63	90.0
	Gestation $<$ 37 weeks	7	10.0

(see Smuts et al., 2003, for more detail). In the overall sample, DHA supplementation produced modest but statistically significant increases in gestation (increased by 6 days), infant length (increased by 0.7 cm), and infant RBC DHA levels (DHA g per 100 g of fatty acids) at delivery (increased by 0.43). However, DHA supplementation did not affect maternal RBC DHA levels at delivery or any other outcome variable.

In the follow-up study, participants were seen at 4, 6, and 8 months of age for infant-controlled visual habituation sessions augmented with heart-rate (HR) measures. Infants were then seen at 12 and 18 months of age for free-play sessions in which looking to objects was measured during a single-object session and in which distractibility was measured during both single- and multiple-object exploration sessions. The blind was broken at the point of the 18-month assessment, but experimenters and observers coding tapes from that final session were in fact functionally blind to the infants' experimental condition and DHA status.

Habituation Sessions (4, 6, and 8 Months)

Procedure

Infants were tested in a 3 m × 3 m room, in which a 0.7 m × 0.7 m rear-projection screen was centered on the front wall. Infants were placed in a car seat 0.8 m from the screen. A Panasonic video camera set at the base of the screen sent an image of the infant's face to a television that was monitored for online recordings by observers. This image was also recorded for archival and reliability purposes. Observers recorded looks online by pressing buttons that were interfaced with a microcomputer that timed looks and controlled the slide projectors. This computer also sent signals to the HR data-acquisition package interface (see the following).

Infants were habituated to stimuli using an infant-control sequence (e.g., Colombo, Shaddy, Richman, Maikranz, & Blaga, in press), with a criterion of two consecutive looks at a 50% decrement from the previous longest look. Looks were considered valid if they were 1 s or longer in duration and were terminated if interrupted for 1 s or more by a look away (Colombo & Horowitz, 1985). When looks were terminated, a dark interstimulus period of 2 s was administered, and the stimulus was then presented for the next trial. A floating-point criterion was used in which the habituation criterion was recalculated if longer looks were encountered later in the habituation sequence (see Colombo & Mitchell,

1990). Reliability for such sessions is typically high; in a large study conducted at the same time as this one and with the same observers, Pearson correlations computed between online and reliability observers within each individual session averaged +.96.

A paired-comparison novelty-preference phase followed habituation in which the familiarized stimulus was simultaneously paired with a novel stimulus in two choice trials administered until infants accumulated predetermined amounts (5 to 10 s, depending on the age tested) of looking to stimuli. An opposite-gender stimulus from the stimulus pair selected for habituation (see the following section) served as the novel stimulus. Infants successfully recognized stimuli at the two older ages, but such discrimination did not vary as a function of the infant's or mother's DHA status. Look duration and novelty preference may, in fact, correlate under conditions in which familiarization is constrained, but in the infant-control procedure used here, infants were allowed ad libitum familiarization; as such, we would expect that recognition performance would be dissociable from attentional functions that form the core basis of this report. The results from the recognition test are thus not considered further in this report.

Stimuli

Stimuli were color slides of children's faces chosen from a larger pool used in Colombo et al. (in press). There were a total of six faces, organized into three pairs varying in ethnicity (African American, Hispanic, and Caucasian) and each pair was composed of a male and a female. During habituation, one of the faces from the chosen pair was rear-projected at midline (25° visual angle). No infant ever saw a face more than once, and the presentation of each stimulus pair was balanced across ages. The gender of the pair presented during habituation was selected randomly for the first visit, and it was alternated at each subsequent testing.

Measurement and Reduction of HR

The electrocardiogram (EKG) was acquired with shielded Ag-AgCl electrodes placed in a triangular configuration on the infants' abdomen and digitized (250 Hz sample rate) through the use of a commercially available data-acquisition package interface (BioPac Inc., Santa Barbara, CA). EKG recording was synchronized with stimulus events and the coding of fixations. Time codes for R waves were obtained

from the digitized EKG and interspersed with time codes from stimulus events (slide onsets and offsets) and infant behaviors (look onsets and offsets) to provide a complete sequential record of the infant's session. The sequential file was then analyzed with custom software that parsed infants' looking into categories of orienting (OR), sustained attention (SA), and attention termination (AT) based on Richards's (1985) framework for defining different phases of attention from HR.

OR is the period during looking that precedes the attainment of a stable HR deceleration during the look. SA is a period of sustained HR deceleration during infant looking and is most closely identified with active stimulus encoding or processing. AT is the period of looking during which the look persists but after which the characteristic HR deceleration has ended; it has been most closely identified with the construct of attentional disengagement. As noted earlier, infants' HR during each trial was parsed into the percentage of time spent in each of these phases during looking.

Toddler Attention Assessments (12 and 18 Months)

Procedure

At all three ages, children received a single-object attention task and a distractibility task embedded in the context of free-play episodes. The order of tasks was constant across age, with the single-object task administered first and the distractibility assessment administered second. Irrespective of task or age, infants were seated on their parent's lap at a table, and parents were asked to refrain from talking and interacting so that their child would freely explore the stimuli. Task durations were timed with a hand-held stopwatch, but variables for analysis were derived from coding of videotapes made of each of the sessions. All sessions were recorded using a Panasonic camcorder, and a time-date generator displayed elapsed time (accurate to 0.1 s) on the videotapes for coding purposes. Coders viewed toddlers' sessions on a large Panasonic monitor and used a jog-shuttle dial on a Panasonic VCR to identify points in time while coding.

Single-object task. In the single-object, free-play task, we assessed toddlers' attention to a complex electronic toy: a V-Tech[®] Nursery Rhyme toy at 12 months, and a V-Tech[®] See-Me-Drive toy at 18 months. Each object had multiple buttons and functions to explore, and toddlers could manipulate the toy to produce interesting visual and auditory effects. The toddler was seated at a table; the toy was

presented to the toddler for 5 min and the toddler was allowed to explore it freely and to manipulate it. The experimenter placed the toy in front of the toddler and encouraged the child to play with a standard script ("[Child's name], look at this toy. There are lots of fun things you can do with this toy. Can you play with this toy? Let me turn it on for you.").

Distractibility assessment. In this procedure, we assessed toddlers' ability to maintain attention to a target object in the context of a competing stimulus. The toddler distractibility session was designed to be similar to distractibility assessments used with both infants (e.g., Oakes & Tellinghuisen, 1994) and children (e.g., Anderson, Choi, & Lorch, 1987; Choi & Anderson, 1991). There were four 3-min episodes (one with each of four developmentally appropriate toys) at each of the two ages. For 12-month-olds, the four target toys included stacking rings, a kaleidoscope sphere that contained mirrored sections and colorful beads, a set of magnetic stacking blocks, and a complex spinning toy that contained multiple colorful components for the infant to spin. For 18-month-olds, the four target toys included nesting cars; a five-component pop-up toy; a lock-and-key garage set with three vehicles; and three minispheres, which contained mirrored sections and colorful beads, in a container. All toys contained manipulable parts and were capable of producing interesting effects.

The distractors were recorded on a videotape and consisted of 7-s segments of a children's television program with intervals of black, blank tape between the television segments. Distractors were presented on a Panasonic 0.75 m (26 in.) monitor located 1 m away from the toddler and at a 45° angle. A mirror located on the wall behind the child reflected the presence of the distractor so that its onset and duration could be recorded for coding purposes. As in Anderson et al. (1987), the intervals of blank tape ranged from 5 s to 25 s, (e.g., 5-, 10-, 15-, 20-, and 25-s intervals), and the order of these intervals was randomly determined.

For the distractibility assessments, the child remained seated at the same table used for the single-object task (see the earlier description). The experimenter introduced each toy and encouraged the child with a standard script ("[Child's name], look at this toy. Can you play with this?") while demonstrating a feature of the toy (e.g., making a cylinder spin on the spinning toy, stacking the nesting cars). At the end of each free-play period with a toy, the experimenter praised the child ("You did a great job playing with that toy. Let me get you a new one."), paused the VCR, collected the toys, and then began

the next period. Toddlers were allowed to manipulate the toys freely, and the experimenter kept her interactions with the child to a minimum.

Videotape Coding

Single-object task. For each infant, coders recorded the time displayed on the videotape at the start and end of each look to the toy and each look away from the toy (i.e., inattention). As a result, it was possible to calculate a mean duration for looks to the toy and to count the number of episodes of inattention (i.e., the number of times toddlers looked away from the toy). Reliability for each behavior was assessed by correlating the duration of each look, or episode, of inattention as recorded by the two coders. At each age, for each task, two coders recorded the behavior for at least 25% of the sample coded for that measure. The average interobserver reliability was .99 for duration of individual looks at both 12 and 18 months, and .98 for durations of individual episodes of inattention at both 12 and 18 months.

Distractibility variables. Three variables were derived from coding in the distractibility task: (a) the percentage of distractors to which the toddler turned away from the target toy, (b) the latency to turn from the target toy to the distractor, and (c) the duration of looking to the television/distractor. For distraction latencies, the average interobserver reliability was .99 at both 12 and 18 months. For duration of looking at the television/distractor, reliability was .96 at both 12 and 18 months.

In addition, coders used established procedures to judge each child's attentional state at the onset of each distractor (e.g., Oakes, Kannass, & Shaddy, 2002; Oakes & Tellinghuisen, 1994; Tellinghuisen, Oakes, & Tjebkes, 1999). Specifically, coders judged whether toddlers were either in a state of casual attention (defined as looking at the toy but not engaged in active learning) or focused attention (defined as engaged in concentration and active learning). A third scoring category was used when the child looked at something other than the target toy (e.g., the experimenter, mother, or video monitor). Coders used a combination of facial cues (e.g., furrowed brow, pursed lips), gaze direction, and manipulation to determine whether the child was in a state of focused, concentrated attention to the toy. Researchers have reliably coded these states of attention and have successfully used it as an indicator of attention and learning (e.g., Oakes, Madole, & Cohen, 1991; Oakes & Tellinghuisen, 1994; Ruff, 1986). Two observers coded each child's attentional state at the onset of each distractor presentation; the

average agreement was 87.6% at 12 months and 91.5% at 18 months, with agreement ranging from 80% to 100%. All disagreements between observers were resolved by attaining consensus, and resolved codings were used in the final analyses. These data allowed us to examine the measures of distractibility as a function of attentional state.

Results

Preliminary Analyses

Preliminary analyses indicated no effects of infant gender or stimulus on infant behavior in any of the attentional follow-up sessions. The method for determining RBC phospholipid DHA is described in Smuts et al. (2003). Owing to the relatively small follow-up sample, the modest reliability of infant measures, and uncertainty about any threshold of effect of DHA, we split the sample at the median for both maternal and infant RBC DHA levels at delivery and examined the effects of high and low delivery RBC DHA as a function of group membership. For maternal DHA, the median was 5.35 g DHA per 100 g of fatty acid; for infant DHA, the median was 7.46 g DHA per 100 g of fatty acid. These medians were drawn from the entire sample described in Smuts et al., but we were reassured to find that these were also the medians for the infants enrolled in the follow-up study. For 4 infants enrolled in the follow-up study, data on maternal DHA at delivery were not available. We imputed their maternal DHA levels from available data on maternal DHA levels at enrollment and infant DHA levels at delivery, and a regression equation derived from the entire RCT sample of 350 infants. Both maternal DHA at enrollment and infant DHA at delivery contributed significant ($p < .001$) independent variance to this prediction, and the R for the overall model as .764.

When categorized into high- and low-DHA groups, infant RBC DHA level was unrelated to subsequent attentional measures, but maternal RBC DHA was consistently predictive of later attentional outcomes (see also Willatts et al., 2003). Having classified infants in this way, it was important to determine whether the high- and low-DHA groupings for maternal DHA were contaminated or correlated with any other variables in the data set relating to demographics, medical history, or participation in the supplementation trials. Table 2 presents the results of these analyses; none of these variables covaried with the designation of high- and low-DHA groups as constructed from maternal DHA levels at delivery.

Table 2
Means (and Standard Deviations) of Potential Covariates of High- and Low-Maternal-DHA Groups

Variable class	Variable	Maternal DHA group		Test statistic
		Low	High	
Demographic	Mother's education	11.47 (1.0)	12.03 (1.3)	1.94
	Father's education	11.68 (0.9)	12.06 (1.7)	1.09
Demographic	Race			
	African American	21 (67%)	33 (87%)	
	Hispanic	1 (2%)	0 (0%)	4.23
	Caucasian	10 (31%)	5 (13%)	
	Gender (female)	12 (38%)	15 (41%)	0.07
Medical	Gestation length (weeks)	39.16 (1.2)	39.39 (1.5)	0.69
	Apgar score (1 min)	8.09 (1.1)	7.82 (1.5)	0.87
	Apgar score (5 min)	8.97 (0.2)	8.66 (0.9)	1.97
	Birth weight (g)	3191 (365)	3296 (414)	1.12
	Length (cm)	50.21 (2.2)	50.92 (2.4)	1.29
	Head circumference (cm)	33.42 (1.1)	34.02 (1.6)	1.84
	Premature (≤ 37 weeks gestation)	4 (12%)	3 (8%)	0.41
	Study	Randomized group (supplemented)	16 (52%)	22 (58%)
Postnatal	Prenatal DHA supplementation (mg)	7785 (6598)	8463 (5565)	0.46
	Any report of breastfeeding (yes - no)	4 (12.5%)	4 (10.5%)	0.67
	Weeks of breastfeeding	1.80 (6.5)	4.79 (13.5)	1.14

Note. DHA = docosahexaenoic acid. For continuous variables, means (and standard deviations) are reported and a t statistic is used. For categorical variables, number (and percentage) of each group is reported per category, and a χ^2 statistic is used. None of the test statistics attains the $p \leq .05$ level of significance.

Analyses of Follow-up Habituation Sessions

Look Duration

Fifty of the 70 infants (71%) enrolled in the follow-up study provided valid data at each of the three time points for the infant-controlled habituation sessions. Past research (e.g., Colombo & Mitchell, 1990; Colombo, Mitchell, O'Brien, & Horowitz, 1987) has indicated that the peak look duration from the habituation sequence is the most robust indicator of both individual and developmental differences in attention. As noted earlier, the normative course for look duration is a decline across much of the 1st year (see Colombo & Mitchell, 1990; Colombo et al., in press), with briefer looking associated with advantages in both concurrent and lagged measures of cognition (Colombo, 1993, 2002, in press).

An Age (4, 6, and 8 months) \times DHA (high vs. low maternal DHA) mixed-design multivariate analysis of variance (MANOVA) was performed on the peak look duration from the habituation sessions. A significant main effect emerged for age, $F(2, 47) = 7.32$, $p < .01$, as the duration of peak look declined with age. In addition, the two-way interaction attained significance, $F(2, 47) = 3.55$, $p < .05$. As Figure 1 shows, infants in the high-maternal-DHA group

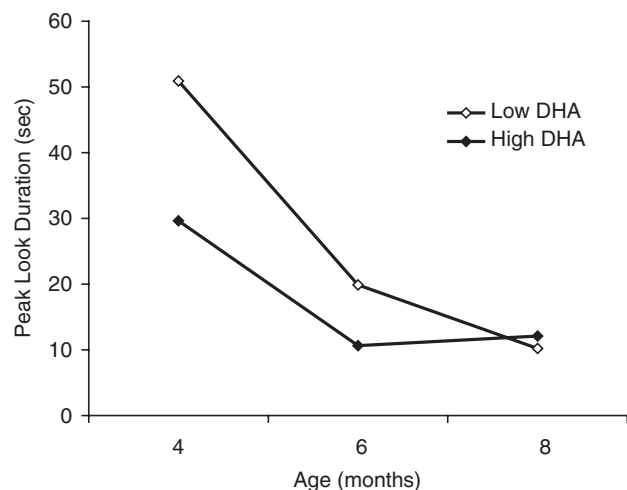


Figure 1. Developmental course of look duration for infants born to mothers with high and low maternal docosahexaenoic acid (DHA) at delivery.

showed an accelerated developmental pattern in looking from 4 to 6 months of age relative to the low-maternal-DHA group, although by 8 months of age the groups were equivalent. Follow-up tests indicated that the high-DHA group showed a decline in look duration from 4 to 6 months ($p < .001$) but a

plateau thereafter (the change from 6 to 8 months was not statistically significant). Analyzed another way, the developmental course for this group was characterized by a significant ($p < .05$) linear trend and a very strong quadratic ($p < .001$) trend. However, the low-DHA group declined from 4 to 6 months ($p < .05$) and then further from 6 to 8 months ($p < .01$). Thus, this group's developmental course was best characterized by a simple linear component ($p < .01$).

HR-Defined Phases of Attention

As noted earlier, infants' HR was measured during the habituation session and parsed into HR-defined phases of attention as initially defined by Richards (1985) and described in Colombo, Richman, Shaddy, Greenhoot, & Maikranz, (2001) and in Colombo et al. (in press). Complete scorable HR protocols were available for 46 of the 50 infants who had complete behavioral data from the longitudinal habituation sessions. For this analysis, we examined the percentage of time spent in each of the phases, which represented the composition of these different phases within infant looking irrespective of look duration. The developmental courses for these phases over the 1st year have been recently described in Colombo et al. (in press). The percentage of time spent in SA tends to decrease from the middle to the end of the 1st postnatal year, and this likely reflects improvements in the efficiency of encoding. Perhaps as a result of this change in SA, the percentage of time spent in OR tends to increase across these ages. The percentage of time spent in AT tends to decrease; this reflects infants' increasing facility to inhibit looking or disengage attention after active processing has ended. Thus, the more mature pattern of HR-defined phases is increasing percentages of OR and decreasing percentages of SA and AT.

We analyzed the percentage time for each phase separately in Age (3) × DHA Group (2) MANOVAs. The main effect of age attained statistical significance ($p < .001$) for each attentional phase, with $F_s(2, 43) = 27.28$ for OR, 14.32 for SA, and 14.98 for AT. The directions of change for each variable mirrored the developmental trends described earlier, with percentage of time spent in OR increasing and percentage of time in both SA and AT decreasing. However, significant main effects emerged for DHA group for percentage of time looking spent both in OR, $F(1, 44) = 4.75, p < .05$, and in SA, $F(1, 44) = 4.34, p < .05$. There were no main effects or interactions involving DHA group for AT. Figure 2 shows the age trends for the three phases broken out for the two

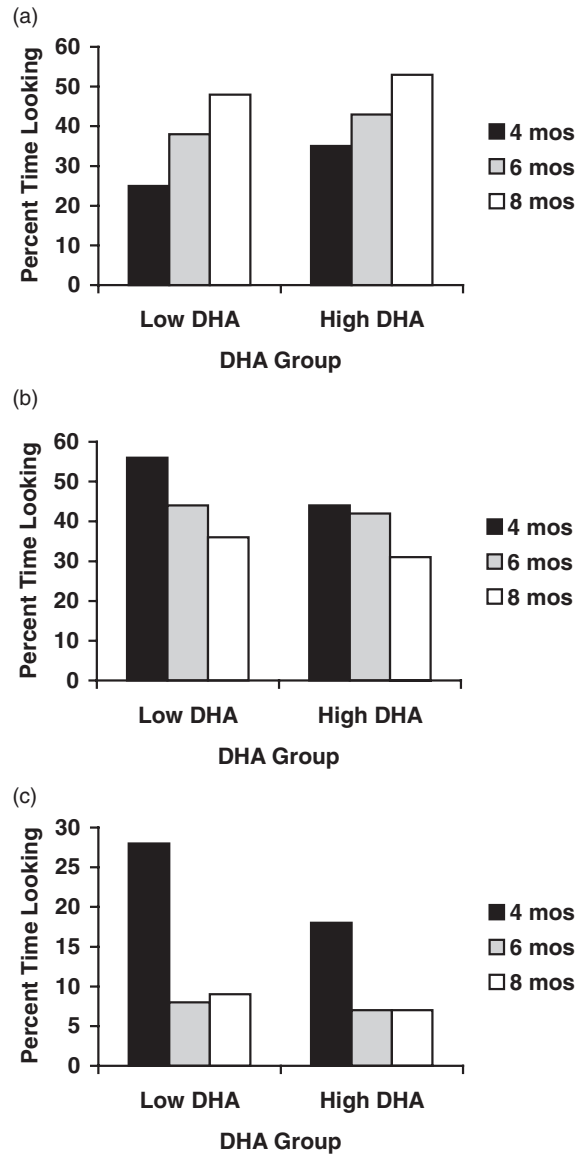


Figure 2. Heart-rate-defined phases of attention for the high- and low-docosahexaenoic-acid (DHA) groups: (a) percentage of time spent looking in orienting, (b) percentage of time spent looking in sustained attention, and (c) percentage of time spent looking in attention termination.

DHA groups. Looking in the high-DHA group was composed of more OR and less SA than that of the low-DHA group.

Summary

Both the behavioral and psychophysiological data suggest that infants whose mothers had higher levels of DHA at birth showed accelerated developmental courses in attention across the 1st year. The decline in look duration reached asymptote earlier for the high-

DHA group, and the composition of attentional components that constitute looking in that group was consistently concordant with patterns seen at older ages. However, the two groups were basically equivalent at 8 months on these measures.

Analyses of Toddler Sessions

Fifty-eight infants returned for the 12-month session ($M = 53.1$ weeks, $SD = 2.2$), and 49 toddlers returned for the 18-month session ($M = 79.1$ weeks, $SD = 3.1$). Two toddlers were excluded because of experimenter error; therefore, there were 47 toddlers (29 males, 18 females) who returned for both sessions. For the distractibility task, 8 toddlers were excluded for parental interference ($n = 1$), fussiness ($n = 2$), parental report of possible hearing problem ($n = 1$), and technical problems ($n = 4$).

Maternal DHA and Single-Object Attention

As noted previously, increased looking time is expected during the 2nd year (Colombo, 2002; Colombo, Harlan, & Mitchell, 1999), and the longer looking during the 2nd year is associated with more positive outcomes (Ruff & Rothbart, 1996).

Episodes of inattention. The number of episodes of attention and the average length of looks to the target toy from the single object task were entered into separate Age (12 and 18 months) \times Maternal DHA (high vs. low) mixed-design MANOVAs. The analysis on the number of inattention episodes revealed only a marginal main effect for age, $F(1, 45) = 3.00$, $p = .09$, as 18-month-olds tended to look away slightly more frequently ($M = 12.6$ times, $SD = 5.9$) than did 12-month-olds ($M = 11.1$ times, $SD = 5.4$). No other significant terms emerged.

Duration of looking to target toy. The analysis on average length of looking to the target toy, however, revealed a significant Age \times Maternal DHA interaction, $F(1, 45) = 4.56$, $p < .05$ (see Figure 3). For toddlers in the high-DHA group, looking levels were low at 12 months and increased between 12 and 18 months, although this change was not significant, $t(26) = 1.22$, ns ; this pattern of attention is consistent with the normative developmental trajectory. However, for toddlers in the low-DHA group, 12-month looking levels were initially high and decreased between 12 and 18 months, $t(19) = 1.89$, $p = .07$. Follow-up analyses revealed a difference ($p = .05$) between the average length of individual looks for toddlers of mothers with high and low DHA at 12 months, although differences at 18 months were not significant.

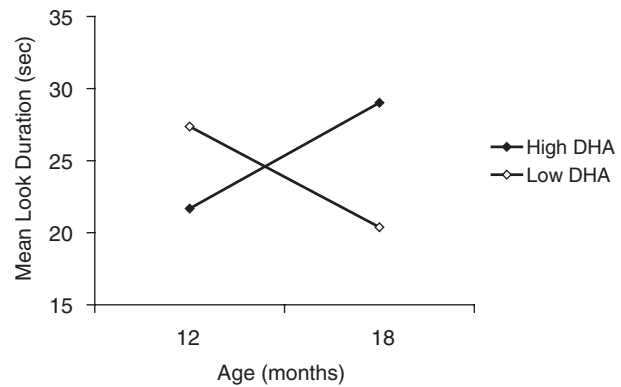


Figure 3. Developmental course of look duration during single-object, free-play sessions at 12 and 18 months as a function of high and low maternal docosahexaenoic acid (DHA) at delivery.

Maternal DHA and Distractibility

We used three indicators of distractibility to assess toddlers' performance in the distractibility task: the percentage of turns to the distractor (i.e., the percentage of times toddlers turned to the distractor when it appeared on the television), distraction latencies during focused and casual attention, and duration of looking to the distractor.

Percentage of turns to the distractor. The percentage of turns to the distractor was also analyzed with an Age \times Attentional State \times Maternal DHA MANOVA. A significant main effect of age, $F(1, 37) = 7.08$, $p < .05$, and a marginally significant main effect of attentional state, $F(1, 37) = 2.82$, $p = .10$ were qualified by a significant Age \times Attentional State interaction, $F(1, 37) = 4.43$, $p < .05$. At 12 months, there were no differences between percentage of toddlers' turns to the distractor as a function of either focused ($M = 37.4\%$, $SD = 24.8$) or casual ($M = 35.4\%$, $SD = 30.6$) attention. However, at 18 months, toddlers turned to the distractor less often ($p < .05$) during periods of focused attention ($M = 43.5\%$, $SD = 25.6$) than they did during periods of casual attention ($M = 54.48\%$, $SD = 29.71$). The analysis also revealed a marginal effect of maternal DHA, $F(1, 37) = 3.37$, $p = .07$ (see Figure 4a); toddlers of high-DHA mothers tended to turn less frequently to the distractor ($M = 37.7\%$, $SD = 26.2$) than did those of low-DHA mothers ($M = 49.2\%$, $SD = 30.2$).

Latencies of turning to distractor. Distraction latencies during focused and casual attention were entered into an Age (12 vs. 18 months) \times Attentional State (casual vs. focused attention) \times Maternal DHA (high vs. low) mixed-design MANOVA. Fourteen toddlers were excluded from this first analysis because they did not contribute data to each of the four

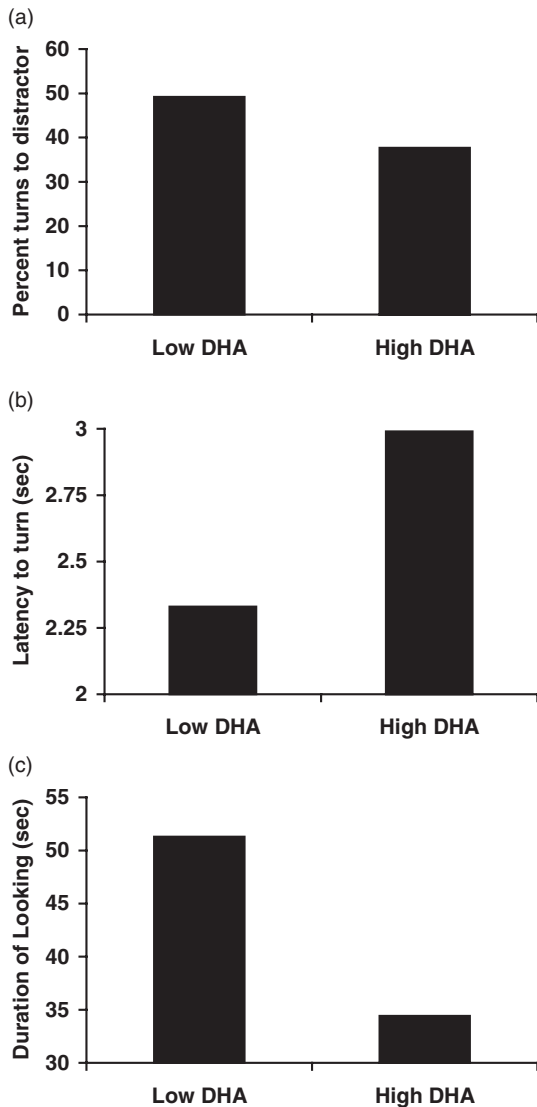


Figure 4. Distractibility indexes for high- and low-docosahexaenoic-acid (DHA) infants. Values reflect main effects for DHA group membership, averaged across 12 and 18 months: (a) percentage of turns to the distractor ($p = .07$), (b) latency to turn to the distractor ($p < .05$), and (c) duration of looking to the television/distractor ($p < .05$).

cells. The analysis revealed a main effect of maternal DHA, $F(1, 23) = 4.22$, $p = .05$, as high-DHA infants had overall longer latencies than low-DHA infants. However, this main effect was qualified by an Attentional State \times Maternal DHA interaction, $F(1, 23) = 4.83$, $p < .05$; toddlers of high-DHA mothers had longer ($p < .01$) latencies during focused attention ($M = 3.2$ s, $SD = 1.7$) than did toddlers of low-DHA mothers ($M = 2.1$ s, $SD = 0.7$), but there were no differences between latencies during periods of casual between the high-DHA group ($M = 2.4$ s, $SD = 1.0$) and the low-DHA group ($M = 2.2$ s, $SD = 1.2$).

High-DHA toddlers therefore showed differentiation in the quality of their attention, being less distractible during states of focused attention. However, low-DHA toddlers performed equivalently whether they were in focused or casual attention at the point when the distractor appeared. No other statistically significant terms emerged from this analysis.

This initial analysis was interesting but disadvantaged by the fact that so many infants were excluded. Exclusions were generally due to a lack of casual attention during the distractibility assessment, which precluded entry into the factorial MANOVA. As such, we conducted a secondary analysis in which latencies were examined only during periods of focused attention in an Age (2) \times Maternal DHA (2) MANOVA. This made theoretical sense, given that focused attention presumably reflects a higher quality of focus than casual attention. It also makes practical sense, however, as only 2 toddlers (rather than 14) were excluded from the analysis. We first analyzed whether the high- and low-maternal-DHA groups varied in terms of the percentage of times they were coded to be in focused attention: They were not different. Both groups were engaged in focused attention most of the time, with means of 74.14% ($SD = 13.4$) for toddlers in the high-DHA group and 67.42% ($SD = 19.3$) for toddlers in the low-DHA group; differences between these groups were not statistically different. This accomplished, we observed that the basic outcome of the prior analysis on distraction latencies was upheld (see Figure 4b). The analysis revealed only a main effect of maternal DHA, $F(1, 35) = 4.16$, $p < .05$, as toddlers from high-DHA mothers had longer latencies to turn to distractors ($M = 2.99$ s, $SD = 1.48$) than did toddlers of low-DHA mothers ($M = 2.33$ s, $SD = 1.19$).

Duration of looking to the television/distractor. Finally, the duration of looking toward the television/distractor during the distractibility session was entered into an Age \times Attentional State \times Maternal DHA MANOVA. This analysis yielded only a significant main effect of maternal DHA, $F(1, 37) = 4.17$, $p < .05$, with toddlers of high-DHA mothers looking at the television/distractor less ($M = 34.42$ s, $SD = 27.37$) than toddlers of low-DHA mothers ($M = 51.30$ s, $SD = 34.98$).

Summary

Collectively, the analyses on the attention and distractibility data during toddlerhood consistently suggest that toddlers of mothers with higher levels of DHA at birth showed more mature developmental

profiles on single-object attention measures and more optimal performance on distractibility assessments than toddlers from mothers with lower DHA.

Discussion

Caution is warranted before a review and interpretive analysis of the results of this study. The focus of this research was the association between maternal DHA levels taken at delivery and the subsequent development of attentional function in infants across the first 2 years of life. The sample was obtained from an RCT of prenatal DHA supplementation during the third trimester of pregnancy, but the DHA supplementation did not affect maternal DHA levels. Thus, the study must be regarded as correlational rather than experimental. Further research will undoubtedly be aimed at manipulating maternal DHA levels more directly in an effort to document a more causal path between DHA and early cognitive function. Despite the fact that the high- and low-DHA groups did not vary on any of the ancillary demographic or medical variables we analyzed (aside from DHA levels *per se*), the results should be interpreted with these design considerations in mind.

That being said, the analyses of attentional outcomes as a function of naturally occurring DHA levels were remarkably consistent. Analyses of several variables showed that infants' classification as being from either a mother with high or low RBC DHA at delivery predicted the differences in the developmental course of attentional variables from habituation measures taken during the 1st year of life and predicted developmental advantages in several attentional measures taken in the 2nd year. In each case, higher levels of DHA were associated with more optimal performance on the outcome measures.

As noted earlier, look duration declines with age during the 1st year of life. On such measures, infants from mothers with high DHA showed an accelerated developmental profile for look duration, with the characteristic decline in looking evident between 4 and 6 months of age, and a plateau evident from 6 to 8 months. Infants from mothers with low DHA, however, started out at a higher level of looking at 4 months but showed a more deliberate decline in look duration, continuing to drop from 4 to 6 months, and then from 6 to 8 months as well. Furthermore, analyses of HR-defined phases of attention (Richards, 1985; Richards & Casey, 1992) taken during the habituation sessions indicated that high-DHA infants showed less SA and more OR across all ages tested, a

profile characteristic of older infants who are more efficient at visual processing or encoding. It is interesting that AT was unaffected, suggesting that the DHA effects may be limited to processing *per se* and not to the inhibition of looking (i.e., attentional disengagement) that AT presumably represents (see Colombo et al., 2001).

Although differences between the high- and low-DHA groups on the habituation measures disappeared at 8 months, measures of endogenous attention revealed that differences between the groups persisted into the 2nd year. Two tasks were administered in which infants' maintenance of attention to a focal object were measured. In one, we measured attention in the absence of salient, competing stimuli; in the other, we measured attention in the face of intermittent and salient distractors. In the single-object task, one would expect a tendency toward increased look duration, which might reflect improved ability to maintain attention to the task at hand. Indeed, that pattern emerged in the data from toddlers of high-DHA mothers. However, toddlers from low-DHA mothers showed a negative slope of change from 12 to 18 months. On the distractibility assessment, toddlers from high-DHA mothers performed consistently better than did those from low-DHA mothers: They tended to turn less to the distractor when it was activated, and when they did turn to the distractor, their latencies were significantly longer and they spent less time overall looking at the distractor or its source during the session. Finally, high-DHA infants showed differentiated performance in distractibility as a function of casual versus focused attention whereas low-DHA infants did not.

Overall, the results may be succinctly summarized as indicating some developmental advantages in attention for infants whose mothers had higher DHA at delivery. These findings are in accord with other research on DHA intake and infant cognition and attention (Carlson & Werkman, 1996; Forsyth et al., 1998; Reisbick et al., 1997; Werkman & Carlson, 1996; Willatts et al., 1998a, 1998b; Willatts et al., 2003). The novel and significant contribution of these findings is its comprehensive developmental approach to assessment across the 1st and 2nd years, and the documentation that higher DHA levels are associated with more optimal or developmentally advanced attentional performance across the entire period of infancy. The effects observed here are not particularly strong or large, which might be expected given the correlational nature of the study and the presumed impact of a single variable on long-term outcomes.

An interesting aspect of these data is the transition in the DHA effects seen from the 1st- to 2nd-year measures of attention. Many past studies of DHA and other LC-PUFA effects show transient effects, in which initial developmental advantages for the supplemented groups dissipate at later ages. This has sometimes been taken to suggest that the effects of supplementation or individual differences are less important. It is worth noting, however, that a developmental systems perspective holds that even such transient advantages may actually be important in the long run (see Colombo, 2001b). The current data support this latter position to some degree, as advantages seen in the high-DHA group on habituation protocols during the 1st year disappear by 8 months of age but then reappear in the 2nd year. This pattern of observations may be a function of the developmental appropriateness of the measures, or it may truly reflect some developmental cascade in which an early developmental advantage in one cognitive domain gives rise to advantages in other, higher order domains.

In summary, the current results are concordant with mounting evidence of associations between DHA and the status of cognitive function in infancy and early childhood. As noted earlier, future work should seek to document these effects within a more causal framework. Two points should be addressed with specific priority: The first would be the demonstration that maternal DHA can be affected by supplementation during pregnancy, either through a longer period or through a higher dosage of supplementation. The second would be an investigation as to why infant DHA levels were not predictive of infant postnatal outcomes; this is the second study in which this finding has been reported (see also Willatts et al., 2003), and therefore it appears to be a phenomenon worthy of investigation.

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