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Omega-3 Fatty Acids in Boys With Behavior, Learning, and Health Problems

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STEVENS, L. J., S. S. ZENTALL, M. L. ABATE, T. KUCZEK AND J. R. BURGESS. *Omega-3 fatty acids in boys with behavior, learning, and health problems.* PHYSIOL BEHAV **59**(4/5) 915–920, 1996.—The purpose of the study reported here was to compare behavior, learning, and health problems in boys ages 6 to 12 with lower plasma phospholipid total omega-3 or total omega-6 fatty acid levels with those boys with higher levels of these fatty acids. A greater frequency of symptoms indicative of essential fatty acid deficiency was reported by the parents of subjects with lower plasma omega-3 or omega-6 fatty acid concentrations than those with higher levels. A greater number of behavior problems, assessed by the Conners' Rating Scale, temper tantrums, and sleep problems were reported in subjects with lower total omega-3 fatty acid concentrations. Additionally, more learning and health problems were found in subjects with lower total omega-3 fatty acid concentrations. (Only more colds and more antibiotic use were reported by those subjects with lower total omega-6 fatty acids.) These findings are discussed in relation to recent findings for omega-3 experimentally deprived animals.

Essential fatty acids   Omega-3 fatty acids   Childhood behaviors
Attention deficit-hyperactivity disorder (ADHD)   Polydipsia   Learning

TWO types of fatty acids are considered essential. Omega-3 (ω-3) and omega-6 (ω-6) fatty acids cannot be synthesized in the body, and as such, must be obtained from the diet. Linoleic acid, an omega-6 fatty acid, and linolenic acid, an omega-3 fatty acid, can undergo carbon chain elongation and desaturation to form longer and more highly polyunsaturated fatty acids, such as dihomogammalinolenic acid (DGLA) (20:3ω-6), arachidonic acid (AA) (20:4ω-6), eicosapentaenoic acid (EPA) (20:5ω-3), and docosahexaenoic acid (DHA) (22:6ω-3) (14). These fatty acids are major structural components of membrane phospholipids, serve as precursors to the biologically active eicosanoids, and influence membrane fluidity and ion transport across cell membranes (14). The omega-6 fatty acids are distributed evenly in most mammalian tissues, while the omega-3 fatty acids are concentrated in a few tissues including brain (26,33).

Deficiency of essential fatty acids (EFA) in mammals is known to lead to reduced growth and increased infertility, as well as to a variety of health symptoms including dry, scaly skin, polydipsia, and polyuria (9). Omega-6 fatty acids are known to be essential for growth and reproduction (9,10). The consequences of omega-6 fatty acid deficiency cannot be totally reversed by omega-3 fatty acid supplementation (19). On the other hand, evidence is accumulating that omega-3 fatty acid deficiency leads to unique symptoms, which may include behavioral problems (15,30).

Studies in animals have indicated both common and distinct symptoms of omega-3 fatty acid deficiency in comparison with omega-6 fatty acid deficiency. Rats fed an omega-3 fatty acid deficient diet had abnormal electroretinograms (7,8) and reduced learning in new environments (perhaps due to reduced visual acuity) (8,15,21). In monkeys fed a pre- and postnatal diet deficient in omega-3 fatty acids, researchers found that the deficient monkeys had lower levels of omega-3 fatty acids in plasma, red blood cells (RBCs), the cerebral cortex, and in the retina (13). Furthermore, the deficient monkeys drank more fluids and excreted more urine and feces (28,29). They also had reduced visual acuity and abnormal electroretinograms (27). In a recent study, home cage behavior was studied in omega-3 fatty acid deficient monkeys (30). These monkeys showed more bouts of stereotyped behavior and increased total locomotion.

In humans, the relationship between omega-3 fatty acid status and behavior is difficult to study experimentally through dietary manipulations. A few case studies of essential fatty acid deficiencies have been reported in humans receiving either total parenteral nutrition or gastric tube feedings (5). Symptoms of deficiency included impaired visual acuity, neurological dysfunction,

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and dermatitis. These symptoms disappeared when feedings were supplemented with oils containing both omega-3 and omega-6 fatty acids. Several descriptive investigations have been reported examining the relationship between behavioral disorders in children and EFA status. Among the behavioral disorders exhibited by children, attention deficit/hyperactivity disorder (ADHD) is one of the most prevalent, affecting 3–5% of the school-age population. Children with ADHD are chronically impulsive, inattentive, and overactive (1). This disorder is believed to be multifactorial, with both genetic and environmental etiologies (3,39). Among the factors assessed, essential fatty acid status is one that may have both genetic and environmental origins (11,24).

In 1981, researchers first hypothesized that children with hyperactivity might have reduced nutritional status of EFA because they showed greater thirst compared to children without hyperactivity (11). In 1987, researchers documented that 48 children with hyperactivity reported significantly greater thirst, more frequent urination, and more health and learning problems than children without hyperactivity (24). Significantly lower plasma levels of two omega-6 fatty acids, dihomogammalinolenic and arachidonic acids, and one omega-3 fatty acid, docosahexaenoic acid, were found in the subjects with hyperactivity.

In initial studies comparing plasma phospholipids levels in 53 boys with ADHD to a control group of 43 boys without ADHD, we found significantly lower levels of arachidonic acid, EPA, DHA, and total omega-3 fatty acids (32). Also, significantly lower levels of arachidonic acid and adrenic acid (22:4n-6) but higher levels of 22:5ω-6 were observed in red blood cells (RBCs) of the subjects with ADHD compared with subjects without ADHD. Overall, approximately 40% of the subjects with ADHD had a greater frequency of symptoms indicative of EFA deficiency (increased thirst, frequent urination, high fluid consumption, and dry hair), relative to 9% of subjects without ADHD.

Both of the investigations described above have grouped subjects by behavioral rather than physiological status, whereas recent animal research provides experimental groupings based on physiological status (30). Thus, we propose to assess the generality of our research with children to the research using rats and monkeys by running a parallel analysis (i.e., by grouping subjects on levels of total omega-3 and total omega-6 fatty acids). This will document the extent to which our findings parallel those reported with omega-3–deficient monkeys and should reveal whether more specific behavioral and learning variables can provide more sensitive outcome measures than an overall criterion behavioral score (Conners' Hyperactivity Index) as used in prior work (24,32). Additionally, we will extend current findings in animal and human research by examining physiological groupings based on total omega-6 fatty acids.

TABLE 1

CONNERS' PARENT RATING SCALES

Hyperactivity Index:	*Conduct Scale:*
Excitable, impulsive	Sassy to grownups
Cries easily or often	Chip on shoulder
Restless in squirmy sense	Destructive
Restless, always up and on the go	Denies mistakes, blames others
Destructive	Quarrelsome
Fails to finish things	Bullies others
Distractibility	Fights constantly
Mood changes	Basically an unhappy child
Easily frustrated	
Disturbs other children	
Impulsive-Hyperactive Scale:	
Excitable, impulsive	
Wants to run things	
Restless in squirmy sense	
Restless, always up and on the go	
Psychosomatic Scale:	*Anxiety Scale:*
Headaches	Fearful
Stomachaches	Shy
Other aches and pains	Worries more than others
Vomiting or nausea	Lets self be pushed around
Learning Scale:	
Difficulty in learning	
Fails to finish things	
Distractibility	
Easily frustrated in efforts	

From Conners' Parent Rating Scale-48. Conners, C.K. Conners' rating scale manual. North Tonawanda, NY: Multi-Health Systems, Inc.: 1990.

METHOD

Subjects

One hundred volunteers from north central Indiana were recruited by newspaper, radio, and television announcements seeking healthy boys, ages 6 to 12, with and without ADHD for a study of various nutritional factors and behavior. Pamphlets outlining the purpose of the study and the steps required (completion of a screening questionnaire, parent and teacher child behavior questionnaires, a 3-day diet record, and a blood test) were sent to each family. Parents and children gave informed written consent for all steps in the study. The protocol was approved by the Purdue University Human Subjects Research Committee. Four of the 100 subjects were later dropped from the study due to discrepancies between teacher and parent scores.

Behavior and Learning Assessment

Parents and teachers were asked to complete the Conners' Parent and Teacher Rating Scales, the most commonly used behavior assessment tools for childhood behavior problems (12,22). Parents evaluated 48 behaviors on a 4-point scale (0 = not at all; 1 = just a little; 2 = pretty much; 3 = very much). Scores for six behavior and learning scales were computed from the parents' responses to the Conners' Parent Rating Scales: Conduct, Impulsivity-Hyperactivity, Anxiety, Psychosomatic, and Learning Scales, and the Hyperactivity Index (see Table 1). As part of the Health Questionnaire parents also rated temper tantrums and sleep problems on a similar 4-point scale. Teachers also completed the Conners' Teacher Scale of 28 items. Scores for four behavior scales from the teachers' responses to the Conners' Teacher Rating Scales were computed: Conduct, Hyperactivity, and Inattentive-Passive Scales, and the Hyperactivity Index. In addition, each teacher was asked to evaluate the learning ability of the target student compared with his peers in reading, math, handwriting, and overall academic ability on a scale of 1 to 5 (1 = poor; 2 = below average; 3 = average; 4 = above average; and 5 = excellent).

Health Assessment

The Health Questionnaire asked parents to rate seven possible symptoms of EFA deficiency [thirst (9), frequent urination (24,29), dry skin (17), dry hair (9), dandruff (9), brittle nails (2), and follicular keratoses (4) on a scale of 0 to 3 (not at all, just a little, pretty much, and very much)]. Parents answered questions about their son's frequency and severity of temper tantrums and sleep problems, symptoms of allergies, and frequency of infections. Parents also reported the incidence and severity of various somatic complaints.

TABLE 2

TOTAL PLASMA PHOSPHOLIPID FATTY ACIDS (MEAN AREA PERCENTS) FOR DATA GROUPED BY RANK INTO LOW, MEDIUM, AND HIGH VALUES (MEAN ± SD)

Fatty Acids	Low (n = 32)	Medium (n = 32)	High (n = 32)
Total omega-3*	2.78 ± 0.22	3.35 ± 0.12	4.11 ± 0.56
Total omega-6†	35.31 ± 2.01	38.20 ± 0.61	39.94 ± 0.64

* Total omega-3 fatty acids = 18:3n-3 + 20:5n-3 + 22:5n-3 + 22:6n-3. Total range omega-3 fatty acids: 2.30–5.84 area %.

† Total omega-6 fatty acids = 18:2n-6 + 18:3n-6 + 20:3n-6 + 20:4n-6 + 22:4n-6 + 22:5n-6. Total range omega-6 fatty acids: 27.64–41.70 area %.

Laboratory Analyses

Venous blood samples were drawn from each subject. As was reported elsewhere (31), a Bligh and Dyer extraction was used to extract plasma lipids (6). Solid phase extraction using a modification of the method of Hamilton and Comai was used to separate neutral from polar lipids (16). The lipids were dried under nitrogen and the fatty acid methyl ester concentrations were prepared and analyzed using the method described previously (37).

Statistical Analysis

Statistical analyses of the data were performed using SAS (SAS Institute, Cary, NC) statistical software on an IBM 3090 computer (32). The subjects were ranked by increasing fatty acid levels and divided into three equally numbered groups ($n = 32$). A separate one-way analysis of variance using PROC GLM was performed on total plasma omega-3 and omega-6 groupings to compare the means of the three groups with various measures of behavior, learning, and health. If statistical significance ($p < 0.05$) were attained, a contrast was performed to compare the means of the lower and higher groups.

RESULTS

Table 2 shows the mean plasma phospholipid fatty acid values for the lower, middle, and higher groups expressed as area percents for the 96 subjects. Approximately 44% (14 out of 32) of the subjects with lower omega-3 fatty acids values also had lower omega-6 fatty acid values. There were no significant differences between groups in age, height, weight, socioeconomic status, or medication status. The results of the comparison of those subjects with lower and higher levels of omega-3 plasma fatty acids for assessment of frequency of symptoms indicative of EFA deficiency, behavior, and learning are shown in Tables 3, 4, and 5.

TABLE 4

FREQUENCY OF BEHAVIOR PROBLEMS IN BOYS COMPARING LOW WITH HIGH TOTAL OMEGA-3 FATTY ACIDS (MEAN ± SD)

Behavior Problems	Low (n = 32)	High (n = 32)	p
Parent scales			
Hyperactivity Index*	16.6 ± 8.4	10.0 ± 7.6	0.002
Conduct*	10.3 ± 6.7	5.6 ± 5.2	0.002
Anxiety*	3.3 ± 2.6	1.8 ± 2.0	0.008
Psychosomatic*	1.5 ± 1.9	1.0 ± 2.0	NS
Impulsivity-hyperactivity*	7.4 ± 4.0	5.0 ± 3.4	0.01
Parent scores			
Temper tantrums†	1.5 ± 1.2	0.7 ± 0.9	0.002
Problems getting to sleep†	1.2 ± 1.3	0.5 ± 0.8	0.02
Problems getting up†	1.2 ± 1.3	0.5 ± 0.8	0.006
Teacher Scales‡			
Hyperactivity Index	11.2 ± 7.4	9.6 ± 8.8	NS
Conduct	5.4 ± 4.8	6.2 ± 7.0	NS
Hyperactivity	7.0 ± 5.9	6.5 ± 6.3	NS
Attention	8.6 ± 6.1	6.8 ± 5.5	NS

* Scores from Conners' Parent Rating Scale—48. Possible scores: Hyperactivity Index (0–30), Conduct (0–24), Anxiety (0–12), Psychosomatic (0–12), Impulsivity-Hyperactivity (0–12).

† Scores from Health Questionnaire. Possible scores: 0–3.

‡ Scores from Conners' Teacher Rating Scale—28. Possible scores: Hyperactivity Index (0–30), Conduct (0–24), Hyperactivity (0–21), Attention (0–24).

Those subjects having lower levels of plasma omega-3 fatty acids reported a significantly greater frequency of symptoms associated with EFA deficiencies compared with subjects with higher levels of omega-3 fatty acids: increased thirst, $F(1, 93) = 17.30$, $p < 0.0001$, frequent urination, $F(1, 93) = 13.46$, $p = 0.0004$, and dry skin, $F(1, 93) = 3.83$, $p = 0.05$. No differences were found in the frequency of reporting dry hair, dandruff, brittle nails, or follicular keratoses. The total EFA deficiency score (the sum of all seven deficiency symptoms) was significantly greater, $F(1, 93) = 15.40$, $p < 0.0001$, in those subjects with lower total omega-3 fatty acid levels.

Behavioral indices obtained from the Conners' Rating Scales and the Health Questionnaire showed that subjects with lower total omega-3 fatty acids scored higher or many different behaviors. On the Conners' Parent Rating Scales, Conduct, $F(1, 93) = 10.50$, $p = 0.002$, Anxiety, $F(1, 93) = 7.38$, $p = 0.008$, Hyperactivity/Impulsivity, $F(1, 93) = 6.44$, $p = 0.01$, scores, and the Hyperactivity Index, $F(1, 93) = 9.80$, $p = 0.002$, were significantly higher for those subjects with lower plasma omega-3 fatty

TABLE 3

FREQUENCY OF ESSENTIAL FATTY ACID DEFICIENCY SYMPTOMS IN BOYS COMPARING LOW WITH HIGH TOTAL OMEGA-3 AND OMEGA-6 FATTY ACIDS (MEAN ± SD)

	Omega-3 Fatty Acids			Omega-6 Fatty Acids		
Symptoms	Low (n = 32)	High (n = 32)	p	Low (n = 32)	High (n = 32)	p
Thirst*	1.4 ± 1.1	0.4 ± 0.8	0.0001	1.0 ± 1.1	0.9 ± 1.0	NS
Frequent urination*	0.9 ± 1.0	0.2 ± 0.6	0.0004	0.6 ± 0.9	0.4 ± 0.8	NS
Dry skin*	0.6 ± 1.0	0.3 ± 0.5	0.05	0.6 ± 1.0	0.2 ± 0.5	0.04
Dry hair*	0.5 ± 1.0	0.2 ± 0.6	NS	0.5 ± 1.0	0.1 ± 0.3	0.03
Total EFA deficiency score†	4.3 ± 3.4	1.7 ± 2.0	0.0001	3.5 ± 3.5	2.0 ± 2.0	NS

* Each subject's symptoms were rated on a four-point scale on the Health Questionnaire: 0 = not at all; 1 = just a little; 2 = pretty much; 3 = very much.

† The total EFA deficiency score is the sum of the scores (on a four-point scale) for each of the seven individual items. Possible scores: 0–21.

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TABLE 5

FREQUENCY OF LEARNING PROBLEMS IN BOYS COMPARING LOW WITH HIGH TOTAL OMEGA-3 FATTY ACIDS (MEAN ± SD)

Learning Problems	Low (n = 32)	High (n = 32)	p
Parent scores			
Learning*	6.6 ± 3.8	3.9 ± 3.2	0.005
Teacher scores			
Math†	3.1 ± 1.1	3.7 ± 1.0	0.05
Reading†	3.2 ± 1.3	3.2 ± 1.3	NS
Handwriting†	2.5 ± 1.2	2.6 ± 1.1	NS
Overall academic ability†	3.1 ± 1.1	3.7 ± 0.9	0.04

* From Conners' Parent Rating Scale—48. Possible scores: 0–12.

† Each subject's academic ability was assessed by teachers on the following scale: 1 = poor; 2 = fair; 3 = average; 4 = good; 5 = excellent.

acid levels vs. those with higher levels. However, no significant differences in the Psychosomatic scores were found. Also, subjects with lower omega-3 fatty acids showed more frequent and excessive temper tantrums, $F(1, 93) = 10.26$, $p = 0.002$, problems getting to sleep, $F(1, 93) = 6.06$, $p = 0.02$, and problems getting up in the morning, $F(1, 93) = 8.02$, $p = 0.006$, than those with higher levels of total omega-3 fatty acids. One somatic complaint that was different between the lower omega-3 fatty acid and higher omega-3 fatty acid groups was stomachaches, $F(1, 93) = 5.07$, $p = 0.03$; but headaches, diarrhea, constipation, allergies, and infections were not significantly different between the two groups.

Some measures of learning problems were also significantly different between the lower and higher total omega-3 fatty acid groups. The Conners' Parent Rating Scale score for learning problem was significantly higher, $F(1, 93) = 8.18$, $p = 0.005$, in the subjects with lower omega-3 fatty acid levels. (No significant differences were found in any of the Conners' Teachers Rating Scales of behavior between lower and higher omega-3 fatty acids.) When teachers were asked to evaluate academic skills, however, math, $F(2, 56) = 4.65$, $p = 0.04$, and overall academic ability, $F(2, 56) = 4.93$, $p = 0.03$, were significantly lower in the lower omega-3 fatty acid group. No significant differences were found in reading or handwriting abilities.

Although no significant differences in behavior and learning were found for groups based on total omega-6 fatty acid levels, differences in several health-related problems were documented. In the group with lower levels of total omega-6 fatty acids, greater frequencies of dry skin, $F(1, 93) = 4.48$, $p = 0.04$, and dry hair, $F(1, 93) = 4.59$, $p = 0.03$, were observed. Also, those subjects with lower total omega-6 fatty acids reported suffering from more colds, $F(1, 93) = 4.15$, $p = 0.04$, and used antibiotics more often since birth, $F(1, 93) = 5.52$, $p = 0.02$, than those with higher omega-6 fatty acid levels.

DISCUSSION

In the study reported here, subjects with lower plasma phospholipid total omega-3 fatty acids showed more problems with behavior, learning, and health than those subjects with higher levels of total omega-3 fatty acids. Also, this group reported more symptoms indicative of EFA deficiency (thirst, frequent urination, and dry skin). Similarly, increased fluid intake and output of urine and feces have been reported in omega-3 deficient monkeys (28,29). The relationship between an omega-3 fatty acid deficiency and polydipsia is not clear, but appears to result from changes in physiological events that are distinct from those that occur as a result of an omega-6 fatty acid deficiency (29). Previous studies of children with hyperactivity have reported a higher frequency of polydipsia and polyuria (11,24,32), as well as lower plasma levels of dihomogammalinolenic acid, arachidonic acid, and DHA (24). Here we report an association between lower n-3 fatty acid status and frequent thirst and urination, but no association was observed between lower n-6 fatty acids and these symptoms.

In this study, an increased frequency of behavior problems (hyperactivity, impulsivity, conduct, anxiety, temper tantrums, and sleep problems) was found in those subjects with lower levels of omega-3 fatty acids. Changes in home cage behavior of omega-3 fatty acid deficient monkeys have been reported: increased locomotion and more bouts of stereotyped behavior (30). Also, mice fed omega-3 deficient diets for three generations showed slightly greater swimming speed in a water maze and more activity in the open field than control animals (36). Thus, it appears that both animals and humans exhibit changes in multiple types of behavior when omega-3 fatty acid status is low.

More learning problems, as reported by both parents and teachers, were also found in those subjects with lower omega-3 fatty acid levels. Studies of omega-3 fatty acid status in animals have reported poorer performance on a variety of learning measures when brain levels were low (8,21,38), while others have reported no effect (36). Many of the learning measures used have involved visual discrimination tasks (21,38), and, thus, it is not clear whether omega-3 fatty acid deficiency effects on learning were due to decreased visual acuity or some other sensory or cerebral function (34,35). In this study visual acuity was not assessed, but in other work, more visual problems have been reported in children with ADHD than in controls (18,24).

It was expected that similar results would be obtained on both the Conners' Parent and the Teacher Rating Scales, because there are several similarly named scales (Hyperactivity Index, Conduct Scale, and Hyperactivity-Impulsivity). In contrast to the parents' scores, no significant mean differences were found on the Teacher Hyperactivity Index, Teacher Conduct Scale, and the Teacher Hyperactivity Scale between the lower and higher omega-3 fatty acid groups. Statistically, this could be attributed to the fact that the parent scores exhibited much larger mean differences than the corresponding teacher scores, although the observed standard deviations were similar.

Close examination of the specific questions comprising the teacher and parent scales (12) show that, although some scales share common titles, the types of behavior rated are different and are evaluated in different environments. Additionally, the parents and teachers have different levels of experience with the subjects.

Furthermore, we anticipated that increased behavioral specificity might lead to increased specificity of outcomes. What we found, however, was that the overall general behavioral criterion (Conners' Hyperactivity Index) was sensitive; but we further identified the following potential indicators in children: temper tantrums, sleep problems (getting to sleep and getting up), conduct, hyperactivity/impulsivity, anxiety, and learning problems.

Subjects with lower levels of omega-6 fatty acids reported more health-related problems of dry skin and dry hair than those subjects with higher omega-6 fatty acid levels. Dry skin (9,17) and thirst (9) have been reported in omega-6 fatty acid deficient rats (9) and infants (17) fed no or low fat diets. Increased transdermal water loss and subsequent dry skin and thirst may occur because of decreased eicosanoid production (23). A deficiency of linoleic acid, a component of skin ceramides, also contributes to these symptoms (23).

In this study, subjects with lower total omega-6 fatty acids reported significantly more colds and greater antibiotic use. Whether the total omega-6 fatty acid status and these physical symptoms are related is unclear. However, animals deficient in omega-6 fatty acids are more susceptible to infection. EFA deficient animals show altered immune response possibly because EFA modulate the production of eicosanoids and affect membrane phospholipid composition (20).

In conclusion, the results presented here show that those subjects with lower plasma phospholipid levels of total omega-3 fatty acids reported more symptoms indicative of EFA deficiency and reported more problems with behavior, learning, and health. Subjects with lower plasma omega-6 fatty acids also reported more symptoms indicative of EFA deficiency and also more health problems. These results, together with other previous descriptive studies, support a relationship between omega-3 fatty acid status and behavior in children that parallels what has been reported with rats and monkeys. What remains to be studied further is the mechanism(s) underlying the relationship between omega-3 fatty acid status and behavior and learning outcomes in children and animals, as well as the genetic and/or environmental causes for lower levels of highly polyunsaturated fatty acids in plasma phospholipids of some children with behavior problems.

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