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
- Omega-6 fatty acids

Attention deficit-hyperactivity disorder (ADHD)

Childhood behaviors

- 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,
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, dihomogammalinoic 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 22:5α-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.

### 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 1

<table>
<thead>
<tr>
<th>CONNERS’ PARENT RATING SCALES</th>
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<tbody>
<tr>
<td><strong>Hyperactivity Index:</strong></td>
</tr>
<tr>
<td>Excitable, impulsive</td>
</tr>
<tr>
<td>Cries easily or often</td>
</tr>
<tr>
<td>Restless in squirmly sense</td>
</tr>
<tr>
<td>Restless, always up and on the go</td>
</tr>
<tr>
<td>Destructive</td>
</tr>
<tr>
<td>Fails to finish things</td>
</tr>
<tr>
<td>Distractibility</td>
</tr>
<tr>
<td>Mood changes</td>
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<tr>
<td>Easily frustrated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Impulsivity-Hyperactivity Scale:</strong></th>
<th><strong>Anxiety Scale:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Excitable, impulsive</td>
<td>Fearful</td>
</tr>
<tr>
<td>Wants to run things</td>
<td>Shy</td>
</tr>
<tr>
<td>Restless in squirmly sense</td>
<td>Worries more than others</td>
</tr>
<tr>
<td>Restless, always up and on the go</td>
<td>Less self be pushed around</td>
</tr>
</tbody>
</table>

FAITY ACIDS IN BOYS and analyzed using the method described previously.

High total

lipids were dried under

0.6 ± 1.0

0.3 ± 0.5

0.6 ± 1.0

0.5 ± 0.5

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 from polar lipids (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 acid 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.

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 Scale—48. Possible scores: Hyperactivity Index (0-30), Conduct (0-24), Anxiety (0-12), Psychosomatic (0-12), Impulsivity/Hyperactivity (0-12).

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In this study, subjects with lower total omega-6 fatty acid levels 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). Feeding low 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 acid levels 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 problems with behavior, learning, and health. 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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REFERENCES


