LCPUFA and functional development of preterm and term infants

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ABBREVIATIONS

BPD  bronchopulmonary dysplasia
DHA  docosahexaenoic acid
EPA  eicosapentaenoic acid
LCPUFA  long-chain polyunsaturated fatty acids
MDI  mental developmental index
PDI  psychomotor developmental index
PMA  postmenstrual age

INTRODUCTION

Monkey infants with $n-3$ fatty acid deficiency have lower docosahexaenoic acid (DHA) levels and differ functionally in several ways from monkeys fed $n-3$ fatty acids. For example, they have poorer retinal physiology, poorer visual acuity, and longer look duration (see Table 1), which has been associated with slower information processing. Infants fed $\alpha$-linolenic acid also have poorer DHA status than infants fed DHA from human milk. On the basis of this observation, we hypothesized that infants born before the normal intrauterine accumulation of brain DHA has been completed could have a conditional need for $n-3$ long-chain polyunsaturated fatty acids ($n-3$ LCPUFA) that was not met by dietary $\alpha$-linolenic acid. Outcomes used in the monkey studies of $n-3$ deficiency have been adapted for studying the essential nature of $n-3$ LCPUFA in preterm and term babies. In two randomized clinical trials DHA status was improved by adding $n-3$ LCPUFA to diets containing $\alpha$-linolenic acid. In each case, the control group received a diet with generous amounts of $\alpha$-linolenic acid but no $n-3$ LCPUFA. The effects of $n-3$ LCPUFA supplementation on visual acuity, look duration, visual recognition memory, and mental and psychomotor development were determined.

METHODS

Preterm infants

Clinical trials included preterm infants of very low birth weight, but who were appropriate for gestational age and did not have medical problems that could adversely
Table 1  Positive effects of feeding diets with α-linolenic acid compared to α-linolenic acid-deficient diets: rhesus monkeys

<table>
<thead>
<tr>
<th>Retinal physiology</th>
<th>Higher amplitudes of cone and rod A-waves at 3–4 months but not at later ages (1)</th>
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<td>Cone- and rod-dominated B-wave implicit times significantly shorter in older monkeys (1)</td>
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<td>Recovery of dark-adapted A- and B-wave amplitudes significantly better at all ages. The difference between groups became more pronounced with age (2)</td>
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<tr>
<td>Visual acuity</td>
<td>Higher at 1, 2 and 3 months of age (the only ages tested) (3)</td>
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<tr>
<td>Look duration</td>
<td>Shorter look duration (4; see also Chapter 10, this volume)</td>
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affect growth and/or development. The infants were randomized to receive either a marine-oil-supplemented formula (containing 0.2 g DHA/100 g fatty acids) or a standard preterm formula until 2 months (this and all subsequent ages relative to expected term). Growth, plasma and erythrocyte phospholipid LCPUFA levels, visual acuity, look duration and visual recognition memory (novelty preference) and the Bayley Mental and Psychomotor development were studied at specific ages until 12 months corrected age. Visual acuity was measured by the Teller Acuity Card procedure, look duration and novelty preference were determined with an experimental version of the Fagan Infantest, and LCPUFA levels were determined by capillary gas liquid chromatography.

The first and second trials differed in several ways, including the level of eicosapentaenoic acid (EPA; 20:5n–3) in the experimental formula, the duration of LCPUFA supplementation, the nutrient composition of the formula given after discharge from the hospital, and the age of the infants at randomization. In the first trial, relative to the second, infants received DHA from marine oil with five times as much EPA (0.3 vs. 0.06% of total fatty acids), were fed DHA until 9 rather than 2 months corrected age, were discharged on a term formula instead of a nutrient-enriched preterm formula, and were older when randomized to their diet group (3.5 weeks vs 3 days). In addition, infants in the first trial were a very select group of the healthiest infants in our nursery. Only three of 67 had bronchopulmonary dysplasia (BPD) whereas 40% of the preterm infants in the second trial had this disease, the incidence typical for 750–1350 g infants in our nursery.

**Term infants**

We also determined the effect of LCPUFA supplementation on visual acuity, look duration and Bayley Mental and Psychomotor developmental indices in healthy term infants randomized to receive either an egg-yolk-supplemented formula (containing 0.1% DHA and 0.43% arachidonic acid of total fatty acids) or a term formula that was