Dietary Protein Intake throughout Childhood Is Associated with the Timing of Puberty¹–³

Anke L. B. Günther,⁴* Nadina Karaolis-Danckert,⁵ Anja Kroke,⁴ Thomas Remer,⁵ and Anette E. Buyken⁵

¹Department of Nutritional, Food and Consumer Sciences, Fulda University of Applied Sciences, 36039 Fulda, Germany; and ²Research Institute of Child Nutrition, Rheinische Friedrich-Wilhelms-University Bonn, 44225 Dortmund, Germany

Abstract

Early puberty onset is associated with hormone-related cancers, but whether diet in childhood influences pubertal timing is controversial. We examined the association of protein intake in early and mid-childhood with the ages at take-off of the pubertal growth spurt (ATO), peak height velocity (APHV), and menarche in girls and voice break in boys using data from the longitudinal Dortmund Nutritional and Anthropometric Longitudinally Designed Study. Among participants who provided 3-d weighed dietary records at 12 mo, 18–24 mo, 3–4 y, and 5–6 y, 112 had sufficient anthropometric measurements between 6 and 13 y to allow estimation of ATO. Life-course plots were used to identify critical periods of total, animal, and vegetable protein intake (percentage of total energy intake) for pubertal timing. At these ages, the association between tertiles of protein intake (T1–T3) and the outcomes was investigated using multiple linear regression analysis. A higher total and animal protein intake at 5–6 y was related to an earlier ATO. In the highest tertile of animal protein intake at 5–6 y, ATO occurred 0.6 y earlier than in the lowest [mean, 95% CI] T1: 9.6, 9.4–9.9 vs. T2: 9.4, 9.1–9.7 vs. T3: 9.0, 8.7–9.3 y; \(P\)-trend = 0.003, adjusted for sex, total energy, breast-feeding, birth year, and paternal university degree]. Similar findings were seen for APHV (\(P\)-trend = 0.001) and the timing of menarche/voice break (\(P\)-trend = 0.02). Conversely, a higher vegetable protein intake at 3–4 and 5–6 y was related to later ATO, APHV, and menarche/voice break (\(P\)-trend = 0.02–0.04). These results suggest that animal and vegetable protein intake in mid-childhood might be differentially related to pubertal timing. J. Nutr. 140: 565–571, 2010.

Introduction

Contemporary data suggests considerable variation in pubertal timing (1) and a secular trend toward earlier sexual maturation may exist (2). In this context, the importance of environmental factors is increasingly acknowledged. Among those early-life environmental exposures that may have the potential to influence pubertal timing, protein intake is of particular interest. High intake levels in infancy and early childhood seem to be associated with later obesity (3), which is itself related to pubertal timing in both boys and girls (4–7).

We have previously shown that animal protein intake [expressed as a percentage of total energy intake (%En)⁶] at age 12 mo, as well as during the adiposity rebound period (5–6 y), might be unfavorably related to body composition at the age of 7 y (8). Similar “critical windows” of early protein consumption may exist for pubertal timing. Previous studies, however, yielded inconsistent results regarding an association between protein intake and puberty markers (9–16). Typically, these studies addressed later pubertal stages, such as menarche, but an earlier menarche could theoretically represent shorter duration of puberty only (4). Thus, it might take early markers of puberty onset, such as age at take-off of the pubertal growth spurt (ATO), to establish associations between childhood diet and the actual onset of puberty.

We investigated whether protein intake at 12 and/or 18–24 mo might be related to pubertal timing, or whether diet in later childhood may be more important. Furthermore, we were interested whether protein from different sources could be decisive. Data were from a contemporary cohort of healthy, free-living girls and boys for whom 1 early (ATO) and 2 later pubertal markers [age at peak height velocity (APHV) and age at menarche/voice break in girls/boys, respectively] could be estimated and who provided repeated dietary assessments in early and mid-childhood. Data for 24-h urinary nitrogen excretion, a biomarker for protein intake (17), was made available in a subsample to corroborate the results from dietary records.

¹ Supported by a research grant from the World Cancer Research Fund International. The Dortmund Nutritional and Anthropometric Longitudinally Designed Study is funded by the Ministry of Science and Research of North Rhine Westphalia, Germany.
³ Supplemental Table 1 and Supplemental Figure 1 are available with the online posting of this paper at jn.nutrition.org.
⁴ Abbreviations used: APHV, age at peak height velocity; ATO, age at take-off; DONALD, Dortmund Nutritional and Anthropometric Longitudinally Designed; % En, percentage of total energy intake; FMI, fat mass index; IGF-1, insulin-like growth factor 1; SDS, SD score.
* To whom correspondence should be addressed. E-mail: anke.guenther@he.hs-fulda.de.
Methods

Study population. The Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study is an ongoing, open cohort study conducted in Dortmund, Germany, since 1985. Details of the study protocol are provided elsewhere (18). The study was approved by the Ethics Committee of the University of Bonn. All assessments, described below in detail, were performed with parental consent.

Among children who had reached adolescence by the time of this analysis, 411 term (37–42 wk gestation) singletons with a birth weight ≥2500 g provided height measurements at 6 and 13 y, as well as ≥5 measurements between these ages, to allow estimation of ATO. Among these, ATO was considered plausible (determined by visual inspection of individual growth curves and by using the cut-offs ATO ≥5 and <13 y) in 376 participants. Finally, plausible dietary records at 12 mo, 18–24 mo (at least 1 of 2 possible), 3–4 y (at least 1 of 2), and 5–6 y (at least 1 of 2) and information on potential confounders were provided by 112 individuals.

The sample resulting from applying all 3 criteria, i.e. 112 children, was used for this analysis. A further subset of 57 children had collected 24-h urine samples at ages 3–4 y (at least 1 of 2) and 5–6 y (at least 1 of 2). APHV could be calculated for 106 children. Information on age at menarche or voice break was available for 92 participants.

Anthropometry, parental, and birth characteristics. As described in detail in the following, DONALD Study participants are measured at each visit according to standard procedures (19), dressed in underwear only. The measuring-trained nurses undergo an annual quality control. From the age of 2 y onwards, standing height is measured to the nearest 0.1 cm. Height measurement is performed by a stationary, digital stadiometer. Weight is measured at the nearest 0.1 kg using an electronic scale (753 E; Seca). Skinfold thicknesses are measured from the age of 6 mo onwards on the right side of the body to the nearest 0.1 mm using a Holtain caliper. Percentage body fat y before ATO was calculated using the Slaughter equations for prepubertal children (20). Percentage body fat was then converted to values of fat mass index (FMI, in kg/m2) and FMI SD scores (FMI SDS) were obtained by internally standardizing logged FMI values (mean = 0, SD = 1, by age and sex).

At their child’s admission to the study, parents provide information about family and socioeconomic characteristics (i.e. school education and professional degree) and are also weighed and measured.

Puberty outcome variables. ATO and APHV were determined using the parametric Preece and Baines model 1 (21). ATO was defined as the age at minimal height velocity at the onset of the pubertal growth spurt (22). Best fit was determined by graphical inspection of each child’s individual growth curve and a comparison of the residual SD (random error had to be smaller than the expected measurement error for height), and by considering the plausibility and the distribution of the pubertal variables estimated. Based on these 4 criteria, data from the following age ranges were selected and entered into Preece and Baines model 1: all measurements from age 5 to 13 y for girls and from age 6 to 13 y for boys.

In addition to growth monitoring, age at menarche in girls and at voice break in boys were assessed and combined to form our 3rd pubertal measure (2).

Dietary data. In the DONALD Study, dietary intake is assessed by 3-d weighed dietary records, as described previously (18). Parents are asked to weigh all foods and beverages consumed by their children to the nearest 1 g for 3 consecutive days. Parents are instructed by trained dieticians, and semiquantitative recording using household measures is allowed when exact weighing was not possible (e.g. foods eaten away from home). Information on recipes or the types and brands of food items is also requested and a dietician visits the family and the record for completeness and accuracy.

The records are analyzed using the in-house nutrient database LEIBTAR (23). For this study, total energy (kJ/d) and protein intakes (g/d) between 12 mo and 6 y were derived for each individual from the mean of the 3 recording days. The reported energy intake was related to the basal metabolic rate (24), and age- and sex-specific cutoffs (25) were used to exclude potentially implausible records (<3%). To represent diet at 18–24 mo, 3–4 y, and 5–6 y, we calculated the mean of the single standardized energy intakes (mean ± SD = 1) or the mean nutrient intakes at the respective time points. Besides total protein intake, we considered animal and vegetable protein, which were further divided into protein from dairy (excluding infant formula), meat, and cereal, as previously described (10).

Urinary nitrogen. Starting at age 3 y, 24-h urine collections are performed on 3 of the 3-d weighed dietary record (20). All micturitions are stored immediately in preservative-free, Extran-cleaned (Extran, MA 03; Merck Darmstadt), 1-L plastic containers at ≤−12°C before they are transported. At the institute, the containers are stored at ≤−20°C before being analyzed. Urinary creatinine was measured according to the kinetic Jaffe technique (26) with a Beckman-2 creatinine analyzer (Beckman Instruments).

For the purpose of this analysis, completeness of 24-h urines was checked via sex- and age-specific, body weight-related reference values of creatinine (27). Urinary nitrogen was measured by the Kjeldahl technique (Buechi 430 Digestor and Buechi Distillation Unit B-324). Protein intake (g/d) was estimated under the assumption that urinary nitrogen reflects 80% of protein ingested (17). Age- and sex-specific reference values for protein requirements for growth were added to allow for protein retention in childhood (28). Consistent with the dietary record data, individual means represented protein intake at 3–4 and 5–6 y.

Statistical analysis and power considerations. To examine when protein intake was important for the different puberty markers, life-course plots were constructed (29). Total, animal, and vegetable protein intakes (from diet records) at 12 mo, 18–24 mo, 3–4 y, and 5–6 y were expressed as %En and standardized by age for comparability. They were then entered into separate multiple linear regression models as independent variables (adjusting for each other) and with ATO, APHV, or age at menarche/voice break as outcomes. All models additionally included sex and the children’s birth year to exclude a potential secular effect in pubertal timing. Furthermore, we added mean energy intake from 1 to 6 y: the individual energy intakes were standardized by age (mean = 0, SD = 1) and the mean was calculated for each child. The resulting regression coefficients were then plotted against age. Both their values (representing the strength of the associations at the single time points) and their changes (representing the associations between puberty markers and change in the dietary variables over the corresponding time interval) were examined to identify important time points and/or periods of protein intake for pubertal timing.

Subsequently, we concentrated on the critical ages identified by the life-course plots. Protein intakes (%En) at those time points were grouped into tertiles. Adjusted mean outcome levels were calculated for each tertile and P-values for linear trends derived from multiple linear regression models (separate model for each continuous protein variable). The Dunnett test for post hoc comparisons was used to examine whether a significant difference to the lowest tertile existed. Tests for interaction were conducted to evaluate whether associations differed by sex. Except for vegetable protein intake at age 5–6 y and ATO and APHV (P = 0.02 for both outcomes), no significant interaction existed for any of the outcomes or protein sources at any time point (P ≥ 0.1). Hence, boys and girls were pooled for analyses, but all models included sex. Similar to the life-course plots, every model contained birth year. We further considered early life and parental characteristics to evaluate confounding by perinatal, lifestyle, and genetic factors: birth weight (n = 3000 g, yes/no), breast-feeding (full breast-feeding ≥4 mo, yes/no), rapid weight gain between birth and age 2 y [increase in weight SDS ≥0.67, yes/no (30)], maternal overweight (BMI ≥25 kg/m2, yes/no), parental education (university entrance qualification, yes/no; university degree, yes/no). Similarly, we considered total energy and fat intake (%En) to evaluate whether any association of protein was due to differences in these dietary factors. Likewise, fiber intake was considered in the analyses on vegetable and cereal protein. Only confounders that modified the associations or predicted the outcomes substantially (P ≤ 0.1) were
Dietary protein and pubertal timing

The present analysis suggests that protein intake during mid-childhood might be differentially related to pubertal timing.
Children with a higher animal protein intake, particularly at 5–6 y, experienced an earlier ATO, APHV, and menarche/voice break, whereas those with a higher vegetable protein at 3–4 and 5–6 y appeared to have a delayed puberty.

Both the greater relevance of diet closer to puberty onset and the opposing effects of animal and vegetable protein are in line with Berkey et al. (9) and their cohort of 67 girls born during the 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both early and late pubertal stages, obtaining remarkably similar results. Others have suggested a role for fat (12,16), energy (11, 1930s and 1940s. We were additionally able to demonstrate an association of animal and vegetable protein with both earlier and later puberty onset, might mainly be due to dairy. This would correspond to results obtained by Wiley et al. (36) who reported that women who drank more milk in childhood (5–12 y) experienced an earlier menarche. In prepubertal boys, skim milk, but not a similar amount of animal protein from meat, stimulated secretion of insulin and insulin-like growth factor 1 (IGF-1) (37,38). Because insulin suppresses IGF binding protein 1 (39), availability of free IGF-1 would be enhanced. IGF-1 is a major regulator of human growth, but a role in adipocyte proliferation and differentiation has also been suggested (40). Indeed, previous analyses of the DONALD Study population yielded positive associations for animal protein (%En), in particular from dairy, at both 12 mo and 5–6 y with body fatness at the age of 7 y (8). But with respect to pubertal timing, protein seems to operate via a pathway that is (partially) independent of body fatness, because adjusting for prepubertal BMI SDS did not fully account for our findings. In fact, prepubertal body composition was critical for later pubertal markers but not the initiation of the pubertal growth spurt in the DONALD Study population (4).

Although frequently used as a reference instrument in validation studies, weighed diet records themselves are prone to measurement error and require a high degree of dedication. Nevertheless, this method represents a method of choice in younger children, such as those studied here (41). In addition, it is a major strength of this analysis that in a subsample, total protein intake could be estimated from 24-h urinary nitrogen. This period of rapid body mass change is perhaps particularly receptive to nutritional influences.

The effect of animal protein intake, which was associated with an earlier puberty onset, might mainly be due to dairy. This would correspond to results obtained by Wiley et al. (36) who reported that women who drank more milk in childhood (5–12 y) experienced an earlier menarche. In prepubertal boys, skim milk, but not a similar amount of animal protein from meat, stimulated secretion of insulin and insulin-like growth factor 1 (IGF-1) (37,38). Because insulin suppresses IGF binding protein 1 (39), availability of free IGF-1 would be enhanced. IGF-1 is a major regulator of human growth, but a role in adipocyte proliferation and differentiation has also been suggested (40). Indeed, previous analyses of the DONALD Study population yielded positive associations for animal protein (%En), in particular from dairy, at both 12 mo and 5–6 y with body fatness at the age of 7 y (8). But with respect to pubertal timing, protein seems to operate via a pathway that is (partially) independent of body fatness, because adjusting for prepubertal BMI SDS did not fully account for our findings. In fact, prepubertal body composition was critical for later pubertal markers but not the initiation of the pubertal growth spurt in the DONALD Study population (4).
perspective. Both early and later markers of puberty could be estimated on the basis of the pubertal growth curve, i.e. based on somatic maturation, and we were not reliant on either recall of pubertal events or more subjective markers of puberty such as Tanner stage, which are difficult to assess and characterized by a high inter-observer variability (42). Also, we were able to control for important potential confounders, e.g. parental and early life characteristics.

Our study has several limitations. DONALD Study participants are characterized by a high socioeconomic status (18). ATO and APHV, however, were in accordance with other European studies (7) and a representative German survey found similar median ages at menarche (12.8 y) and voice break (13.5 y) (43). Furthermore, data on parental pubertal characteristics are not available in the DONALD Study; hence, genetic influences on pubertal timing could not be adjusted for. A 3rd limitation is the small sample size, which is why we could not reliably examine potential sex differences and were also forced to create a variable combining age at menarche and voice break. In the present examination, statistical tests for interactions did not support differences between boys and girls. Stratified analyses, however, suggested that the associations of protein intake with pubertal timing might be stronger in boys, but this finding could be due to chance (data not shown). Recent studies suggested that factors influencing pubertal timing, such as adiposity, may not differ between sexes (4–7).

An earlier puberty onset has been related to an increased risk for hormone-related cancers in adulthood (44–46). For example, a meta-analysis of 26 epidemiological studies reported a 9% risk reduction for breast cancer with every additional year at menarche (47). Additionally, recent study results demonstrated that a 1-y delay in menarche was associated with a 2.4 (48) to 4.5% (49) lower total mortality. The difference of a 0.4–0.8 y earlier puberty onset in the highest compared with the lowest tertile of animal protein intake observed in our final models thus suggests that the present findings, if confirmed, could have substantial public health implications. The same might be true for vegetable protein intake, where differences were only slightly smaller and pubertal timing was delayed by 0.3–0.5 y in the highest tertiles of intake compared to the lowest.

In conclusion, dietary protein in mid-childhood may differentially influence pubertal timing. Whereas higher animal protein intake at 5–6 y might be related to an earlier ATO, APHV and menarche/voice break, higher intakes of vegetable protein at 3–4 and 5–6 y were associated with a delayed puberty. These findings need to be confirmed in future studies with sufficient power to examine differences between boys and girls and the ability to consider hormonal status.

**FIGURE 1** Life-course plots with ATO (y) as the dependent variable and standardized total protein (A), animal protein (B), and vegetable protein intakes (C) (%En) throughout childhood as the explanatory variables. Values are regression coefficients (95% CI), n = 92–112, adjusted for each other, for mean energy intake from 1–6 y, sex, and birth year, *P < 0.05.

| TABLE 3 Association between dietary protein intake in childhood and ATO |  |
|---|---|---|---|---|
| | Tertiles of protein intake | 1 | 2 | 3 | P-trend$^2$
| Total protein, %En | Age 3–4 y | 9.5 (9.2; 9.8) | 9.5 (9.2; 9.8) | 9.2 (8.9; 9.5) | 0.2
| Age 5–6 y | Model 1 | 9.7 (9.4; 10.0) | 9.2 (8.9; 9.5)* | 9.2 (8.9; 9.5)* | 0.02
| | Model 2 | 9.7 (9.4; 10.0) | 9.2 (8.9; 9.5)* | 9.2 (8.9; 9.5)* | 0.03
| Animal protein, %En | Age 3–4 y | 9.7 (9.4; 10.0) | 9.5 (9.2; 9.8) | 9.0 (8.7; 9.3)* | 0.01
| Age 5–6 y | Model 1 | 9.6 (9.3; 9.9) | 9.5 (9.2; 9.8) | 9.0 (8.7; 9.3)* | 0.07
| | Model 2 | 9.6 (9.3; 9.9) | 9.4 (9.1; 9.7) | 9.0 (8.7; 9.3)* | 0.003
| Vegetable protein, %En | Age 3–4 y | 9.1 (8.8; 9.4) | 9.4 (9.1; 9.7) | 9.6 (9.2; 9.9) | 0.01
| Age 5–6 y | Model 1 | 9.1 (8.8; 9.4) | 9.4 (9.1; 9.7) | 9.6 (9.3; 9.9) | 0.02
| | Model 2 | 9.1 (8.8; 9.4) | 9.4 (9.1; 9.7) | 9.6 (9.3; 9.9) | 0.07

1 Values are adjusted means (95% CI), n = 112. *Different from the lowest tertile, P < 0.05 (Dunnett’s test for post hoc comparisons).

2 Multiple linear regression models (continuous variables). Model 1: adjustments for sex, total energy intake, full breast-feeding for ≤4 mo (yes/no), birth year, and paternal university degree (yes/no); model 2: model 1 + FMI SDS 1 y before ATO.
TABLE 4 Association between dietary protein intake in childhood and APHV

<table>
<thead>
<tr>
<th>Tertiles of protein intake</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total protein, %(\text{EN})</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 3–4 y</td>
<td>Model 1</td>
<td>12.4 (12.0; 12.7)</td>
<td>12.5 (12.1; 12.8)</td>
<td>12.3 (11.9; 12.6)</td>
</tr>
<tr>
<td></td>
<td>Model 2</td>
<td>12.3 (12.0; 12.6)</td>
<td>12.5 (12.1; 12.8)</td>
<td>12.3 (11.9; 12.6)</td>
</tr>
<tr>
<td>Age 5–6 y</td>
<td>Model 1</td>
<td>12.8 (12.5; 13.1)</td>
<td>12.1 (11.8; 12.5)*</td>
<td>12.1 (11.8; 12.5)*</td>
</tr>
<tr>
<td></td>
<td>Model 2</td>
<td>12.8 (12.4; 13.1)</td>
<td>12.1 (11.8; 12.4)*</td>
<td>12.1 (11.8; 12.5)*</td>
</tr>
<tr>
<td><strong>Animal protein, %(\text{EN})</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 3–4 y</td>
<td>Model 1</td>
<td>12.5 (12.2; 12.9)</td>
<td>12.5 (12.2; 12.9)</td>
<td>12.0 (11.7; 12.3)</td>
</tr>
<tr>
<td></td>
<td>Model 2</td>
<td>12.4 (12.1; 12.8)</td>
<td>12.6 (12.2; 12.9)</td>
<td>12.0 (11.7; 12.3)</td>
</tr>
<tr>
<td>Age 5–6 y</td>
<td>Model 1</td>
<td>12.8 (12.5; 13.1)</td>
<td>12.3 (12.0; 12.6)</td>
<td>12.0 (11.7; 12.3)*</td>
</tr>
<tr>
<td></td>
<td>Model 2</td>
<td>12.8 (12.4; 13.1)</td>
<td>12.3 (12.0; 12.6)</td>
<td>12.0 (11.6; 12.3)*</td>
</tr>
<tr>
<td><strong>Vegetable protein, %(\text{EN})</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 3–4 y</td>
<td>Model 1</td>
<td>12.1 (11.8; 12.5)</td>
<td>12.3 (12.0; 12.7)</td>
<td>12.6 (12.3; 13.0)</td>
</tr>
<tr>
<td></td>
<td>Model 2</td>
<td>12.1 (11.8; 12.5)</td>
<td>12.3 (12.0; 12.6)</td>
<td>12.6 (12.2; 13.0)</td>
</tr>
<tr>
<td>Age 5–6 y</td>
<td>Model 1</td>
<td>12.2 (11.8; 12.6)</td>
<td>12.3 (11.9; 12.6)</td>
<td>12.6 (12.2; 13.0)</td>
</tr>
<tr>
<td></td>
<td>Model 2</td>
<td>12.2 (11.8; 12.6)</td>
<td>12.3 (11.9; 12.6)</td>
<td>12.5 (12.2; 12.9)</td>
</tr>
</tbody>
</table>

1 Values are adjusted means (95% CI), \(n = 112\). *Different from the lowest tertile, \(P < 0.05\) (Dunnett’s test for post hoc comparisons).

2 Multiple linear regression models (continuous variables). Model 1: adjustments for sex, total energy intake, full breast-feeding for >3 mo (yes/no), birth year, and paternal university degree (yes/no); model 2: model 1 + FMI SDS 1 y before ATO.

Acknowledgements

A.L.B.G., N.K-D., A.K., and A.E.B. designed research. A.L.B.G. had primary responsibility for final content. All authors made substantial contributions to and approved the final manuscript.

Literature Cited