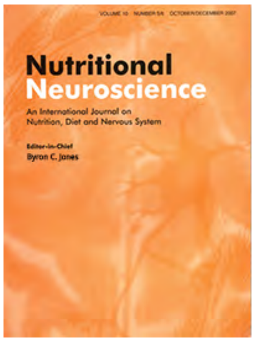

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Dietary patterns are associated with attention-deficit hyperactivity disorder (ADHD) symptoms among preschoolers in South Korea: a prospective cohort study

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Dietary patterns are associated with attention-deficit hyperactivity disorder (ADHD) symptoms among preschoolers in South Korea: a prospective cohort study

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ABSTRACT
Objectives: Attention-deficit hyperactivity disorder (ADHD) is a prevalent neurobehavioral disorder in children. There are limited studies for diet or dietary supplement effects on ADHD in preschool children in Asia. This study aimed to determine the association between dietary patterns in 4-year-old children and ADHD symptoms in 6-year-old children. Methods: We estimated dietary intake in 4-year-old children using a food frequency questionnaire. Using 33 food groups, major dietary patterns were identified in relation to the consumption of sweets, vegetables, meats, and carbohydrates. Parents of 6-year-old children used the Korean version of the ADHD Rating Scale for ADHD symptom assessment. Results: A sweet dietary pattern was associated with a higher risk of attention deficit (AD) (relative risk [RR], 1.34; confidence interval [CI], 1.17–1.55), hyperactivity (RR, 1.40; CI, 1.19–1.64), and ADHD symptoms (RR, 1.37; CI, 1.23–1.52). A vegetable dietary pattern was associated with a lower risk of ADHD symptoms (RR, 0.81; CI, 0.72–0.90). Food item analysis of the sweet dietary pattern showed that intake scores for chocolate, chips, and fruit jams positively correlated with AD, hyperactivity, and ADHD symptoms. Discussion: These findings can be useful to further understand the roles of dietary factors in ADHD.

Abbreviations: CAS study: Congenital Anomaly Study; EDC study: Environment and Development of Children study; K-ARS: ADHD Rating Scale; ADHD: Attention-deficit hyperactivity disorder; RR: relative risk; FFQ: food frequency questionnaire; PCA: principal component analysis; SD: standard deviation

KEYWORDS
Attention-deficit hyperactivity disorder; Dietary pattern; Korean; Sweets

Introduction

The worldwide-pooled prevalence rate for attention-deficit hyperactivity disorder (ADHD) has been reported to be 3.4–7.2% in children and adolescents [1,2]. ADHD is characterized by both internalizing problems, such as depression and anxiety, and externalizing problems, such as impulsivity and hyperactivity [3]. Children with ADHD have significantly poorer school-work performance, family relationships, and social interaction [4,5]. The etiology of ADHD is considered to be due to multifactorial causes. Risk factors for ADHD include perinatal stress, low birth weight, traumatic brain injury, maternal smoking and alcohol use during pregnancy, lead exposure, social disadvantages, such as low educational level or divorced parent, and family history [6]. Several studies have suggested that ADHD in children is associated with nutritional issues, such as vitamin D or mineral deficiencies [7], low level of omega-3 fatty acids [8], high zinc level in hair [9], and low adherence Mediterranean dietary pattern [6]. However, the association between dietary intake or dietary patterns and behavioral problems in children has only been constantly reported in Western countries, whereas few studies have been conducted involving Asian children. Because people who lived in Western countries and Asian countries have very different dietary habits or nutritional intake according to the type of meals, research studies on dietary pattern and ADHD symptom in Asia children are needed. One study in China reported the relationship between dietary patterns and ADHD symptoms during

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the preschool period. That study observed that a higher dietary intake of processed and snack foods and a lower intake of vegetarian foods was associated with a significantly higher risk of ADHD symptoms. Two recent Korean studies have investigated the association between dietary patterns and behavioral problems in children. Park et al. showed that a high intake of sweets, fried food, and salt were related to learning disabilities in children. However, a well-balanced diet, regular eating, and an intake rich in dairy products and vegetables had beneficial effects on learning difficulties, attention spans, and behavior in school-age children [10]. In another Korean study, the Korean traditional dietary pattern was found to be associated with lower risks of children having ADHD [11]. However, no study has reported an association between dietary patterns and ADHD symptoms in preschool children in Korea, despite an increasing global prevalence of ADHD symptoms having been reported in preschool children [12].

To further understand the relationship between dietary patterns and ADHD in preschool children, we aimed to examine the longitudinal relationship between dietary patterns of 4-year-old children and ADHD symptoms in the same children at age 6.

Materials and methods

Study participants

We used data from an Environment and Development of Children (EDC) prospective cohort study, as previously described by Kim et al [13], to investigate the effects of childhood environmental exposures on the development of physical and neurological behavior. Briefly, we conducted the Congenital Anomaly Study (CAS) to analyze the association between environmental exposure of the fetus and congenital birth defects. In that study, 13,484 pregnant women from eight local hospitals in the Seoul and Gyeonggi provinces of South Korea were enrolled from August 2008 to July 2010. After the CAS ended in 2011, we individually contacted mothers, who were randomly selected from the CAS participant list, to be recruited for the EDC study using telephone calls.

We compared mothers with children enrolled to not enrolled in the EDC study, the proportion of active smokers (6.1% vs 5.9%; p-value: 0.736), proportion of cesarean section deliveries (35.2% vs 33.5%; p-value: 0.951), maternal age at enrollment (31.3 ± 3.6 years vs 30.5 ± 3.5 years; $p\text{-value} < 0.0001$) and birth weight (3.2 ± 0.04 kg vs 3.2 ± 0.05 kg; p-value: 0.801) did not differ significantly except for maternal age at enrollment. We started their follow-up between 2012 and 2013, and every 2 years thereafter. From 2013 to 2015, 645 4-year-old children were followed up and, from 2015 to 2017, 575 6-year-old children were followed up. In 2014 and 2015, 52 and 29 more children were randomly added, respectively, after the invitation of the CAS study participants to make up for previous losses at follow-up time.

We obtained data from 535 children who had been followed up at both ages 4 and 6 years. Figure 1 shows the process of selecting participants throughout the study. Detailed information concerning the study was provided to all participants' parents, and prior written consent was obtained at every survey. The study protocol was approved by the Institutional Review Board of the Seoul National University Hospital (IRB No. 1201-010-392).

Dietary assessment

Dietary intake for each child was assessed using a validated semi-quantitative food frequency questionnaire (FFQ), which was administered during the follow-up visits at ages 4 and 6 years. Previous research shows that FFQ is reliable($r = 0.5$–0.8) and valid($r = 0.3$–0.6) for a range of nutrients [14–16]. The FFQ included 91 food items, with nine response categories ranging in frequency from 'rarely use' to 'three or more times per day'. For all foods, the questionnaire specified the intake of a small portion (50% smaller than the average), an average portion, or a large portion (50% larger than the average) of food. The parents were asked to indicate their child's average intake frequency and the portion size of foods consumed. The amount of each food item included in the FFQ was converted into grams, from which the daily intake of nutrients was calculated using the Computer-Aided Nutritional Analysis Program 5.0, developed by the Korean Nutrition Society.

ADHD

To evaluate ADHD symptom in 6-year-old children, parents of the participating children were asked to respond to the Korean version of the ADHD Rating Scale (K-ARS) [17]. The K-ARS is a standardized screening tool for ADHD [18]. The K-ARS includes 18 items selected from 18 symptoms listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, in relation to ADHD criteria. Nine items are related to inattention and nine items are related to hyperactivity and impulsivity, and each item is rated from 0 to 3 points, and the score ranges from 0 to 54. The reliability and validity of the K-ARS has been previously well established in studies involving Korean children [19,20]. To conduct a prevalence of ADHD in our study, we

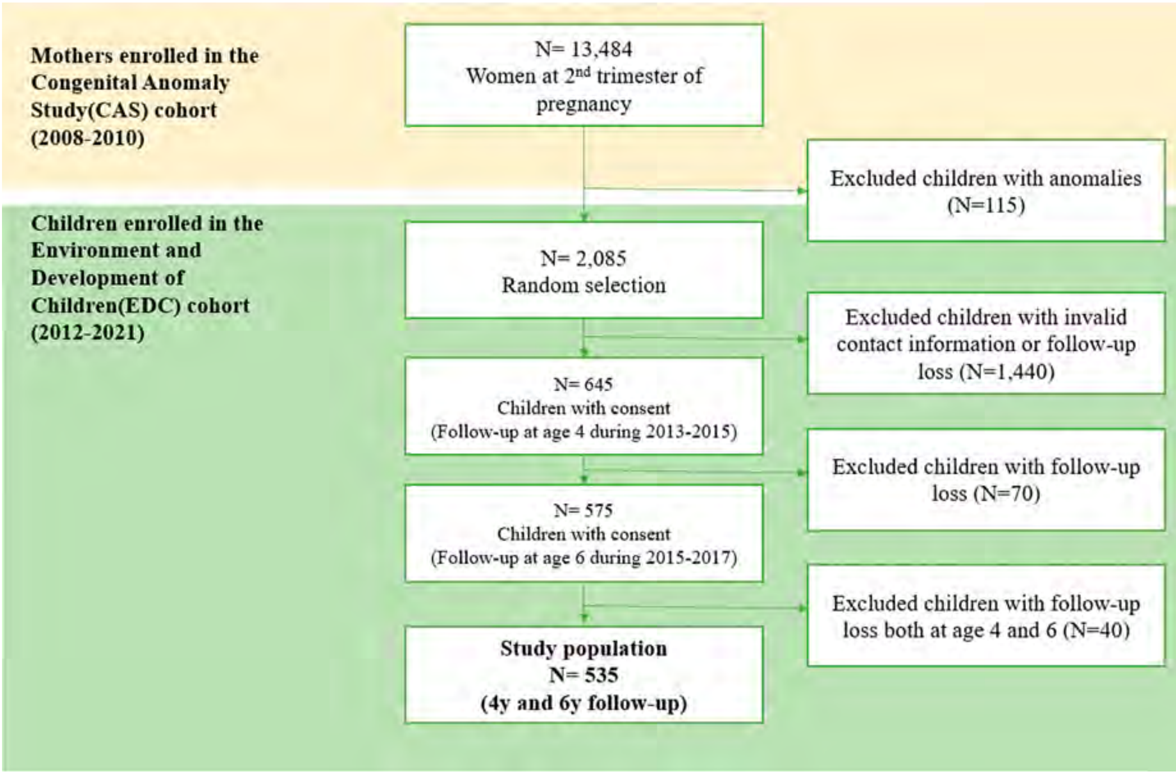

Figure 1. The flow of participants though the study.

classified children as having ADHD if the ADHD scores measured by the K-ARS were ≥19 [21].

Covariates

To determine covariates for the association between dietary pattern and ADHD symptom, univariate regression analysis was performed to find the significant possible covariates associated with AD, HD, and ADHD scores at age 6 (Table S2). Covariates were selected at the significance level under 0.2 of *p*-value in the univariate analysis, then were included in the multivariate-adjusted model. We determined children's sex, age (month), body mass index z-score, paternal education levels, daily energy intake, exposure to second-hand smoke, maternal age during pregnancy, and gestational age.

A trained technician measured the children's height and weight, following standard recommended procedures at each visit. Based on the 2007 Korean National Growth Charts [22], body mass index (BMI) z-scores for corresponding ages were determined. In addition, we added in the cross-sectional model for adjusting the monthly household income information, which was asked to the parents at 6-year-olds (Table S5 and Table S6).

Statistical analysis

Ninety-one food items were classified into 33 food groups, based on the nutritional profile of each food item, to evaluate dietary patterns (Table S1). Because the association between dietary intake and ADHD score variables could be the result of differences in total energy intake between comparison groups, the total energy intake was further controlled [23]. We used the amount of each food item which was obtained after the control of a residual of total intake. A factor analysis on the intake frequency values of 33 food groups was performed to derive a dietary pattern using orthogonal rotation to determine the major dietary patterns, and we conducted a principal component analysis (PCA) to extract the relevant dietary patterns. We determined the number of dietary patterns after reviewing both the Scree plot and the coherence of apparent dietary patterns. We divided into four groups (Q1 (below 25%), Q2 (25% – 50%), Q3 (50%–75%), Q4 (over 75%)) with factor loadings in children for each dietary pattern. Because a higher factor loading value indicates a larger association with each food group, the children, who were in quartile 4 (over 75%) group, were likely to be the highest intake of the food group.

Table S4 shows the factor loadings for four groups of each dietary pattern in 4- and 6-year-old children.

The associations of each dietary pattern with ADHD scores were evaluated, adjusting for the children's age (months), sex, exposure to second-hand smoke, BMI z-score, and energy intake, as well as paternal education levels, maternal age, and gestational age using SAS (version 8.2, SAS Institute Inc.).

We modeled the K-ARS as a Poisson distribution using PROC GENMOD in SAS. To estimate the risk of ADHD on each dietary pattern, the beta estimates of the Poisson distribution were transformed to relative risk as the following formula:

We interpreted the relative risk as an increase of risk of ADHD for a 1 quartile increase of each dietary intake [24].

When analyzing the association between dietary patterns in 4-year-old children and attention deficit (AD), hyperactivity, and ADHD symptoms in 6-year-old children, we selected the environmental covariates when the children were aged 4. In addition, we also adjusted for the environmental covariate when the children were age 6Relative risk $=$ exponential (ß), $95\%CI =$ exponential(ß $\pm$ 1.96 $\times$ Standard error). (see Table S5).

In the additional cross-sectional analysis for the association between dietary pattern and AD, hyperactivity, and ADHD symptoms in 6-year-old children, we used the relevant covariates when the children were age 6 (Table S6). The result showed a similar pattern with our longitudinal design. In addition, we found that there are highly correlated dietary patterns between 4 and 6 years (p-value was below 0.0001) (Table S3).

Table 1. Demographic characteristics of children in this study during visits at ages 4 and 6 years.

Characteristics	Category	4-year-olds	6-year-olds
		$N = 535$	$N = 535$
Age (months)		47.26 ± 1.82	71.05 ± 1.53
Boys, n (%)		279 (52.15)	
Paternal education	High school graduate or lower	80 (14.95)	
	University graduate	380 (71.03)	
	Graduate school	75 (14.02)	
Maternal age during pregnancy		31.34 ± 3.58	
Gestational age		38.68 ± 1.53	
Exposure to second-hand smoke	Yes	137 (25.6)	127 (23.7)
Daily energy intake	Kcal	1424.66 ± 397.67	1484.68 ± 362.14
BMI z-score		−0.10 ± 1.02	−0.10 ± 1.04
Screen positive for ADHD ($19 \leq$ K-ARS) (%)		3.52	2.24

Note: BMI, body mass index.

Results

General characteristics

Table 1 shows the demographic characteristics of the 535 children during the follow-up visits at ages 4 and 6 years. The mean ages of the 4- and 6-year-old children were 47.26 months (standard deviation [SD], 1.82) and 71.05 months (SD, 1.53), respectively. The number and percentage of fathers who had graduated from university were 380 and (71.3%), respectively. The mean value for the gestational age was 38.68 (SD, 1.53). The proportions of those exposed to second-hand tobacco smoke among the 4- and 6-year-old children comprised 25.6% and 23.7%, respectively. The daily nutrient intakes were 1424.66 kcal (SD, 397.67) at age 4 years and 1484.68 kcal (SD, 362.14) at age 6 years. The means of BMI z-score at each follow-up of children were −0.10 (SD, 1.02) at age 4 years and −0.10 (SD, 1.04) at age 6 years. The defined high-risk group of ADHD (positive screen) measured by K-ARS was 3.52% at age 4 and 2.24% at age 6.

Dietary components

Four major dietary patterns were identified using PCA among the 33 food groups from the 91 food items in FFQ (Table S1). The dietary pattern loadings for each food group in the 4-year-old children are shown in Figure S1. A high intake of snacks, chocolate, sweet drinks, and ice cream characterized the sweet dietary pattern. The vegetable dietary pattern included a high intake of vegetables, potatoes, fruit, anchovies, beans, and kimchi. The meat dietary pattern included a high intake of pork, chicken, fresh fish, and processed fish. Finally, the carbohydrate dietary pattern was characterized with a high intake of processed bread, sweet bread, fats, noodles, and dumplings.

The daily nutrient intakes, according to the quartiles of the four dietary pattern scores, are presented in Table S7. Total energy intake and animal protein, plant protein, animal fat, plant fat, vitamin A, retinol, folate, and vitamin E intakes differed significantly across the quartiles in relation to the scores for the four dietary patterns. Beta-carotene, vitamin C, monounsaturated fatty acid, and polyunsaturated fatty acid intakes significantly differed across the quartiles of the vegetable, meat, and carbohydrate dietary pattern scores. Saturated fatty acid intake significantly differed across the quartiles of the meat and carbohydrate dietary pattern scores.

Associations between dietary patterns and ADHD symptoms

The associations between dietary patterns in 4-year-old children and AD, hyperactivity, and ADHD symptoms in 6-year-old children are presented in Table 2. Children in the higher quartiles of the sweet dietary pattern showed a higher risk of ADHD symptoms than those in the lower quartiles (relative risks [RRs] and 95% confidence intervals [CIs] from Q4 to Q1: 1.37 [1.23–1.52], 1.23 [1.10–1.37], 1.08 [0.97–1.21], and 1.00). Moreover, children in the highest quartile of the carbohydrate dietary pattern showed a higher risk of AD, hyperactivity, and ADHD symptoms than those in the lowest quartile (RRs [95% CIs] from Q4 to Q1 for ADHD: 1.31 [1.17–1.46], 1.25 [1.12–1.40], 1.22 [1.09–1.36], and 1.00).

However, children in the third highest quartile (Q3) of the vegetable dietary pattern showed a significantly lower risk of ADHD symptoms than those in the lowest quartile (Q1) in the adjusted model (RR, 0.81; 95% CI, 0.72–0.90). Children in the second (Q2) of the meat dietary pattern showed a significantly highest risk of ADHD symptoms among the quartile groups (RR, 1.17; 95% CI, 1.05–1.30).

We conducted an additional analysis of the cross-sectional association between dietary patterns and AD, hyperactivity, and ADHD symptoms in the 6-year-old children (Table S6). The association between the sweet dietary pattern and ADHD symptoms showed a similar result as shown in Table 2. Children in the highest quartile of the meat and carbohydrate dietary pattern still demonstrated a higher risk of AD, hyperactivity, and ADHD symptoms than those in the lowest quartile. The vegetable dietary pattern was associated with a lower risk of ADHD symptoms in the highest quartiles than in the lowest quartiles.

Food item analysis for the sweet dietary pattern and ADHD symptoms

Table 3 shows the food item analysis for the association between the sweet dietary pattern and AD, hyperactivity, and ADHD symptom scores. A 10 g increased intake of chocolate, chips, crackers, sweet bread, traditional sweet drinks, and jam was associated with an increased risk of ADHD symptoms in the adjusted model. Meanwhile, a 10 g increased intake of tomato juice and other fruit juices significantly decreased the risk of hyperactivity symptoms, and a 10 g increased intake of diet drinks decreased the risk of AD and ADHD symptoms. Therefore, the intake scores for chocolate, chips, and jam were significantly associated with AD, hyperactivity, and ADHD symptoms, whereas tomato juice, fruit juices, and diet drinks may reduce the risk of symptoms.

Discussion

This study found that a sweet dietary pattern in children at age 4 years significantly increased the risk of AD, hyperactivity, and ADHD symptoms at age 6 years. The study also found that a vegetable dietary pattern at age 4 years was negatively associated with ADHD at age 6 years, suggesting that an intake of vegetables may play a protective role against ADHD symptoms in children.

Previous studies have reported associations between several nutritional factors and childhood behavioral disorders such as ADHD. In children with a high intake of Western food [25], junk and snack food [26], soft drinks

Table 2. Associations between dietary patterns in 4-year-old children and attention deficit (AD), hyperactivity, and attention-deficit hyperactivity disorder (ADHD) symptoms in 6-year-old children ($N = 535$).

Factor 1 (Sweets)	AD symptoms RR (CI)	Hyperactivity symptoms RR (CI)	ADHD symptoms RR (CI)
Q1 (Lowest)	1.00	1.00	1.00
Q2	1.11 (0.96–1.29)	1.04 (0.87–1.23)	1.08 (0.97–1.21)
Q3	1.22 (1.05–1.41)**	1.24 (1.05–1.47)**	1.23 (1.10–1.37)**
Q4 (Highest)	1.34 (1.17–1.55)**	1.40 (1.19–1.64)**	1.37 (1.23–1.52)**
Factor 2 (Vegetables)	RR (CI)	RR (CI)	RR (CI)
Q1 (Lowest)	1.00	1.00	1.00
Q2	0.96 (0.84–1.11)	0.91 (0.78–1.07)	0.94 (0.85–1.04)
Q3	0.82 (0.71–0.95)**	0.79 (0.67–0.93)**	0.81 (0.72–0.90)**
Q4 (Highest)	1.02 (0.89–1.17)	0.98 (0.84–1.14)	1.00 (0.90–1.11)
Factor 3 (Meats)	RR (CI)	RR (CI)	RR (CI)
Q1 (Lowest)	1.00	1.00	1.00
Q2	1.19 (1.03–1.36)*	1.14 (0.97–1.34)	1.17 (1.05–1.30)**
Q3	0.97 (0.84–1.13)	1.10 (0.93–1.29)	1.03 (0.92–1.15)
Q4 (Highest)	1.07 (0.93–1.24)	0.93 (0.79–1.10)	1.01 (0.91–1.12)
Factor 4 (Carbohydrates)	RR (CI)	RR (CI)	RR (CI)
Q1 (Lowest)	1.00	1.00	1.00
Q2	1.30 (1.12–1.50)**	1.12 (0.95–1.32)	1.22 (1.09–1.36)**
Q3	1.28 (1.10–1.49)**	1.21 (1.03–1.44)*	1.25 (1.12–1.40)**
Q4 (Highest)	1.32 (1.14–1.53)**	1.29 (1.10–1.52)**	1.31 (1.17–1.46)**

Note: Values are adjusted for age (months), sex, paternal education, exposure to second-hand smoke, body mass index *z*-score, energy intake, maternal age, and gestational age. RR, relative risk; CI, confidence interval.
* <0.05, ** <0.01.

Table 3. Associations between intake of sweets in 4-year-old children and attention deficit (AD), hyperactivity, and attention deficit hyperactivity disorder (ADHD) symptoms in 6-year-old children (per 10 g increase).

Food groups	Food	AD symptoms RR (95% CI)	Hyperactivity symptoms RR (95% CI)	ADHD symptoms RR (95% CI)
Chocolate	Chocolate	**1.15 (1.05––1.26)****	**1.15 (1.04–1.27)****	**1.15 (1.07–1.23)****
Fruit juice	Orange juice	1.00 (0.99–1.01)	0.99 (0.98–1.01)	1.00 (0.99–1.01)
	Tomato juice	0.99 (0.97–1.02)	**0.95 (0.92–0.99)***	0.98 (0.96–1.00)
	Other fruit juices	0.99 (0.98–1.00)	**0.98 (0.96–0.99)***	**0.98 (0.97–0.99)***
Ice cream	Ice cream	1.00 (0.98–1.01)	0.98 (0.97–1.00)	0.99 (0.98–1.00)
Snacks	Chips	**1.09 (1.02–1.16)****	**1.19 (1.11–1.27)****	**1.13 (1.08–1.19)****
	Crackers	1.05 (0.97–1.14)	**1.09 (1.00–1.18)***	**1.07 (1.01–1.13)***
Sweet bread	Sweet bread	**1.08 (1.04–1.13)****	1.04 (0.98–1.09)	**1.06 (1.03–1.10)****
Sweet drinks	Traditional sweet drinks	**1.06 (1.00–1.12)***	**1.06 (1.00–1.13)***	**1.06 (1.02–1.10)****
	Cocoa	**1.03 (1.00–1.07)***	0.97 (0.93–1.02)	1.01 (0.98–1.04)
	Soft drinks	1.00 (0.98–1.02)	1.00 (0.98–1.02)	1.00 (0.99–1.01)
	Diet drinks	**0.89 (0.80–0.98)***	0.95 (0.87–1.05)	**0.92 (0.86–0.99)***
	Sport drinks	0.98 (0.95–1.01)	1.01 (0.98–1.04)	0.99 (0.97–1.01)
Sweets	Candies	0.87 (0.47–1.62)	1.33 (0.68–2.61)	1.05 (0.67–1.66)
	Jam	**1.16 (1.05–1.27)****	**1.18 (1.07–1.31)****	**1.17 (1.09–1.25)****

Note: Values are adjusted for age (months), sex, paternal education, exposure to second-hand smoke, body mass index *z*-score, energy intake, maternal age, and gestational age. RR, relative risk; CI, confidence interval.
* <0.05, **<0.01.

[27], and sweets, an association with greater odds ratios (ORs) for ADHD has been reported than for children with a low intake of these foods. The Western food, such as higher total fat, saturated fat, and sodium intake, was found to increase odds ratio for ADHD [25]. The hypothesis was that higher intake of Western food leads to eat a higher intake of food additives, flavors, or colors, which may change neurotransmitter function because of poor micronutrient intake [28]. Two studies showed that inadequate micronutrient intake was associated with increasing anxiety symptoms among children [29] or ADHD symptom in adult cohort [30]. The junk and snack food also have many additives and food colorings as well as poor nutritional quality [26]. In addition, a higher junk food diet tends to contain lower levels of fatty acid such as omega-3 and omega-6 [31]. It was reported that lower level was associated with hyperactive children [32]. Lien et al. showed a strong relationship between soft drink consumption and hyperactivity among Norway adolescents [27]. They explained that substances, such as a high sugar intake and caffeine in soft drink, may trigger mental health problems among adolescents.

However, Mediterranean dietary patterns [6] were inversely associated with a diagnosis of ADHD. Ríos-Hernández, Alejandra, et al. showed the association between ADHD diagnosis and lower intake of Mediterranean dietary pattern among 9-year-old children [6] They explained that lower plasma level of some nutrients, such as iron, ferritin, and zinc, according to the lower intake of Mediterranean dietary pattern, was related to ADHD among children.

Recently, associations between dietary patterns and ADHD have been investigated in studies in Asian countries. In one study in China, preschoolers in the highest quintile of the processed and snack food dietary pattern categories had higher ORs for having ADHD symptoms than those in the lowest quintile after adjusting for potential confounders. Those with the lowest score in the vegetarian category were reported to be more likely to have ADHD symptoms [33]. In another study in China, a dietary pattern, involving a high intake of shellfish, deep water fish, freshwater fish, white meat, fungi and algae, and organ meat, and a nutrient dietary pattern with a high intake of zinc, protein, phosphorus, selenium, calcium, and riboflavin, was inversely associated with having ADHD [34]. There are two association studies between dietary intake and ADHD in Korean children. S. Park et al. examined the association dietary behaviors using 10 mini-dietary assessments for Koreans and learning disabilities and related externalizing problems including ADHD [10]. The result showed that high intake of sweetened desserts instead of a balanced diet and regular meals is associated with increasing behavioral problems. Our result was consistent with this because one of the risk factors on ADHD symptom was a high intake of sweetened desserts. Woo et al. reported that ORs for ADHD symptoms were negatively associated with a traditional Korean dietary pattern, involving a high intake of kimchi and grains and a low consumption of fast foods and beverages, in Korean children [11]. It was also consistent with our result that a high intake of vegetables was beneficially associated with the risk of ADHD. This study explained that the traditional Korean dietary pattern, which contained high intakes of polyunsaturated fatty acids (PUFAs), has beneficial effects on ADHD [11]. Our result showed that the highest quartile of vegetable groups lead to the highest PUFA intake (see Table S7).

An association between a high sugar intake and mental health in children has been reported in previous studies. Lien et al. found an association between the consumption of sugar-rich nutrients and attention and depression issues in children [27]. An unhealthy prenatal diet such as one high in fat and sugar is linked with ADHD [35]. The positive association between sugar consumption and ADHD was reported in a cohort study [36] and a meta-analysis [37]. Although a high sugar-rich intake has been constantly reported to be associated with the risk of ADHD including our study, a more longitudinal study should be needed to investigate a causal relationship. A key contribution of our study is to expand the knowledge based on current studies by reporting on the longitudinal relations of dietary pattern at age 4 and ADHD symptom at age 6. We also found that the association between the 'sweet' dietary pattern at age 6 as well as at age 4, and attention deficit or ADHD symptom at age 6, are consistently significant (see Table S3 and Table S6).

There are several mechanisms concerning the association between sugar intake and behavioral problem. Mergenthaler et al. showed that glucose metabolism is linked to brain activity. The review article showed the evidence that glucose metabolism is strongly associated with neuronal activity from functional brain imaging [38]. High sugar intake causes high levels of insulin secretion in the pancreas resulting in delayed hypoglycemia, which stimulates an increase of epinephrine to activate neurological and behavioral disorders [39]. Other study has shown that long-term sugar intakes cause dopaminergic signaling dysfunction, such as a gradual decrease in dopamine reactions. These dysfunctions are reported to involve the frontal cortex, a direct area responsible for the control mechanism of ADHD [36].

Our results showed protective effects between fruit juice, including tomato juice, and hyperactivity, and diet drinks and ADHD (see Table 3). However, we observed opposite effects for jams. Because fruit juices are high in fructose and jams are high in sucrose, the difference in fructose and sucrose may raise a question of different roles in ADHD. Jam contains much more sugar per volume compared to fruit juice, which is high in micronutrients such as vitamin C that is known well to be good for mental health [40].

Diet drink in Korea contains aspartame which is an artificial sweetener instead of sugar. There are several studies showing the association between consumption of aspartame and neurophysiological symptoms. However, it should be investigated more before conclusion is reached about the association [41].

Our results showed a negative association between a vegetable dietary pattern and ADHD symptoms. The protective effect of vegetable and fruit intake against ADHD symptoms has been mainly attributed to the antioxidant effect of dietary polyphenols present in fruits and vegetables [42]. Dietary polyphenol intake has been reported to have provided positive effects on psychiatric patients in terms of modulating behavior, mood, and cognition [43].

This study had some limitations. First, we could not clearly establish a causal relationship because of additional complicating factors. For example, our study cannot reflect a parental style and their inability to control the food intake or behavior of the child [44]. Furthermore, eating large amounts of sweetened desserts and having an unbalanced diet among children with ADHD symptoms may be due to the children's non-responsiveness to their parents' efforts to encourage improved eating behaviors [10]. Second, childhood behavioral problems were measured using the parental K-ARS. Parents may have underestimated the extent of behavioral issues in relation to their children's conduct. However, any misclassification would have attenuated any association toward the null hypothesis. In addition, there is low prevalence of ADHD in our study population because only a few met the cutoff of clinical diagnosis. A recent study showed that children with subthreshold ADHD symptoms had a higher rate of negative behavior problems, such as deficits in cognitive, interpersonal, and school functions, than non-ADHD children [45].

Therefore, our result with subthreshold scores of ADHD also merits attention. Further studies on the association between sugar dietary intake and behavioral problems among children regarding academic performance, attention, and learning ability are needed.

Finally, healthy children may also require higher energy when they increase in sport and physical activity. Therefore, when interpreting 'energy' intake of ADHD children, we need to consider energy increase of normal children when they increase physical activity.

Nevertheless, this study had several strengths. First, our study used the dietary pattern analysis, which was an overall consideration of diet rather than the selection of isolated foods or nutrients. The results of the analysis can be useful for dietary recommendations as they reflect the effects of many foods and their combinations simultaneously [46]. Second, we estimated dietary patterns in children using data from a prospective cohort study. Therefore, we could analyze the association between dietary patterns in 4-year-old children and ADHD symptoms in 6-year-old children. So, one consideration of our study was that we tried to analyze in a longitudinal design to conclude the causal nature of ADHD instead of a cross-sectional study. Finally, because we utilized data from a cohort study involving a general population of children rather than a study of children diagnosed with ADHD, the findings of the present study can be useful in guiding public health policies for children.

In sum, our study showed that a sweet dietary pattern in children at age 4 years was positively associated with AD, hyperactivity, and ADHD symptoms at age 6 years, while a vegetable dietary pattern was negatively associated with ADHD symptoms. Such findings can be useful for further understanding the roles of dietary factors in ADHD. Further studies on the effects of dietary patterns on mental health in children are warranted.

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Conflicts of interest

The authors declare no conflict of interest.

Disclosure statement

To the best of our knowledge, the named authors have no conflict of interest, financial or otherwise(s).

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References

[1] Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual research review: a meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. J Child Psychol Psychiatry. 2015;56(3):345–65.
[2] Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics. 2015;135(4):e994–e1001.
[3] Trapp GS, Allen KL, Black LJ, Ambrosini GL, Jacoby P, Byrne S, et al. A prospective investigation of dietary patterns and internalizing and externalizing mental health problems in adolescents. Food Sci Nutr. 2016;4(6):888–96.
[4] Biederman J, Faraone S, Spencer T, Mick E, Monuteaux M, Aleardi M. Functional impairments in adults with self-reports of diagnosed ADHD. J Clin Psychiatry. 2006;67(4):524–40.
[5] Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: adaptive functioning in major life activities. J Am Acad Child Adolesc Psychiatry. 2006;45(2):192–202.
[6] Ríos-Hernández A, Alda JA, Farran-Codina A, Ferreira-García E, Izquierdo-Pulido M. The Mediterranean diet and ADHD in children and adolescents. Pediatrics. 2017;139(2):e20162027.
[7] Mohammadpour N, Jazayeri S, Tehrani-Doost M, Djalali M, Hosseini M, Effatpanah M, et al. Effect of vitamin D supplementation as adjunctive therapy to methylphenidate on ADHD symptoms: a randomized, double blind, placebo-controlled trial. Nutr Neurosci. 2018;21(3):202–9.
[8] Gow RV, Hibbeln JR, Parletta N. Current evidence and future directions for research with omega-3 fatty acids and attention deficit hyperactivity disorder. Curr Opin Clin Nutr Metab Care. 2015;18(2):133–8.
[9] Tippairote T, Temviriyanukul P, Benjapong W, Trachootham D. Hair zinc and severity of symptoms are increased in children with attention deficit and hyperactivity disorder: a hair multi-element profile study. Biol Trace Elem Res. 2017;179(2):185–94.
[10] Park S, Cho SC, Hong YC, Oh SY, Kim JW, Shin MS, et al. Association between dietary behaviors and attention-deficit/hyperactivity disorder and learning disabilities in school-aged children. Psychiatry Res. 2012;198(3):468–76. Epub 2012/09/25. doi: 10.1016/j.psychres.2012.02.012. PubMed PMID: 22999993.
[11] Woo H, Kim D, Hong Y-S, Kim Y-M, Seo J-H, Choe B, et al. Dietary patterns in children with attention deficit/hyperactivity disorder (ADHD). Nutrients. 2014;6(4):1539–53.
[12] Sayal K, Prasad V, Daley D, Ford T, Coghill DJTLP. ADHD in children and young people: prevalence, care pathways, and service provision. Lancet Psychiatry. 2018;5(2):175–86.
[13] Kim K-N, Lim Y-H, Shin CH, Lee YA, Kim B-N, Kim JI, et al. Cohort profile: The Environment and Development of children (EDC) study: a prospective children's cohort. Int J Epidemiol. 2018;47(4):1049–50.
[14] Lim Y. Reliability and validity of a semi-quantitative food frequency questionnaire for Korean pre-school children. Seoul: Kyung Hee University; 2001.
[15] Oh S, Chung J, Kim M, Kwon S, Cho B. Antioxidant nutrient intakes and corresponding biomarkers associated with the risk of atopic dermatitis in young children. Eur J Clin Nutr. 2010;64(3):245.
[16] Chung J, Kwon S-O, Ahn H, Hwang H, Hong S-J, Oh S-YJN. Association between dietary patterns and atopic dermatitis in relation to GSTM1 and GSTT1 polymorphisms in young children. Open Access. 2015;7(11):9440–52.

[17] Pappas D. ADHD Rating Scale-IV: Checklists, norms, and clinical interpretation. J Psychoeduc Assess. 2006;24(2):172–8.
[18] Kim J-w, Park K-h, Cheon K-a, Kim B-n, Cho S-c, Hong K-EM. The child behavior checklist together with the ADHD rating scale can diagnose ADHD in Korean community-based samples. Can J Psychiatry. 2005;50(12):802–5.
[19] So YK, Noh JS, Kim YS, Ko SG, Koh YJ. The reliability and validity of Korean parent and teacher ADHD rating scale. J Korean Neuropsychiatr Assoc. 2002;41(2):283–9.
[20] Hong S-B, Im M-H, Kim J-W, Park E-J, Shin M-S, Kim B-N, et al. Environmental lead exposure and attention deficit/hyperactivity disorder symptom domains in a community sample of South Korean school-age children. Environ Health Perspect. 2015;123(3):271.
[21] Kim MJ, Park I, Lim MH, Paik KC, Cho S, Kwon H-J, et al. Prevalence of attention-deficit/hyperactivity disorder and its comorbidity among Korean children in a community population. J Korean Med Sci. 2017;32(3):401–6.
[22] Moon JS, Lee SY, Nam CM, Choi J-M, Choe B-K, Seo J-W, et al. Korean National Growth Charts: review of developmental process and an outlook. Korean J Pediatr. 2007;51(1):1–25.
[23] Willett W. Implications of total energy intake for epidemiologic analyses. Nutritional Epidemiology. 1998: 273–301.
[24] McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. Am J Epidemiol. 2003;157(10):940–3. Epub 2003/05/15. doi: 10.1093/aje/kwg074. PubMed PMID: 12746247.
[25] Howard AL, Robinson M, Smith GJ, Ambrosini GL, Piek JP, Oddy WH. ADHD is associated with a 'Western' dietary pattern in adolescents. J Atten Disord. 2011;15(5):403–11. doi: 10.1177/1087054710365990. PubMed PMID: 20631199.
[26] Wiles NJ, Northstone K, Emmett P, Lewis G. 'Junk food' diet and childhood behavioural problems: results from the ALSPAC cohort. Eur J Clin Nutr. 2009;63(4):491–8. doi:10.1038/sj.ejcn.1602967. PubMed PMID: 18059416; PubMed Central PMCID: PMCPMC2664919.
[27] Lien L, Lien N, Heyerdahl S, Thoresen M, Bjertness E. Consumption of soft drinks and hyperactivity, mental distress, and conduct problems among adolescents in Oslo, Norway. Am J Public Health. 2006;96(10):1815–20.
[28] McCann D, Barrett A, Cooper A, Crumpler D, Dalen L, Grimshaw K, et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. The Lancet. 2007;370(9598):1560–7.
[29] Kaplan BJ, Crawford SG, Gardner B. Farrelly GJJoc, psychopharmacology a. Treatment of mood lability and explosive rage with minerals and vitamins: two case studies in children. J Child Adolesc Psychopharmacol. 2002;12(3):205–19.
[30] Kaplan BJ, Fisher JE, Crawford SG, Field CJ, Kolb B. Psychopharmacology a. improved mood and behavior during treatment with a mineral-vitamin supplement: an open-label case series of children. J Child Adolesc Psychopharmacol. 2004;14(1):115–22.
[31] Lauritzen LJPLR. The essentiality of long chain n-3 fatty acids in relation to development and function of the brain and retina. Prog Lipid Res. 2001;40:1–94.
[32] Schnoll R, Burshteyn D, Cea-Aravena JJAP. Biofeedback. Nutrition in the treatment of attention-deficit hyperactivity disorder: a neglected but important aspect. Appl Psychophysiol Biofeedback. 2003;28(1):63–75.
[33] Yan S, Cao H, Gu C, Ni L, Tao H, Shao T, et al. Dietary patterns are associated with attention-deficit/hyperactivity disorder (ADHD) symptoms among preschoolers in mainland China. Eur J Clin Nutr. 2018;72(11):1517–23.
[34] Zhou F, Wu F, Zou S, Chen Y, Feng C, Fan G. Dietary, nutrient patterns and blood essential elements in Chinese children with ADHD. Nutrients. 2016;8(6):352.
[35] Murcia C. Unhealthy prenatal diet linked to ADHD: first-of-its-kind study connects high-fat, high-sugar diet with ADHD in offspring. Contemp Pediatr. 2017;34(1):27–8.
[36] Del-Ponte B, Anselmi L, Assunção MCF, Tovo-Rodrigues L, Munhoz TN, Matijasevich A, et al. Sugar consumption and attention-deficit/hyperactivity disorder (ADHD): a birth cohort study. J Affect Disorders. 2019;243:290–6.
[37] Del-Ponte B, Quinte GC, Cruz S, Grellert M, Santos IS. Dietary patterns and attention deficit/hyperactivity disorder (ADHD): a systematic review and meta-analysis. J Affect Disord. 2019;252:160–73. doi:10.1016/j.jad.2019.04.061. PubMed PMID: 30986731.
[38] Mergenthaler P, Lindauer U, Dienel GA, Meisel A. Sugar for the brain: the role of glucose in physiological and pathological brain function. Trends Neurosci. 2013;36(10):587–97.
[39] Yu C-J, Du J-C, Chiou H-C, Feng C-C, Chung M-Y, Yang W, et al. Sugar-sweetened beverage consumption is adversely associated with childhood attention deficit/hyperactivity disorder. Int J Environ Res Public Health. 2016;13(7):678.
[40] Lamport DJ, Saunders C, Butler LT, Spencer JP. Fruits, vegetables, 100% juices, and cognitive function. Nutr Rev. 2014;72(12):774–89.
[41] Choudhary AK, Lee YY. Neurophysiological symptoms and aspartame: what is the connection? Nutr Neurosci. 2018;21(5):306–16.
[42] Han X, Shen T, Lou H. Dietary polyphenols and their biological significance. Int J Mol Sci. 2007;8(9):950–88.
[43] Trebatická J, Ďuračková Z. Psychiatric disorders and polyphenols: can they be helpful in therapy? Oxid Med Cell Longevity. 2015;2015:248529.
[44] Deheeger M, Rolland-Cachera M, Fontvieille A. Physical activity and body composition in 10 year old French children: linkages with nutritional intake? Int J Obes. 1997;21(5):372.
[45] Kirova A-M, Kelberman C, Storch B, DiSalvo M, Woodworth KY, Faraone SV, et al. Are subsyndromal manifestations of attention deficit hyperactivity disorder morbid in children? A Systematic Qualitative Review of the Literature with Meta-Analysis. 2019;274:75–90.
[46] Schulze MB, Hu FB. Dietary patterns and risk of hypertension, type 2 diabetes mellitus, and coronary heart disease. Curr Atheroscler Rep. 2002;4(6):462–7.