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Review

Empirically derived dietary patterns and food groups intake in relation with Attention Deficit/Hyperactivity Disorder (ADHD): A systematic review and meta-analysis

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SUMMARY

Background and aims: Attention Deficit Hyperactivity Disorder (ADHD) is a prevalent chronic psychiatric condition in children world wide. This study was aimed to provide an overview of food groups and dietary patterns in ADHD children as a systematic review.
Methods: The relation between dietary patterns and this disorder was also investigated through meta-analysis. Databases including Google Scholar, SCOPUS, ISI Web of science, and PubMed were searched up to June 2017. Studies on posteriori derived dietary patterns and food intakes of ADHD children were included. The achieved Relative Risks (RR) and Odds Ratio (OR) were pooled together for ADHD to compare the most and the least adherence to major dietary patterns. The heterogeneity was assessed by Cochran's Q test and I-squared methods.
Results: This systematic review consisted of 6 dietary patterns and 6 foods or macronutrients studies. In this regard, 6 dietary patterns studies (n: 8816) were included in the meta-analysis. The pooled analysis established that "healthy" dietary pattern significantly decreased the risk of ADHD (OR: 0·63; 95% CI: 0·41, 0·96), whereas "Western" (OR: 1.92; 95% CI: 1.13, 3.26; p:0.016) and "junk food" (OR: 1.51; 95% CI: 1.06, 2.16; p: 0.024) dietary patterns increased it.
Conclusions: "Healthy" dietary pattern highly loaded with vegetables, fruits, legumes, and fish has decreased the odds of ADHD up to 37%. In addition, adherence to "junk food" pattern containing sweetened beverages and desserts as well as "Western" dietary pattern including red meat, refined grains, processed meats, and hydrogenated fat increased it.

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common chronic mental disorders among children [1]. The prevalence of ADHD was 7.2% all over the world in 2015 and has been growing every year [2,3]. ADHD children are disturbed by learning disorders, depression, anxiety, and adverse social impact [4–6]. They will also have academic problems, antisocial behavior, addictive behavior, and obesity in their adulthood [7].

Genetic, environmental and biological factors (i.e. existence of toxic chemicals in the environment, head injury, complications during pregnancy) have long been attributed to the incidence of ADHD [8,9]. However, the relation between nutrition and ADHD has been investigated from 1996 [10–12]. Diet as one of the most effective modifiable factors plays a fundamental role in neurological and behavioral symptoms [13]. Earlier findings have established the role of nutrients such as zinc [14], copper [15], iron [16], magnesium [17], and ratio of w3 to w6 intake [18] on ADHD. Unhealthy foods consumption such as sweetened beverages, desserts, snacks, and chocolates following by increase of energy intake

Abbreviations: ADHD, Attention deficit hyperactivity disorder; PUFAs, Poly unsaturated fatty acids; LC-PUFAs, Long chain poly unsaturated fatty acids; FFQ, Food frequency questionnaire; ERC-Mg, Magnesium of eritrocyte; BMI, Body mass index; OR, Odds ratio; RR, Risk ratio; CI, Confidence interval; SDQ, Strengths and difficulties questionnaire; DASH, Dietary approaches to stop hypertension; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders IV.

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among children have been concerned during the last decade [19,20].

Dietary patterns analysis is the newest approach in diet and ADHD that showed more comprehensive view of the diet and the nutriens interaction than a single food or nutrient [21–23]. Up to now, two methods of hypothesis-oriented approach or priori used diet quality scores based on the recommended diet or dietary guidelines [24,25] and posteriori or empirically analysis for derived dietary patterns have been applied. Previous studies over the relationship between dietary patterns and ADHD have yielded inconclusive results. For example in a cohort study, western dietary pattern loaded with red meat, refined grains, processed meats, and hydrogenated fat increased the incidence of ADHD, but no significant relation was found in the literature. Similarly one study showed that healthy dietary pattern highly loaded with vegetables, fruits, legumes, and fish could significantly decrease ADHD risk, while other studies did not [26–28]. The relation between refined grains intake and ADHD have been strongly approved [27,29,30]. Therefore, it is interesting to explore the relation of "sweet" and "junk" dietary patterns highly loaded with refined grain with ADHD. The relation between meat, fish, fruits, vegetables, sweetened beverages, desserts, and dairy products consumption and ADHD were explored in food group studies [31–33]. To the best of our knowledge, only one review study assessed the effects of nutrition (including single nutrient, food and diet) on ADHD [34]. Moreover, there have not been any systematic review and meta-analysis exploring dietary patterns and food groups in ADHD children. Thus, this systematic review and meta-analysis aimed to assess the relation of food groups and dietary patterns using posteriori approach with ADHD.

2. Materials and methods

2.1. Search strategy

An electronic literature search was conducted in Google Scholar, SCOPUS, ISI Web of science, and PubMed in June 2017. The search strategies used text words and relevant indexings [medical subject heading (MeSH) terms] to obtain English studies assessing the relation of food groups and dietary patterns with ADHD children up to 2017. Our search included a combination of MeSH and text-based terms keywords: attention deficit hyperactivity disorder, ADHD, inattention, impulsivity, minimal brain dysfunction, attention deficit and disruptive behavior disorder, hyper kinesia, attention, hyperactivity disorder, attention deficit, children, adolescence, dietary pattern, dietary patterns, food pattern, food patterns, eating, eating pattern, diet, food intake, eating behavior, Mediterranean, prudent, food frequency, food-frequency questionnaire, FFQ, Dietary approaches to stop hypertension, DASH, vegetables, fruits, meat, legume, cereal, dairy products, whole grain, Western diet, western dietary, Reduced rank regression, posteriori, priori, cluster analysis, factor analysis, and principle component analysis. The search was updated in February 2017. The process of study selection is shown in Fig. 1.

2.2. Inclusion and exclusion criteria

Studies that diagnosed ADHD by behavioral questionnaire such as DSMIV, SDQ or Conner's scale among participants in the age range of 6–14 years and focused on assessing food intake and dietary pattern were included. In this regard, only studies that

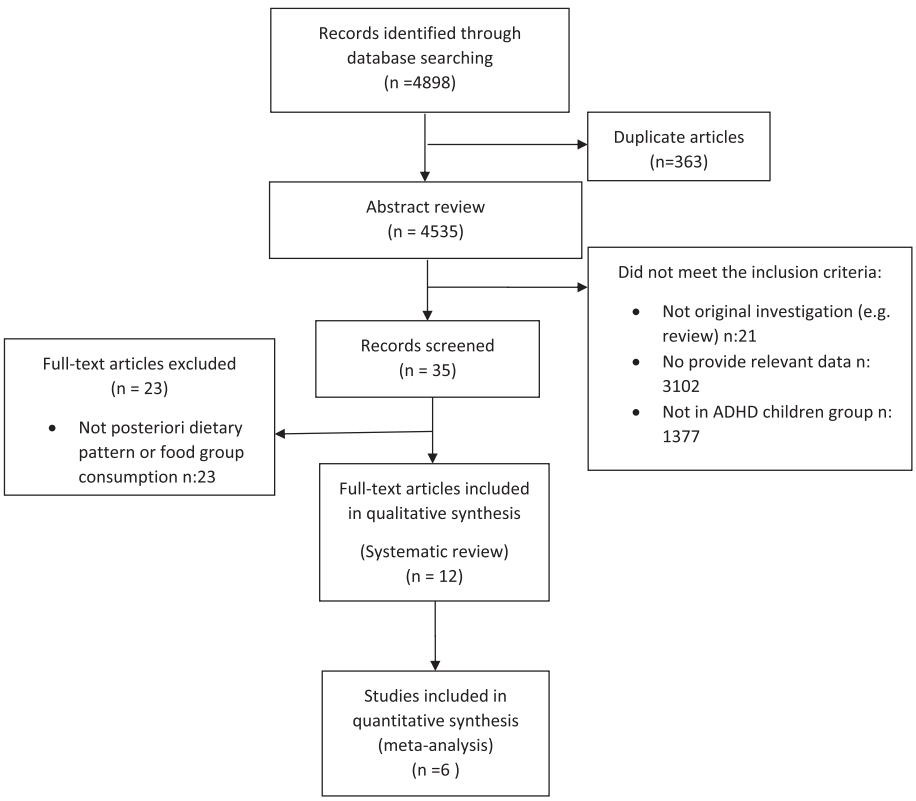

Fig. 1. Flowchart of the study selection process.

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reported ORs of ADHD and measures of variability (SEs or 95% CIs from which these could be derived) were included.

2.3. Data extraction and data synthesis

Information extracted from each study included: first author's family name, publication year, geographic region in which the study was conducted and designed, participants' gender, participants' age, sample size, duration of follow-up, dietary assessment method, the number of ADHD cases, OR with their corresponding confidence intervals (CIs), and confounding factors adjusted in analysis. Two independent reviewers read the abstract of articles retrieved in the first search to identify the relevant studies. Both reviewers agreed on relevant abstracts and then the full-text of articles were reviewed to extract researches on food consumption or dietary pattern by factor analysis and/or principle component analysis in ADHD children. To minimize error, only the most common patterns were identified from the remaining articles and the selected dietary patterns similar in foods' factor loadings were categorized under the same dietry pattern group. For instance, if food groups were highly loaded in fruits, vegetables, grains, and fish, they were named “healthy” dietary pattern. But if unhealthy food groups such as red meat, processed meat, animal fat, and salt were consumed, the dietary pattern was categorized as “Western”. Dietary pattern highly loaded with food groups such as sweets, sweetened beverages, snaks, ice creams, and fastfoods were named " junk food” dietary pattern as a separate main dietary pattern.

The achieved RR and OR were pooled together for ADHD to compare the most and the least adherence to major dietary patterns. Since some studies used several models to adjust for confounding variables, the models with the most number of variables were entered in the meta-analysis. The derived dietary patterns and informations were independently categorized by two reviewers (E SH and MH) and discrepancies were resolved through consulation with another author (A.S.A). This study was designed and reported based on PRISMA guidelines [35].

2.4. Quality assessment of studies

The quality of relevant articles was assessed by using the Newcastle–Ottawa quality assessment scale for cohort, cross-sectional and case control studies. An eight-question checklist was filled for eligible studies [36]. Study selection, data extraction, and quality assessment were performed independently by 2 reviewers.

2.5. Statistical analysis

Odds ratios and their corresponding 95% CIs were used to estimate log OR and its standard error as effect size of different dietary patterns on likelihood of ADHD. Random effects model was used to combine effect sizes because it takes between-studies heterogeneity and deign difference into account [37]. The between-studies heterogeneity was checked using Cochran's Q test and I-squared. To explore the sensitivity of analyses to a specific study or a particular group of studies, sensitivity analysis was carried out. Publication bias was also checked plotting log ORs against their corresponding standard errors (SEs) in Begg's funnel plots [38]. Furthermore, the statistical asymmetry of the funnel plot was assessed using Egger's regression asymmetry test and Begg's adjusted rank correlation test [37]. All analyses were conducted by STATA software, version 11.2 (STATA Corp, College Station, TX). P value of lower than 0.05 was considered as statistically significant.

3. Results

In the initial search, 4898 articles were found, among which 363 studies were repeated. By scanning titles and abstracts and based on the inclusion criteria, 12 relevant articles were eligible [26–28,30–33,39–44]. Further investigations showed that 6 studies were about dietary patterns in ADHD children [26–28,30,40,42] and 6 of them were about food consumption [30–33,41,43,44]. Dietary pattern studies consisted of 2 cohort [26,30], 2 cross-sectional [27,40], and 2 case–control [28,42] studies in ADHD children. Totally, 4886 children with and without ADHD were included in the selected studies.

Studies were adjusted according to the estimated odds or risk for confounding variables such as age, sex, physical activity, energy intake, BMI, and socio-economic factors.

Detailed information about the eligible studies in the systematic review and meta-analysis are reperesented in Table 1.

3.1. Results of systematic review

3.1.1. Food groups associated with risk of ADHD

Three studies found that high intake of sweetened beverages are associated with ADHD children, even after adjustment for dopaminergic gene variations [41]. One study did not prove the protective effect of fish consumption in ADHD children [33]. High intakes of sweetened desserts, fried foods, and salt were associated with increasing learning, attention, and behavioral problems. However, a balanced diet of regular meals with high intake of dairy products and vegetables were related with decrease of learning, attention, and behavioral problems [31]. A case–control study reported that consumption of cereals, meat, pulses and fruits was significantly higher in healthy children than ADHD [44].

3.2. Results of meta-analysis

3.2.1. Dietary patterns decreasing the odds of ADHD

The meta-analysis showed that “healthy” food pattern highly loaded with fruits, vegetables, and fish is protectively related with ADHD (OR: 0.63; 95% CI: 0.41, 0.96; Fig. 2). Moreover, heterogeneity was not observed among studies (Cochrane Q test, $p = 0.113$; $I^2 = 46.5\%$). Five researches evaluated the association between “healthy” dietary pattern and ADHD among children [26–28,42]. One of them conducted in Korean population indicated that “traditional-healthy” dietary pattern significantly decreased the risk of ADHD [28]. In addition, a case–control study which investigated three dietary patterns of “vegetable-fruit”, “fish-white meat”, and “grain-bean” showed that food groups highly loaded with healthy foods could significantly decrease the risk of ADHD in Chinese children [42]. In addition, “varied Norwegian” pattern indicated decrease of ADHD odds in children [40]. Yet, two studies did not prove this significant relation [26,27].

3.2.2. Dietary patterns increasing the odds of ADHD

There were 2 studies dealing with the Western dietary pattern in meta-analysis [26,27]. The comparison between intake categories of Western dietary pattern and meta-analysis showed significant association with increased odds of ADHD (OR: 1.92; 95% CI: 1.13,3.26; $p = 0.016$) and no heterogeneity was observed (Cochrane Q test, $p = 0.406$; $I^2 = 0.0\%$; Fig. 2). Only one cohort study on 115 adolescents showed that “Western” dietary pattern can significantly increase the risk of ADHD [26], however in a cross-sectional study no significant correlation was reported [27]. The results of pooled analysis from five studies [27,28,30,40,42] represented a significant relation between “junk food” dietary pattern and ADHD (OR = 1.51; 95% CI: 1.06, 2.16; $p = 0.024$; Fig. 2). The heterogeneity

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Table 1
Characteristics of included studies in this systematic review and meta-analysis.

study	location	design	Sample size	Diet-assessment method	Dietary patterns identified	Odds ratio (OR)	Factors adjusted in analyses (multivariable)	Study quality
Howard et al. [26] (2011)	Australia	cohort	2868 (115) 14 year old adolescence	Food-frequency questionnaire (38:past year)	"Healthy" "Western"	1.02 (0.61,1.70) 2.21 (1.18,4.13)	Sex, maternal education, maternal smoking during pregnancy, biological father living with family, family income, Maternal stress events, single-parent family, physical activity, sedentary activity, total energy intake	9/9
Hae Dong Woo et al. [28] (2014)	Korea	Case control	Cases 96 Controls 96 7–12 year old children	24-h recall (3 nonconsecutive)	"traditional" "seaweed-egg" "traditional-healthy" "snack"	0.76 (0.26,2.24) 0.84 (0.36,1.94) 0.31 (0.12,0.79) 1.59 (0.65,3.91)	Gestation age, birth weight, mother's age, birth order, father's education, and father's occupation, total energy intake, omega-3 fatty acids, lead, and mercury consumption	6/9
Leila Azadbakht et al. [27] (2012)	Iran	Cross sectional	375 5–10 year old children	semi quantitative food-frequency questionnaire (134:past year)	"Healthy" "Western" "sweet" "fast food"	0.84 (0.28,2.21) 1.34 (0.58,4.29) 3.95 (1.16,15.31) 3.21 (1.05,10.90)	Sex, age, socioeconomic status, and family history of ADHD, energy intake	9/10
Inger M Oellingrath et al. [40] (2014)	Norway	Cross sectional	789 (44) 12–13year old adolescence	Food-frequency questionnaire (40: last 6 month)	"varied Norwegian" "junk/Convenient" "snacking" "dieting"	0.4 (0.2, 0.8) 3.4 (1.3,8.6) 1.6 (0.7, 3.5) 1.3 (0.6,2.7)	Sex, maternal and paternal education, family income, family structure, child physical activity, sedentary activity, BMI	9/10
Fankun Zhou [42] (2016)	China	Case control	Case 296 Control 296 6–14 years old children	Food-frequency questionnaire (144 items:past year)	"vegetable-fruit" "fish-white meat" "grain-bean" "fast food-sweet"	0.69 (0.42, 1.13) 0.44 (0.27, 0.73) 0.60 (0.36, 1.05) 1.25 (0.76, 2.06)	BMI, energy intake, family history of ADHD, household composition, maternal smoking during pregnancy, maternal drinking during pregnancy, paternal smoking before childbirth, paternal smoking after childbirth, maternal abortion history, maternal age at childbirth, parents' education, household income, labor or delivery complications, birth weight, twin, full-term pregnancy, breast feeding, emotional abuse, and family conflicts	7/9
NJ Wiles et al. [30] (2007)	UK	cohort	9550 (4000) 7 year old children	food frequency questionnaire	"Junk food"	1.19 (1.10,1.29)	Sex, maternal smoking (during pregnancy and when the child was aged 4), maternal age at the birth of the child, number of siblings, socio-economic markers (maternal education, housing tenure, household overcrowding and car ownership), birth weight, gestational age, maternal depression and anxiety, maternal enjoyment and single-parent household	8/9
Ching-Jung Yu [41] (2016)	Taiwan	Case control	173 159 Aged 4-15	Food recall questionnaire (previous month)	Sweetened beverages Meat Milk Vegetables Fruits	3.69 (1.29,10.60) [a]14.02 v.s 18.14 (P-value:0.04) 3.33 v.s 5.01 (P-value:0.02) 16.61 v.s 11.97 (P-value:<0.01) 5.70 v.s 4.78 (P-value:0.02)	Sex, consumption of milk/meat/fruit/vegetables, family history of nervous system diseases, parental education levels, maternal alcohol consumption during pregnancy, gene polymorphism of DRD4 at rs752306	6/9
Gabriele Kohlboeck et al. [43] (2012)	Germany	Cross sectional	3361 (435) Aged 11	Food-frequency questionnaire (82:past year)	OMD diet (lower in fat and saturated fatty acids and contains ample amounts of plant foods)	0.91 (0.83,0.99)	Sex, study center, socio demographic characteristics, BMI, physical exercise, television viewing/PC use and total energy intake	9/10

Subin Park et al. [31] (2012)	Korea	Cross sectional	986	mini-dietary assessment (MDA)	sweetened desserts fried food salt balanced diet dairy products vegetables	1.41 (0.73, 2.10) 0.74 (−0.01, 1.50) 1.21 (0.36, 2.07) −1.15 (−1.86, −0.43) −0.71 (−1.45, 0.03) −0.86 (−1.57, −0.14)	Sex, age, IQ, paternal and maternal educational years, socio-economic state, residential area, and body mass index.	10/10
R.H.M. de Groot [33] (2012)	Netherlands	Cross sectional	700	self-report questionnaire (by the parents/guardians of the participants)	No significant relationship was found between fish consumption and ADHD	F (3,681) = 0.94 P = 0.42	Sex, age, and level of parental education	10/10
Deborah L. Schwartz [32] (2015)	USA	Cross sectional	1649 (242) 11–13 year old	24 h recall (5 item)	Sweetened beverage	1.14 (1.04, 1.25)	Sex, age, race/ethnicity, school lunch eligibility, family structure and sugary food consumption	9/10
T. Durá Travé [44] (2013)	New Mexico	Case control	250 (100)	food intake recall (3 consecutive days)	Consumption of cereals, meat, pulses and fruits lower in ADHD group	$P < 0.05$	Educational years, doses of MPH-ER	7/9

[a] Mean intake (serving per week).

of this pattern was moderate but not statistically significant (Cochrane Q test, $p = 0.099$; $I^2 = 48.7\%$). The "Fast food" and "Sweet" dietary patterns derived from 375 school-age children [27] as well as the "snack" dietary pattern in a Korean study were significantly related with increase of ADHD [28].

Sensitivity analysis revealed that by excluding Howard study, the result of Western dietary pattern in pooled analysis turned into non-significant. About healthy and junk food dietary patterns, the results remained significant with excluding any of the studies.

4. Discussion

To the best of our knowledge, this study is the first systematic review and meta-analysis exploring the association between dietary patterns and ADHD. The results showed that more adherence to the "Western" dietary pattern was related to increased risk of ADHD by 1.92 times. Western dietary pattern contains high amounts of confectionery, red meat, refined grains, processed meats, potatoes (fried, crisps), soft drinks, as well as animals' and hydrogenated fats. Similar to our findings, researches on the relation between dietary pattern and mental disorder proved that Western dietary pattern significantly increased anxiety [45], depression [46], learning and memory function odds [47]. In a systematic review, unhealthy dietary patterns were also related to poor mental health in children and adolescents [39]. In addition, another systematic review reported that high consumption of processed food was associated with an increased depression chance [48]. In contrast to our study, no significant association was observed between the Western dietary pattern and depression in a recent meta-analysis [49]. Western foods have high amounts of sodium and saturated fat, while they have low concentration of essential fatty acids such as polyunsaturated fatty acids (PUFAs), magnesium and vitamins [50]. The available evidence suggests that western diets with high amounts of fat and sugar can affect brain-derived neurotropic factor proteins that are important in brain development [51]. Western dietary patterns have also shown impaired glucoregulation and structural integrity of the blood–brain barrier [47]. In addition, they can reduce levels of neurotrophins and increase neuroinflammation [47].

Pooled analysis on children who consumed junk foods more frequently revealed that they were 1.83 times more likely to develop ADHD. "Junk food" dietary pattern that is popular among children consists of chocolate, biscuits, chocolate bars, cakes/buns, pizza, sweets, crisps, cola, and other fizzy drinks. The analysis showed that this dietary pattern strongly increased the odds of ADHD. This pattern is low in vitamins and minerals, but it has high amounts of artificial food colors and sugar [30]. Confining the results of this study, a systematic review and meta-analysis suggested that 8% of symptoms of ADHD children were related to food colors [52]. "Junk food" dietary pattern is characterized with high glycemic index components. In this regard, higher glycemic index foods were related to poorer memory performance in non-diabetic children [53]. The most consistently reported cognitive deficits were associated with insulin resistance and poor glycemic control in humans [54,55]. In contrast, previous systematic reviews did not find any relationship between sweetened beverages, desserts, and sweets intake on the one hand and ADHD on the other hand [56].

Our systematic review over the studied food groups showed that high vegetables, fruits, and dairy products intake was protectively related to attention deficit risk in children [31,41]. In contrast, sweetened beverages [32,41], desserts, salt [31] and processed meat consumption [43] exacerbated symptoms in children.

Healthy dietary pattern was also associated with decreased ADHD chance in our meta-analysis. Similar to the present study, previous systematic reviews in this area have established that

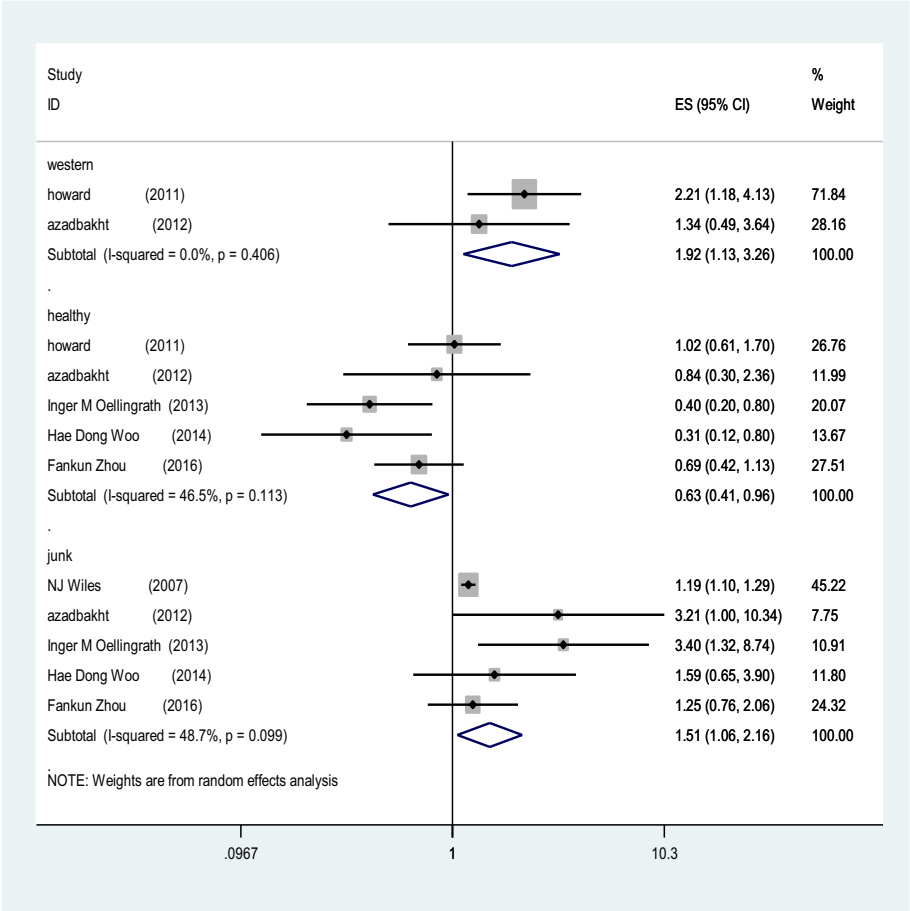

Fig. 2. Forest plot illustrating weighted OR using a random-effects model for the comparison of odds in ADHD participants with highest v.s lowest adherence to "healthy", "junk" and "western" dietary patterns.

healthy dietary pattern may improve mental health [39,49]. This dietary pattern consists of high vegetables, fruits, sea food, PUFAs, magnesium, zinc, and phytochemicals. An other comprehensive review revealed that ADHD children had lower serum, RBC, hair, urine, and nails zinc levels compared with non ADHD children [57]. Magnesium and calcium affect synaptic nerve cell signaling and cerebral blood flow and may have impact on proper brain function [20,58]. In addition, it was found that magnesium of eritrocyts (ERC-Mg) decreased in excitable children [59]. Healthy dietary patterns highly loaded with fish, as a source of long chain LC-PUFAs are associated with normal brain function and nervous system development [60]. A previous study showed less concentration of this essential fatty acid in children with ADHD [61].

However, there are no conclusive evidences proving that mega-dose vitamin supplementation can ameliorate ADHD symptoms. In other words, recent dietary pattern interventions concluded that priori oriented dietary pattern such as "Mediterranean diet" with high amounts of vegetables, fruits, unrefined cereals, legumes, and fish which is low in western and junk foods can improve mental health [62,63]. It is therefore suggested that dietary pattern modification can be a more comprehensive and safe approach than supplementation of individual nutrient or food.

The findings of our study may however be affected by strengths of various study designs and measurement errors of the assessment tools. Dietary patterns are also different based on the region, so that the same food can have different contents in various regions. For example, the mercury in fishes which was considered as the healthy pattern is different based on the environmental circumstances [64]. Moreover, another limitation of this study was the differences in factor loadings of dietary pattern studies which was unavoidable. Data collection was carried out by FFQ in all studies, except the study of Hae Dong Woo in which three nonconsecutive 24-h recalls were used. But, this deference did not have any significant influence on meta-analysis because by removing this study no change was observed. In addition, there were some inconsistencies in the confounding factors adjusted among included studies.

In conclusion, "healthy" dietary pattern consisting of vegetables, fruits, and fish decreased ADHD odds. However, "junk food" and "Western" dietary patterns highly loaded with sweetened beverages, desserts, high fat dairy products, fast food, animal fat, red meat and salt can significantly increase ADHD chance in children.

Statement of authorship

M. H and A. S designed the survey.
E.SH and Z. S. S collected and extracted the data.
M. H and A. S conducted the statistical analysis.
E.SH and Z. S. S wrote the draft of the manuscript.
M. H critically revised the manuscript and approved the final version of paper to be submitted. All authors read and approved the final version of the article.

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Declaration of Competing Interest

Authors declared no conflict of interest.

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