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REVIEW ARTICLE

The use of diet interventions to treat symptoms of ADHD in children and adolescents – a systematic review of randomized controlled trials

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ABSTRACT

Background: For over forty years diet interventions have been investigated as a treatment of ADHD in children and adolescents and, with the new discoveries of the microbiota-gut-brain axis, this research becomes more relevant than ever. The aim of this systematic review was therefore to investigate the current knowledge of diet interventions as a treatment of ADHD in children and adolescents

Methods: A systematic literature search in PubMed was conducted, identifying randomized controlled trials investigating diet interventions to treat ADHD in children and adolescents.

Results: The study populations were generally small and the studies varied in duration and nature of the exposure. Overall 10 out of 12 studies spoke in favour of an elimination diet, 2 out of 6 of eliminating artificial food colourings from the diet and none in favour of eliminating sucrose or aspartame from the diet to treat ADHD.

Conclusion: The current evidence is not enough to recommend treating ADHD with diet interventions, but a subgroup of children and adolescents might warrant from elimination of certain food-items. Further investigations of the mechanism and effect of diet interventions to treat ADHD is needed.

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KEYWORDS
Systematic review; ADHD; diet-intervention; children; adolescents

Introduction

Attention deficit hyperactivity disorder (ADHD) is a behavioural disorder affecting approximately 5% of all children [1]. The disorder is multifactorial and considered heritable but also associated with non-heritable risk factors. The mechanism by which these genetic and non-heritable risk factors interact and cause ADHD remains unknown, making ADHD challenging to treat [2].

In Denmark, ADHD in children and adolescents is most often treated with a combination of pharmacological treatments and psychosocial interventions [3]. Though, several alternative treatments have been investigated, including diet interventions.

In the seventies Ben F. Feingold proposed that the Feingold diet (FD), also called the Kaiser Permanente diet [4], eliminating salicylates and artificial food colourings (AFC) and flavourings, could improve behaviour and learning in children with hyperkinetic behaviour and learning disabilities [5]. Since then, other diets consisting of elimination of different foods have been suggested, based on the theory that some children are more sensitive to certain foods and that this sensitivity could cause ADHD symptoms [6]. This has led to the development of a restricted diet, called the oligoantigenic diet (OAD), consisting of few food items to avoid items that are believed to cause symptoms [7,8]. Though different, these diets are all eliminating food items and can therefore be referred to as a collected group of elimination diets.

Sugar has through anecdotes also been associated with hyperactivity in children [9]. A substitute for sugar is the sweetener aspartame, that consists of methanol, phenylalanine and asparteic acid [10]. Asparteic acid acts as an excitatory neurotransmitter and phenylalanine is suspected of altering the concentration of neurotransmitters in the brain, such as the monoamines dopamine and serotonin, by various mechanisms [11–13]. These observations have led to theories of whether or not aspartame elimination can reduce ADHD symptoms.

Though research of diet interventions as a treatment of ADHD has been conducted since the seventies, the new findings of a possible bidirectional connection between the brain and the gut microbiota [14–16], and possible association of the microbiota to autism spectrum disorder, depression and anxiety [17–19], warrant new investigations of dietary treatment of ADHD.

This systematic review will therefore investigate the current knowledge of diet interventions as a treatment of ADHD in children and adolescents.

Methods

Data search

The studies were identified using the predefined search string: (ADHD or hyperactivity or hyperkinetic syndrome)

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AND (children or youth or adolescents) AND (randomized controlled trial or RCT or clinical trial) AND (diet or diet intervention or food or nutrition or food colours). The search was conducted in PubMed in February 2020 and restricted to articles in English, but with no restrictions as to the date of publication. Supplementary studies were also identified by hand search of references in relevant articles. All records were screened by title and abstract by both raters, and the possibly eligible articles were read in full text. The articles fulfilling the eligibility criteria were then included in the study.

Eligibility criteria

To be eligible a study had to be a randomized controlled trial and had to be investigating the efficacy of a diet intervention as a treatment of ADHD in individuals <18 years of age. To focus on diet interventions, supplements such as omega fatty acids, amino acids, vitamins and minerals were excluded.

The outcome of the studies had to be an effect on ADHD symptoms; several different tools could measure this.

Data collection

For each article included, the following data were collected: Name of first author and year of publication, number of participants, age of participants, outcome measure, intervention and result of the study.

Risk of bias in the individual studies was evaluated using the RoB 2 tool [20]. This tool is used to estimate the risk of bias depending on the randomization process, assignment to intervention, starting and adhering to intervention, missing data, measurement of outcome and selection of the reported result [20]. Based on these subsidiary scores, a final score was given to each study (low risk, some concerns, high risk).

Results

The search string identified 252 studies and the hand search identified 6 studies (Figure 1). After reading through the titles and abstracts, 36 articles were selected for full-text assessment. Twenty-two studies were found eligible and included, with one article containing 2 separate included studies [21].

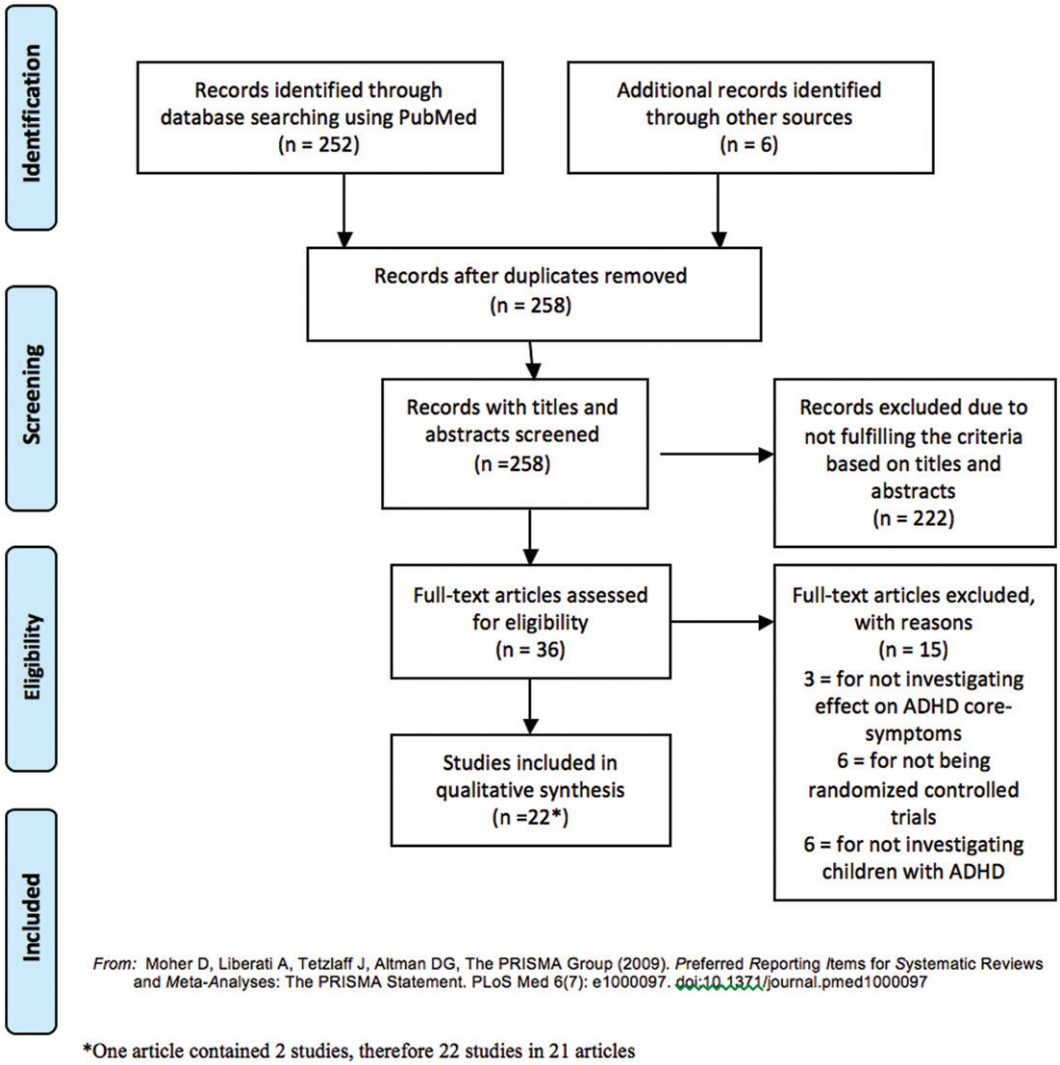

Figure 1. Prisma Flow Diagram.

Of the studies excluded, 3 were excluded for not investigating effect on ADHD symptoms, 6 for not being randomized controlled trials and 6 for not investigating children with ADHD. The raters were in agreement about the included and excluded studies.

Elimination diets

Table 1 summarizes the 12 studies investigating elimination diets as a treatment of ADHD.

Three of them explored what they called an elimination diet (ED) [27,29,30], four the Feingold diet (FD) [22–25], three the oligoantigenic diet (OAD) [7,8,28], one investigating an Alberta Children's hospital (ACH) diet, similar to the FD [26] and one investigating recommending avoidance of unfavoured and encouraging favoured foods [31]. Three of the studies were parallel-group trials [29–31], the remaining were crossover studies.

Overall, all studies except one [25], spoke in favour of an elimination diet and reported an effect of the diet on ADHD symptoms [7,8,22–24,26–31] (Figure 2).

Four studies were challenge studies, where individuals adhering to a diet were reintroduced to incriminated foods [7,8,25,27]. Two were conducted in children with ADHD responding to an OAD [7,8], where both found that antigenic foods affected behavioural ratings negatively compared to placebo [7,8]. Interestingly, in the study by Egger et al. [8] the placebo scores were higher when the placebo preceded the antigenic food compared to when reversed. .

A study in children with ADHD responding to an ED found an increase in parent scores of hyperactivity associated with the challenge with incriminated foods [27].

The only study with overall negative findings was also a challenge study, investigating children with a parent-reported response to the FD, finding no significant deterioration in symptoms associated with FD violating snacks [25].

Seven of the studies compared diet interventions to control diets [22–24,26,28–30].

Two of them with the diet interventions conducted in a controlled manner. One study investigated the OAD in children living in the hospital, and found significant improvement in ADHD symptoms on the OAD [28]. The other study delivered packaged food to be heated at home and saw a positive response in 42% of children [26]. Two were parallel trials where the parents had to prepare the meals according to instructions, and they were therefore not blinded [29,30]. Both studies showed an effect of the ED according to the un-blinded parents [29,30], and one also an effect according to a blinded paediatrician [30]. The mentioned lack of a blinded assessment in the Pelsser et al. [29] study, is the reason why it was classified as in high risk of bias, as there is risk of the outcome being based on knowledge of the intervention.

The last study compared children receiving methylphenidate to children receiving both methylphenidate and dietary recommendations. The dietary recommendations consisted of a list of favoured and unfavoured foods. No significant change in un-blinded scores of ADHD symptoms was found when comparing the groups, but there was a negative association between inattentiveness scores at the end of the study and the mean change in diet scores based on the list of favoured and unfavoured foods [31].

Three of the studies had results where parent ratings and teacher ratings differed [22–24]. Two studies found only an effect of the diet in parent ratings [23,24]. One of them with the parent ratings depending on the order of the diets, with a larger effect of the FD when the control diet preceded the FD [23]. The other by Eich et al. [24] found that the FD was significantly effective in mother-ratings, but it was possible that the mothers through the dietary instructions had figured out which was the FD and which was the control diet. This also caused the study to be classified as in high risk of bias, due to the risk of classification of outcome based on intervention (Table 1).

In contrast, the last study found that the FD gave a significant reduction in teacher ratings and not parent ratings [22]. But similar to the Harley et al. [23] study, the bulk of the positive changes occurred in the group randomized to start with the control diet.

Analysis of the risk of bias in the individual studies (Table 1) revealed that two studies were at a low risk of bias [7,8]. Six studies were considered to be associated with some concerns [22,23,25,26,28,30].

The remaining four studies were considered to be associated with a high risk of bias [27,29,31]. One of these studies was classified as such due to doubt as to whether or not there was any randomization [27]. Three were classified as such due to blinding issues [24,29,31].

Artificial food colourings

Table 2 summarizes the results regarding elimination of AFCs as a treatment of ADHD. Six studies fulfilled the criteria for inclusion. All six were crossover challenge studies in children on a diet without AFCs [21,32–35]

Goyette et al. [21] conducted 2 challenge studies. In the first they found no significant difference in hyperkinetic symptoms, but younger children demonstrated more symptoms when challenged and symptoms tended to occur earlier than the evaluation of the children. The second study was therefore conducted like the first, but in younger children and with earlier assessment of the outcome, resulting in significant deterioration in parent scores during the AFC challenge compared to placebo [21].

The challenge study by Williams et al. [32], tested AFCs compared to placebo in combination with either medication to treat ADHD or placebo, and found that the most effective treatment combination was a combination of medication and no AFCs. This positive effect was only present in parent scores and not the teacher ratings. Contrarily the teacher ratings showed significant effect of no AFCs when the child did not receive medication.

No association was found in a fourth study, where they investigated the effect of AFCs on classroom behaviour [33].

One study tested only with the yellow AFC tartrazine, and found no significant deterioration during the tartrazine

Table 1. Elimination diets.

Study	Outcomes and measure	Intervention	Summary of results	Risk of bias[a] R	D	Mi	Me	S	O
Conners et al. [22]. (n = 15) 4–12 years old Conducted as a crossover trial.	Blinded teachers and parents using Conner's hyperkinesis index rating scales. Double blinded study.	FD compared to a control diet. Each for a period of 4 weeks.	The FD was associated with reduced hyperkinetic symptoms. The teachers, but not the parents noted a significant reduction in ADHD symptoms.	?	+	+	+	?	?
Harley et al. [23]. (n = 26) 6–13 years old Conducted as a crossover trial	Conner's ratings by parents and teachers. Classroom observations. Neuropsychological and laboratory observations. Double-blinded study.	3 weeks of FD or 3 weeks of control diet with these ingredients.	Parents reported significant effect of the diet, especially when the control preceded the experimental diet. Teacher ratings and laboratory observations proved no effect.	+	+	+	+	?	?
Eich et al. [24]. (n = 16) unknown age Conducted as crossover trial.	Conner's hyperactivity index scales by the parents and teachers. Walker problem behaviour checklist by teachers. Nurse practitioner conducting tests: Human figure drawing, Beery Buchtenica test of visual motor integration, Porteus maze test. Digit subspan test of WISC, Quick neurology screening test. Blinded teachers and nurse practitioner. Parents could have been unblinded.	1 month of FD or 1 month of placebo diet in varying order.	Significant effect of the diet in parent ratings, but not in teacher ratings or the testing by the nurse.	+	?	+	–	?	–
Adams [25]. (n = 18) 4–12 years old Conducted as crossover challenge	Activity, auditory and visual attention. Gross and fine motor skills. Observations by blinded personnel and by parents in a 3–4 hour period after consummation of snack. Double blinded study	In children adhering to FD for 3 months. A snack either adhering to or challenging Feingold diet.	No significant difference between the two snacks.	?	+	+	+	?	?
Egger et al. [8]. (n = 28) 2–15 years old Conducted as crossover challenge	Daily abbreviated Conner's scores by parents. Overall double-blinded assessment of overactivity by parents and a paediatric neurologist. Psychological testing: • Behaviour testing • Actometer • Matching familiar figures • Porteus mazes Double blinded study	In children adhering to an OAD for 4 weeks. Challenge with cows milk, orange juice, wheat or placebo.	Higher means of Conner's scores during challenge than placebo. Higher scores during placebo period if placebo was before active agent.	+	+	+	+	+	+
Kaplan et al. [26]. (n = 24) 3–6 years old Conducted as crossover study	Abbreviated Conner's ratings scales by blinded parents and day care and assessment of physical symptoms by parents. Tests in the lab of learning, memory and various psychometric tests Double blinded study	3 weeks of regular diet (placebo) or 4 weeks of a diet with fewer additives and sugars and more vitamins.	Parent reported data showed improvement while on test diet, but no effect on the scores from the day care. Incomplete data from test in laboratory setting.	?	?	+	+	+	?

(*continued*)

Table 1. Continued.

Study	Outcomes and measure	Intervention	Summary of results	Risk of bias[a]					
				R	D	Mi	Me	S	O
Carter et al. [7]. (n = 19) 3–12 years old Conducted as crossover challenge	Conner's rating scales by blinded parents Hyperactive behaviour during testing was observed by a blinded psychologist. Tests: paired associated learning test and matching familiar figures test. Double blinded study.	Children responding to a OAD for 3–4 weeks were reintroduced to one or more incriminated foods or placebo for one week each.	Significant deterioration in behaviour rated by the parents and during testing by psychologists. Significant effect on the matching familiar figures test.	+	+	?	+	+	+
Boris and Mandel [27]. (n = 16) > 7 years old Conducted as crossover challenge	Conner's rating scales for hyperactivity score conducted by blinded parents.	Responders to 2 weeks of elimination diet received either 7 days of placebo or 7 day challenge with foods reported to produce symptoms.	Significant deterioration in scores on challenge days compared to placebo.	–	+	?	+	+	–
Schmidt et al. [28]. (n = 49) 6–12 years old Conducted as crossover study.	Performance testing • Paired associate learning task (PAT) • Continuous performance task (CPT) Behaviour rating with Conner's abbreviated scale during class, and behaviour rating while in the ward and during performance testing. Double blinded study	9 days of OAD compared to 9 days of a control diet containing food colorants and additives.	24% of children had a significant improvement on the OAD both in the ward and during testing. There was no effect in the classroom setting.	?	+	+	+	+	?
Pelsser et al. [29]. (n = 27) 3–9 years old Conducted as parallel study	Abbreviated Conner's Scales and ADHD DSM-IV rating scale by parents and teachers. No blinding.	Randomization to 5 weeks of individually composed ED or waiting list (regular diet).	Children in the ED group had a significant improvement in both scores.	+	?	+	–	+	–
Pelsser et al. [30]. (n = 100) 4–8 years old Conducted as parallel study	Abbreviated Conner's scales by unmasked parents and teachers. ADHD rating scale by a blinded paediatrician.	Randomization to 5 weeks of restricted ED or to instructions for a healthy diet	Significantly lower Conner's scores as well as masked ADHD rating scale scores associated with the ED.	+	?	+	?	+	?
Ghanizadeh and Haddad [31] (n = 106) 5–14 years old Conducted as a parallel study	Assessment of ADHD severity using ADHD checklist. No blinding	A list with favoured (vegetables, low fat meat etc.) and unfavoured foods (sugar, soft drinks, sauces) + methylfenidate compared to children only receiving methylfenidate. The duration was one month	A negative association between the inattentiveness scores and the mean change of intake of favoured foods when both the control and intervention groups were combined. No significant difference in mean change of hyperactivity/impulsivity and inattentiveness between the two groups.	+	?	?	–	+	-

[a]R: randomization process, D: deviations from intended interventions, Mi: missing outcome data, Me: measurement of the outcome. S: selection of the reported result. O: overall risk of bias. + = low risk of bias, ? = some concerns, – = high risk of bias.

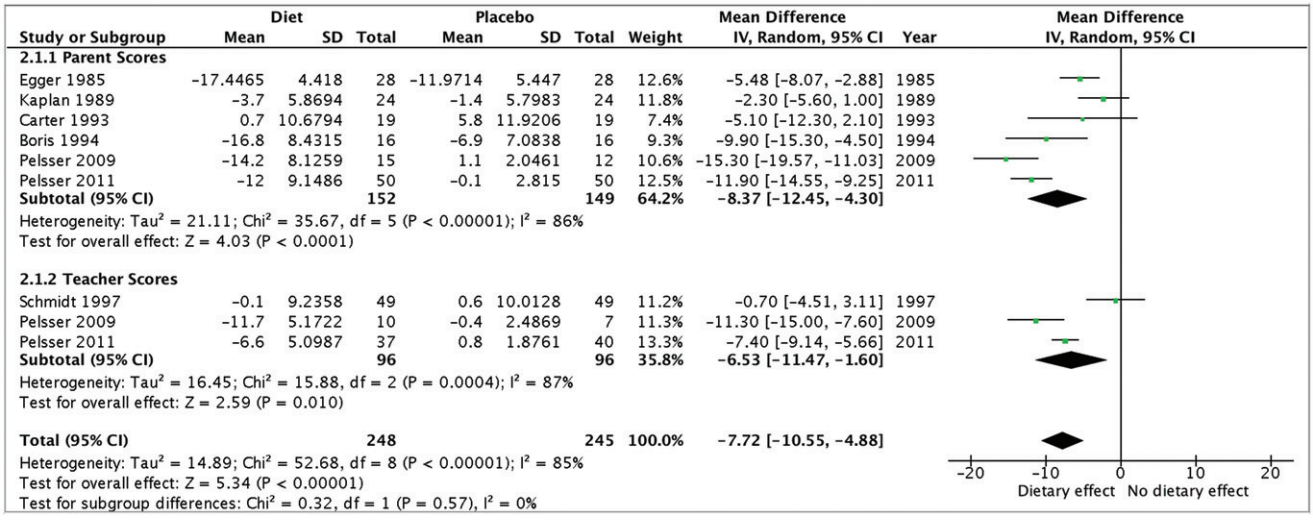

Figure 2. Forest plot of elimination diet vs placebo, outcome: change from baseline abbreviated conner's scores.

challenge, even though mothers reported an improvement during 4 weeks of ED [34]. The last study similarly found no difference in blinded parent, teacher, psychiatrist or psychologist scores when ingesting AFCs, even though it was conducted in a group of children with parent reported dramatic deterioration when receiving AFCs [35].

All six studies were found to be associated with some concerns in relation to the risk of bias [21,32–35] (Table 2), this mostly due to a lack of reporting of the process of randomization and the data analysis performed.

Overall, two studies reported an association between ADHD symptoms and artificial food colorants [21,32] while four studies found no association [21,33–35].

Sucrose and aspartame

Table 3 summarizes the results regarding elimination of sucrose or aspartame from the diet as a treatment of ADHD. Four studies were included, all were challenge studies, and none of the studies found a significant effect of sucrose or aspartame on symptoms of ADHD [9,36–38].

Two of the 4 studies were conducted by the parents in the home [9,38] and 2 were conducted in a laboratory or hospital setting [36,37].

Two of the studies compared sucrose to placebo in the form of aspartame [36,37]. One, conducted during a day-treatment programme, found no difference in behaviour during the two days of sucrose-sweetened drinks compared to the two placebo days [37]. The other, conducted in children with parent reported adverse reactions to sucrose, similarly found no difference when evaluating behaviour and cognition. Here they also found that it was independent of fasting status of the children [36].

One study by Gross [9] compared sucrose to placebo in the form of saccharine in children with mother reportings of sugar causing the child's symptoms. They found no difference in behaviour ratings.

The last study by Shaywitz et al. [38] compared the sweetener aspartame to placebo and found no significant difference in behaviour, cognition or monoamine metabolism between the two.

In the analysis of bias, three of the studies were found to be associated with some concerns [9,36,37]. This was mostly due to a lack of reporting of the randomization process. One study was judged to be at a low risk of bias [38].

Discussion

Overall, most of the studies were of older date and had varying duration and nature of exposure. All, but three [29–31], were crossover studies, which increases the risk of a carry-over effect of a diet intervention to a following placebo period. In general, interpretation of the results of all studies should be done with care as they were all generally done in small study populations (Tables 1–3).

We identified no studies conducted after 2015. Our search string revealed that the studies conducted after 2015 have shown a trend towards investigating the effects of supplements such as omega fatty acids as a treatment of symptoms of ADHD.

Elimination diets

The diets were labelled as the FD [22–25], OAD [7,8,28], the ACH diet [26] or ED [27,29,30] and one diet intervention consisted of recommendations of favoured and unfavoured foods [31]. This makes it hard to compare the individual diet interventions, as they varied in the exact contents. Of note is also that not all studies were completely blinded [29–31].

In all four of the challenge studies, only children who responded to a diet eliminating the challenge item were investigated [7,8,25,27]. This could mean that the external validity of the studies could be limited to a potential distinct group of children with a diet responsive ADHD.

Of further note is that one of the Pelsser et al. [30] studies recruited children through media announcements. This could cause recruitment of families especially interested in diet

Table 2. Artificial food colourings.

Study	Outcomes and measure	Intervention	Results	Risk of bias[a]					
				R	D	Mi	Me	S	O
Williams et al. [32]. (n = 28) 5–12 years old Conducted as a crossover challenge.	Conner's rating scales by parents and teachers. Double-blinded study.	After 5 weeks of FD, the children received a combination of medication or placebo and AFC challenge or placebo – each combination for one week.	Medication + placebo cookie was most effective. Diet was most effective while receiving medication in parent ratings and while receiving placebo in teacher ratings.	?	+	+	+	?	?
Harley et al. [33]. (n = 9) Mean age: 111 months old Conducted as a crossover challenge	Conner's rating scales by parents and teachers. Classroom observations. Neuropsychological and laboratory observations Double-blinded study.	Strict FD. Then the children with the best response to the diet were challenged with cookies and candy bars with AFCs or placebo, each for 2–3 weeks at a time.	No significant differences between AFC challenges compared to placebo.	?	+	+	+	?	?
Levy et al. [34]. (n = 22) 4–8 years old Conducted as crossover challenge	Conner's ratings by mother, teacher and psychiatrist and psychologist. Psychiatrist and psychologist evaluations conducting tests: Continuous performance test, Draw-a-line-slowly test, Motor-accuracy and Figure-Ground subtest, Auditory Memory task, Wechsler preschool and primary scale, Maze subtest. Double blinded study.	4 weeks of ED and hereafter 2 weeks of either cookies containing tartazine or placebo cookies in random order.	No significant deterioration in behaviour during tartrazine challenge.	?	+	?	+	?	?
Goyette et al. [21]. (n = 16) 4–11 years old Conducted as crossover challenge	Conner's rating hyperkinesis index by parents and teachers. Zero input tracking analyzer and auxillary distraction task (ZITA/ADT) Double blinded study.	In children responding to an ED. Cookies containing AFCs or placebo for 4 weeks each.	No significant differences. ZITA/ADT testing after only 1–2 hours of ingestion had trend towards deterioration after AFC challenge. Younger children had a tendency to show a more pronounced response to challenge.	?	+	+	+	?	?
Goyette et al. [21]. (n = 13) 3–10 years old Conducted as crossover challenge	Conner's hyperkinesis index by parents and teachers. Zero input tracking analyzer and auxillary distraction task (ZITA/ADT)	In children responding to ED. Challenge with cookies containing AFCs or placebo cookies for 1 week each.	There was a significant deterioration in behaviour when challenged with AFCs compared to placebo.	?	+	+	+	?	?
Mattes and Gittelman [35]. (n = 11) 4–13 years old Conducted as crossover challenge	Abbreviated Conner's rating scales completed by parents and teachers. Psychiatric evaluation and children's diagnostic scale. Test of distractability The study is double blinded	All children responding to Feingold diet. Cookies containing placebo or cookies containing AFCs. 1 week of each in random order.	No significant differences between placebo or AFC cookie.	?	+	+	+	?	?

[a]R: randomization process, D: deviations from intended interventions, Mi: missing outcome data, Me: measurement of the outcome. S: selection of the reported result. O: overall risk of bias.
+ = low risk of bias, ? = some concerns, – = high risk of bias.

interventions and cause bias as the study also used unmasked parent ratings.

The masked study by Adams [25] investigating children who were reported by parents to benefit from the FD, found that the results of their masked challenge did not show a significant change in behaviour of the children. This could point towards that in general, any parent report of response to a diet should be interpreted with care.

However it is important to note that in the Pelsser et al. [30] study a blinded paediatrician also observed an effect.

Four of the studies showed a difference in parent and teacher observed effects [22–24,32]. One of those studies had a greater reduction in ADHD symptoms in teacher scores [22], and two had a greater reduction in parent scores [23,24].

The observed effect by the parents in the Eich et al. [24] study, could be due to the difficulties in blinding the parents to the diet intervention. The parents could have figured out whether or not their child was randomized to the FD based on the instructions for the diet and their potential knowledge of the FD [24]. When the parents later scored the behaviour of the children, the possible knowledge of the intervention could have affected their reporting of the outcome.

However it is possible that the overall variance in effect observed by parents and teachers could be due to chance, as the number of children investigated in the 4 studies varied from 16 to 28 children (Table 1). But other than chance, it could be due to the different structures and situations associated with the home and the classroom, or maybe the timing of potential medication. This might be because a potential morning dose of medication could have a larger impact during the day and therefore, the true effect of the diet is only visible to the teacher when the effect of the medication is not present. This of course also presumes that medication is superior to diet in treating ADHD.

This theory is consistent with the findings in the study Conners et al. [22] where the ADHD medication was discontinued before the study and only teachers reported a significant dietary effect. However, in the study by Harley et al. [23] where medicine was also discontinued, only the parents noted a significant effect of the diet.

Any possible association between medication and teacher ratings can probably not alone explain the discrepancies found between parent and teacher ratings in the studies.

Of further note is that the study by Harley et al. [23] also showed an order-effect, where the efficacy of the diet intervention proved greater when the control diet was randomized to occur before the FD [23]. The same order-effect, with the bulk of the significant effects being seen when the control diet came before the FD, was seen in the study by Conners et al. [22]. Another example is the study by Egger et al. [8] where the Conner's scores were greater during the placebo period if this was placed before the challenge.

It is possible that this could be due to chance as the studies ranged from 15 to 28 children. But it does raise concern, as the higher early placebo score of ADHD symptoms could be caused by the parents getting used to the symptoms of their child with the repeated scoring. The result of the possible order effect could be an overestimation of the effect of the later diet intervention.

It is also possible that a lower placebo score when the control diet followed the diet intervention could be due to a carry-over effect by the intervention. Although, this would not account for the effect in the Egger et al. challenge study as any carry-over effect should cause a deterioration in placebo scores if this was after the challenge.

If an elimination diet has an effect on the symptoms of ADHD, as most of these studies suggest, then what causes it? As mentioned earlier, the effect of a diet eliminating certain foods has been suggested to be through hypersensitivity, causing a distinct type of food responsive ADHD [6]. It has been suggested that this association could be allergic but no association between atopic disease or asthma and ADHD has been found, and therefore this theory has been questioned [39,40].

Other than allergy, maybe the deterioration in ADHD symptoms could be caused by discomfort due to bodily symptoms causing the child distress. Rapp et al. [41] investigated the effect of an ED on hyperactivity symptoms and other symptoms in non-asthmatic children with a hyperactivity diagnosis, and found that gastrointestinal symptoms, muscle pain and headaches had moderately to markedly improved in 15 of 23 children, while hyperactivity symptoms improved in 12 of 23 after one week of an ED. Whether or not these groups were overlapping is not clear. Another study found that sleep and physical complaints significantly decreased in children with ADHD on an ED, with a further positive correlation between behavioural symptoms and the reduction of physical symptoms [42].

Lastly, in relation to the ED interventions, it should be mentioned that in the two studies by Pelsser et al. and the study by Ghanizadeh et al. the diet intervention was compared to no diet intervention [29–31]. This could mean that possible extra attention associated with a diet intervention and added structure of the every day life might influence the results. This could also be part of why the study by Adams [25] found no association, even though the parents had reported that the children had responded to the FD at home. Maybe the positive effect observed at home, was due to the possible structure and extra attention associated with a diet intervention and not the diet itself.

Artificial food colourings

The studies investigating AFCs also varied greatly in relation to the nature of the challenge and dosage and agent that the children were challenged with.

It is possible that some children are more sensitive to AFCs than others. Though the results from the Levy et al. [34] study were generally negative, they did find that some children seemed to react more to the challenge with AFCs than others.

But what could make some children more sensitive to AFCs than others? In the first experiment by Goyette et al. [21] where the mean age of the participants was 8.3 years,

Table 3. Sucrose and aspartame.

Study	Outcomes and measure	Intervention	Results	Risk of bias[a]					
				R	D	Mi	Me	S	O
Gross [9]. (n = 50) 5–17 years old Conducted as crossover challenge	Rating of change in behaviour by mother. Double-blinded study.	Lemonade sweetened with sucrose or placebo (saccharin). Each tried 3 times.	No significantly altered response to sucrose compared to placebo.	?	+	+	+	?	?
Wolraich et al. [36]. (n = 16) 7–12 years old Conducted as a crossover challenge.	Playroom observations. Various testing: Continuous performance test, paired-associate learning test, nonsense-word spelling task, matching familiar figures test, draw-a-line-fast test, draw-a-line-slowly test. Overall behaviour rating during testing. Double-blinded study.	Drink sweetened with sucrose or placebo (aspartame). Each tried 1 time.	No difference in the behaviour between the two drinks ingested.	?	+	+	+	+	?
Milich and Pelham [37]. (n = 16) 6–10 years old Conducted as a crossover challenge	Observations during playtime: Following rules, positive peer (prosocial behaviors), noncompliance, negative verbalizations. Observations of behaviour in the classroom: Math tasks, reading tasks Double-blinded study.	Drink sweetened with sucrose or placebo (aspartame), 2 days of each.	No difference in behaviour or learning between the two drinks ingested.	?	+	+	+	?	?
Shaywitz et al. [38]. (n = 15) 5–13 years old Conducted as a crossover study	Conner's rating scales by parents and teachers Behaviour observations and cognitive testing in hospital: Matching familiar figures, children's checking task, the airplane test, the Wisconsin card sorting test, the subjects treatment emergent symptom scale, multigrade inventory for teachers. Double-blinded study.	Aspartame or placebo capsules for alternating 2 week periods.	No significant difference in behaviour or cognition between aspartame or placebo.	+	+	+	+	+	+

[a]R: randomization process, D: deviations from intended interventions, Mi: missing outcome data, Me: measurement of the outcome. S: selection of the reported result. O: overall risk of bias. + = low risk of bias, ? = some concerns, – = high risk of bias.

they found, when dissecting the data, that younger children tended to demonstrate a larger response to AFCs. In the second experiment they investigated younger children (mean age of 5.3 years), and found a significant difference in behaviour between the AFC and the placebo challenges [21]. However, they also measured the effect at an earlier time after the challenge than in the first study, and this could also have affected the results. But one could still question whether or not the sensitivity to AFCs in children with ADHD is age dependent. A study that further supports the theory of younger children being more susceptible to adverse effects of AFCs is a study by Bateman et al. [43]. They showed that 3-year-old children, receiving a diet eliminating AFCs and benzoate preservatives, had significant reductions in hyperactive behaviour and they also found significant increases in hyperactive behaviour associated with reintroduction in a double blind crossover study [43]. This study was not conducted in children with ADHD, suggesting that younger children in general might be more sensitive to AFCs.

An explanation for why AFCs are linked to hyperactivity, could be that children with ADHD are more prone to ingesting foods with AFCs compared to children without ADHD and therefore not because AFCs cause ADHD. A study from 1975 investigated the weekly ingestion of food additives in hyperactive boys compared to boys from the general population and found no significant difference in the ingestion between the two groups [44]. The same study also found that the ingestion of food additives was independent of whether or not the hyperactive boys received medication for their hyperreactivity [44].

Sucrose and aspartame

Comparing these studies should be done with caution as only one compares aspartame to placebo [38], two studies sucrose to aspartame [36,37] and one sucrose to saccharine [9]. This makes it difficult differentiate the effect of either intervention and to compare the effects observed.

As mentioned previously, it has been indicated that aspartame could affect monoamine metabolism in the brain. The study by Shaywitz et al. [38] measured not just the effect of aspartame on cognition and behaviour but also, through measurements in blood and urine, the effect on neurotransmitter metabolism. There was no indication in these peripheral measurements that aspartame affects brain neurotransmitter metabolism [38].

As the studies were generally small (Table 3), hypersensitivity in some children with ADHD to sucrose or aspartame might still exist, but in a rarity that leads to it not being detected in studies of these sizes. As an example, in the study by Milich and Pelham [37] the investigators went through the results again and here both evaluators identified one boy that might react adversely to sucrose in 4 of 25 measures.

Overall none of these studies suggest that symptoms of ADHD are significantly increased when ingesting sucrose or aspartame.

One explanation for the anecdotal theory that children with ADHD exhibit deterioration in symptoms when ingesting foods containing sucrose or aspartame could be caused by the situations in which they are ingested. These foods could more often be ingested in non-structured settings such as children's birthday parties or for example trips to the circus, and therefore any association between these foods and any deterioration in behaviour might be due to the difference in setting rather than the diet.

Another theory could be that a higher intake of sugar is seen in children with ADHD compared to children without ADHD, leading to the belief that it causes the symptoms. A theory supported by a recent study showing that intake of sugar-sweetened beverages was higher among children with ADHD than children without [45].

Conclusion and perspectives

Overall, the current evidence is not enough to warrant a recommendation of diet interventions to treat ADHD, but the evidence presented could indicate that some children with ADHD, maybe certain age groups, could warrant from elimination of some food items.

This however would need to be further investigated in well-conducted, reproducible double-blinded studies. Future investigations should also include research into how any sensitivity to food items may arise, such as a possible relation to the gut microbiota.

Disclosure statement

Nanna Maria Uldall Torp has nothing to disclose. Per Hove Thomsen has received speakers fee from Shire and Medice during last three years.

Author contributions

Study idea and design: NMT, PHT; acquisition of data: NMT; analysis and interpretation of data: NMT, PHT; drafting of manuscript: NMT, PHT; critical revision: PHT.

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