

ADHD, a Food-Induced Hypersensitivity Syndrome: in Quest of a Cause

**The effects of a restricted elimination diet (RED) on ADHD,
ODD and comorbid somatic complaints,
and a preliminary survey of the mechanisms of an RED**

Een wetenschappelijke proeve op het gebied van de
Medische Wetenschappen

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9.7. Practical implications and implementation of the RED in general practice: a proposal for a multi-modal algorithm for diagnosis and treatment

The results of the RED studies, convincingly showing that ADHD may be caused by food in the majority of young children with ADHD, may incite a child psychiatric paradigm shift when ADHD and ODD are concerned. Implementation of RED research in the ADHD diagnostic procedure, as suggested in *Chapter 6*, provides an opportunity to prevent ADHD and ODD in those children responding to the RED. A comparison of the pros and cons of both medication and an RED will elucidate why it is timely to implement an RED in ADHD.

Medication has two advantages: First of all it is a “quick fix”: soon after ingesting the tablet the child’s behaviour will improve and the improvement will last until the moment the tablet has lost its effect. An RED is the opposite of a quick fix and asks for commitment of parents and child. It takes a year to establish to which foods a child reacts and during that year the child has to comply with a more or less strict diet. Second: medication is easy to apply and thus convenient for all families, while an RED needs a great deal of commitment and is not easy to apply.

An RED also has some advantages. First of all, although medication used to be the most powerful treatment of ADHD with effect sizes varying from 0.6-0.9,⁹ to date an RED may be considered the most effective ADHD treatment with a mean effect size of 1.2. Second, psychostimulants like methylphenidate, the most commonly used drug in ADHD, have a duration of action of 3-12 hours. This implicates that this medication does not solve the behavioural problems in the early morning and in the evening. Conversely, the effects of an RED last 24/7. Third, despite initial symptom improvement when treating ADHD with medication, the follow-up study in the Multimodal Treatment Study of children with ADHD (MTA),⁸⁹ showed that children who received medication exhibited significant impairment in adolescence, in fact comparable to children who had not received any medication at all. Follow-up research in RED studies, lasting 1 year, has shown beneficial effects throughout the year, but further follow-up studies are necessary. Fortunately, the prospects are promising: the initial RED will, slowly but surely, be expanded to a more or less normal dietary pattern, thus increasing the feasibility of diet with a limited number of restrictions. Fourth, almost 60% of children do not continue medication despite initial favourable behavioural effects,

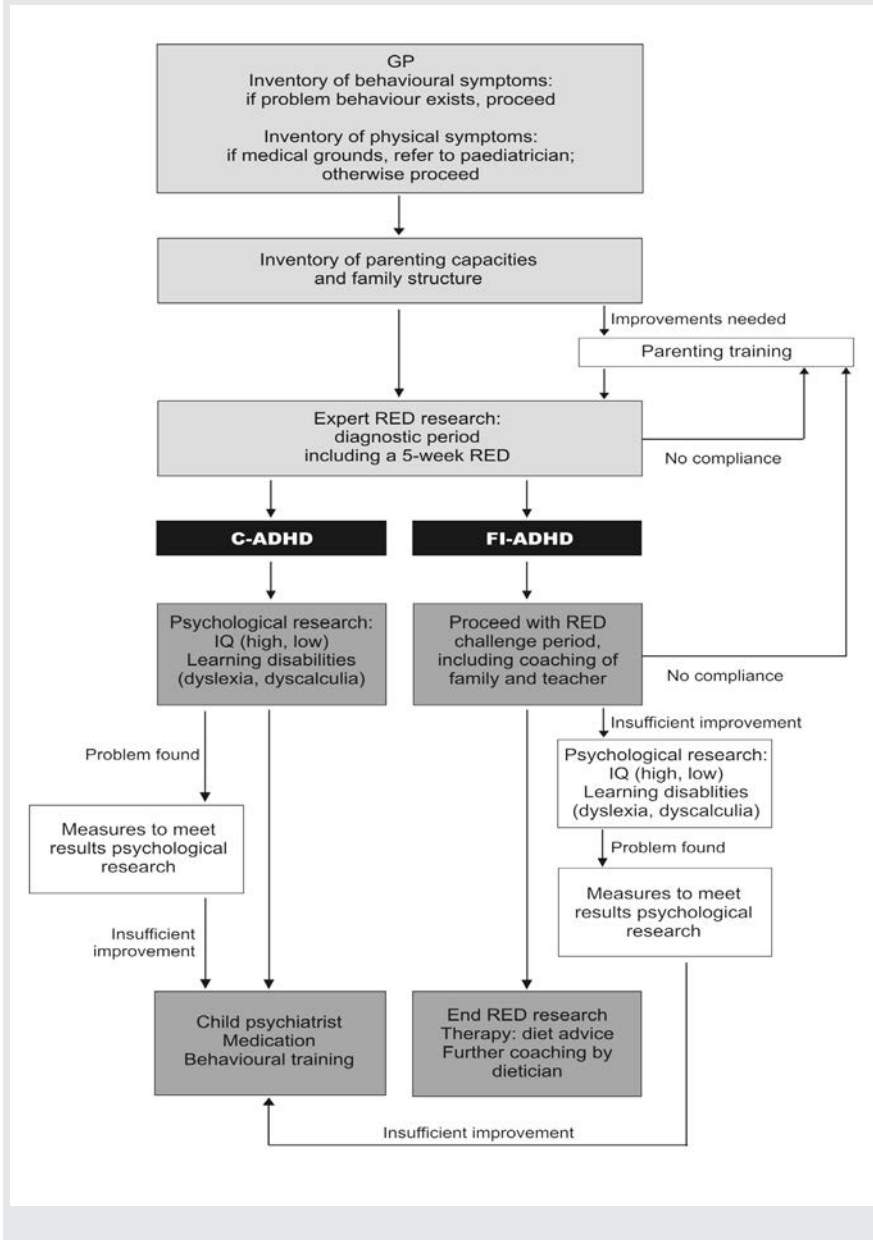
mostly because of adverse side effects like loss of appetite and perceived tolerability.⁹⁰ Conversely, an RED has a beneficial effect on somatic and sleep problems. Still, the diet itself, with concurrent limitations when attending parties or celebrations, may especially during the first year be interpreted as an adverse side effect. Fifth, not all children with ADHD respond favourably to medication; children show individual variability in medication response and in duration of effect and for this reason determining the optimal dose and the choice of medication is a matter of trial and error.⁹¹ Of course neither do all children respond to an RED, but in 5 weeks it is clear whether the child suffers from FI-ADHD or C-ADHD.

In sum, medication, the most applied treatment of ADHD, has some disadvantages while the RED has some advantages, accordingly, innovative treatment approaches like the RED would be welcome in ADHD. Therefore it is timely to present a proposal for new ADHD guidelines which include RED research. Once before, in 2001, an RED was included in a basic algorithm for treatment of ADHD, based on the 6 RED RCTs available at that time. Somehow this part of the algorithm has never been put into effect, probably as a result of the false claims that additives were the main cause of ADHD.²⁰ The negating of the RED trials and of the 2001 algorithm for treatment may ensue from these false claims or may be due to change blindness.⁹² Now, ten years later, additional RED RCTs have been performed, confirming and strengthening the previous study results in unselected groups of children with ADHD, and thus warranting a revised algorithm for multimodal diagnosis and treatment of ADHD (see **figure 4**).

9.7.1. The parenting part of the algorithm

In this algorithm a multidisciplinary and multimodal approach is proposed, including educational therapists, RED experts, psychologists, psychiatrists and dieticians. It goes without saying that communication between these professionals is of the essence to optimise the diagnostic and therapeutic procedure. First, the GP or child health centre physician will make an inventory of the behavioural and physical problems. Subsequently, if applicable, the parenting capacities and family environment and structure may be considered by an educational specialist. If parents show at least average parenting qualities, the RED research may start. Conversely, if improvement of parenting capabilities (e.g. consistency, family interaction, affection and clear communication) seems important, this should first

Figure 4 Algorithm for Multimodal Diagnosis and Treatment of ADHD



be attended to. Still, it is conceivable that parenting incapacities are consequential and not causal of the child's behavioural problems. Consequently, if the child's behaviour does not improve sufficiently despite parent training, the RED research should start. If a family proves to be unable to comply with the 5-week diet, it is worthwhile to consider the parenting capacities once more and offer expert educational advice in order to help the family to comply with the RED.

In addition to the inventory of parenting capabilities prior to the RED, it is also important to investigate whether parents are willing and motivated to follow an RED. In families who do not want to start RED research or who repeatedly fail to adhere to the dietary restrictions, treatment as usual is indicated. Still, the results of the RED studies are striking and to such an extent, that no efforts should be spared to grant every child the opportunity to participate in RED research. For this reason it would be in the interest of children whose parents are not motivated to follow an RED to offer all assistance required to help these parents to see the RED through, and it is important to inform all parents in great detail of the pros en cons of participation in RED research and of treatment as usual.

9.7.2. The RED research part of the algorithm

When it has been established that parents are motivated to start an RED and that parenting capabilities are sufficient, the RED research may start. This research needs expert supervision by trained staff, i.e. a physician. There are several reasons why expert supervision is important to meet the conditions required for high quality diagnostic research in accordance with the model as applied in the INCA study (*Chapter 6*). First of all, most children with ADHD suffer from other disorders as well, and comorbidity is rule rather than exception, i.e., the problems involved are complex and in most children not limited to ADHD. This implicates that the RED research covers various areas of health problems and the RED expert must be capable to handle the variety of problems involved. Second, in children starting the RED and already taking medication the RED physician will monitor the reduction of medication which will take place in due course during the RED, consequently the RED expert must be clearly aware of all medical ins and outs of the child. Third, the RED expert will, depending on the child's behaviour during the 5-week RED, not only adapt the medication but also adapt the diet, in order to maximize the behavioural improvements. Unremitting consultation with parents and teacher on the effects of the RED is compulsory in order to maintain

the high quality and the impressive effect sizes achieved in the RED studies. Adaptations are made based on behavioural questionnaires, in accordance with the questionnaires used in the INCA study. It is important to emphasize the disadvantages of unsupervised elimination diets which may be prescribed undeservedly, which may lead to dietary insufficiencies or the results of which may be interpreted incorrectly because of missing reliable information. Finally, children diagnosed FI-ADHD who proceed with the challenge period and who subsequently show a severe behavioural relapse due to one of the challenged foods, may be advised to start or restart medication for a short period of time, i.e. until the effects of the challenged foods have faded away, in order to sooth the effect of the challenged food and to decrease the behavioural problems, especially at school. This is an important aspect of the challenge period which has to be monitored by an expert. At the end of the 5-week RED the diagnosis FI-ADHD or C-ADHD will be made, based on the results of the questionnaires and the information of parents and teachers.

9.7.3. Follow-up strategy in children with C-ADHD

Parents need to be informed about the procedure that will take place when their child is diagnosed with C-ADHD. It will be obvious that these children, not responding to an RED, are allowed to eat anything again. They may proceed with psychological research to establish any other problems that may underly ADHD symptoms, e.g. learning disorders or learning problems, including an above average or high IQ. Unrecognised high talented children, similarly to children with unrecognised nonverbal learning disability (NLD) or dyslexia, may have problems at school, may show inattention problems or become restless and fidgety, may underperform and may eventually be diagnosed with ADHD because they are showing the symptoms of ADHD. It must be acknowledged that ADHD is a symptomatic disorder, based on the number of symptoms and the concurrent problems in daily life. Consequently, unrecognised learning problems and disorders may lead to the diagnosis ADHD, and it is of the utmost importance to investigate and determine any psychological conditions which may be underlying of C-ADHD. If none of these psychological conditions are present or if an adequate approach of established psychological conditions does not improve the behavioural problems, then referral to a child psychiatrist is imperative, and medication as well as behavioural interventions should be considered.

9.7.4. Follow-up strategy in children with FI-ADHD

Children diagnosed FI-ADHD will proceed with the RED challenge period, in order to define the incriminated foods which may differ per child and per amount of food. This period is considered aggravating for parents and teacher, due to the recurrent behavioural relapses. Consequently, expert coaching of parents and teacher is important to increase the feasibility of the challenge period. Families showing compliance problems may be offered complementary parenting training, including video home training. The results of the RED in children with FI-ADHD is to such an extent, that it is important to strain every nerve in order to help families to see this period through. At the end of the challenge period the child's diet has returned to almost normal, the incriminated foods have been pin-pointed and the individual sensitivity for each incriminated food has been established, resulting in an dietary advice to what extent these foods have to be avoided, i.e. partially or completely, thus preventing ADHD.

If in the course of the RED challenge period a relapse in behaviour occurs or if the behavioural improvements manifest themselves predominantly at home and are less prominent at school, then also in children with FI-ADHD psychological research must be considered. Co-occurrence of ADHD with learning disabilities or learning problems is a conceivable option which might be the reason for less behavioural improvements at school. It is worth mentioning that in this algorithm psychological research consciously has been placed after the RED, to improve the reliability of the test results, because children with ADHD tend to underperform which may affect the test results. Executing the psychological research following the RED will offer, at least in children with FI-ADHD and provided that the child has complied with the diet preceding the test, more reliable results because in these children the effects of ADHD are ruled out. Still, if in children with FI-ADHD the underlying cause of the relapse in behaviour cannot be established, and if the relapse is causal of malfunctioning at school or at home, then medication needs to be considered.

It has to be acknowledged that the challenge period is the most poignant part of the RED research. Expert monitoring and coaching of family and teachers is of paramount importance, first of all in order to pull everyone through this period; secondly, in order to define to which foods a child reacts; and most of all to give the child a chance of a better future, without ADHD. There is no reason to expect, provided that the child sticks to the diet, the dietary effects to disappear or diminish.

Two RED studies and the INCA follow-up have shown that the effects of an RED may continue unabated for a one-year period. Consequently, although more long-term research needs to be done especially to verify whether children may outgrow their specific vulnerability, it is timely to implement RED research in ADHD.

The concurrent economical effects of every child completing the RED research will be gigantic. According to a Dutch report, making a rough inventory of some of the costs of ADHD while comparing the costs including RED research with the current costs of ADHD, implementation of RED research may yield savings of 7.000 euros per year per child starting the RED research.⁷⁴ This sum is applicable to each child starting the RED research, independent of the fact whether the child proves to be a responder or a nonresponder. The height of the sum may be explained by the fact that children diagnosed C-ADHD need expert supervision and medication for a great many years, while children diagnosed FI-ADHD need expert supervision for 1 year only. Consequently, if 100 children would start the RED research right now, the financial proceeds would, in a 10-year period, amount to 7 million euros (100 children x 7.000 euros x 10 years). Imagine the savings if all children with ADHD would start RED research!

9.7.5. An overview of the RED research according to the algorithm

- 1) RED research may be very effective, but certainly is not a quick fix method,
- 2) parents need to be motivated and need to have sufficient parenting capacities,
- 3) in the course of RED research a 5-week RED is necessary to establish whether the child is suffering from FI-ADHD (the RED diagnostic phase),
- 4) the diagnostic phase ends with making either the diagnosis FI-ADHD or the diagnosis classic ADHD (C-ADHD),
- 5) children diagnosed C-ADHD start assessment and treatment as usual,
- 6) children diagnosed with FI-ADHD will proceed with a challenge period to establish which foods are causal of the behavioural problems (the RED therapeutic phase),
- 7) the challenge period will take an average of 15 months,
- 8) following the challenge period the child's diet will be almost back to normal, the child only having to avoid a small number of foods,
- 9) the therapeutic phase ends with an individually dietary advice about which foods are incriminated and about the frequency in which the child is allowed to eat the incriminated foods,



- 10) it is not clear whether the child has to stick to the individual dietary restrictions perpetually, or whether children may overgrow the hypersensitivity,
- 11) occasional non-compliance with the therapeutic dietary advice will not be a problem, because in most children the behavioural problems occur only if the incriminated food is eaten for several days in succession and if the amount of the food exceeds an individually established threshold.

9.8. Suggestions for DSM-V

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) will be published in May 2013. The DSM is a renowned and widely used standard handbook describing and classifying mental disorders. Most classifications are based on specific symptoms which have to occur for a determined period of time and which have to cause significant impairment, consequently, most DSM diagnoses are symptomatic, i.e. based on symptoms instead of on causes (causal diagnoses). Of course, in psychiatric disorders it is common practice and justifiable to make symptomatic diagnoses, considering that the aetiology of most disorders is complex and unclear. Nevertheless, in some psychiatric disorders the diagnoses do refer to the cause, e.g. in Substance-Induced Delirium, Alcohol-Related Disorders, Amphetamine-Related Disorders and Cocaine-Induced Disorders. In accordance with these cause-related diagnoses the impact of an RED on ADHD has clearly been established, as a consequence of which part of the causal puzzle of this disorder is solved. Naming and blaming food as a cause of ADHD and integrating this knowledge (which was already incorporated in an algorithm for treatment of ADHD in 2001) in the DSM-V would be a considerable step forward towards understanding and treating ADHD, with concurrent beneficial effects for the children suffering from this disorder.

In addition to the suggestion to include food-induced ADHD (FI-ADHD) in the DSM-V, it is worth considering to substitute the current dichotomic symptom inventory ("often" versus "not often") by an inventory that specifies the rather vague and ambiguous indication "often". It is important to define the exact meaning of "often" in order to make a correct inventory of the behaviour of the child. The absence of a specific definition of "often" may lead to misinterpretation of the child's behaviour in parents with a lack of resilience as well as in parents