

# **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

## **Proefschrift**

ter verkrijging van de graad van doctor  
aan de Radboud Universiteit Nijmegen  
op gezag van de rector magnificus prof. mr. S.C.J.J. Kortmann  
volgens besluit van het college van decanen  
in het openbaar te verdedigen op maandag 10 oktober 2011  
om 15.30 uur precies

door

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geboren op 8 januari 1956  
te Epen (Wittem)

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Cover illustration and cartoons by: Rob van Barneveld, Utrecht ([www.roodgras.nl](http://www.roodgras.nl))

Layout by: In Zicht Grafisch Ontwerp, Arnhem ([www.promotie-inzicht.nl](http://www.promotie-inzicht.nl))

Printed by: Ipskamp Drukkers, Enschede ([www.ipskampdrukkers.nl](http://www.ipskampdrukkers.nl))

ISBN 978-90-817682-0-7

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## Preface: how it all began

When I practised as a veterinary surgeon it occurred to me that I often spent more time listening to the personal problems of the owner than treating their pets. Although I was not trained to be a human physician or psychiatrist, I felt that I failed in my duty. Consequently, in the evenings I took psychology classes and I became fascinated by one specific book, the *Modern Synopsis of the Comprehensive Textbook of Psychiatry* by Kaplan and Sadock. I was puzzled by the fact that in the human psychiatric diagnostic procedure it seemed to be common practice to start a therapy – of course after making an inventory of symptoms and their impact on everyday life – without a search for a cause. How totally different that was from what I had learned as a vet.

According to my veterinary medical education it was considered malpractice to start a therapy without at least trying to find a cause of the problems. This golden standard – first making an inventory of symptoms, then a search for the cause of the symptoms (i.e. differential diagnostic research), and finally starting a therapy specifically aimed at eliminating the cause – is common practice in both veterinary and human somatic medicine. Still, I now was dealing with psychiatric conditions. Could it be, so I pondered on this issue, that psychiatric diagnostic rules did not correspond to somatic diagnostic rules?

On the other hand, although we had not yet unravelled the mysteries of the brain, it is an organ like other organs, so there should be a cause to find in case of malfunction, even in psychiatric disorders. What did psychiatric researchers focus on to resolve this problem, I wondered. I remembered treating a little dog suffering from fly catcher's syndrome, compulsively trying to catch imaginary flies. Definitely mad. This dog happened to suffer from eczema as well and I prescribed a restricted elimination diet, an effective treatment of eczema in veterinary practice in many patients. What happened following a 6-week period of diet was striking: the dog trotted into the surgery without a twitch or snatch, the owner following with a big smile on his face. I was astounded to find that not only the eczema had vanished but also the fly catching. What a strange and puzzling coincidence it seemed to be at the time, but now I wondered whether there might have been a connection between the somatic and the psychiatric problems of the little dog.

Several weeks later I happened to hit upon a study investigating the effects of a restricted elimination diet on ADHD in children. Reading it I got truly interested, I searched for more literature on this subject, thought about the little mad dog and I kept on reading. That was how I spent my evenings, reading, writing, thinking and rethinking, with my children fast asleep. I discovered that the answers to my questions inevitably led to even more questions and I enjoyed it to the full. I realised I had found my future: science. You may find the results of my thoughts and research in this thesis, and I would highly recommend chapters 1, 8 and 9, which in particular comprise the results of my considerations on the cause of ADHD.

## Postface: how it all turned out

I wrote my first research protocol on ADHD and food, the “Validation of early Intervention and Prevention (VIP)” study, fifteen years ago. The VIP study was meant to be the continuation of the Restricted Elimination Diet (RED) studies conducted between 1985 and 1994, all showing convincing evidence for the effects of an RED on ADHD. The study consisted of a 5-year research including 2 groups of young children with behavioural problems, a VIP group and a control group. The VIP group was not only to follow the RED but also to receive Very Important Person (VIP) treatment (i.e. psychological research, improvement of parenting capacities, and coaching of parents, siblings and teachers), whilst the control group would neither follow the RED nor the VIP treatment, but would receive treatment as usual only.

Unfortunately, in spite of all efforts to find a university to support and a sponsor to fund this study, I did not succeed. Daring to think outside the box makes one vulnerable and my research proposal was ridiculed and dismissed, many times. There was nothing else for it but to try a different approach. I decided to start all over again and write a new proposal as though no RED research ever had been conducted. Now I found a professor (thank you, Jan), we found a sponsor (thank you, Stichting Kinderpostzegels Nederland) and the results of this study are described in chapter 2.

The reader may have noticed the time span between the first (2002) and the second study (2009), which is attributable to several factors: 1) fund raising of the second study took some time; 2) recruitment of subjects proved difficult: parents willing to participate were often discouraged to do so by GP, psychologist or psychiatrist; and 3) editors' and reviewers' unfamiliarity with the subject. Most editors dismissed the manuscript by return of post, and even when it survived the editor's scrutiny, the reviewers dealt summarily with it. One reviewer motivated his rejection as follows: “... this means that 83.3% of the children responded to dietary intervention!” Apparently this reviewer was shocked by the results, which may be understandable considering the subject, but rejecting a paper based on the surprising results is not quite a scientific attitude.

While the above mentioned manuscript was sent from one journal to the other, I wrote a hypothesis paper (see chapter 5), I wrote the protocol for the INCA study, I tried to raise the funds necessary to start the INCA study, and I stubbornly went

on studying. I was especially interested in fish oil. Could it be true that a simple capsule a day would keep ADHD away? I was very keen to find out, because if it were true it would be a much more convenient and easier therapy than an RED. I contacted companies manufacturing fish oil and presented a research proposal to compare the effects of an RED with the effects of fish oil. Surprisingly, none of them were interested, and one of the companies politely explained the rejection as follows: "We will not cooperate in this study because the risks for negative results with respect to the effectiveness of the supplements are substantial". My further study into this subject showed that the anxiety reflected by the polite company was appropriate, indeed. In chapter 1.7 and chapter 9.6 the negative results of recent studies investigating the effect of fish oil on ADHD are discussed.

Studying fish oil (omega-3 fatty acid) also means studying sunflower oil (omega-6 fatty acid), and I read a lot about the differences between omega-3 and omega-6 fatty acids. Not only do they differ in biochemical structure, they also differ in function (omega-3 inhibiting inflammation, omega-6 promoting inflammation). The most striking distinction, though, is the at least tenfold increased omega-6/omega-3 ratio in our food during the last 50 years. Given that omega-6 and omega-3 compete for the same enzymes it seems rather useless to supply omega-3 without a concurrent drastic decrease of omega-6. There is evidence that the huge increase of omega-6 fats in our food may be causal of the Western world's lifestyle diseases characterised by an increase of inflammation, like type 2 diabetes and obesity (see chapter 9.6). I am convinced that it would be worthwhile to investigate whether a major decrease of omega-6 in our food might result in an equally major decrease of our chronic Western diseases, and I earnestly stand wondering why scientists continue to focus on less saturated fats and more unsaturated fats (omega-6 and omega-3), while simultaneously lifestyle diseases unabatedly increase.

I would have loved to study this subject more comprehensively, but my fatty acid adventures were interrupted by a sudden rapid development of the ADHD research. The protocol of the INCA study was accepted by *The Lancet* (see appendix), the manuscript that had travelled from one editor to another for more than 3 years was finally accepted for publication (see chapter 3), and the long-lasting fund-raising campaign to raise money for the INCA study ended with a passionate plea broadcasted by EenVandaag, a Dutch television station, after which a maecenas generously donated the money needed to start.

And here we are now. The INCA study has been published in *The Lancet* (see chapter 6), which of course may be considered the crowning glory of this thesis. Still, there it is, in my drawer, the protocol of the VIP study. Unabated a highly topical subject, and I would love to conduct this implementation study as well as the other RED-ADHD studies I have in mind (see chapter 9.6). It is evident that many children may benefit from our findings, as you may read in chapter 9.7, describing the pros and cons of both treatment-as-usual and RED treatment. It would be truly sad if it took another fifteen years before follow-up research like the VIP study might be realised. I sincerely hope that this thesis may lead to an RED-ADHD Research Centre and may instigate a paradigm shift necessary to improve child psychiatric health care (whether that be an RED or, if necessary, medication and psychological interventions or any combination of these), thus offering our children suffering from ADHD the ultimate chance of a more favourable future.