

 **ADHD, a Food-Induced Hypersensitivity Syndrome**

Scientific Research
into the Effects of a
Restricted Elimination Diet (RED)
on ADHD




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 **Why innovative investigations are needed**


- The current treatment (medication) is good, but not good enough
- Despite short-term efficacy of drugs, long-term beneficial effects have not been convincingly established
- 50% of children with ADHD discontinue medication within 2 years

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 **Limitations of current treatment**


- The current treatment (predominantly methylphenidate) is more care than cure: problems in mornings/evenings are not solved
- Growing concerns about side effects and safety of available medication
- In 75% of children the problems persist into adolescence and adulthood

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 **Current knowledge of ADHD is limited**

- Our knowledge concerning pathogenesis and causes of ADHD is limited
- Finding new causes may instigate new, tailor made, treatments, instead of a “one size fits all” approach
- There is increased interest and knowledge of the effects of environmental factors such as food

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 **ADHD - Food Research 2 types**

Additive Research
some foods involved:
(colourings, sugar, preservatives)

RED Research
many foods involved:
(**R**estricted **E**limination **D**iet [**RED**])


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 **Additive research results:
ADHD not caused by sugar or additives**




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**RED research results:
ADHD caused by common foods**



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Restricted Elimination Diet (RED)-RCTs

1. Egger, *Lancet*, 1985, **DBPC** Food challenge
2. Kaplan Pediatrics, 1989, **DBPC**, Placebo diet
3. Carter, Arch Dis Child, 1993, **DBPC** Food challenge
4. Boris, Ann Allergy, 1994, **DBPC** Food challenge
5. Schulte-Korne, Z Kinder Jugendpsych, 1996, Open RCT
6. Schmidt, ECAP, 1997, **DBPC**, Placebo diet
7. Pelsser, ECAP, 2009, Open RCT
8. Pelsser, *Lancet*, 2011, Open RCT, blinded measurements

- 5/8 studies **Double-blind Placebo-Controlled Design**
- 3 open RCT's (1 with blinded measurements)
- Two lancet publications

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**Results 5 DBPC RED RCTs
(1985-1997)**

Statistically significant and clinically relevant effects of an RED on ADHD, some in selected subgroups

- Behavioural effects: **effect size 0.6 - 1.1**
(Effect size medication 0.5 - 0.9)
- 2001: advice to implement an RED in subgroup of children with ADHD (Hill & Taylor, Arch Dis Child, 2001)
- This advice has found no response
- 2001: Start RED research in The Netherlands

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Dutch RED research (2001-2011)

2 open pilot studies

- *Dutch Medical Journal (NTVG)*, 2002 (n=40) (Pubmed)
- *Dutch Psychology Journal*, 2003 (n=64)

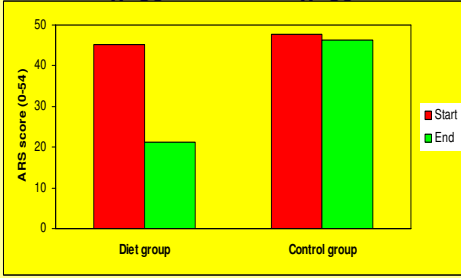
2 RCTs, one with blinded measurements

- *Eur Child Adolesc Psychiatry*, 2009 (n=27)
- *The Lancet*, 2011, INCA study (n=100)
(Impact of Nutrition on Children with ADHD)

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**INCA results ADHD, phase 1
blinded ratings, locf**

n=50 n=50

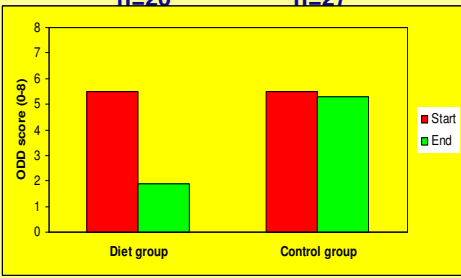


Group	Start	End
Diet group (n=50)	~45	~20
Control group (n=50)	~48	~45

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**INCA results ODD, phase 1
blinded ratings**

n=20 n=27



Group	Start	End
Diet group (n=20)	~5.5	~2
Control group (n=27)	~5.5	~5

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Results RED Responders

Definition responder: improvement > 40%

Number of RED responders: 32/50 = 64%
(Average behavioural improvement: 79%)

End of RED:
behaviour of responders normalized.
Children did neither meet ADHD nor ODD criteria according to parents, teachers and blinded paediatrician

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Effect RED on ADHD (combined type)

Group	n	before	end	ES
All children	50	16.4	5.1	2.0
All children who responded RED	41	16.3	4.0	5.9
Responders	32	16.3	1.7	5.9
Nonresponders	9	16.3	15.8	0.3

ADHD ↑
NO - ↓
ADHD

Number of ADHD symptoms

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Conclusion INCA

- A. In 64% of children with ADHD/ODD the behavioural problems disappear after an RED
- B. Mechanism: IgE and IgG not involved
no improvement of family structure
- C. RED implementation is advised in young children
- D. Necessary conditions:
 - motivated parents
 - expert supervision

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Time for a paradigm shift?

Question, based on all RED RCTs:
is implementation of RED research in practice and inclusion of RED in the DSM-V timely?

500 psychiatrists and paediatricians attended the Nordic Psychiatry Congress and voted...

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Yes, time for a paradigm shift!

The majority (57%) voted that it is timely to implement RED research in children with ADHD and to include food as a causal factor of ADHD in the DSM-V!

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What ADHD have you got?

To date: therapy based on symptoms
In future: therapie based on cause

Food-Induced ADHD? **RED**

Classic ADHD? **MED**

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Follow-up after RED research

- Children with **Classic ADHD** (behavioural improvement < 40% following **RED research**) should be referred for standard treatments like medication (MED)
- Children with **Food-Induced ADHD** (behavioural improvements > 40% following **RED research**) should start a follow-up period of food provocation and elimination in order to define the incriminated foods (each child reacts to different foods, with an average of 5 foods per child)

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RED in practice

Necessary conditions:

1. Parents have to be motivated to follow a 5 week **RED**. The younger the child, the easier the diet
2. Expert supervision is necessary
RED research implicates more than just a diet
3. Random diet advice is discouraged
-First investigation is needed to define IF a child reacts to food (**RED research**).
-If so, a follow-up period is needed to define to **WHAT** foods a child reacts
4. Keeping a diary to define whether ADHD is caused by foods does not provide useful information and is discouraged

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Implementation in The Netherlands

In The Netherlands physicians are trained to apply **RED research** in general practice according to the INCA protocol.

First results of an independent practice in Rotterdam (2009 - 2011):

167 subjects, age 2-15, ADHD and/or ODD, mainly boys

5% left study during 5-week RED: 8/167

26% nonresponders: 43/167

69% ADHD and ODD responders: 116/167

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Implementation action points



Training physicians to apply RED research

Training coaches to assist and guide parents and teachers during the follow-up period

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Further research

Not IF but HOW an RED affects behaviour

- Mechanism?
- Bowel-Brain interaction?
- Long term effect?
- Biomarkers?
- Epigenetic effect?

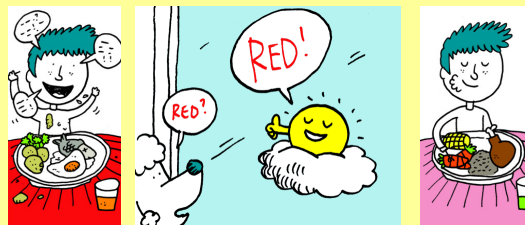


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Prevention is better than cure



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