

# NON-PHARMACOLOGIC TREATMENTS FOR ATTENTION- DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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A Card Trick. John George Brown. Joslyn Art Museum, Omaha, NE, US

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This chapter complements and should be read in conjunction with [Chapter D.1](#) of the IACAPAP Textbook. Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders of childhood, with an estimated prevalence of about 5% in school-age children. Core symptoms include impaired attention and/or hyperactivity/impulsivity (American Psychiatric Association, 2013). ADHD often has a chronic course with up to 65 % of affected individuals displaying impairing symptoms during adulthood (Faraone et al, 2006). ADHD is associated with high levels of both externalizing (oppositional defiant disorder and conduct disorder) and internalizing (depression and anxiety) comorbidities. ADHD impacts on in multiple domains of functioning across the lifespan, including school and work performance, social relationships, and family interactions (Faraone et al, 2006).

Given its impact and associated burden, considerable effort has been directed at developing effective treatments. Multimodal treatments, which combine pharmacologic and psychologic approaches, are currently recommended (National Institute for Health and Clinical Excellence, 2008). ADHD medication—i.e., stimulants (e.g., methylphenidate, d-amphetamine) and non-stimulants (e.g., atomoxetine, guanfacine)—are effective in the short and medium term in randomized controlled trials in relation to core symptoms, externalizing comorbidities, and daily functioning (Faraone & Buitelaar, 2010; Banaschewski et al, 2013). Medication can also reduce neuropsychological impairment: executive functions, executive and non-executive memory, reaction time, reaction time variability, response inhibition, aversion to delayed reward, and intrinsic motivation (Ni et al, 2013; Coghill et al, 2013).

Despite its proven short-term efficacy, treatment with medication has several limitations. These include (Sonuga-Barke et al, 2013):

- Partial or no-response in a proportion of cases
- Adverse effects
- Questionable long term benefits and costs
- Poor adherence, and
- Negative attitudes of patients, parents, or clinicians to medication.

Limitations of existing pharmacologic treatments highlight the need for therapeutic innovation to develop effective non-pharmacologic interventions that improve short and long term outcomes in core symptom domains, neuropsychological deficits and, more generally, in the pattern of impairment (Graham et al, 2011; Cortese et al, 2013). To date, a variety of non-pharmacological interventions are available to treat ADHD including psychologic treatments and dietary approaches. Effectiveness of some of these therapies has been partly supported by several systematic reviews and meta-analyses. However, some of these studies have significant methodological shortcomings—for example, by including non-randomized designs, non-ADHD samples, or non-ADHD outcomes—not allowing firm conclusions to be drawn (Arns et al, 2009; Fabiano et al, 2009; Bloch & Qawasmi, 2011; Nigg et al, 2012).

In this chapter we describe commonly available non-pharmacologic approaches, their rationale, delivery, evidence of effectiveness, clinical considerations, and future directions for research and practice. It is important to note that our findings *do not* imply recommendation for their use.

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## EXCLUSION DIETS AND DIETARY SUPPLEMENTS

There is increasing interest in the relationship between lifestyle, diet and mental health. For example, a report from a prospective birth cohort study described a significant association between a “Western” dietary pattern—high in fat, refined sugars, and sodium, and low in fiber, folate, and omega-3 fatty acids—and ADHD (Howard et al, 2011). This section focuses on four dietary interventions—exclusion of artificial colors and preservatives; restrictive elimination diets/oligo-antigenic diets; supplementation with omega-3 fatty acids; supplementation with vitamins and micronutrients—and their clinical relevance for ADHD.

### ARTIFICIAL FOOD COLORS AND PRESERVATIVES

Feingold was the first to suggest that allergy to food color additives, synthetic flavors, and food preservatives could lead to an increase in ADHD symptoms (Feingold, 1985). He based this on observations that salicylates could not only cause asthma or eczema but also behavioral reactions, such as an increase of hyperkinetic behavior, in some patients. Hence, he proposed a diet free of foods with natural salicylates and synthetic colors and flavors. The supposed mechanism could be either an allergic reaction or hypersensitivity to salicylates and related substances.

#### Treatment Delivery and Available Treatments

The Feingold program is a form of elimination diet where foods containing certain additives are replaced with foods free of those additives. When starting the program, certain foods and non-food items containing aspirin-like chemicals called salicylates are eliminated and later tested for tolerance. These foods include:

- Artificial colorings (e.g., petrochemical dyes)
- Artificial flavors and fragrances
- Some preservatives
- Artificial sweeteners
- And foods and products containing salicylates.

Initially the diet is used as a diagnostic tool to determine if any of the eliminated items trigger some or all of the problems observed. When successful, it is continued as a treatment, and can be combined with other medical treatments.

#### Effectiveness

A meta-analysis across 20 studies of elimination diets including 794 participants found a small effect size (0.18) based on parent reports, that decreased to 0.12 when possible publication bias was taken into account (Nigg et al, 2012). Effect on teachers’ reports and observer measures was not significant (Nigg et al, 2012). About 8% of children with ADHD were estimated to have symptoms related to food colors. Another meta-analysis of 8 studies including 294 participants reported a similar effect size (0.32 to 0.42 depending on the informant). However, the effect size became non-significant when the analysis was limited to studies with few or no concurrent medication (Sonuga-Barke et al, 2013). There are no long-term studies.

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[Click on the image to view a very brief summary of the meta-analysis by Sonuga-Barke et al \(2013\) on the different non-pharmacologic treatments for ADHD](#)

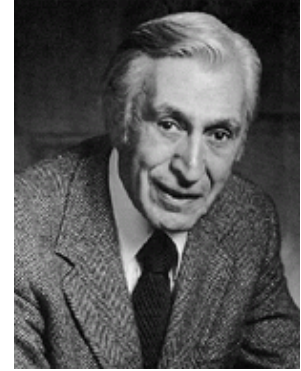
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### THE INTERNATIONAL NUMBERING SYSTEM FOR FOOD ADDITIVES (INS)

This is a European-based naming system for food additives aimed at providing a short designation for what may be a lengthy chemical name. It is defined by the Codex Alimentarius of the international food standards organization. The information is published in the document “[Class Names and the International Numbering System for Food Additives](#)”. The INS is an open list, subject to the inclusion of additional additives or removal of existing ones. INS numbers consist of three or four digits. Approved food additives are written with a prefix of E on food packaging in the European Union. Australia and New Zealand do not use a prefix letter. INS numbers generally correspond to E numbers for the same compound, e.g. INS 102 (tartrazine), is also E102. INS numbers are not unique and, in fact, one number may be assigned to a group of similar compounds. The US does not use the INS numbering system (Wikipedia).



Benjamin F Feingold MD (1899, 1982) was a US pediatrician who proposed that salicylates and food additives, such as artificial colors and artificial flavors, cause hyperactivity in children. Eliminating these foods (Feingold diet) would be expected to reduce hyperactivity.

### Clinical Implications

Despite the long-standing controversy on the effects of food colors and preservatives on ADHD symptoms, the evidence available still has many gaps. Most if not all studies are of small size, the mechanisms and predictors of response are unknown, and it is unclear which chemicals and at which dose have a clinical impact. Nevertheless, the effect size on ADHD symptoms of exclusion diets is small, not large enough to justify it being recommended as stand-alone treatment. It may be a useful adjunctive treatment for some cases.

Decisions to explore the clinical utility of such diets in individual cases should be weighed against difficulty and expense (e.g., it is hard to implement in a household with several children, requires intrusive monitoring of compliance that in itself could impact negatively on the parent-child relationship, and it is expensive to source additive-free foodstuffs).

### Future Directions

- There is a need for rigorous large-scale studies on the effects of food colors and preservatives on ADHD symptoms and related behaviors such as aggression, oppositionality and emotional lability
- Though the effect size of food exclusion diets is small from a clinical perspective, it may be substantial from a population-wide, health care, and food policy perspectives. The prevention paradox states that most cases derive from low-risk individuals and that a rather small protective

**Table D.1.1.1** Preservatives to be eliminated from the diet (www.feingold.com)

ABBREVIATION	NAME	E-NUMBER*
BHA	Butylated hydroxyanisole	E 320
BHT	Butylated hydroxytoluene	E 131
TBHQ	Tertiary butylhydroquinone	E 319

\*Codes for substances that are permitted as food additives within the European Union and Switzerland (see Box).

effect on the wider population could reduce caseness more often than an intervention targeting clinical cases or high-risk individuals (Rose, 1981)

## RESTRICTIVE ELIMINATION OR OLIGOANTIGENIC DIETS

Adverse physical reactions (e.g., eczema, asthma, allergic rhinitis, and gastrointestinal problems) to some foods have led to the hypothesis that specific foods might also have an impact on the brain, resulting in adverse behavioral effects. In oligoantigenic diets the focus is on foods other than artificial colors and preservatives that may trigger ADHD symptoms in some children by acting as food antigens or allergens. Foods often found to be allergenic include cow's milk, cheese, eggs, chocolate, and nuts. Thus, an individually constructed oligoantigenic or restricted elimination diet might be an effective treatment for ADHD (Nigg et al, 2012; Pelsser et al, 2011).

A typical food allergy is a reaction to foods involving specific antibodies (e.g., IgE). It has been hypothesized that in non-IgE-mediated reactions to food, determination of IgG may be a helpful adjunct, and IgG blood tests are widely offered to establish a relationship between foods and ADHD symptoms, especially in complementary medicine settings. According to the IgG-ADHD theory, foods associated with high IgG-levels would result in a significant behavioral deterioration when eating these foods, while foods associated with low IgG-levels would not. However, evidence of the value of these tests is lacking. Further, in a restricted elimination study, worsening of ADHD symptoms occurred independently of IgG levels of the challenging foods, thus questioning the role of IgG-mediated mechanisms (Pelsser et al, 2011).

### Treatment Delivery and Available Treatments

Restrictive elimination diet interventions typically involve a temporary (2-5 weeks) total change of diet, in which the child is only allowed to consume a few hypo-allergenic foods (e.g., rice, turkey, lettuce, pears, and water). If it results in a substantial decrease in ADHD symptoms (i.e., it shows to be "food sensitive"), a 12-18 month reintroduction phase is conducted to find out which specific foodstuffs trigger ADHD symptoms. The rationale is that a person may show adverse reactions to a variety of foods and that it is important to determine the individual's susceptibility to the specific foods that cause the adverse reactions.

### Effectiveness

A meta-analysis reported an effect size of 0.29 across 6 controlled trials including 195 participants and concluded that about one third of the children with ADHD show an excellent (>40% symptom reduction) response (Nigg et al, 2012). Another meta-analysis estimated an effect size of 1.48 for the most proximal assessment (by the person applying the treatment). However, effect size dropped to 0.51 when probably blind raters were used (Sonuga-Barke et al, 2013). There was considerable heterogeneity across studies due to different designs and on how strict was the food elimination. Studies included a small number of participants. There are no studies reporting medium to long-term effectiveness and cost-effectiveness.

## ANTIBODIES

**Antibodies** are formed from short light chains (with low molecular weight) and long heavy chains (with high molecular weight). Of these, there are five types of heavy chains, and the type of antibody is determined by differences in these heavy chains (IgG, IgM, IgA, IgD, IgE).

IgE is believed to be related to immunity reactions to parasites and has recently become known as a key factor in allergies such as hay fever.

IgG is the main antibody in the blood. It is the only one that can pass through the placenta, and IgG transferred from the mother's body protects a newborn until a week after birth. IgG is widely distributed in the blood and tissues, and protects the body.

### Clinical Considerations

- A strictly supervised elimination diet is a valuable approach to assess whether ADHD in a given child might be food-sensitive. As IgG blood tests do not provide information about which foods might provoke ADHD symptoms, the prescription of diets based on these tests should be discouraged
- Children with ADHD and their parents who are interested in elimination diets need to be supervised closely because adherence to the diet requires efforts and motivation by the whole family
- Implementation of this diet requires a drastic change of lifestyle; success will depend on the family's organizational skills and parents' level of control over the child's diet

### Future Directions

- Large scale, multisite clinical trials into the feasibility, effectiveness and cost-effectiveness of elimination diets for children with ADHD are needed. These studies should aim to identify predictors of response and establish the long-term effectiveness
- Future research might also need to target the gut microbiota/brain connection as a potential mechanism underlying the effects of elimination diets

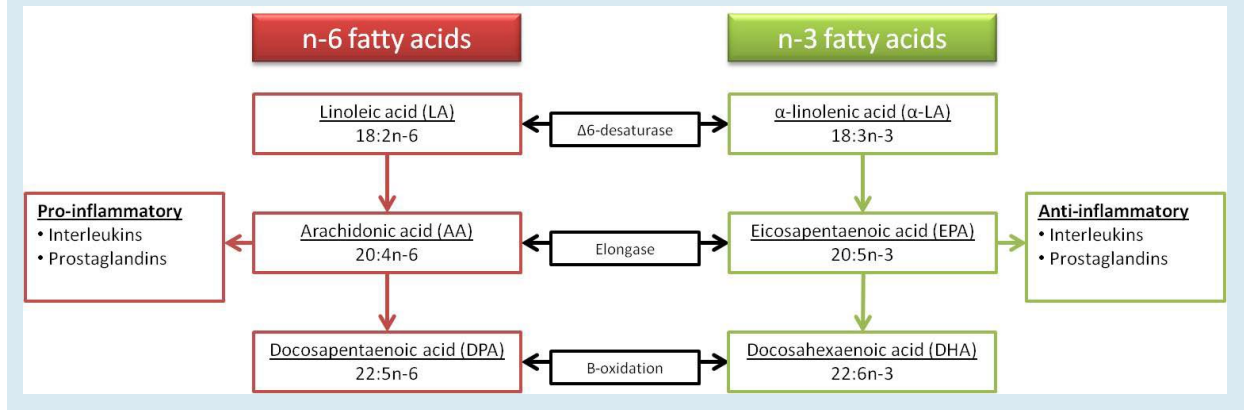
## SUPPLEMENTATION WITH OMEGA-3 AND OMEGA-6 FATTY ACIDS

Around 25-30% of all fatty acids in the brain are polyunsaturated. They play an important role in the structure and function of neuronal cell membranes in the brain, retina and myelin sheath. Two fatty acids, also called “essential”,  $\alpha$ -linolenic (an omega-3 fatty acid) and linoleic (an omega-6 fatty acid) cannot be synthesized by humans and need to be acquired through the ingestion of foods (see Figure D.1.1.1). Whereas  $\alpha$ -linolenic is sparsely distributed in soybean, canola, and flax seeds oil, linoleic acid is more abundant; over 50% of all fatty acids in soybeans, corn and sunflower oil is linoleic. Omega-6 and omega-3 fatty acids are not interchangeable; the former have anti-inflammatory properties, whereas the latter is pro-inflammatory.

Several studies have reported lower concentrations of omega-3 fatty acids in plasma and erythrocyte membranes in children and adults with ADHD (Bloch 2011). Abnormally low essential fatty acids in children with ADHD may be due to reduced intake, reduced conversion of essential fatty acids to long chain polyunsaturated fatty acids, and increased metabolism of long chain polyunsaturated fatty acids, but none of these alternatives have been properly studied (Millichap et al, 2012).

### Treatment Delivery and Available Treatments

There are numerous commercial products (gels, capsules, and liquids) available to supplement omega-3 fatty acids in the diet. Most supply eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (see Figure D.1.1.1) in amounts that vary up to ten-fold. Additionally, many products also contain other micronutrients or vitamins hypothesized to be deficient in patients with behavior disorders.

**Figure D.1.1.1** Fatty-acid synthesis pathway

### Effectiveness

Two meta-analyses concluded that supplementation with these fatty acids was associated with a small but reliable reduction of ADHD symptoms, with effect sizes ranging from 0.18 to 0.31 (Sonuga-Barke et al, 2013; Bloch, 2011). Higher doses of omega-3 supplements were significantly associated with a larger reduction of ADHD symptoms (Bloch, 2012). A third meta-analysis did not find statistically significant differences on parent and teacher ratings of ADHD symptoms between fatty acids supplementation and placebo (Gilles et al, 2012). None of the studies monitored plasma levels of free fatty acids. This and other methodological limitations should lead to caution when interpreting the significance of these effects. There are no studies on the long-term effectiveness and cost-effectiveness.

### Clinical Considerations

- The clinical relevance of fatty acid supplementation in treating ADHD remains unclear. Some researchers have suggested that fatty acid supplements be considered as an add-on treatment in children who show partial response to medication. If so, the recommended doses are 300 to 600 mg/day of omega-3 and 30-60 mg/day of omega-6 fatty acids for at least 2 or 3 months, or longer if indicated (Millichap et al, 2012). Given the low effect sizes, it is important to monitor carefully whether supplements have any benefit and to continue using them only if this is the case
- Side effects are minor and include fishy taste and odor, stomach upset, loose stools, and nausea.

### Future Directions

- There is a need for high-quality, large sample, controlled studies with fatty acid supplementation that include patients with different ages (preschoolers, school age children and adolescents) and monitor the plasma levels of fatty acids at baseline and during treatment.

## SUPPLEMENTATION WITH MICRO-NUTRIENTS

Neurotransmitter metabolism requires enzymes, and enzyme function is dependent upon the presence of adequate quantities of multiple coenzymes

(cofactors), such as vitamins and minerals. Conditions such as ADHD and other psychiatric disorders may be associated with metabolic dysfunctions that limit the availability of vitamin and mineral cofactors and results in slowed metabolic activity (Kaplan et al, 2007; Ames et al, 2002). This may be remediated by supplementation with micronutrients. Deficiencies of micronutrients may play a role in the cognitive deficits associated with ADHD (Mikirova et al, 2013; Sarris et al, 2011; Scassellatti et al, 2012). Further, outside the context of ADHD, the quality of the nutrition in the first years of life is associated with children's later cognitive and academic abilities (Nyaradi et al, 2013; Prado & Dewey, 2014).

### **Treatment Delivery and Available Treatments**

There is a multitude of commercially available products that follow a “broad spectrum approach” by providing multi-ingredient and/or multivitamin supplementation and claim effectiveness in reducing symptoms of ADHD and other psychiatric conditions such as bipolar illness, anxiety disorders, and depression.

#### **Effectiveness**

Micronutrient treatment trials vary but for the most part have focused on single nutrients such as iron, magnesium and zinc. They have demonstrated modest to negligible effects (Cortese et al, 2012; Ghanizadeh et al, 2013; Rucklidge et al, 2009). A well-designed, blinded, randomized clinical trial has shown large improvements in ADHD symptoms in adults after a broad spectrum vitamin-mineral treatment (Rucklidge et al, 2014). An open label pilot trial using the same micronutrient formula in 14 children with ADHD reported significant improvement in parent reported ADHD symptoms (Gordon et al, 2015).

#### **Clinical Considerations**

- Dose and variety of ingredients in micronutrient supplementation may be important in effecting change in ADHD, but no specific guidance can be given since data are lacking
- Current studies did not raise safety issues, but very high doses can become toxic with no associated benefit as demonstrated by earlier studies that gave mega doses (Arnold et al, 1978)

#### **Future Directions**

- Good quality, large controlled studies with micronutrient supplementation that include patient with different age ranges are needed
- These studies should be combined with biochemical assessments to probe for real deficiencies and to examine the combined effects of micronutrient supplementation with other dietary interventions



## PSYCHOSOCIAL TREATMENTS

### BEHAVIORAL INTERVENTIONS

Psychosocial treatments based on social learning and behavior modification principles have been widely used, often through parent training-based approaches. Behavioral interventions can be defined broadly as therapies using learning principles to target ADHD or ADHD-related behaviors (Sonuga-Barke et al, 2013).

Behaviorally focused treatments can be delivered by therapists, parents, or by other “facilitators” (for example teachers). Facilitators are taught to use basic operant conditioning principles—behavior is modified through positive (e.g., praise) and negative (e.g., ignoring inappropriate behavior) reinforcement—to shape more appropriate behavior in the child; this is also called “contingency management”.

A daily report card is an example of a tool based on operant learning principles; teachers reinforce appropriate behaviors daily by giving feedback (for example by sticking stars or “smilies” on the report card) for appropriate behaviors in the school. Moreover, this tool can go between home and school facilitating interaction and communication between parents and teachers (see Figure D.1.1.2).

Another objective of these behavior-focused treatments is to reduce maladaptive behavior. To achieve this, parents and teachers are trained to use a more structured approach when dealing with a child with ADHD about everyday issues—for example, by giving clear instructions, one instruction at a time, or by providing in the morning a clear and realistic plan for the day—so that children know what is expected of them. Finally, an important aspect of these treatments is to enhance enjoyable parenting and positive interactions between parent and child, as a negative coercive cycle between parent and child often develops (Van der Oord & Daley, 2015). These interventions are typically used for pre-school and primary school-aged children rather than for adolescents.

Skills-based interventions assume that individuals with ADHD have core deficits in certain skills (e.g., planning and organization) and seek to enhance these skills either directly with the individual or through parents and teachers (Evans et al, 2014). These interventions can be provided in the clinic (Abikoff et al, 2015; Boyer et al, 2015) or the school, mainly through after school programs (Evans et al, 2016) that focus on enhancing skills such as planning, organization, and social

**Figure D.1.1.2** Example of a daily report card

Daily Report Card for: <u>Billy</u>		Date: _____		
Target Behavior	Reading	Writing	Math	Art
Write names on worksheet	★	★	★	★
Minds the fighting rule	★			★
Has book/materials for lesson		★	★	
7 stars = 1 prize from reward menu		Total # of stars earned: 8		

Click [here](#) for advice to teachers on how to design daily report cards

interaction. Skills based interventions are useful for both school-age children and adolescents.

Cognitive interventions for ADHD may also target children's negative schemas or thoughts, based on the premise that thoughts, feelings and behaviors are interrelated and that changing one element of this triad will modify the others (Antshel & Olszewski, 2014). They are typically delivered individually and are particularly useful for adolescents.



[Click on the image to access a video on parent and teacher training for ADHD](#)

## **Treatment Delivery and Available Treatments**

Should behavioral treatments be provided in a group or individually, at home, at school, or in a mental health service? Are there lower-cost alternatives such as self-help interventions that are effective?

### ***Parent training***

The National Institute for Health and Clinical Excellence (2008) of the UK recommends group behaviorally-focused parent training interventions (see [Chapter A.12 of the Textbook](#)). These interventions are effective for children with, or at risk of, ADHD (Webster-Stratton et al, 2011; Jones et al, 2007), but there is no evidence to suggest that group is more effective than individual intervention.

Parents of children with ADHD often display symptoms of ADHD themselves and may struggle with the organizational challenges of attending group-based sessions in clinic or community settings. To enhance effectiveness, treatments should be adapted to the needs of the target group, and be provided in the setting where maladaptive behavior is manifested (Kazdin & Blase, 2011). An unpublished study by Sonuga-Barke et al compared the relative efficacy of an individual home-based parenting program for ADHD (New Forest Parenting Program) with a group-based parenting intervention run in the community (Incredible Years), and with treatment as usual for a large group of hard to engage and difficult to treat parents of preschool children at risk of ADHD. Results suggested no clear advantage of the home based intervention in terms of symptom severity, but the individual intervention was more cost effective. However, the individual home-based intervention was preferred by parents (see Wymbs et al, 2015 for a discussion of parents' treatment preferences).

### ***School-based interventions***

School-based interventions are very diverse and it is a challenge to reach general conclusions. Not all school-based treatments aim at reducing ADHD symptoms specifically, some seek to deal with the academic problems commonly shown by children with ADHD.

Specific manipulation of academic instructions and materials can have a positive effect on ADHD children's learning efficiency (e.g., sitting closer to the teacher, providing shorter assignments, note-taking training, assisted oral reading, structured schedules and rules, alternating easier with more difficult exercises, allowing regular breaks, intra-task stimulation by adding colors or highly engaging stimuli) (Raggi & Chronis, 2006; Schultz et al, 2011). Peer tutoring (i.e., pairing an ADHD pupil with a highly achieving, supportive student) (DuPaul et al, 1998), as well as computer enhanced learning, applying a multi-sensory approach and

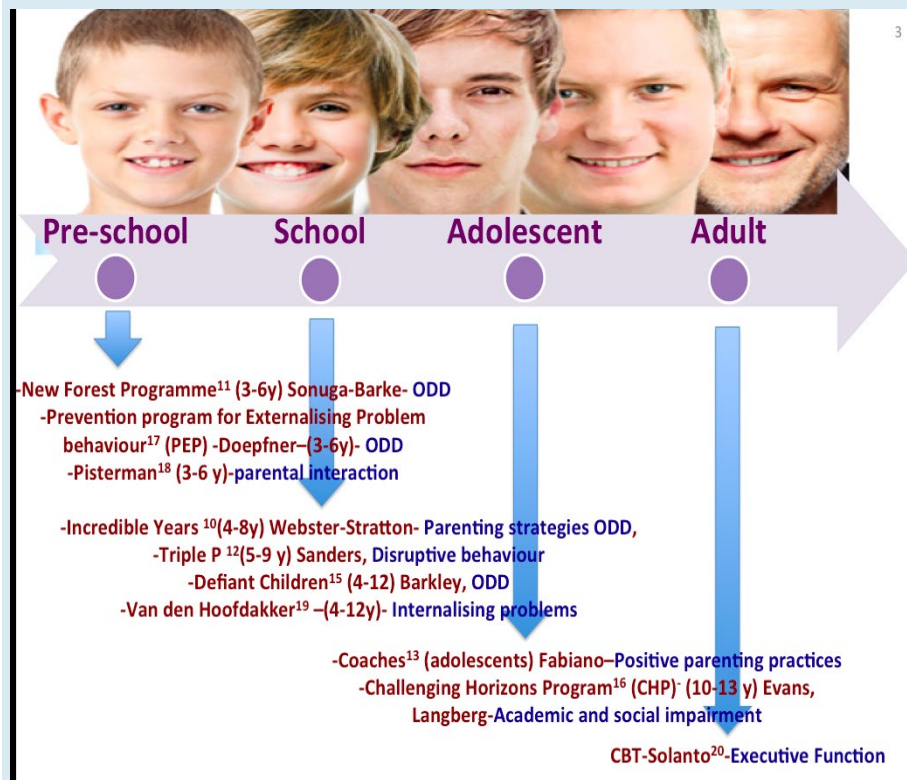
immediate feedback (Clarfield & Stoner, 2005; Ota & DuPaul, 2002) have shown beneficial effects but have not been studied in controlled designs.

A review of research conducted over 32 years has identified more than 50 studies (including 36 randomized controlled trials) of non-pharmacological interventions in school settings addressing ADHD symptoms (Richardson et al, 2015). The majority targeted children at elementary/primary school level. Four categories of interventions were defined based on common ingredients:

1. Reward and punishment (contingency management)
2. Skills training and self-management
3. Creativity-based therapies and
4. Physical treatments

Contingency management has been studied the most, followed by academic skills training, emotional skills training, self-regulation, biofeedback, daily report card, social skills training, cognitive skills training, adaptation to the learning environment, music therapy, motivational beliefs, psychoeducation, play therapy, and massage. A large proportion of the interventions was delivered by teachers within the classroom but often mental health providers were involved. The length of the intervention varied widely (between 1 and 156 weeks, with a mean of 15.5 weeks). Across all these different interventions there was some beneficial effect on inattention and hyperactivity/impulsivity assessed with neurocognitive tasks and on teacher-rated inattention (Richardson et al, 2015). However, there was little effect according to parent-observed ADHD symptoms. There was a small effect on

**Figure D.1.1.3** Summary of recommended behavioral interventions for ADHD throughout the lifespan\*



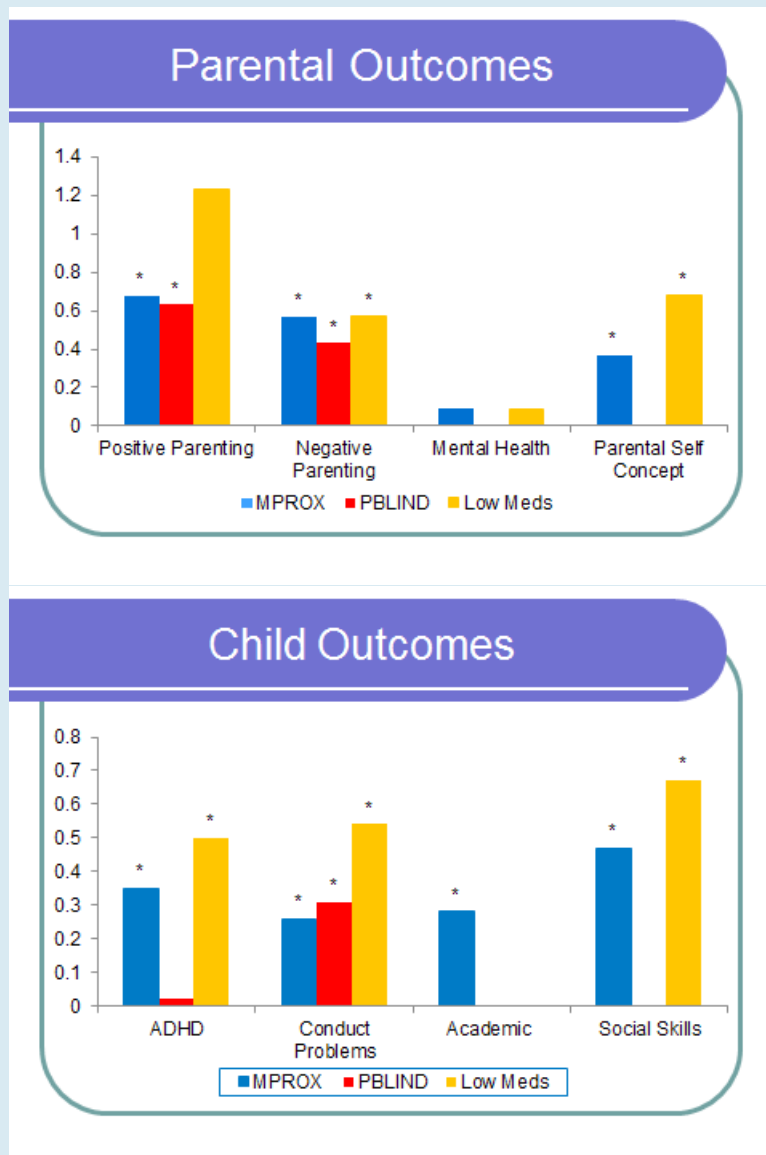
\*M Ferrin, with permission.

standardized achievement tests and on teacher reported externalizing symptoms.

### Effectiveness of Behavioral Interventions

Two meta-analyses explored the short-term effectiveness of behavioral interventions (broadly defined) compared to control conditions (Sonuga-Barke et al, 2013; Daley et al, 2014). Results were presented separately for outcomes that may be biased towards favorable reporting because of involvement in the treatment (e.g., parent ratings), and for other outcomes that could represent more objective

**Figure D.1.1.4** Child and parents outcomes of behavioural interventions in ADHD according to informant.\* MPROX is based on reports by individuals who may be biased towards favorable reporting because of involvement in the treatment (e.g., parent ratings); PBLIND is based on more objective measures (e.g., teacher ratings). Low Meds represents the results of studies with less than 30% of the children in the sample receiving medication.



\*With permission from Daley et al

measures (e.g., teacher ratings). Results (see Figure D.1.1.4) showed a significant improvement in ADHD symptoms when reports from the person applying the treatment were considered (“most proximal”), but there was no change according to the more objective informants (“probably blind”). However, both groups of informants reported a significant benefit in relation to conduct problems, positive parenting, and for reduction in negative parenting. Significant effects were also found on social skills and academic performance; however, blinded outcomes were not available for these variables. Finally, no impact was found on parental wellbeing.

Studies exploring the long-term efficacy of behavioral interventions are sparse and typically they are naturalistic follow-ups where other treatments (e.g., medication) are often used concurrently. Therefore it is difficult to disentangle the specific long-term effects of the behavioral interventions. For parent training, positive effects on parenting behavior and parent reports of child’s behavior are maintained for up to 3 months to 3 years after treatment, depending on the study (Lee et al, 2012).

### **Clinical Considerations**

- According to most studies, children with comorbid ODD/CD and comorbid anxiety disorders are the most likely to benefit from behavioral interventions
- Larger effect sizes were observed in preschoolers and in children not taking medication (Daley et al, 2014)
- Lower parental education, greater parental mental health problems and greater child complexity and comorbidity are likely to be related to worse outcomes (Daley & O’Brien, 2013)
- A challenge for behavioral approaches has been to generalize the benefits from the treatment setting to other settings
- Since some reliable effects have been shown on relatively objective measures of neurocognitive assessments and academic achievement, these offer some support for the effectiveness of non-drug treatment in school settings. Because many different intervention packages or combinations are used, it is impossible to identify the potentially active ingredients
- Barriers are that these treatments are expensive, both in terms of time and money, and parents need to be motivated
- Evidence supports the efficacy of educational interventions with parents (Ferrin et al, 2014; Ferrin et al, 2016) and of self-help interventions either on their own or in combination with telephone or media support (Sanders et al, 2007). According to a Cochrane review (Montgomery et al, 2006) self-help interventions can: (i) reduce the amount of time therapists have to devote to each case; (ii) increase access to the intervention; (iii) release clinician time to concentrate on more complex cases; (iv) reduce or eliminate costs, transport and timing difficulties for families.



## Future Directions

- More evidence from blind studies is required before behavioral interventions can be supported as a first-line treatment for core ADHD symptoms
- Despite the many randomized controlled trials assessing school interventions in ADHD—which already show a large improvement when compared with earlier reviews (DuPaul et al, 1998)—there is a need for better designed studies (Richardson et al, 2015)
- Self-help approaches may work best within a stepped care clinical model, with self-help targeted at parents who are waiting to access face-to-face treatment. Also, self-help could be used in combination with face-to-face treatment or on a triage basis. It could be offered as an initial intervention that may be enough for some highly functioning parents or those with children with less complex problems
- More research is needed on how to engage parents in self-help interventions and to clarify who may benefit the most

## COGNITIVE TRAINING

ADHD is associated with a broad range of neuropsychological impairments encompassing multiple brain networks known to underpin diverse cognitive and motivational processes (Willcutt et al, 2008). There has been an increasing interest in, and use of, computer-based cognitive training as a treatment for ADHD with different approaches used to target different neuropsychological deficits (i.e., working memory, attention, inhibition). Cognitive training is grounded on the notion of neural plasticity and the reorganization of brain structure and function in patients experiencing lesion-based deficits and cognitive impairments (Jolles & Crone, 2012; Willis & Schaie, 2009). Models rely on the assumptions that particular neuropsychological deficits mediate ADHD pathogenesis, and that repeatedly loading a limited cognitive resource would eventually lead to its strengthening and improved functioning. However, specific neurobiologic models of the effects of cognitive training strategies used with ADHD patients are lacking.

### Treatment Delivery and Available Treatments

Cognitive training for ADHD is typically delivered using computers. Training sessions may be conducted at school, home, or in the clinic. The duration of each session, number, and frequency vary according to the specific protocol employed—they typically involve a large number of sessions spread over several weeks. The difficulty level is automatically adjusted by the software on a session by session basis to match the improving working memory of the subject on each task, to drive learners to increasingly higher levels of performance as training proceeds. This includes an individualized reward schedule. Table D.1.1.2 lists commonly used, computerized cognitive training programs.

### Effectiveness

The first controlled trial that examined the benefits of cognitive training for ADHD was reported by Klingberg and colleagues (2005). They reported a large positive effect on parent ratings of ADHD but this did not generalize to teacher



[Click on the image to view an example of how Cogmed, one of the cognitive training programs, is supposed to work.](#)

**Table D.1.1.2.** Commonly used computer-based cognitive training programs\*

PROGRAM	TARGET FUNCTION
AixTent (CogniPlus)	Attention: selective, divided, focused and constant
Captain's Log	Attention, working memory, visuomotor function, problem solving
Cogmed (RoboMemo)	Visuospatial and spatial-verbal working memory
CogniPlus	Attention, working memory, visuomotor function, executive functions, long-term memory
Locu Tour	Acoustic, visual, and verbal attention, executive functions, acoustic and visual memory
Play Attention	Attention
RehaCom	Attention, memory, executive functions, visuomotor functions
Braingame Brian (in Dutch)	Training working memory, inhibition and flexibility

\*Adapted from Sonuga-Barke et al, 2014. Click on the name of the program to access.

ratings. The meta-analysis by Sonuga-Barke et al (2013) reported data from 126 participants and 123 controls. Overall, there was a moderate and significant effect in favor of the intervention by the end of treatment. However, the effect dropped substantially and became not significant when ratings by (probably) blind raters were considered. Similar results were reported in another meta-analysis (Cortese et al, 2015).

### Clinical Considerations

- There is no definitive evidence of the effectiveness of cognitive training in ADHD
- Cognitive training may improve working memory, however the impact on academic functioning is not yet determined (Cortese et al, 2015)
- Contraindications and side effect of these treatments are not well known

### Future Directions

- Approaches targeting multiple neuropsychological processes may optimize the transfer of effects from cognitive deficits to clinical symptoms, but this requires further research
- There is a particular need for studies examining the relative value of combining cognitive training with medication, dietary, or other psychological approaches (Vinogradov et al, 2012)
- Future research should explore whether cognitive training may also play a role in early intervention approaches for ADHD

- Trials in the future need to compare the response of clinical subtypes and neuropsychological sub-groups to different forms of training.

## NEUROFEEDBACK

Neurofeedback has been seen as a promising treatment for core ADHD symptoms based on the results of some controlled studies (Arns et al, 2009). The increasing acceptance of neurofeedback as a treatment for ADHD derives from observations of altered brain activation in many children with ADHD detected in EEG and imaging studies. Neurofeedback is based on the principle that the types of waves registered by EEG represent different psychological states, e.g., whether the individual is concentrating in an activity or distracted, day-dreaming. By giving real time information about the type of wave observed at any given time and rewards, children can be taught to produce the brain-wave pattern associated with concentrating on a task. This would reduce symptoms of ADHD.

Two different protocols for treatment are available to address deviant cortical activity in ADHD children:

- *EEG frequency band training*, which seeks to reduce slow wave activity and increase faster (alpha wave) activity
- *Event-related cortical potentials training*. Event-related potentials allow the examination of electrical responses reflecting preparatory and pre-attentive processes, auditory and visual attention, frontal inhibition, and time processing. A lower amplitude, longer latency and different topography of the P300 component has been the most replicated finding in ADHD children when compared to healthy controls (Brandeis et al, 2002). The characteristics of P300 and other components of the evoked potentials have been used for neurofeedback.

### Treatment Delivery and Available Treatments

A conventional neurofeedback protocol to reduce inattention and impulsivity consists of rewarding the suppression of theta activity and enhancement of beta activity. Using visual feedback, the trainee receives a large amount of rewards throughout the training. In some programs, the cortical activity is represented by the height or speed of an object, such as a ball, a plane, or a cartoon character moving across the screen. If the EEG activity is regulated in the desired way, the object rises, falls, or advances more quickly. In other animations, the patient is asked to view a movie, or change the color of an object in the screen by generating the target brain wave activity. Successful trials are immediately rewarded by a tone, a smiley face, coins, or points. Individual parameters are adjusted throughout the course of the training to ensure positive feedback in some trials, while other trials operate without feedback in order to extend the results to the everyday life of the patient.

### Effectiveness

Several controlled studies support the short-term improvement in core symptoms, neuropsychological function, and electrophysiological correlates of ADHD achieved with neurofeedback (Gevensleven et al, 2012; Fabiano et al, 2009; Nigg et al, 2012; Sonuga-Barke et al, 2013; Micoulaud-Franchi et al, 2014). However, a more recent meta-analysis has found no reduction in core symptoms



[Click on the image to view Dr Selim R. Benbadis talking about whether ADHD can really be diagnosed by EEG?](#)

## ELECTROENCEPHALOGRAM (EEG)

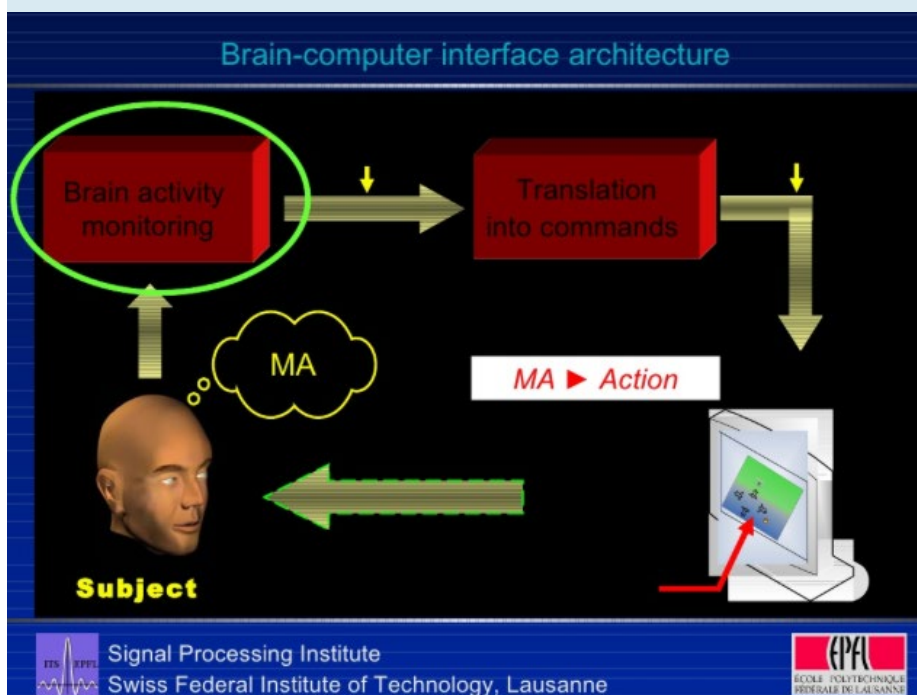
Electroencephalogram refers to the recording of brain electrical activity. It is typically obtained by placing electrodes on the scalp, not very differently from those used to obtain electrocardiograms. EEG measures voltage fluctuations resulting from electrical currents in brain regions, not in individual neurons. Related techniques are evoked potentials or event-related potentials, which measure stereotyped electrical brain responses to specific sensory, cognitive, or motor stimuli. Evoked potentials are obtained by averaging EEG activity triggered by the presentation of a stimulus (visual, somatosensory, or auditory).

Five frequency bands have been traditionally defined in EEG recordings: delta (1.5–3.5 Hz), theta (3.5–7.5 Hz), alpha (7.5–12.5 Hz), beta (12.5–30 Hz), and gamma (30–70 Hz). The type of brain activity recorded depends on many factors, e.g., whether persons are awake or in different stages of sleep, what they are doing, and if their eyes are open or closed.

Quantitative EEG (qEEG)—also called brain mapping and brain electrical activity mapping (BEAM)—is a method of analyzing the electrical activity of the brain to show a topographic display and analysis of brain electrophysiological data. The clinical significance of the various patterns of brain wave activity is unknown and the value of quantitative EEG in diagnosis and treatment of ADHD and other conditions has not been demonstrated unequivocally.

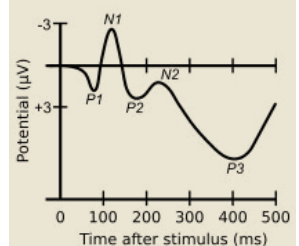
EEG in children differs from adult EEG because of developmental maturation—lower frequency bands are most prominent during the first years of life, decreasing with increasing age. A substantial group of ADHD children have shown elevated levels of slow wave (delta and theta) activity in the frontal regions. An increase in the theta/alpha and theta/beta ratios have been claimed to be reliable measures of the presence of ADHD (Monastra et al, 1999). However, this has low specificity and the usefulness of the theta/beta ratio as a specific marker for ADHD has been questioned.

**FIGURE D.1.1.5** The picture describes the brain-computer interface architecture sequence: brain activity monitoring, translation into commands, electrophysiological signals, commands subject and action feedback.



## P300

The **P300 wave** (P3 in the figure below) of an event related potential has received particular attention in relation to ADHD. P300 is a positive wave complex that occurs about 300–500 milliseconds after the stimulus. It is obtained when the individual's attention is focused on a signal that is rare, especially if the signal has a motivational or emotional meaning. P300 is thought to reflect processes involved in stimulus evaluation or categorization. It is typically elicited using the "oddball paradigm", in which low-probability stimuli are mixed with high-probability non-target (or standard) items. For example, in a visual oddball task, a square (standard) is presented 95% of the time and a circle (oddball) 5%. When the targets (e.g., circles) appear, the subject must make a response, such as pressing a button or updating a mental count. The characteristics of the P300 wave in this situation are often used as measures of cognitive function in decision making.





or in any neuropsychological outcomes explored (e.g., inattention and response inhibition) (Cortese et al, in press). Results are difficult to interpret because of the weak experimental design of many studies (e.g., lack of controls, non-random allocation, or the use of non-blind measures). No differences were observed when using quantitative EEG or evoked potentials as the basis for biofeedback (Gevensleven et al, 2009). Trials that compared neurofeedback with medication alone or in combination reported conflicting results (Duric et al, 2012; Meisel et al, 2013; Li et al, 2013; Ogrim et al, 2013).

### Clinical Considerations

- A number of factors might contribute to clinical response, including training intensity and number of sessions; visual imagery of the individual; parenting style; use of reinforcement techniques at home; and motivation (effort, attention, and time invested)
- Epilepsy might be a contraindication
- Potential side effects include headaches and fatigue

### Future directions

- The question whether one training protocol is more effective than the other is not yet resolved (Holtmann et al. 2014).
- Techniques such as near-infrared spectroscopy and fMRI neurofeedback may offer advantages in terms of targeting well defined brain regions (Mihara et al, 2012). Notably, real time fMRI may additionally open the possibility of more rapid learning to regulate deep structures such as dopaminergic midbrain regions implicated in ADHD (Cortese et al, 2012).



[Click on the image to view how neurofeedback works in practice](#)

- Do you have questions?
- Comments?

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Ma Haifang. Children at school.



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# Appendix D.1.1.1

## SELF-DIRECTED LEARNING EXERCISES AND SELF-ASSESSMENT

**MCQ D.1.1.1 Restrictive elimination diets for ADHD:**

- A. Have been shown to be an effective treatment
- B. Have a small effect size on ADHD symptoms, not large enough to justify recommending it as a stand-alone treatment
- C. Are only effective in adolescents
- D. Are effective on comorbid depressive symptoms
- E. Are simple and cheap to implement

**MCQ D.1.1.2 Oligoantigenic diets focus on foods other than artificial colors and preservatives that may trigger ADHD symptoms. Implementation of these diets:**

- A. Requires all the family to be on the diet
- B. Do not show results for at least 6 months
- C. Usually excludes cow's milk, cheese, egg, chocolate, rice and nuts
- D. Should be tried in all cases
- E. Is very effective

**MCQ D.1.1.3 Fatty-acid supplementation for ADHD:**

- A. Has significant side effects
- B. Requires supplementation with omega-3 fatty acids only
- C. Requires supplementation with omega-6 fatty acids only
- D. Requires supplementation with both omega-3 and omega-6 fatty acids
- E. Has been found to be ineffective

**MCQ D.1.1.4 Psychosocial treatments based on social learning and behavior modification principles have been widely used for ADHD. The intervention most widely supported by evidence for younger children is:**

- A. Contingency management
- B. Skills training
- C. Creativity-based therapies
- D. Self-management
- E. Parent training programs

**MCQ D.1.1.5 Children most likely to benefit from behavioral interventions are those who:**

- A. Come from lower socio-economic status families
- B. Have parents with mental health problems
- C. Have comorbid ODD/CD
- D. Are older (e.g., adolescents)
- E. Have higher levels of family conflict

**MCQ D.1.1.6 A form of neurofeedback is called EEG frequency band training. This intervention seeks to:**

- A. Reduce slow wave activity and increase faster (alpha wave) activity
- B. Modify event-related cortical potentials
- C. Help the child control epileptiform EEG activity
- D. Induce brain maturation
- E. Increase neuronal metabolism

**ANSWERS**

**MCQ D.1.1.1 Answer: B**

**MCQ D.1.1.2 Answer: C**

**MCQ D.1.1.3 Answer: D**

**MCQ D.1.1.4 Answer: E**

**MCQ D.1.1.5 Answer: C**

**MCQ D.1.1.6 Answer: A**