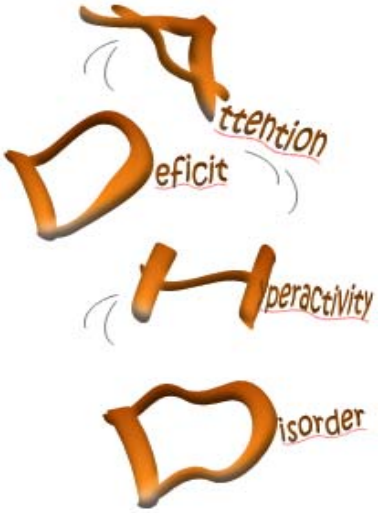
NEWSLETTER



INDICE:

MARIO NEGRI
ISTITUTO DI RICERCHE FARMACOLOGICHE
1961 - 2011

BIBIOGRAFIA ADHD GENNAIO 2011

Environ Health Perspect. 2010;118:1646-53.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A FOCUSED OVERVIEW FOR CHILDREN'S ENVIRONMENTAL HEALTH RESEARCHERS.

Aguiar A, Eubig PA, Schantz SL.

Objectives: Attention deficit/hyperactivity disorder (ADHD) is the most frequently diagnosed childhood neurobehavioral disorder. Much research has been done to identify genetic, environmental, and social risk factors for ADHD; however, we are still far from fully understanding its etiology. In this review we provide an overview of diagnostic criteria for ADHD and what is known about its biological basis. We also review the neuropsychological functions that are affected in ADHD. The goal is to familiarize the reader with the behavioral deficits that are hallmarks of ADHD and to facilitate comparisons with neurobehavioral deficits associated with environmental chemical exposures.

Data Sources: Relevant literature on ADHD is reviewed, focusing in particular on meta-analyses conducted between 2004 and the present that evaluated associations between measures of neuro-psychological function and ADHD in children. Meta-analyses were obtained through searches of the PubMed electronic database using the terms "ADHD," "meta-analysis," "attention," "executive," and "neuro psychological functions." Although meta-analyses are emphasized, nonquantitative reviews are included for particular neuropsychological functions where no meta-analyses were available.

Data Synthesis: The meta-analyses indicate that vigilance (sustained attention), response inhibition, and working memory are impaired in children diagnosed with ADHD. Similar but somewhat less consistent meta-analytic findings have been reported for impairments in alertness, cognitive flexibility, and planning. Additionally, the literature suggests deficits in temporal information processing and altered responses to reinforcement in children diagnosed with ADHD. Findings from brain imagining and neurochemistry studies support the behavioral findings.

Conclusions: Behavioral, neuroanatomical, and neurochemical data indicate substantial differences in attention and executive functions between children diagnosed with ADHD and non-ADHD controls. Comparisons of the neurobehavioral deficits associated with ADHD and those associated with exposures to environmental chemicals may help to identify possible environmental risk factors for ADHD and/or reveal common underlying biological mechanisms.

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J Psychiatr Res. 2011;45:150-55.

PREDICTORS OF PERSISTENT ADHD: AN 11-YEAR FOLLOW-UP STUDY.

Biederman J, Petty CR, Clarke A, et al.

Objective: Despite the existence of several follow-up studies of children with ADHD followed up into adulthood, there is limited information on whether patterns of persistence and remission in ADHD can be predicted over the long term. The main aim of this study was to evaluate predictors of persistence of ADHD in a large sample of boys with and without ADHD followed prospectively for 11 years into young adulthood.

Method: Subjects were Caucasian, non-Hispanic boys with (N = 110) and without (N = 105) ADHD who were 6-17 years old at the baseline assessment (mean age 11 years) and 15 to 31 years old at the follow-up assessment (mean age 22 years). Subjects were comprehensively and blindly assessed with structured diagnostic interviews and assessments of cognitive, social, school, and family functioning.

Results: At the 11-year follow-up, 78% of children with ADHD continued to have a full (35%) or a partial persistence (subsyndromal (22%), impaired functioning (15%), or remitted but treated (6%)). Predictors of

persistence were severe impairment of ADHD, psychiatric comorbidity, and exposure to maternal psychopathology at baseline.
Conclusions: These findings prospectively confirm that persistence of ADHD over the long term is predictable from psychosocial adversity and psychiatric comorbidity ascertained 11 years earlier.

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Acta Neuropsychol. 2008;6:107-21.
SUSTAINED ATTENTION IN CHILDREN WITH ADHD.
Borkowska AR, Tomaszewski W.
Introduction. The symptoms that comprise inattentive behaviour in ADHD include problems with focusing on a task and sustaining attention over a long period, even in advantageous external conditions. There is also a character-istic excessive distractibility under the influence of other, unimportant stimuli. Thus attention processes are one of the main variables which form the clini-cal picture of ADHD. The research published to date on this topic does not, however, lead to an unequivocal conclusion concerning the existence of sus-tained attention deficits (vigilance deficits). The aim of our research was to assess this aspect of attention processes in children with the combined and inattentive type of ADHD.
Material and Methods. The research group consisted of 132 children, age 9;06-12;02 (combined type-64 children, inattentive type-21 children, control group-47 children). The level of sustained attention was defined as the capability to sustain attention over a long period (the 20-minute Stop Signal Task requires a high level of vigilance), and to perform effectively a monotonous, easy, but rather long task (the 20-minute Continuous Performance Task).
Results. The results obtained by the children from both clinical groups differ significantly in all parameters from the controls. This suggests that there exists an attention alertness network deficit in ADHD. No significant differences were observed between the combined and inattentive type.
Conclusions. Our results confirmed problems with sustained attention during long-lasting and monotonous tasks in ADHD children. The deficits of sustained attention in combined ADHD and inattention ADHD are alike, so those deficits are common for all children with ADHD.

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J Urol. 2011;185:663-68.
LOWER URINARY TRACT CONDITIONS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: CORRELATION OF SYMPTOMS BASED ON VALIDATED SCORING SYSTEMS.
Burgu B, Aydogdu O, Gurkan K, et al.
Purpose We investigated whether certain voiding problems have a higher incidence in patients with attention deficit disorder with hyperactivity compared to age matched controls. Materials and Methods We used the Conners Parent Rating Scale-revised for attention deficit disorder with hyperactivity and lower urinary tract symptom score to evaluate voiding problems. A total of 62 children with attention deficit disorder and 124 healthy controls were enrolled. We evaluated uroflowmetry patterns in both groups. Residual urine volumes and Bristol stool scale were noted. We examined the correlation between total Conners Parent Rating Scale-revised and lower urinary tract symptom score in patients with attention deficit disorder. Additionally we analyzed each index of the Conners Parent Rating Scale-revised separately in terms of correlation with symptom subgroups for lower urinary tract symptom scores. Results Mean (plus or minus) SD total lower urinary tract symptom score was 11.1 (plus or minus) 2.9 in patients with attention deficit disorder with hyperactivity and 3.2 (plus or minus) 1.3 in controls, a difference that was statistically significantly ($p < 0.001$). With the exception of constipation, mean scores of all lower urinary tract symptom subindices were significantly higher in patients with attention deficit disorder compared to controls. Symptoms evaluated in lower urinary tract symptom score were mostly correlated with attention deficit disorder index of the Conners Parent Rating Scale-revised. If a child with attention deficit disorder has a high index in the Conners Parent Rating Scale-revised, he or she is more likely to have urgency. Also, if a child with attention deficit disorder has a high hyperactivity subscale score, he or she is more likely to have enuresis. Conclusions Voiding problems are more common in children with attention deficit

disorder with hyperactivity than in age matched controls. Urgency and enuresis are the outstanding problems in children with attention deficit disorder. Simultaneous use of the Conners Parent Rating Scale-revised and lower urinary tract symptom score questionnaire should be encouraged in patients with attention deficit disorder to allow a structured and quantitative evaluation of these overlapping problems.

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J Child Adolesc Psychopharmacol. 2010;20:495-502.

SERUM FERRITIN AND AMPHETAMINE RESPONSE IN YOUTH WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Calarge C, Farmer C, Disilvestro R, et al.

Introduction: Iron deficiency (ID) has been associated with attention and behavioral problems, in general, and with attention-deficit/hyperactivity disorder (ADHD), in particular. The study aim was to explore whether iron stores, as reflected by serum ferritin concentration, predicted response to psychostimulants.

Methods: Six-to 14-year-old children with ADHD enrolled in a multiphase, double-blind, randomized, placebo-controlled trial investigating zinc supplementation in treating ADHD and optimizing response to psychostimulants. The Swanson, Nolan, and Pelham (SNAP) ADHD rating scale was the primary clinical instrument. Serum ferritin concentration was obtained at baseline and 8 weeks later. Partial correlations, adjusting for age and sex, were computed.

Results: Fifty-two participants (83% males) had a mean age of 10 years. Their ADHD symptoms were moderately severe at baseline (SNAP item mean=2.1). Their mean ferritin concentration was 18.4ng/mL, with 23% of the participants having a level below 7, the assay-defined threshold for ID. Serum ferritin was inversely correlated with baseline inattention, hyperactivity/impulsivity, and total ADHD symptom scores (Partial Spearman's r=-0.31, p=0.04; r=-0.42, p<0.006; and r=-0.43, p<0.004, respectively) and with the weight-adjusted dose of amphetamine used to optimize clinical response (Partial Spearman's r=-0.45, p<0.007). Psychotropic-treatment history moderated some, but not all, of these associations, with previously medicated children showing a stronger association between ferritin concentration and ADHD symptom severity.

Conclusion: These findings add to the growing literature implicating ID in ADHD. The prediction of amphetamine optimal dose by ferritin concentration suggests that iron supplementation should be investigated as a potential intervention to optimize response to psychostimulants at a lower dose in individuals with low iron stores and ADHD.

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Neuropsychology. 2011 Jan;25:15-24.

MEMORY CAPACITY, SELECTIVE CONTROL, AND VALUE-DIRECTED REMEMBERING IN CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Castel AD, Lee SS, Humphreys KL, et al.

Objective: The ability to select what is important to remember, to attend to this information, and to recall high-value items leads to the efficient use of memory. The present study examined how children with and without attention-deficit/hyperactivity disorder (ADHD) performed on an incentive-based selectivity task in which to-be-remembered items were worth different point values.

Method: Participants were 6–9 year old children with ADHD (n = 57) and without ADHD (n = 59). Using a selectivity task, participants studied words paired with point values and were asked to maximize their score, which was the overall value of the items they recalled. This task allows for measures of memory capacity and the ability to selectively remember high-value items.

Results: Although there were no significant between-groups differences in the number of words recalled (memory capacity), children with ADHD were less selective than children in the control group in terms of the value of the items they recalled (control of memory). All children recalled more high-value items than low-value items and showed some learning with task experience, but children with ADHD Combined type did not efficiently maximize memory performance (as measured by a selectivity index) relative to children with ADHD Inattentive type and healthy controls, who did not differ significantly from one another.

Conclusions: Children with ADHD Combined type exhibit impairments in the strategic and efficient encoding and recall of high-value items. The findings have implications for theories of memory dysfunction in childhood ADHD and the key role of metacognition, cognitive control, and value-directed remembering when considering the strategic use of memory.

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Clin Neurophysiol. 2011 Jan;122:73-80.

CHILDHOOD EEG AS A PREDICTOR OF ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Clarke AR, Barry RJ, Dupuy FE, et al.

OBJECTIVE: The aim of this study was to determine whether EEG differences exist between children with attention-deficit/hyperactivity disorder (AD/HD) who later outgrow the disorder and those who continue to be symptomatic as adults.

METHODS: Thirty-eight boys, diagnosed with AD/HD as children, were reassessed 11 years later to determine who met criteria for adult AD/HD. At the childhood assessment, an EEG was recorded from the AD/HD group and a control group, during an eyes-closed resting condition. This was analysed for absolute and relative power in the delta, theta, alpha and beta bands, and the theta/beta ratio.

RESULTS: At the childhood assessment, the AD/HD group had an EEG profile typical of the disorder, with increased absolute and relative theta, reduced relative alpha, and increased theta/beta ratio. EEG differences were found between those who outgrew the disorder and those who did not - the adult AD/HD group had greater childhood global relative beta, reduced frontal relative theta, and increased frontal absolute and relative beta.

CONCLUSIONS: These results suggest the existence of specific CNS differences in childhood AD/HD that may be used to predict the developmental course of the disorder.

SIGNIFICANCE: This is the first study to investigate childhood EEG markers of adult AD/HD.

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Youth Violence and Juvenile Justice. 2011 Jan;9:43-58.

FLEDGLING PSYCHOPATHY IN THE CLASSROOM: ADHD SUBTYPES, PSYCHOPATHY, AND READING COMPREHENSION IN A COMMUNITY SAMPLE OF ADOLESCENTS.

DeLisi M, Vaughn M, Beaver KM, et al.

The current study explores characteristics that are associated with fledgling psychopathy and educational outcomes relating to reading comprehension performance in a community sample of 432 middle school students. Latent class analysis (LCA) produced a four-class solution. Class 1 was a large (71.5% of sample) "control" group of youths with no attention/hyperactivity deficits and the highest reading comprehension scores. Class 2 was 11.6% of the sample and was consistent with traits associated with attention deficit hyperactivity disorder (ADHD) predominantly inattentive type. Class 3 was 7.4% of the sample and was consistent with traits associated with ADHD predominantly hyperactive-impulsive type. Class 4 was 9.5% of the sample and was consistent with traits associated with ADHD combined type. Classes 2 and 4 were characterized by elevated levels of psychopathic and callous-unemotional (CU) traits and lower educational performance. This study extends the utility of fledgling psychopathy to educational outcomes, which has broad implications for adolescent development, delinquency, and youth violence.

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Res Autism Spectr Disord. 2011 Jan;5:126-34.

EMPATHIC ACCURACY IN ADOLESCENTS WITH AUTISM SPECTRUM DISORDERS AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Demurie E, De Corel M, Roeyers H.

In research on theory of mind (ToM) in individuals with an autism spectrum disorder (ASD) mainly static mind-reading tasks were used. In this study both a static (Eyes Test) and a more naturalistic (empathic accuracy task) ToM measure were used to investigate the perspective taking abilities of adolescents with ASD (n=13), adolescents with attention-deficit/hyperactivity disorder (ADHD; n=13) and typically developing adolescents (n=18). An innovative aspect concerns the standard stimulus tapes of the empathic accuracy task, which showed interactions between dyads of one adolescent with ADHD and one adolescent without ADHD. In this way, we were able to compare the 'readability' of the thoughts and feelings of adolescents with and without ADHD. The results clearly demonstrate the impairment in perspective taking abilities of adolescents with ASD, both on the static and naturalistic mind-reading task. Moreover, the empathic accuracy task seems to be a useful and promising method to assess ToM abilities in adolescents, with or without clinical problems. Finally, thoughts and feelings of target persons with ADHD seemed to be less easy to read than the thoughts and feelings of typically developing target persons.

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Biol Psychiatry. 2010 Dec;68:1084-91.

ATYPICAL DEFAULT NETWORK CONNECTIVITY IN YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Fair DA, Posner J, Nagel BJ, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a major public health concern. It has been suggested that the brain's default network may provide a crucial avenue for understanding the neurobiology of attention deficit/hyperactivity disorder. Evaluations of the default network have increased over recent years with the applied technique of resting-state functional connectivity magnetic resonance imaging (rs-fcMRI). These investigations have established that spontaneous activity in this network is highly correlated at rest in young adult populations. This coherence seems to be reduced in adults with ADHD. This is an intriguing finding, as coherence in spontaneous activity within the default network strengthens with age. Thus, the pathophysiology of ADHD might include delayed or disrupted maturation of the default network. If so, it is important to determine whether an altered developmental picture can be detected using rs-fcMRI in children with ADHD.

Methods: This study used the typical developmental context provided previously by Fair et al. (2008) to examine coherence of brain activity within the default network using rs-fcMRI in children with (n=23) and without attention deficit/hyperactivity disorder (n=23).

Results: We found that functional connections previously shown as developmentally dynamic in the default network were atypical in children with attention deficit/hyperactivity disorder - consistent with perturbation or failure of the maturational processes.

Conclusions: These findings are consistent with the hypothesis that atypical consolidation of this network over development plays a role in attention deficit/hyperactivity disorder.

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Pediatrics. 2011;127:e188-e196.

CONTRASTING PARENTS' AND PEDIATRICIANS' PERSPECTIVES ON SHARED DECISION-MAKING IN ADHD.

Fiks AG, Hughes CC, Gafen A, et al.

OBJECTIVE: The goal was to compare how parents and clinicians understand shared decision-making (SDM) in attention-deficit/hyperactivity disorder (ADHD), a prototype for SDM in pediatrics.

METHODS: We conducted semi-structured interviews with 60 parents of children 6 to 12 years of age with ADHD (50% black and 43% college educated) and 30 primary care clinicians with varying experience.

Open-ended interviews explored how pediatric clinicians and parents understood SDM in ADHD. Interviews were taped, transcribed, and then coded. Data were analyzed by using a modified grounded theory approach.
RESULTS: Parents and clinicians both viewed SDM favorably. However, parents described SDM as a partnership between equals, with physicians providing medical expertise and the family contributing in-depth knowledge of the child. In contrast, clinicians understood SDM as a means to encourage families to accept clinicians' preferred treatment. These findings affected care because parents mistrusted clinicians whose presentation they perceived as biased. Both groups discussed how real-world barriers limit the consideration of evidence-based options, and they emphasized the importance of engaging professionals, family members, and/or friends in SDM. Although primary themes did not differ according to race, white parents more commonly received support from medical professionals in their social networks.
CONCLUSIONS: Despite national guidelines prioritizing SDM in ADHD, challenges to implementing the process persist. Results suggest that, to support SDM in ADHD, modifications are needed at the practice and policy levels, including clinician training, incorporation of decision aids and improved strategies to facilitate communication, and efforts to ensure that evidence-based treatment is accessible.

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Kindheit und Entwicklung. 2011;20:21-30.
SCHNELLE AUGENBEWEGUNGEN UND VISUELLE FIXATION BEI KINDERN MIT ADHS.
Folta K, Mähler C.
Attention deficit hyperactivity disorder (ADHD) is a prevalent developmental disorder,which is characterized by symptoms of impulsiveness, hyperactivity, and/or inattention. The neurobiological foundations of this disorder are still a matter of debate. Here, we discuss important implications of modern eye-tracking systems in ADHD research. In addition, we report a dual-task study, investigating the ability of time-reproduction (interval timing), prosaccade inhibition, and prosaccade initiation in healthy control children and in medicated children with a diagnosis of ADHD. The results showed comparable abilities in the two groups with regards to precise time-reproduction, active inhibition, and initiation of prosaccades. In addition, our data revealed a comparable number, latency, amplitude, and duration of prosaccades in medicated ADHD children and in control subjects. The data suggest that ADHD medication is effective at compensating for deficits in executive control. However, compared to unmedicated healthy control subjects medicated children demonstrated accelerated peak velocities in trials requiring a prosaccade to peripheral targets, indicating changes in brainstem processing. Precise measurement of peak velocities might be useful to further improve the diagnosis of ADHD.

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Environ Int. 2011.
EFFECTS OF PRE AND POSTNATAL EXPOSURE TO LOW LEVELS OF POLYBROMODIPHENYL ETHERS ON NEURODEVELOPMENT AND THYROID HORMONE LEVELS AT 4 YEARS OF AGE.
Gascon M, Vrijheid M, Martinez D, et al.
There are at present very few studies of the effects of polybromodiphenyl ethers (PBDEs), used as flame retardants in consumer products, on neurodevelopment or thyroid hormone levels in humans. The present study aims to examine the association between pre and postnatal PBDE concentrations and neurodevelopment and thyroid hormone levels in children at age 4 years and isolate the effects of PBDEs from those of PCBs, DDT, DDE and HCB. A prospective birth cohort in Menorca (Spain) enrolled 482 pregnant mothers between 1997 and 1998. At 4 years, children were assessed for motor and cognitive function (McCarthy Scales of Children's Abilities), attention-deficit, hyperactivity and impulsivity (ADHD-DSM-IV) and social competence (California Preschool Social Competence Scale). PBDE concentrations were measured in cord blood (N=88) and in serum of 4 years olds (N=244). Among all congeners analyzed only PBDE 47 was quantified in a reasonable number of samples (LOQ = 0.002 ng/ml). Exposure to PBDE 47 was analyzed as a dichotomous variable: concentrations above the LOQ (exposed) and concentrations below (referents). Scores for cognitive and motor functions were always lower in children pre and

postnatally exposed to PBDE47 than in referents, but none of these associations was statistically significant ((beta) coefficient (95%CI) of the total cognition score: -2.7 (-7.0, 1.6) for postnatal exposure, and -1.4 (-9.2, 6.5) for prenatal exposure). Postnatal exposure to PBDE 47 was statistically significantly related to an increased risk of symptoms on the attention deficit subscale of ADHD symptoms (RR (95%CI) = 1.8 (1.0, 3.2)) but not to hyperactivity symptoms. A statistically significant higher risk of poor social competence symptoms was observed as a consequence of postnatal PBDE 47 exposure (RR (95%CI) = 2.6 (1.2, 5.9)). Adjustment for other organochlorine compounds did not influence the results. Levels of thyroid hormones were not associated to PBDE exposure. This study highlights the importance of assessing the effects of PBDE exposure not just prenatally but also during the early years of life. In the light of current evidence a precautionary approach towards PBDE exposure of both mothers and children seems warranted.

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Kindheit und Entwicklung. 2011;20:41-48.

KOGNITIVE KONTROLLE UND SELBSTREGULATION BEI KINDERN MIT ADHS.

Gawrilow C, Schmitt K, Rauch W.

Children with ADHD are inattentive, impulsive, and hyperactive. These symptoms result in disorders of learning as well as in frequent conflicts with parents, teachers, and peers. ADHD symptoms are explained by self-regulation deficits. Hence, difficulties shown by children, adolescents, and adults with ADHD are assumed to be related to self-regulation deficits as well as to executive function deficits and mainly deficits in cognitive control. Therefore, interventions that aim to facilitate self-regulation in children with ADHD(i. e., if-then-plans) are particularly promising.

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Child Neuropsychol. 2011 Jan;17:67-81.

COGNITIVE-MOTIVATIONAL DEFICITS IN ADHD: DEVELOPMENT OF A CLASSIFICATION SYSTEM.

Gupta R, Kar BR, Srinivasan N.

The classification systems developed so far to detect attention deficit/hyperactivity disorder (ADHD) do not have high sensitivity and specificity. We have developed a classification system based on several neuropsychological tests that measure cognitive-motivational functions that are specifically impaired in ADHD children. A total of 240 (120 ADHD children and 120 healthy controls) children in the age range of 6-9 years and 32 Oppositional Defiant Disorder (ODD) children (aged 9 years) participated in the study. Stop-Signal, Task-Switching, Attentional Network, and Choice Delay tests were administered to all the participants. Receiver operating characteristic (ROC) analysis indicated that percentage choice of long-delay reward best classified the ADHD children from healthy controls. Single parameters were not helpful in making a differential classification of ADHD with ODD. Multi-nominal logistic regression (MLR) was performed with multiple parameters (data fusion) that produced improved overall classification accuracy. A combination of stop-signal reaction time, posterror-slowing, mean delay, switch cost, and percentage choice of long-delay reward produced an overall classification accuracy of 97.8%; with internal validation, the overall accuracy was 92.2%. Combining parameters from different tests of control functions not only enabled us to accurately classify ADHD children from healthy controls but also in making a differential classification with ODD. These results have implications for the theories of ADHD.

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Acta Paediatrica. 2010 Oct;99:1536-39.

ADHD SYMPTOMS AND MATURITY—A FOLLOW-UP STUDY IN SCHOOL CHILDREN.

Gustafsson P, Holmström E, Besjakov J, et al.

Aim: To test the hypothesis that there is a subgroup of children with attention deficit hyperactivity disorder (ADHD) who show a decline in ADHD-symptoms that is associated with signs of biological maturation, a phenomenon referred to as a 'maturation catch-up'.

Methods: The parents of 147 children who were given an examination in grades one and two 1999–2000 that included assessment of ADHD-symptoms and estimation of skeletal bone-age by use of hand radiographs (which was repeated in the eighth grade), were contacted 2008–2009 and were asked to answer questions concerning ADHD symptoms and behavioural maturity in their children. The response frequency was 67%. A complete dataset was achieved in 57 children. A reduction of Conners scores for ADHD-symptoms of eight or more between the evaluations was defined as a marked reduction in symptoms.

Results: When the children with a marked symptom reduction (n=6) were compared with children without such a reduction (n=51), we found a significant difference in skeletal maturation ($p<0.05$).

Conclusion: This study gives support to the theory that there is a group of children with ADHD-symptoms who have a biological maturational-lag who will show a decrease in their ADHD-symptoms as they show a maturation catch-up with increasing age.

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Kindheit und Entwicklung. 2011;20:1-3.

LERN- UND AUFMERKSAMKEITSSTÖRUNGEN.

Hasselhorn M, Hartmann U.

This paper provides an introduction to the special issue on learning disabilities and attention deficit disorders in children. Initially, the authors sketch the current state of research on these types of disorders, especially with regard to assessment and prevailing comorbidities. The paper also includes an overview of the studies described in this issue. Most of them were conducted at the IDeA Center in Frankfurt, Germany. Taken together, these studies point to a more differentiated view on the neurobiological foundations of learning disabilities and attention deficit disorders. This will probably lead to improvements with respect to assessment, prevention, and intervention for these kinds of disorders.

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Zeitschrift für Psychiatrie, Psychologie und Psychotherapie. 2010 Oct;58:299-308.

INTELLIGENZ- UND AUFMERKSAMKEITSLEISTUNGEN VON JUNGEN MIT ADHS.

Hellwig-Brida S, Daseking M, Petermann F, et al.

In the present study we compared the performance of boys with ADHD with the norms from the general population. We measured the performance of 85 boys with newly diagnosed ADHD aged 6 to 13 in the Working Memory Index and the Processing Speed Index of the German version of the Wechsler Intelligence Scale for Children (WISC-IV) as well as the performance of 68 of those children (aged 6 to 10) in the Test of Attentional Performance for Children (KITAP). Additionally to the comparison between the results of the complete sample with the standardization data we conducted analyses for children with the Combined and the Primarily Hyperactive subtypes and children with the Primarily Inattentive subtype separately. The children showed deficits in working memory, stability of reaction time, inhibition, cognitive flexibility, sustained attention and divided attention with effect sizes lying in the moderate to large range. Differences to the norm in processing speed were shown only in the group of children with the Primarily Inattentive subtype. In all investigated parameters a maximum of 50 % of children showed performance below average.

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J Magn Reson Imaging. 2011;33:17-23.

PRELIMINARY EVIDENCE OF ALTERED GRAY AND WHITE MATTER MICROSTRUCTURAL DEVELOPMENT IN THE FRONTAL LOBE OF ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A DIFFUSIONAL KURTOSIS IMAGING STUDY.

Helpern JA, Adisetiyo V, Falangola MF, et al.

Purpose To investigate non-Gaussian water diffusion using diffusional kurtosis imaging (DKI) to assess age effects on gray matter (GM) and white matter (WM) microstructural changes in the prefrontal cortex (PFC) of adolescents with attention-deficit hyperactivity disorder (ADHD) compared to typically developing controls (TDC). Materials and Methods In this preliminary cross-sectional study, T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) and DKI images were acquired at 3T from TDC (n = 13) and adolescents with ADHD (n = 12). Regression analysis of the PFC region of interest (ROI) was conducted. Results TDC show a significant kurtosis increase of WM microstructural complexity from 12 to 18 years of age, particularly in the radial direction, whereas WM microstructure in ADHD is stagnant in both the axial and radial directions. In ADHD, GM microstructure also lacked a significant age-related increase in complexity as seen in TDC; only kurtosis measures were able to detect this difference. Conclusion These findings support the prevailing theory that ADHD is a disorder affecting frontostriatal WM. Our study is the first to directly quantify an aberrant age-related trajectory in ADHD within GM microstructure, suggesting that the assessment of non-Gaussian directional diffusion using DKI provides more sensitive and complementary information about tissue microstructural changes than conventional diffusion imaging methods.

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Child Neuropsychol. 2011 Jan;17:34-50.

RETROSPECTIVE AND PROSPECTIVE TIME DEFICITS IN CHILDHOOD ADHD: THE EFFECTS OF TASK MODALITY, DURATION, AND SYMPTOM DIMENSIONS.

Hurks PPM, Hendriksen JGM.

Time estimation is believed to be an adaptive function in human life. In the present study, prospective and retrospective time estimation are studied in both clinical-referred school-aged children with ADHD-C and healthy community control children, while examining more specifically the effects of type of time estimation task, length of time intervals (i.e., ranging from 3-90 s), and continuous scaling of the main ADHD symptom clusters (i.e., inattention vs. hyperactivity/impulsiveness). On a prospective verbal time estimation test, children with ADHD-C showed significant more overestimation compared to controls. For the majority of short-to-medium time intervals, this overestimation was predicted only by the continuous levels of impulsiveness or a disturbed self-regulation, indicating a dysregulation of the internal clock in ADHD. The same holds for the retrospective time estimation task. In contrast, an ADHD-related underestimation on the prospective time reproduction task was found for the longer intervals. In contrast to verbal time estimation, levels of inattention, and not the levels of impulsiveness, predicted underestimation on the time reproduction task. Our results point thereby towards parallel networks for regulating attention/working memory versus impulse regulation/inhibition as potential loci for dysfunction. These results are in contrast to the frequently cited global inhibitory executive function deficit hypothesis.

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BMC Psychiatry. 2010;10.

Genetic influences on attention deficit hyperactivity disorder symptoms from age 2 to 3: A quantitative and molecular genetic investigation.

Ilott NE, Saudino KJ, Asherson P.

Background: A twin study design was used to assess the degree to which additive genetic variance influences ADHD symptom scores across two ages during infancy. A further objective in the study was to observe whether genetic association with a number of candidate markers reflects results from the quantitative genetic analysis.

Method: We have studied 312 twin pairs at two time-points, age 2 and age 3. A composite measure of ADHD symptoms from two parent-rating scales: The Child Behavior Checklist/1.5 - 5 years (CBCL) hyperactivity scale and the Revised Rutter Parent Scale for Preschool Children (RRPSPC) was used for both quantitative and molecular genetic analyses.
Results: At ages 2 and 3 ADHD symptoms are highly heritable (h2 = 0.79 and 0.78, respectively) with a high level of genetic stability across these ages. However, we also observe a significant level of genetic change from age 2 to age 3. There are modest influences of non-shared environment at each age independently (e2 = 0.22 and 0.21, respectively), with these influences being largely age-specific. In addition, we find modest association signals in DAT1 and NET1 at both ages, along with suggestive specific effects of 5-HTT and DRD4 at age 3.
Conclusions: ADHD symptoms are heritable at ages 2 and 3. Additive genetic variance is largely shared across these ages, although there are significant new effects emerging at age 3. Results from our genetic association analysis reflect these levels of stability and change and, more generally, suggest a requirement for consideration of age-specific genotypic effects in future molecular studies.

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Indian Pediatr. 2010;47:955-58.

IRON DEFICIENCY IN INDIAN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Juneja M, Jain R, Singh V, et al.

A case control study was conducted at the Child Development and Early Intervention Clinic to determine the body iron status of children with ADHD, and study the correlation between the body iron status and ADHD symptoms. Serum ferritin was measured in newly diagnosed cases with ADHD and compared with that of controls. Correlation was studied between serum ferritin levels and the severity of ADHD symptoms as determined by Conners' Rating Scale. Serum ferritin was found to be significantly lower in children with ADHD (6.04 (plus or minus) 3.85 ng/ mL) as compared to controls (48.96 (plus or minus) 41.64 ng/mL, P value<0.001). There was a significant negative correlation between serum ferritin levels and oppositional subscore on Conners' Rating Scale.

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Arch Gen Psychiatry. 2010 Dec;67:1317-23.

GENOTYPE LINK WITH EXTREME ANTISOCIAL BEHAVIOR: THE CONTRIBUTION OF COGNITIVE PATHWAYS.

Langley K, Heron J, O'Donovan OD, et al.

Context: As genes associated with common disorders are increasingly identified, we need to progress from observing associations to identifying risk pathways. The high-activity COMT genotype, in the presence of attention-deficit/ hyperactivity disorder (ADHD), has previously been shown to be associated with extreme antisocial behavior. The same genotype has also been implicated in affecting cognitive function in healthy individuals. Impaired cognitive function might therefore lie on the risk pathway from genotype to clinical outcome.
Objectives: To replicate the association between COMT genotype and antisocial behavior in ADHD and to then test whether (1) impaired executive control or (2) impaired social understanding act as intermediate phenotypes for this association and lie on the risk pathway between COMT genotype and antisocial behavior. Design: Prospective epidemiological cohort sample.
Setting: The Avon Longitudinal Study of Parents and Children.
Participants: Four thousand three hundred sixty-five children with data on COMT Val158Met genotype, ADHD symptoms and diagnoses, and measures of social cognition/ understanding and executive control. Main Outcome Measures: Antisocial behavior at age 7.5 years assessed using DSM-IV conduct disorder symptoms.
Results: We replicated the association of the high activity COMT genotype, in the presence of ADHD, with extreme antisocial behavior (odds ratio, 2.82; 95% confidence interval, 2.02-3.94; P .001 for the most severe antisocial behavior). The high-activity COMT genotype was associated with both executive control and impaired social understanding. The strength of the association between genotype and antisocial

behavior was unchanged by including executive control in the model but dropped when impaired social understanding was included (odds ratio, 1.87; 95% confidence interval, 1.26- 2.76; P=.002).
Conclusions: The high-activity COMT genotype in ADHD is associated with antisocial behavior in part via impaired social understanding. Impaired executive control was also associated with the high-activity COMT genotype but may not lie on the risk pathway to antisocial behavior. The findings demonstrate the importance of testing links between genotype, intermediate phenotype, and clinical outcome in the same sample to identify potential risk pathways.

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2011;35:47-52.
THE INCREASE IN THETA/BETA RATIO ON RESTING-STATE EEG IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IS MEDIATED BY SLOW ALPHA PEAK FREQUENCY.
Lansbergen MM, Arns M, van Dongen-Boomsma Martine M, et al.
Attention-deficit/hyperactivity disorder (ADHD) was found to be characterized by a deviant pattern of electrocortical activity during resting state, particularly increased theta and decreased beta activity. The first objective of the present study is to confirm whether individuals with slow alpha peak frequency contribute to the finding of increased theta activity in ADHD. The second objective is to explore the relation between resting-state brain oscillations and specific cognitive functions. From 49 boys with ADHD and 49 healthy control boys, resting-state EEG during eyes open and eyes closed was recorded, and a variety of cognitive tasks were administered. Theta and beta power and theta/beta ratio were calculated using both fixed frequency bands and individualized frequency bands. As expected, theta/beta ratio, calculated using fixed frequency bands, was significantly higher in ADHD children than control children. However, this group effect was not significant when theta/beta ratio was assessed using individualized frequency bands. No consistent relation was found between resting-state brain oscillations and cognition. The present results suggest that previous findings of increased theta/beta ratio in ADHD may reflect individuals with slow alpha peak frequencies in addition to individuals with true increased theta activity. Therefore, the often reported theta/beta ratio in ADHD can be considered a non-specific measure combining several distinct neurophysiological subgroups such as frontal theta and slowed alpha peak frequencies. Future research should elucidate the functional role of resting-state brain oscillations by investigating neurophysiological subgroups, which may have a clearer relation to cognitive functions than single frequency bands.

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Epilepsy Res. 2011;93:53-65.
ATTENTIONAL PROCESSES AND ADHD-RELATED SYMPTOMS IN PEDIATRIC PATIENTS WITH EPILEPSY.
Liu ST, Tsai FJ, Lee WT, et al.
Objective: To investigate the attentional processes and symptoms of attention-deficit hyperactivity disorder (ADHD) in pediatric patients with epilepsy and IQ greater than 70 in Taiwan.
Methods: We assessed 61 children (male, 62.3%; full-scale IQ >70) with epilepsy, ages 6-16 years, and 61 sex-, age-, and parental education-matched typically developing children (controls). All participants completed the intelligence (WISC-III) and attention assessments (Conners' Continuous Performance Test, CPT). The parents reported on the ADHD symptoms of their children.
Results: Children with epilepsy had more omission errors and deviant response style ((beta)) and scored lower in the Hit Reaction Time (RT) Block Change, reflecting inattention and slowness. Epileptic children with ADHD symptoms had longer and more variable Hit RT than those without ADHD and controls. Higher full-scale IQ was significantly associated with less change in Hit RT, Hit RT block, standard error, and inter-stimulus intervals. There were no effects from age of onset, duration of having epilepsy, etiology of epilepsy, and brain anomaly on the CPT profiles.

Conclusion: The findings suggest that children with epilepsy, despite not mentally retarded, may have attention deficits. Hence, screening for attention problems among patients with epilepsy regardless of intelligence level and ADHD symptoms is recommended to offset possible learning adversities of this population.

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Brain Res. 2011;1368:159-62.

THE FUNCTION OF HYPOTHALAMUS-PITUITARY-ADRENAL AXIS IN CHILDREN WITH ADHD.

Ma L, Chen YH, Chen H, et al.

Objective: To explore the relationship between hypothalamus-pituitary- adrenal (HPA) axis and Attention Deficit Hyperactivity Disorder (ADHD) in non-stress states.

Method: 128 male children with ADHD aged between 6 and 14 years old were recruited, while 30 healthy male children were chosen as a control group. The diagnostic material was based on DSM-IV. The included ADHD children were further classified into the three sub-groups: ADHD-predominantly inattention type (ADHD-I) (n=44), ADHD-predominantly hyperactive impulsive type (ADHD-HI) (n=32), and ADHD-combined type (ADHD-C) (n=52). The levels of cortisol and adrenocorticotropin hormone (ACTH) were evaluated by the automatic particle enzyme immunoassay and electrochemiluminescence respectively per morning (8:00 am). Intelligence test was assessed by the Raven's Standard Progressive Matrices.

Results: The children with ADHD had significantly lower intelligence quotient (IQ) (84.5 (plus or minus) 11.3) in contrast to the control group (98.6 (plus or minus) 12.4, P<0.01), although the lower level of IQ in ADHD-C group (79.2 (plus or minus) 10.7) was also found when compared with other two sub-groups [ADHD-I (85.6 (plus or minus) 10.4) and ADHD-HI (91.3 (plus or minus) 12.6)]. In addition, no significant difference between the ADHD-HI group and the control group regarding the level of IQ were revealed. The level of cortisol in the ADHD group (226.47 (plus or minus) 129.12 nmol/L) was significantly lower than that of the control group (384.53 (plus or minus) 141.43 nmol/L, P < 0.001). The level of cortisol of the ADHD-HI group (154.36 (plus or minus) 71.62 nmol/L) was significantly lower than that of other two groups [ADHD-I group (219.42 (plus or minus) 117.66 nmol/L) (P < 0.01) and ADHD-C group (258.30 (plus or minus) 136.39 nmol/L) (P<0.01)]. There were no significant differences in the ACTH level either between the ADHD and the control group (P>0.05), or between sub-groups in ADHD (P>0.05).

Conclusion: In the non-stress states, the existence of dysfunction of the HPA axis (lower plasma cortisol) in children with ADHD might be due to the under-reactivity of the HPA axis; the low plasma cortisol level might contribute less to the outcomes of cognitive behavior of ADHD children and instead more closely relate to the core domains of attention deficit, hyperactivity and impulsive behavior of ADHD patients.

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J Clin Exp Neuropsychol. 2011 Jan;33:74-84.

NEUROPSYCHOLOGICAL FACTORS DIFFERENTIATING TREATED CHILDREN WITH PEDIATRIC BIPOLAR DISORDER FROM THOSE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Mattis S, Papolos D, Luck D, et al.

To determine the specificity of suggested endophenotypes of pediatric bipolar disorder (PBD), the performance of 15 euthymic children with PBD was contrasted with that of 20 children with attention-deficit/hyperactivity disorder (ADHD), a population with reportedly similar executive dysfunction, and 18 children with both PBD and ADHD. Children with PBD and PBD+ADHD (ages 8 to 17) demonstrated higher intraindividual variability in reaction time, slower processing speed, and more sluggish motor preparedness than did children with ADHD. The findings support the contention that processing speed, intraindividual variability, and slower and more variable reaction time as interstimulus interval lengthens are likely specific endophenotypes of PBD.

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Child Adolesc Psychiatry Ment Health. 2010;4.

ECONOMIC BURDEN AND COMORBIDITIES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG PEDIATRIC PATIENTS HOSPITALIZED IN THE UNITED STATES.

Meyers J, Classi P, Wietecha L, et al.

Background: This retrospective database analysis used data from the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample (NIS) to examine common primary diagnoses among children and adolescents hospitalized with a secondary diagnosis of attention- deficit/hyperactivity disorder (ADHD) and assessed the burden of ADHD.

Methods: Hospitalized children (aged 6-11 years) and adolescents (aged 12-17 years) with a secondary diagnosis of ADHD were identified. The 10 most common primary diagnoses (using the first 3 digits of the ICD-9-CM code) were reported for each age group. Patients with 1 of these conditions were selected to analyze demographics, length of stay (LOS), and costs. Control patients were selected if they had 1 of the 10 primary diagnoses and no secondary ADHD diagnosis. Patient and hospital characteristics were reported by cohort (i.e., patients with ADHD vs. controls), and LOS and costs were reported by primary diagnosis. Multivariable linear regression analyses were undertaken to adjust LOS and costs based on patient and hospital characteristics.

Results: A total of 126,056 children and 204,176 adolescents were identified as having a secondary diagnosis of ADHD. Among children and adolescents with ADHD, the most common diagnoses tended to be mental health related (i.e., affective psychoses, emotional disturbances, conduct disturbances, depressive disorder, or adjustment reaction). Other common diagnoses included general symptoms, asthma (in children only), and acute appendicitis. Among patients with ADHD, a higher percentage were male, white, and covered by Medicaid. LOS and costs were higher among children with ADHD and a primary diagnosis of affective psychoses (by 0.61 days and $51), adjustment reaction (by 1.71 days and $940), or depressive disorder (by 0.41 days and $124) versus controls. LOS and costs were higher among adolescents with ADHD and a primary diagnosis of affective psychoses (by 1.04 days and $352), depressive disorder (by 0.94 days and $517), conduct disturbances (by 0.86 days and $1,330), emotional disturbances (by 1.45 days and $1,626), adjustment reaction (by 1.25 days and $702), and neurotic disorders (by 1.60 days and $541) versus controls.

Conclusion: Clinicians and health care decision makers should be aware of the potential impact of ADHD on hospitalized children and adolescents.

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Clin Neurophysiol. 2011;122:311-19.

NEUROCOGNITIVE ASSESSMENT AND SLEEP ANALYSIS IN CHILDREN WITH SLEEP-DISORDERED BREATHING.

Miano S, Paolino MC, Urbano A, et al.

Objective: To assess possible correlations between intelligence quotient (IQ) and attention deficit hyperactive disorder (ADHD) rating scale values and sleep (including cyclic alternating patterns analysis) and respiratory parameters in children with sleep-disordered breathing (SDB).

Methods: Thirteen children who satisfied the criteria for primary snoring and 31 children for obstructive sleep apnea syndrome (OSAS) underwent polysomnography in a standard laboratory setting and a neurocognitive assessment. Sixty normal controls recruited from two schools underwent the neurocognitive assessment.

Results: The IQ estimates of controls were higher and the ADHD rating scale scores lower than those of children with SDB. Children with OSAS had a higher REM sleep latency and arousal index as well as a lower N3 and A mean duration than children who snored. In our sample of children with SDB, the percentage of wakefulness after sleep onset, of N1, of A2, of arousal and A2 index correlated positively with global intelligence. Total and hyperactivity scores correlated positively with the A2 index. Regression analysis mostly confirmed the correlations between neurocognitive measures and sleep parameters and further demonstrated a negative correlation between the hyperactivity rating score and oxygen saturation during the night.

Conclusions: Our results support the hypothesis that arousal is a defensive mechanism that may preserve cognitive function by counteracting the respiratory events, at the expense of sleep maintenance and NREM sleep instability.

Significance: We believe that our study makes an interesting contribution to research on the relationship between sleep fragmentation and cognitive function.

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2011.

GENOME-WIDE ASSOCIATION STUDY OF BLOOD PRESSURE RESPONSE TO METHYLPHENIDATE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Mick E, McGough JJ, Middleton FA, et al.

Objective: We conducted a genome-wide association study of blood pressure in an open-label study of the methylphenidate transdermal system (MTS) for the treatment of attention-deficit/hyperactivity disorder (ADHD).

Method: Genotyping was conducted with the Affymetrix Genome-Wide Human SNP Array 6.0. Multivariate association analyses were conducted using the software package PLINK. After data cleaning and quality control we tested 316,934 SNPs in 140 children with ADHD.

Results: We observed no genome-wide statistically significant findings, but a SNP in a K+-dependent Na+/Ca2+ exchanger expressed in vascular smooth muscle (SLC24A3) was included in our top associations at p < 1E-04. Genetic enrichment analyses of genes with (greater-than or equal to) 1 SNP significant at p < 0.01, implicated several functional categories (FERM domain, p=5.0E-07; immunoglobulin domain, p=8.1E-06; the transmembrane region, p=4.4E-05; channel activity, p=2.0E-04; and type-III fibronectins, p = 2.7E-05) harboring genes previously associated with related cardiovascular phenotypes.

Conclusions: The hypothesis generating results from this study suggests that polymorphisms in several genes consistently associated with cardiovascular diseases may impact changes in blood pressure observed with methylphenidate pharmacotherapy in children with ADHD.

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J Child Neurol. 2011;26:6-11.

FREQUENCY OF EPILEPTIFORM DISCHARGES IN THE SLEEP-DEPRIVED ELECTROENCEPHALOGRAM IN CHILDREN EVALUATED FOR ATTENTION-DEFICIT DISORDERS.

Millichap JJ, Stack CV, Millichap JG.

The authors determined the frequency of epileptiform discharges in the electroencephalogram (EEG) of a cohort of children and adolescents referred to a neurology specialty clinic for evaluation of attention-deficit disorders. Of 624 records, 461 (73.9%) were normal and 163 (26.1%) abnormal. Of abnormal EEGs, 70 (42.9%) had focal epileptiform discharges only, 68 (41.7%) had generalized epileptiform discharges only, and 19 (11.6%) had both independent focal and generalized spikes. Focal spikes were localized chiefly in central, frontal, and temporal regions. Of 163 records with abnormalities, 154 (94.5%) were sleep deprived and 159 (97.5%) were sleep records. One-quarter of the nonepileptic children evaluated for attention-deficit disorder have epileptiform discharges in the EEG, and just more than half are focal. Sleep-deprived sleep is essential to exclude epileptiform abnormalities. The utility of the EEG in the management of attention-deficit disorders and selection of stimulant or nonstimulant medication deserves further study.

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J Child Neurol. 2011;26:31-36.

CHANGES OF URINE DIHYDROXYPHENYLGLYCOL TO NOREPINEPHRINE RATIO IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) TREATED WITH ATOMOXETINE.

Montoya A, Escobar R, Garcia-Polavieja MJ, et al.

This study investigated changes in the urine dihydroxyphenylglycol to norepinephrine ratio in patients with attention-deficit hyperactivity disorder (ADHD) treated with atomoxetine. The possible relationship with clinical response was also explored. Newly ADHD diagnosed, treatment-naive children or adolescents were

double-blindly randomized (2:1) to atomoxetine (n=28) or placebo (n=13). The dihydroxyphenylglycol to norepinephrine ratio decreased in both groups, showing significantly greater changes with atomoxetine than with placebo at week 6 (-42% versus -14%; P =.001), when dosed at 1.2 mg/kg/day, than at week 2 (-20% versus -2%; P =.118) with a dose of 0.5 mg/kg/day. Although the significant dihydroxyphenylglycol to norepinephrine ratio decrease with atomoxetine indicated norepinephrine transporter blockade, no association with ADHD clinical response (ADHD Rating Scale-IV-Parent:Investigator) was found. Therefore, dihydroxyphenylglycol to norepinephrine ratio might be a useful pharmacodynamic/pharmacokinetic biomarker, although not sufficiently sensitive to predict clinical efficacy. It remains a possibility that this ratio might have value to facilitate personalized atomoxetine pharmacotherapy in ADHD patients.

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Eating Weight Disord. 2010;15:e144-e151.
INCREASED RESTING ENERGY EXPENDITURE IN CHILDREN WITH ATTENTION-DEFICIT- HYPERACTIVITY DISORDER.
Mueller TF, Brielmaier S, Domsch H, et al.
BACKGROUND: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequently reported neuropsychiatric disorders in childhood. However, there is limited data on the biological basis for this disorder. Disturbances in neurotransmitters have been suggested to play a pathophysiologic role. Phenotypically an increased prevalence of obesity has been reported.
OBJECTIVE: To investigate resting energy expenditure (REE) and diet-induced thermogenesis in stimulant medication-naive children with ADHD.
DESIGN: Case control study of 12 pre-pubertal boys with ADHD of the hyperactive-impulsive type and 12 control boys without ADHD. Anthropometric testing and indirect calorimetry were performed before and after a standardized meal. REE and thermogenesis were measured in each subject at 2 time points. In an independent group of 60 boys with ADHD, BMI standard deviation scores (BMI-SDS) were compared to age-adapted reference values.
RESULTS: REE was on average 6.5 kcal/kg fat free mass/day higher in the ADHD compared to the control group (p<0.01). In contrast, the thermogenic effect of food was not different between the two groups (average increase by 16%, p=n.s.). The repeat measurements, an average of 5(plus or minus)1 months apart, were highly reproducible in all subjects. Age and restlessness did not explain the differences in REE. Boys with ADHD had similar BMI-SDS values (mean BMI-SDS -0.10(plus or minus)0.98) as reference groups.
CONCLUSIONS: REE, in contrast to diet-induced thermogenesis, is higher in medication-naive boys with ADHD. The normal BMI levels suggest increased energy intake in these children.

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Tidsskr Nor Laegeforen. 2011 Jan;131:14.
[MISLEADING ABOUT ADHD].
Neraal T.

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Journal of Emotional and Behavioral Disorders. 2010 Dec;18:247-55.
CLINICAL USEFULNESS OF THE OPPOSITIONAL DEFIANT DISORDER RATING SCALE (ODDRS).
O'Laughlin EM, Hackenberg JL, Riccardi MM.
The present study examined the reliability, validity, and clinical utility of the Oppositional Defiant Disorder Rating Scale (ODDRS) in a population of children referred for ADHD evaluation. The diagnostic benefit of using a rating scale specific to Oppositional Defiant Disorder (ODD), in addition to a broad range behavior scale, was also investigated. Parents and teachers of 177 clinic-referred children provided ratings on the

ODDRS. The average correlation between parent and teacher ratings was minimal (r = .13). Children diagnosed with ODD through structured parent interviews were found to have elevated scores on the parent version of the ODDRS, as compared to children without a research diagnosis of ODD. However teacher ratings did not discriminate between the ODD and no-ODD groups. There was minimal evidence of incremental validity as classification rates for the ODDRS were almost identical to classification rates based on the Aggression subscale of the Behavior Assessment System for Children (BASC-2).

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Journal of Attention Disorders. 2011 Jan;15:67-78.

SUBCLINICAL ADHD, STRESS, AND COPING IN ROMANTIC RELATIONSHIPS OF UNIVERSITY STUDENTS.

Overbey GA, Snell WE, Jr., Callis KE.

Objective: To examine how the subclinical symptoms of adult ADHD and those of oppositional-defiant disorder (ODD) affect relationship satisfaction and stress and to determine whether different patterns of coping strategies emerge when undergraduates have symptoms of one or both disorders.

Method: Participants (N=497) complete self-report surveys assessing ADHD and ODD symptoms, relationship satisfaction, stress, and coping strategies used in their intimate relationships.

Results: ADHD and ODD symptoms are significantly related to a number of stressors and different patterns of coping strategies. University students with symptoms of both ADHD and ODD display a different pattern of stressors and different patterns of coping than those with symptoms of ADHD only.

Conclusion: Screenings for both ADHD and ODD and the provision of services that offer students more constructive coping alternatives to deal with stress in their intimate relationships are needed on university campuses.

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Neuropsychology. 2011 Jan;25:25-35.

NEUROCOGNITION AND FUNCTIONAL OUTCOME IN EARLY-ONSET SCHIZOPHRENIA AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A 13-YEAR FOLLOW-UP.

Øie M, Sundet K, Ueland T.

Objective: The relation between neurocognitive impairments and functional outcome has been documented in both early onset schizophrenia (EOS) and attention-deficit/hyperactivity disorder (ADHD), but less is known about the long-term relation between these factors. The present study investigates how neurocognition at baseline is related to measures of functional outcome at 13-year follow-up in subjects with EOS and ADHD.

Method: Subjects with EOS (n = 15), ADHD (n = 19), and healthy controls (n = 30) were followed up 13 years after initial assessment. All subjects were between 12 and 18 years of age at baseline and between 24 and 30 at follow-up. They were retested at T2 with the same comprehensive neurocognitive test battery as used at T1, and reassessed with various symptom and behavior ratings and functional outcome measures.

Results: Both groups were characterized by reduced functional outcome at follow-up, although of different magnitude and type, compared with healthy controls. In the EOS group, neurocognitive baseline measures were associated with social functioning at follow-up (?2 between .26 and .41), while for the ADHD group, no significant predictions were found.

Conclusions: Adolescents with EOS and ADHD are characterized by poor functional outcome compared with healthy controls when reassessed as young adults. Executive function, memory and attention were related to social and community functioning in EOS. For ADHD no significant predictions were found although functional outcome was poor. For both groups treatment should focus on training of social skills and activities of daily living to enhance the long-term functional outcome. For EOS cognitive remediation should also be considered.

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Mol Cell Proteomics. 2011;10.

HUMAN PLASMA GLYCOME IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDERS.

Pivac N, Knezevic A, Gornik O, et al.

Over a half of all proteins are glycosylated, and their proper glycosylation is essential for normal function. Unfortunately, because of structural complexity of nonlinear branched glycans and the absence of genetic template for their synthesis, the knowledge about glycans is lagging significantly behind the knowledge about proteins or DNA. Using a recently developed quantitative high throughput glycan analysis method we quantified components of the plasma N-glycome in 99 children with attention-deficit hyperactivity disorder (ADHD), 81 child and 5 adults with autism spectrum disorder, and a total of 340 matching healthy controls. No changes in plasma glycome were found to associate with autism spectrum disorder, but several highly significant associations were observed with ADHD. Further structural analysis of plasma glycans revealed that ADHD is associated with increased antennary fucosylation of biantennary glycans and decreased levels of some complex glycans with three or four antennas. The design of this study prevented any functional conclusions about the observed associations, but specific differences in glycosylation appears to be strongly associated with ADHD and warrants further studies in this direction.

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J Clin Exp Neuropsychol. 2011 Jan;33:147-56.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND WILLIAMS SYNDROME: SHARED BEHAVIORAL AND NEUROPSYCHOLOGICAL PROFILES.

Rhodes SM, Riby DM, Matthews K, et al.

We compared verbally matched attention-deficit/hyperactivity disorder (ADHD), Williams syndrome (WS), and typically developing individuals (N=19 each group) on behavioral symptoms (Conners ADHD rating scale) and neuropsychological functioning. Neuropsychological tasks included those that assessed short-term memory and executive functions from the CANTAB (Cambridge Neuropsychological Test Automated Battery) neuropsychological battery. Children with WS scored within the abnormal range and did not differ in severity from ADHD children on the Conners Oppositionality, Cognitive Problems/Inattention, Hyperactivity, and ADHD Index subscales. The WS and ADHD groups also showed similar patterns of neuropsychological functioning, particularly in working memory (WM) strategy use and delayed short-term memory (STM). The findings may have clinical implications for the management of individuals with WS, highlighting the potential significance of behavioral, educational, and pharmacological strategies and treatments known to be useful in the treatment of children with ADHD for individuals with WS.

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J Int Neuropsychol Soc. 2010 Nov;16:1056-63.

EXECUTIVE DYSFUNCTION IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1: A STUDY OF ACTION PLANNING.

Roy A, Roulin JL, Charbonnier V, et al.

In this study, we tested the hypothesis that action planning is impaired in children with neurofibromatosis type 1 (NF1). Thirty-six children with NF1 were pair-matched to 36 healthy controls (HC) on age (range, 7-12 years), sex, and parental education level, and both groups were administered three action-planning tasks. To examine the relation of task performance to attention deficit hyperactivity disorder (ADHD), the NF1 group was divided into subsets of children who met or did not meet criteria for ADHD. Children with NF1 performed less well than HC on all planning tasks, and differences remained when controlling for IQ or a measure of visuospatial skill. Both the NF1 with ADHD subset and NF1 without ADHD subset performed more poorly than HC on two of the tasks, whereas only the NF1 with ADHD subset performed worse than HC on the third planning task. The results underscore the importance of evaluating executive function in children with NF1 and suggest that deficits in this domain may be only partially related to ADHD. Planning

deficits in children with NF1 may be part of their cognitive phenotype. Identifying these deficits is relevant in determining factors contributing to learning problems and in developing appropriate interventions.

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Hum Brain Mapp. 2010 Dec;31:1823-33.

DISORDER-SPECIFIC INFERIOR PREFRONTAL HYPOFUNCTION IN BOYS WITH PURE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMPARED TO BOYS WITH PURE CONDUCT DISORDER DURING COGNITIVE FLEXIBILITY.

Rubia K, Halari R, Cubillo A, et al.

Background: Problems with cognitive flexibility have been observed in patients with attention deficit hyperactivity disorder (ADHD) and in patients with conduct disorder (CD), characterized by the violation of societal rules and the rights of others. Functional magnetic resonance imaging (fMRI) of cognitive switching, however, has only been investigated in patients with ADHD, including comorbidity with CD, finding frontostriatal and temporoparietal underactivation. This study investigates disorder-specific functional abnormalities during cognitive flexibility between medication-naïve children and adolescents with noncomorbid CD and those with noncomorbid ADHD compared to healthy controls.

Methods: Event-related fMRI was used to compare brain activation of 14 boys with noncomorbid, childhood-onset CD, 14 boys with noncomorbid ADHD, and 20 healthy comparison boys during a visual–spatial Switch task.

Results: Behaviorally, children with ADHD compared to children with CD had significantly slower reaction times to switch compared to repeat trials. The fMRI comparison showed that the patients with ADHD compared to both controls and patients with CD showed underactivation in right and left inferior prefrontal cortex. No disorder-specific brain underactivation was observed in patients with CD. Only when compared with controls alone, the disruptive behavior group showed reduced activation in bilateral temporoparietal and occipital brain regions.

Conclusions: The findings extend previous evidence for disorder-specific underactivation in patients with ADHD compared to patients with CD in inferior prefrontal cortex during tasks of inhibitory control to the domain of cognitive flexibility. Inferior prefrontal underactivation thus appears to be a disorder-specific neurofunctional biomarker for ADHD when compared with patients with CD.

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CONTINUUM Lifelong Learn Neurol. 2009;15:78-97.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN, ADOLESCENTS, AND ADULTS.

Schachar R.

Attention deficit hyperactivity disorder (ADHD) is a common and impairing disorder characterized by developmentally atypical levels of inattention, impulsiveness, and hyperactivity. It startsin childhood and persists into adulthood in about half of affected individuals. ADHD affects many aspects of affected persons' lives and adds substantially to their overall health care costs. Although ADHD starts in childhood, patientsmay present for the first timein adolescence or adulthood. Neurologists often play a significant role in the assessment and treatment of ADHD at all ages. Assessment should not only evaluate the symptoms of ADHD but also weigh the impairment arising from these symptoms, including associated psychiatric disorders and learning problems, and the presenceof precipitating or aggravating medical problems. A number of pharmacologic and nonpharmacologic interventions play a role in treatment.

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Journal of Attention Disorders. 2011 Jan;15:56-66.

IS BEHAVIORAL REGULATION IN CHILDREN WITH ADHD AGGRAVATED BY COMORBID ANXIETY DISORDER?

Sørensen L, Plessen KJ, Nicholas J, et al.

Background: The present study investigated the impact of coexisting anxiety disorder in children with ADHD on their ability to regulate behavior.

Method: Parent reports on the Behavior Rating Inventory of Executive Function (BRIEF) in a comorbid group of children with ADHD and anxiety (n = 11) were compared to BRIEF reports in a group of children with a "pure" ADHD (n=23), a "pure" anxiety (n = 24) and a group without any diagnosis (n=104) in a 2 (ADHD vs. no ADHD) × 2 (anxiety vs. no anxiety) design.

Results: The children with ADHD and anxiety disorder scored significantly higher on the Inhibit scale than children within the other three groups. Main effects of diagnosis appeared in ADHD children on the Inhibit, Emotional Control, and Working Memory scales, and on the Shift and Emotional Control scales in anxious children.

Conclusion: The results indicate that a behavioral dysregulation in ADHD children is aggravated by comorbid anxiety.

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Prim Care Companion J Clin Psych. 2010;12.

OSMOTIC RELEASE ORAL SYSTEM (OROS) METHYLPHENIDATE?INDUCED DOUBLE INCONTINENCE: A CASE REPORT.

Tang CS, Chou WJ, Cheng ATA.

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J Clin Exp Neuropsychol. 2010 Nov;32:929-36.

ATTENTION PROCESSING ABNORMALITIES IN CHILDREN WITH TRAUMATIC BRAIN INJURY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: DIFFERENTIAL IMPAIRMENT OF COMPONENT PROCESSES.

Thaler NS, Allen DN, Park BS, et al.

Individuals with acquired and neurodevelopmental brain disorders often exhibit deficits in attention. Recent models of attention have conceptualized it as a multicomponent system. One influential model proposed by Mirsky et al. (1991) consists of factors that include focus, sustain, shift, and encode components. This model has been used to examine the structure of attention in a variety of clinical populations although few studies have contrasted performance of various clinical groups in order to determine whether these components are differentially affected. To address this issue, the current study investigated the differential sensitivity of these attention components in 90 children: 30 who had sustained traumatic brain injury (TBI), 30 who were diagnosed with attention-deficit/hyperactivity disorder (ADHD), and 30 normal controls. Results demonstrated that the TBI group had significantly lower focus factor scores, the ADHD group had significantly lower sustain scores, and that both clinical groups had lower encode factor scores than controls. Stepwise discriminant function analysis (DFA) retained the focus and encode factors in predicting clinical groups from controls with 75.6% accuracy. A second DFA retained the focus factor in differentiating the two clinical groups with 70.0% accuracy. These findings provide evidence of differential attention deficits resulting from TBI and ADHD.

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Z Psych Psychol Psychother. 2011;59:25-36.

EFFECTIVENESS OF BEHAVIORAL THERAPY ON ATTENTION REGULATION AND EXECUTIVE FUNCTIONING IN CHILDREN AND ADOLESCENTS WITH ADHD.

Toussaint A, Petermann F, Schmidt S, et al.

The present study examined whether learning theory-based techniques in a multimodal training lead to an improvement in attention regulation and executive functioning of children and adolescents with ADHD. 45 children and adolescents with ADHD participated for two weeks in a Summercamp Program which included a systematic Response-Cost-Token approach (RCT) and specific attention training. In an experimental pre-post design executive functions were assessed using the Test for Attention Performance (TAP) and the Trail-Making-Test (TMT). The results showed significant improvement in specific neuropsychological functions like attention regulation and inhibitory control. Since all participants discontinued medication before and during the training, these effects refer predominantly on RCT and attention training. Thus, fundamental learning theory-based techniques lead to substantial improvement in neuropsychological functioning of children with ADHD.

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J Child Adolesc Psychopharmacol. 2010;20:503-11.

EXECUTIVE FUNCTION DEFICITS IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND IMPROVEMENT WITH LISDEXAMFETAMINE DIMESYLATE IN AN OPEN-LABEL STUDY.

Turgay A, Ginsberg L, Sarkis E, et al.

Objective: To assess the effects of lisdexamfetamine dimesylate (LDX) on executive function (EF) behaviors in children with attention-deficit/ hyperactivity disorder (ADHD).

Methods: This observational, open-label, 7-week, dose-optimization study of LDX (20-70mg/day) in children with ADHD evaluated efficacy with the ADHD Rating Scale IV; safety measures included adverse events (AEs). EF was assessed with the Behavior Rating Inventory of Executive Function (BRIEF). Post hoc analyses examined BRIEF scores by sex, ADHD subtype, comorbid psychiatric symptoms, and common treatment-emergent AEs (TEAEs). ADHD Rating Scale IV scores were assessed in subjects categorized by baseline BRIEF global executive composite T scores with clinically significant ((greater-than or equal to)65) or not clinically significant (<65) impairment in EF.

Results: Mean (standard deviation) change from baseline to endpoint for BRIEF of-17.9 (12.5) for Global Executive Composite,-15.4 (12.6) for Behavioral Regulation Index, and-17.6 (12.3) for Metacognition Index demonstrated improvement with LDX (pooled doses; $p<0.0001$ for all). Improvements in BRIEF scores were seen regardless of sex, ADHD subtype, comorbid psychiatric symptoms, common TEAEs, or baseline EF impairment category. TEAEs included decreased appetite, decreased weight, irritability, insomnia, headache, upper abdominal pain, and initial insomnia.

Conclusions: Improvements were demonstrated in EF behaviors and ADHD symptoms with LDX. LDX safety profile was consistent with long-acting stimulant use.

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J Neural Transm. 2010;117:1213-28.

TIME PROCESSING IN CHILDREN AND ADULTS WITH ADHD.

Valko L, Schneider G, Doehnert M, et al.

A time-processing deficit has been proposed as a neuropsychological candidate endophenotype for Attention Deficit Hyperactivity Disorder (ADHD), but its developmental trajectory still needs to be explored. In the present study, children (N=33) and adults (N=22) with ADHD were compared to normal controls on two time-processing tasks. For time reproduction, ADHD-related impairment was found in the full group, but not when adults were analyzed separately. For the discrimination of brief intervals, children and adults with

ADHD showed different patterns of deficit. We conclude that in ADHD some time-processing deficits are still present in adults, but may take on age-related different forms.

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Educational and Psychological Measurement. 2010 Dec;70:1042-59.

PARENT REPORT OF ADHD SYMPTOMS OF EARLY ADOLESCENTS: A CONFIRMATORY FACTOR ANALYSIS OF THE DISRUPTIVE BEHAVIOR DISORDERS SCALE.

Van Eck K, Finney SJ, Evans SW.

The Disruptive Behavior Disorders (DBD) scale includes the Diagnostic and Statistical Manual of Mental Disorders (4th ed.) criteria for attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder, and conduct disorder. This study examined only the ADHD items of the DBD scale. This scale is frequently used for assessing parent- and teacher-reported ADHD symptoms. Although some research on teacher report exists, little is known about the factor structure of parent-reported ADHD for this scale, particularly for early adolescents. Confirmatory factor analysis was used to assess the fit of a priori specified, theoretically based models of ADHD. Participants were 250 parents of early adolescents (M = 12 years, SD = 1.53), who completed the ADHD items of the DBD scale. A two-factor model of hyperactivity/impulsivity and inattention provided the best fit to item responses, but localized areas of misfit were present. Alternate wording for a few items was proposed. Implications of the findings and directions for future research are discussed.

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Child Adolesc Psychiatry Ment Health. 2010;4.

DIFFERENCES BETWEEN CHILDREN AND ADOLESCENTS IN TREATMENT RESPONSE TO ATOMOXETINE AND THE CORRELATION BETWEEN HEALTH-RELATED QUALITY OF LIFE AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER CORE SYMPTOMS: META-ANALYSIS OF FIVE ATOMOXETINE TRIALS.

Wehmeier PM, Schacht A, Escobar R, et al.

Objectives: To explore the influence of age on treatment responses to atomoxetine and to assess the relationship between core symptoms of attention deficit/hyperactivity disorder (ADHD) and health-related quality of life (HR-QoL) outcomes.

Data Sources: Data from five similar clinical trials of atomoxetine in the treatment of children and adolescents with ADHD were included in this meta-analysis.

Study Selection: Atomoxetine studies that used the ADHD Rating Scale (ADHD-RS) and the Child Health and Illness Profile Child Edition (CHIP-CE) as outcome measures were selected.

Interventions: Treatment with atomoxetine.

Main Outcome Measures: Treatment group differences (atomoxetine vs placebo) in terms of total score, domains, and subdomains of the CHIP-CE were compared across age groups, and correlations between ADHD-RS scores and CHIP-CE scores were calculated by age.

Results: Data of 794 subjects (611 children, 183 adolescents) were pooled. At baseline, adolescents showed significantly ($p < 0.05$) greater impairment compared with children in the Family Involvement, Satisfaction with Self, and Academic Performance subdomains of the CHIP-CE. Treatment effect of atomoxetine was significant in both age groups for the Risk Avoidance domain and its subdomains. There was a significant age-treatment interaction with greater efficacy seen in adolescents in both the Risk Avoidance domain and the Threats to Achievement subdomain. Correlations between ADHD-RS and CHIP-CE scores were generally low at baseline and moderate in change from baseline and were overall similar in adolescents and children.

Conclusions: Atomoxetine was effective in improving some aspects of HR-QoL in both age groups. Correlations between core symptoms of ADHD and HR-QoL were low to moderate.

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Zh Nevrologii Psihiatrii im S S Korsakova. 2010;110:50-55.

ATTENTION DEFICIT - HYPERACTIVITY DISORDER AND ENURESIS IN CHILDREN AND ADOLESCENTS.

Zavadenko NN, Kolobova NM, Suvorinova NY.

Frequency of comorbid disorders and neuropsychological state, executive functions (EF), were studied in two groups of patients aged from 5 to 14 years: 53 patients with attention-deficit hyperactivity disorder (ADHD) in the association with enuresis and 71 patients with ADHD without enuresis. The most cases of enuresis (50 out of 53 patients) were represented by primary nocturnal enuresis. The significant increase of total number of ADHD cases with comorbidity for oppositional-defiant disorder, anxiety disorder, tics or encopresis (77,7%) was found in the first group compared to the second one (60,6%). The presence of enuresis in ADHD was associated with the significant increase of frequency of anxiety disorders (54,7% versus 39,4%). Moreover, in the group of patients with ADHD and enuresis, the frequency of oppositional-defiant disorder and encopresis was higher in the age of 5-9 years while the frequency of obsessive-compulsive disorder and tics increased in the period of 10-14 years as compared to patients without enuresis. The assessment of executive functions with the Wisconsin Card Sorting Test did not reveal any differences between patients of two groups.

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Neurosci Behav Physiol. 2011 Jan;41:52-56.

ATTENTION DEFICIT HYPERACTIVITY SYNDROME: THE ROLE OF PARENT AND TEACHER QUESTIONNAIRES IN ASSESSING THE SOCIAL AND PSYCHOLOGICAL ADAPTATION OF PATIENTS.

Zavadenko NN, Lebedeva TV, Schasnaya OV, et al.

The “Strengths and Difficulties” questionnaire was put to the parents and teachers of 342 schoolchildren aged 7–11 years using a non-randomized method. Questionnaire data from parents and teachers on children with ADHD and their peers were then compared. The spectrum of impairments arising in ADHD was found not to be restricted to the main symptoms of ADHD. Questionnaires completed by both parents and teachers showed that emotional impairments, behavioral problems, difficulties interacting with peers, and underdevelopment of social behavior were significantly more severe in children with ADHD as compared with healthy children. These results demonstrate the need for treatment to extend beyond addressing the basic symptoms to consider more general measures of patients’ quality of life.

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Eur J Paediatr Neurol. 2011;15:48-52.

AN ASSOCIATION STUDY BETWEEN SNAP-25 GENE AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Zhang H, Zhu S, Zhu Y, et al.

Attention-Deficit Hyperactivity Disorder (ADHD) is the most common behavioral disorder in childhood. Genetic associations have been reported between ADHD and polymorphic variants within or near dopamine pathway genes. Synaptosomal-associated protein, 25 kDa (SNAP-25), a presynaptic plasma membrane protein with an integral role in synaptic transmission, has shown association with ADHD in several datasets. We characterized two single-nucleotide polymorphisms (rs362549, rs363006) and one microsatellite [5'-UTR (TAAA)n] of SNAP-25. The association of these variants with ADHD was assessed in 102 trios collected from 90 male and 12 female probands. Transmission disequilibrium test (TDT) analysis showed that none of the polymorphic alleles were preferentially transmitted to the probands. Quantitative analysis was also conducted to assess the relationship between these marker alleles and the severity of ADHD symptoms. Analysis of the DSM-IV subtypes indicated that a significant association was identified between SNP rs362549 and ADHD subtypes (P = 0.0047). This is the first report of an association between SNAP-25 and ADHD in Chinese subjects of Han descent. We still support the premise that SNAP-25 is a genetic susceptibility factor for ADHD.

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J Clin Psychopharmacol. 2011;31:51-55.

EFFECT OF METHYLPHENIDATE ON INTELLIGENCE QUOTIENT SCORES IN CHINESE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Zhang L, Jin X, Zhang Y.

Background: Stimulants are the most effective drugs for attention-deficit/hyperactivity disorder (ADHD) symptoms. The purpose of this study was to explore the intervention effect of methylphenidate, a commonly used stimulant, on cognitive performance in ADHD children and whether the effect is associated with age, sex, different subtypes of ADHD, and drug dosage.

Methods: Children with ADHD were divided into the following subtypes: combined type, predominantly inattentive type, and hyperactive/impulsive type. The intervention group consisted of 159 children treated with methylphenidate, and the control group consisted of 78 untreated patients. All 237 subjects were given a Wechsler Intelligence Scale for Children - Revised test at baseline, and 6 months later, they were retested. The scores of Verbal Intelligence Quotient (IQ) test, Performance IQ (PIQ) test, Full Scale IQ (FSIQ) test, and subtests were compared before and after the intervention.

Results: At baseline, scores were not statistically different between the 2 groups. After 6 months, PIQ and FSIQ scores of intervention group were higher than those of the control group ($P<0.05$). Compared with baseline scores, the intervention group, but not the control group, showed significant increases in Verbal IQ ($P<0.05$), PIQ ($P<0.01$), and FSIQ ($P<0.01$). In the intervention group, the 5 subtests scores of PIQ improved significantly ($P < 0.01$). In the control group, none of the scores from the subtests showed statistical differences. Furthermore, there was no statistical difference between the change of IQ scores and children's age, sex, different subtypes of ADHD, and drug dosage.

Conclusions: Methylphenidate can enhance cognitive performance in ADHD patients thus evaluating their IQ scores, although the effect size seems to be relatively small. The result should not be indicated as an increase in intelligence.

Effects of a restricted elimination diet on the behaviour of children with attention-deficit hyperactivity disorder (INCA study): a randomised controlled trial

Lidy M Pelsser, Klaas Frankena, Jan Toorman, Huub F Savelkoul, Anthony E Dubois, Rob Rodrigues Pereira, Ton A Haagen, Nanda N Rommelse, Jan K Buitelaar

Lancet 2011; 377: 494–503
See Comment page 446

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Summary

Background The effects of a restricted elimination diet in children with attention-deficit hyperactivity disorder (ADHD) have mainly been investigated in selected subgroups of patients. We aimed to investigate whether there is a connection between diet and behaviour in an unselected group of children.

Methods The Impact of Nutrition on Children with ADHD (INCA) study was a randomised controlled trial that consisted of an open-label phase with masked measurements followed by a double-blind crossover phase. Patients in the Netherlands and Belgium were enrolled via announcements in medical health centres and through media announcements. Randomisation in both phases was individually done by random sampling. In the open-label phase (first phase), children aged 4–8 years who were diagnosed with ADHD were randomly assigned to 5 weeks of a restricted elimination diet (diet group) or to instructions for a healthy diet (control group). Thereafter, the clinical responders (those with an improvement of at least 40% on the ADHD rating scale [ARS]) from the diet group proceeded with a 4-week double-blind crossover food challenge phase (second phase), in which high-IgG or low-IgG foods (classified on the basis of every child's individual IgG blood test results) were added to the diet. During the first phase, only the assessing paediatrician was masked to group allocation. During the second phase (challenge phase), all persons involved were masked to challenge allocation. Primary endpoints were the change in ARS score between baseline and the end of the first phase (masked paediatrician) and between the end of the first phase and the second phase (double-blind), and the abbreviated Conners' scale (ACS) score (unmasked) between the same timepoints. Secondary endpoints included food-specific IgG levels at baseline related to the behaviour of the diet group responders after IgG-based food challenges. The primary analyses were intention to treat for the first phase and per protocol for the second phase. INCA is registered as an International Standard Randomised Controlled Trial, number ISRCTN 76063113.

Findings Between Nov 4, 2008, and Sept 29, 2009, 100 children were enrolled and randomly assigned to the control group (n=50) or the diet group (n=50). Between baseline and the end of the first phase, the difference between the diet group and the control group in the mean ARS total score was 23·7 (95% CI 18·6–28·8; p<0·0001) according to the masked ratings. The difference between groups in the mean ACS score between the same timepoints was 11·8 (95% CI 9·2–14·5; p<0·0001). The ARS total score increased in clinical responders after the challenge by 20·8 (95% CI 14·3–27·3; p<0·0001) and the ACS score increased by 11·6 (7·7–15·4; p<0·0001). In the challenge phase, after challenges with either high-IgG or low-IgG foods, relapse of ADHD symptoms occurred in 19 of 30 (63%) children, independent of the IgG blood levels. There were no harms or adverse events reported in both phases.

Interpretation A strictly supervised restricted elimination diet is a valuable instrument to assess whether ADHD is induced by food. The prescription of diets on the basis of IgG blood tests should be discouraged.

Funding Foundation of Child and Behaviour, Foundation Nuts Ohra, Foundation for Children's Welfare Stamps Netherlands, and the KF Hein Foundation.

Introduction

Attention-deficit hyperactivity disorder (ADHD) affects 5% of children worldwide and is characterised by excessive and impairing inattentive, hyperactive, and impulsive behaviour.[1] Genetic and environmental factors are involved,[2] and ADHD is often accompanied by oppositional defiant disorder.[3] Children with ADHD and comorbid oppositional defiant disorder are difficult for parents, guardians, and teachers to handle, give rise to substantial parenting stress, and have a worse prognosis for adverse outcomes (ie, an increased risk of developing conduct disorder and antisocial personality disorder) than have children without comorbidity.[4] At present, ADHD is treated with psychoeducation, parent training, child behavioural interventions, and drugs,[5] but follow-up studies have reported limited long-term effects of multimodal treatment.[6,7]

One of the risk factors for ADHD that could be targeted for intervention is food.[8] Reports of adverse physical reactions to foods (eg, eczema, asthma, and

gastrointestinal problems) that affect various organ systems[9] have led to the suggestion that foods might also affect the brain, resulting in adverse behavioural effects.[10] Colourings and preservatives might have some effect on the behaviour of children with or without ADHD, but additives do not cause ADHD.[2,5,11,12] An individually constructed restricted elimination diet, which consists of some hypoallergenic foods, might be effective for treatment of ADHD.[8,11] The rationale of this diet for children with ADHD is to investigate whether ADHD is triggered by foods—ie, to identify a hypersensitivity reaction to foods. In a small randomised controlled trial that investigated the effects of a restricted elimination diet,[13] we reported statistically significant and clinically relevant effects on ADHD and oppositional defiant disorder.

In children with ADHD that is triggered by foods, ADHD meets the criteria of hypersensitivity according to allergy nomenclature.[14] Accordingly, we postulated that ADHD might be an allergic or non-allergic hypersensitivity disorder in some children.[15] IgE is implicated in typical food allergies. In reactions to food that are not mediated by IgE, assessment of IgG levels might be useful,[16] and IgG blood tests are offered—especially in complementary care[17]—with the aim of establishing a relation between foods and ADHD. According to this theory, eating foods that induce high IgG levels would lead to a substantial behavioural relapse whereas eating those that induce low IgG levels would not. However, there is no evidence for the effectiveness of these tests.[18]

The primary aim of the Impact of Nutrition on Children with ADHD (INCA) study was to investigate the effects of a restricted elimination diet on behaviour in children with ADHD. The secondary aim was to differentiate between non-allergic and allergic mechanisms in food-induced ADHD.

Methods

Participants

Children were recruited at medical health centres and through media announcements in the Netherlands and Belgium. Interested parents or guardians (hereafter called parents) were provided with verbal and written information about the study. Eligible children were assessed for ADHD and comorbid disorders by a senior paediatrician (JT) using a structured psychiatric interview (SPI). Children were included if they had been diagnosed with ADHD of any subtype.[1] Further inclusion criteria were children's age 4–8 years (sufficiently young to maximise dietary compliance), and parents with adequate knowledge of Dutch and who were motivated to follow a 5-week restricted elimination diet. Exclusion criteria were children receiving drugs or behavioural therapy for ADHD, children already following a diet, or family circumstances that were likely to prevent completion of the study. The presence of comorbid psychiatric disorders was not a reason for exclusion.

The INCA study was approved by the medical ethics committee of Wageningen University and by the executive board and ethics committee of Catharina Hospital Eindhoven. The parents of children who participated in the trial provided written informed consent before week 1 of the study.

Randomisation and masking

INCA consisted of two phases. The first phase was an open-label phase with masked paediatrician measurements. After the baseline assessment, eligible children were randomly assigned to either a diet group or a control group. Randomisation was individually done by random sampling. Ten blocks of ten identical, sealed envelopes containing concealed treatment codes were made by a masked epidemiologist (KF) to prevent unbalanced assignment of treatment over time. Parents randomly picked and opened an envelope. Staff who recruited and assessed patients were not involved in the procedure used to generate group allocations.

Because the diet was individually tailored and restricted, a reliable placebo diet was not possible, thus parents and teachers could not be masked to group allocation. Also, the researcher (LP) who provided expert advice to parents and teachers during the diet period could not be masked. Parents were instructed not to reveal dietary information to the paediatrician (JT) who did masked assessments.[19]

The second phase was a double-blind crossover food challenge phase in the diet group. Eligible children from the diet group were randomly assigned, by simple sampling, to one of two challenge groups. Each group was offered either three foods that induce low IgG levels or three that induce high IgG levels in a crossover design. The three foods within each group were selected by an independent dietician who was masked to group assignment. The researcher, paediatrician, parents, and teachers were masked to IgG allocation. KF did the data entry for both phases and was masked to the assigned treatment.

For the trial protocol see http://www.adhdresearchcentre.nl/english

Procedures

During the trial, we used four questionnaires to assess outcome: the 18-item ADHD rating scale (ARS),[20] ten-item abbreviated Conners' scale (ACS),[21] strengths and difficulties questionnaire (SDQ),[22] and SPI.[23] The ARS, which is based on the diagnostic and statistical manual of mental disorders part IV (DSM-IV) criteria for ADHD, consists of nine inattention and nine hyperactivity and impulsivity criteria, with a four-point scale (0=never [less than once a week], 1=sometimes [several times a week], 2=often [once a day], and 3=very often [several times a day]). Three measures were taken from the ARS: total score (0–54), inattention score (0–27), and hyperactivity and impulsivity score (0–27). The ACS, also a four-point rating scale, covers hyperactivity, impulsivity, attention, mood, and temper tantrums. The DSM-IV-based SPI was

See Online for webappendix

used to assess oppositional defiant disorder (with the eight DSM-IV oppositional defiant disorder criteria) and conduct disorder (with seven of the 15 DSM-IV conduct disorder criteria relevant to this young group of patients—ie, criteria 1–5, 9, and 11). The SDQ provides a total difficulties score on the basis of the results of four problem subscales: emotional symptoms, and conduct, hyperactivity–inattention, and peer problems. Unmasked parent and teacher assessments (ACS, ARS, and SPI) and masked paediatrician assessments (ARS and SPI) were done at baseline and at the end of the first phase (week 9 in the diet group and week 13 in the control group; table 1). The masked paediatrician based his ratings on information obtained from the parents as well as on his own observation and assessment of the child's behaviour and presentation. The masked measurements were used for all analyses in the first phase, apart from the ACS score and the week 9 measurements in the control group. Blood samples were taken at the start and end of the first phase.

After the baseline assessments, randomisation was done, and parents started a 2-week baseline period during which they did not exclude any foods from their child's diet. Parents kept extended diaries (containing information on the child's diet, behaviour, activities, physical complaints, and medications; webappendix p 1) and closely monitored their child's behaviour. After the baseline period (in week 3), the second unmasked parent assessment took place (ACS and ARS) and parents and teachers filled in the SDQ.

During week 4 (start of the first phase), the diet group started a 5-week individually designed restricted elimination diet, which has been described elsewhere[24] (webappendix p 2). Briefly, the diet consisted of the few-foods diet (ie, rice, meat, vegetables, pears, and water)[8,24] complemented with specific foods such as potatoes, fruits, and wheat. The aim was to create an elimination diet as comprehensive as possible for each individual child, to make the intervention easy for children and their parents to follow.[10,11] If the parents reported no behavioural changes by the end of the second diet week, the diet was gradually restricted to the few-foods diet only.[10] At the end of the first phase, all children were assessed by the masked paediatrician (ARS and SPI), unmasked parent and teacher ratings (ACS, ARS, and SPI) were done, the SDQ was completed by all parents and teachers, and blood samples were taken. Children in the diet group who had behavioural improvement of at least 40% on the ARS—ie, clinical responders—entered the challenge phase; the non-responders left the trial.

IgE and IgG levels were analysed from the blood samples taken at week 1. Total IgE, food-specific IgE (to chicken egg, peanut, soy, milk, fish, and wheat), and food-specific total IgG levels to 270 different foods were assessed with ELISA. Based on the levels of IgG (μg/mL) in serum, measured with a certified IgG-specific food screening test (ImuPro test), each analysed food was categorised as a low-IgG food or a high-IgG food.

In the diet group responders, in the second phase (double-blind crossover challenge phase; weeks 10–13), two groups of foods consisting of either three high-IgG or three low-IgG foods were consecutively added to the restricted elimination diet, each for 2 weeks. For every child, the composition of the food challenge groups was tailored by the dietician on the basis of total IgG levels to 270 different foods, which were assessed in the first blood samples. Any of the 270 foods could be chosen by the dietician, except for foods that caused increased IgE levels (to preclude an anaphylactic reaction), were disliked by the child, or were already part of the diet. Thus, the foods added in the challenge phase were individually chosen and differed per child. All children were to complete both challenges, and each challenge food group had to be eaten every day in equal amounts during the 2-week period or until behavioural changes occurred.

All behavioural measurements in the challenge phase were double-blind. Parent ACS and ARS assessments were done after each challenge; the other measurements were done at week 13 or at week 11 if there was a relapse in behaviour during the first challenge (table 1). If the child's behaviour showed no relapse (according to the double-blind parent ARS score) during

	Diet group	Control group
Baseline period		
Weeks 1–3	No foods excluded	No foods excluded
Week 1	ACS, ARS, SPI (LP: P, T) ARS, SPI (JT) Blood samples taken	ACS, ARS, SPI (LP: P, T) ARS, SPI (JT) Blood samples taken
End of week 1	Randomisation	Randomisation
During week 3	ACS, ARS (LP: P) SDQ (P, T)	ACS, ARS (LP: P) SDQ (P, T)
First phase		
Weeks 4–9	Restricted elimination diet	Healthy food advice
During week 9	ACS, ARS, SPI (LP: P, T) ARS, SPI (JT) SDQ (P, T) Blood samples taken	ACS, ARS, SPI (LP: P) SDQ (P)
Second phase*		
Weeks 10–11	First double-blind challenge	Healthy food advice
Week 11	ACS, ARS, SPI† (LP: P, T) ARS†, SPI† (JT) SDQ† (P, T) Blood samples taken†	ACS, ARS (LP: P)
Weeks 12–13	Second double-blind challenge	Healthy food advice
End of week 13	ACS, ARS, SPI‡ (LP: P, T) ARS‡, SPI‡ (JT) SDQ‡ (P, T) Blood samples taken‡	ACS, ARS, SPI (LP: P, T) ARS, SPI (JT) SDQ (P, T) Blood samples taken

Masking (paediatrician only) during the first phase (diet group and control group) is for group assignment, masking (paediatrician, researcher, parent, and teacher) during the second phase (diet group only) is for challenge assignment. ACS=abbreviated Conners' scale. ARS=attention-deficit hyperactivity disorder rating scale. SPI=structured psychiatric interview. LP=researcher assessor. P=parent. T=teacher. JT=paediatrician assessor. SDQ=strengths and difficulties questionnaire. *Diet group responders only. †Responders who relapsed only. ‡Those who had not relapsed at 11 weeks.

Table 1: Measurement points during baseline, and the first and second phases

the first challenge period (weeks 10–11), the child proceeded with the second challenge (weeks 12–13), and a third blood sample was taken at week 13. Conversely, if the ADHD problems returned during the first challenge, the third blood sampling was brought forward, after which the challenge foods were eliminated again. After a washout period, the length of which depended on the remission of the behavioural problems, the second challenge would start, after which the randomised controlled trial ended.

After the baseline period, the control group followed the first phase until week 13 and received healthy food advice according to the guidelines of the Dutch Nutrition Centre. Parents continued to keep an extended diary until the end of the trial (week 13). Measurements took place at comparable times to the measurements in the diet group (table 1). At week 13, the second blood sample was taken, after which all parents of children who did not show behavioural improvements were offered the possibility of starting the diet.

The first phase primary endpoints were the difference in ARS (masked paediatrician assessment) and ACS scores (parent; unmasked assessment) between baseline and the end of the first phase. The challenge phase primary endpoints, in the clinical responders, were the change in ARS and ACS score from the end of the first phase to week 11 (after the first challenge) and week 13 (after the second challenge). A relapse in ADHD behaviour was defined as an ARS increase of at least 40% of the ARS score at the end of the first phase, and up to at least 60% of the ARS baseline score.

The first phase secondary endpoints were the IgE blood levels at the start of the trial associated with the behavioural changes at the end of the first phase, and the child's comorbid behavioural problems, assessed by the change in SPI[13] scores (masked paediatrician) from week 1 and SDQ[22] scores (parent) from week 3 to the end of the first phase. The challenge phase secondary endpoints were the food-specific IgG levels at baseline related to the behaviour of the diet group responders after IgG-based food challenges. The other secondary endpoints of physical and sleep problems assessed with the other complaints questionnaire,[24] and other blood tests, as specified in the INCA protocol, will be assessed in a separate paper.

Statistical analysis

In our previous randomised controlled trial,[11] 11 of 15 children in the diet group and none of 12 children in the control group showed behavioural improvements of 40% or more. We therefore assumed that a behavioural improvement of at least 40% would occur in 60% of children in the diet group and in 20% of those in the control group in this study. To achieve 80% power (α=0·05, two sided test), taking into account a potential block effect and 10% dropouts, we calculated that 40 children per group were needed. To allow for a potentially higher percentage of dropouts, we included ten extra children per group.

We did statistical analyses with Stata (version 10) and SPSS (version 15). In the first phase, masked measurements were done at Catharina Hospital Eindhoven by JT and unmasked measurements were done at the ADHD Research Centre Eindhoven by LP. In the second phase, double-blind measurements were done by JT and LP. The

For the Dutch Nutrition Centre see http://www.voedingscentrum.nl

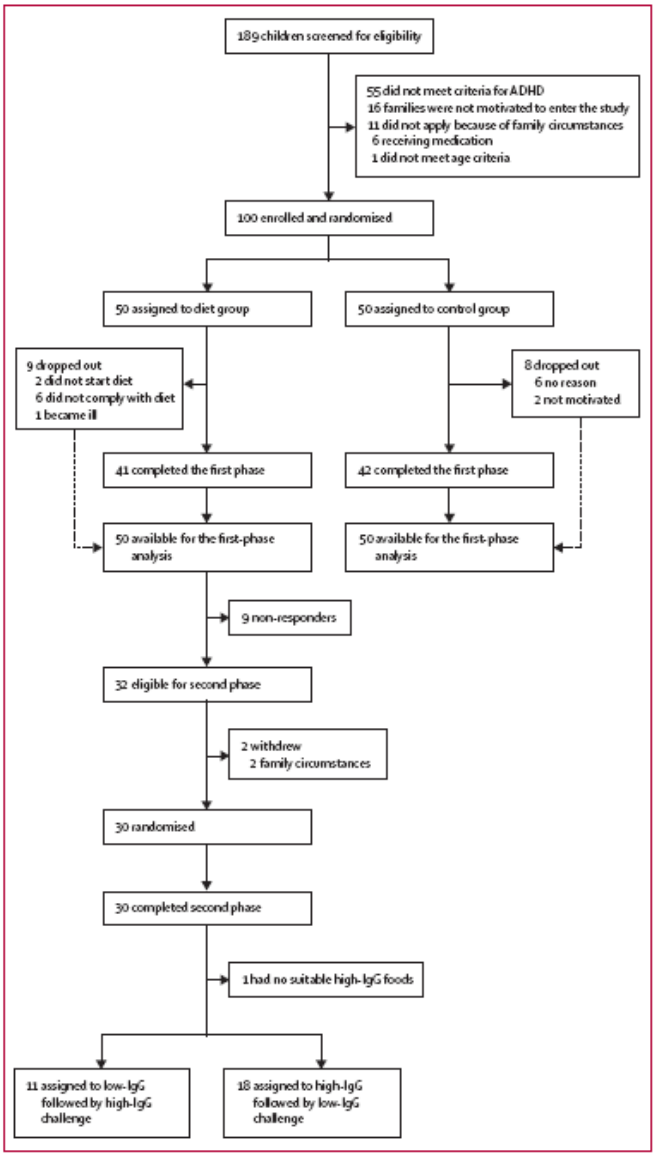

Figure 1: Trial profile

	Diet group (n=50)	Control group (n=50)
Boys	44 (88%)	42 (84%)
Age (years)	6·8 (1·3)	7·0 (1·3)
Pregnancy and birth*		
Mother smoked during pregnancy	5 (10%)	2 (4%)
Pregnancy ≤36 weeks	4 (8%)	4 (8%)
Problems at birth (hypoxia, incubated)	5 (10%)	4 (8%)
Parental data		
Non-native parent(s)	5 (10%)	7 (14%)
1 parent or co-parenting	3 (6%)	3 (6%)
Adopted or foster child	3 (6%)	1 (2%)
Age of onset of behavioural problems		
<2 years	33 (66%)	38 (76%)
2–4 years	16 (32%)	11 (22%)
>4 years	1 (2%)	1 (2%)
Psychiatric history		
Referred because of ADHD symptoms	40 (80%)	44 (88%)
On ADHD drugs before start of trial	6 (12%)	8 (16%)
Allergy data at start of trial		
Increased total IgE level	8 (16%)	6 (12%)
Increased food-specific IgE level	5 (10%)	9 (18%)
ADHD diagnoses at start of trial		
Combined type	41 (82%)	44 (88%)
Inattentive type	3 (6%)	3 (6%)
Hyperactive type	6 (12%)	3 (6%)
Other psychiatric diagnoses at start of trial		
Oppositional defiant disorder	20 (40%)	27 (54%)
Conduct disorder	3 (6%)	5 (10%)

Data are number (%) or mean (SD). ADHD=attention-deficit hyperactivity disorder. * Data missing for two adopted children in the diet group and one in the control group.

Table 2: Demographics and characteristics during week 1

For *The Lancet* protocol see http://www.thelancet.com/protocol-reviews/06PRT-7719

first phase ARS and SPI analyses were done with the masked measurements and were by intention to treat, last observation carried forward. The challenge phase analyses were per protocol. To assess the agreement between the unmasked (parent) and masked paediatrician measurements for ARS and SPI, we calculated kappa values,[25] and intra-cluster correlation coefficients (ICCs)[26] for categorical and continuous parameters, respectively. Kappa values greater than 0·75 (ICC >0·80) were taken to represent excellent agreement beyond chance; values below 0·40 (ICC <0·40) suggested poor agreement.

Behavioural endpoint scores were analysed by a general linear model with treatment (diet group *vs* control group), block, and their interaction as independent variables and baseline scores as covariates. The most reduced model was selected but treatment and block were forced in each model. We assessed the fit of the models with the link test command of Stata. The association between clinical response (yes or no) and treatment, and its association with IgE blood levels was calculated with Fisher's exact test. We analysed the effect of the crossover challenges (low-IgG or high-IgG) on the child's behaviour with the Mainland-Gart procedure.[27] We did a second analysis that also included those children who responded equally to both challenges with the Prescott test.[27] The effect of the challenges (low-IgG, high-IgG) was expressed as odds ratios (ORs) and estimated by generalised estimated equations (binomial distribution, logit link), with adjustment for challenge period and intra-patient correlation.

INCA is registered as an International Standard Randomised Controlled Trial, number ISRCTN 76063113. The protocol for this study was peer reviewed and accepted by *The Lancet*; a summary of the protocol was published on the journal's website, and the journal then made a commitment to peer review the primary clinical manuscript.

Role of the funding source

The sponsors of the study had no role in the study design, data collection, data analysis, data interpretation, writing of the manuscript, or in the decision to submit for publication. All authors had full access to the data in the study and LMP, NNR, and JKB had final responsibility for the decision to submit for publication.

Results

Between Nov 4, 2008, and Sept 29, 2009, 100 children were enrolled and randomly assigned to the control group (n=50) or the diet group (n=50; figure 1). Most children were boys and the mean age was 6·9 years (SD 1·3; table 2). Of the 41 children in the diet group who completed the first phase, the diet of 17 was restricted to the few-foods diet only.

Table 3 and figure 2 show the ARS results from the first phase. Of the 41 (82%) of 50 children in the diet group who completed the first phase, nine (22%) of 41 did not and 32 (78%) of 41 did respond to the diet (figure 1). The mean difference in ARS score between baseline and the end of the first phase was significantly lower in the diet group than in the control group for both the masked paediatrician (p<0·0001) and unmasked teacher ratings (p<0·0001; table 3). When comparing the unmasked (parent; LP) with the masked (JT) ARS and SPI measurements from the first phase, both kappa and ICC of inter-rater agreement were greater than 0·40 (mean 0·90 [SD 0·07] for ICC and 0·83 [0·20] for kappa). The ACS score between baseline and the first phase was also significantly lower in the diet group than in the control group for both parent (p<0·0001) and teacher (p<0·0001) ratings (table 3).

The difference between groups on the oppositional defiant disorder criteria measured by the SPI at the end of the first phase was also significant for both the masked paediatrician (p<0·0001) and teacher ratings (p=0·0320; table 3; figure 2). Because only three children in the diet group met the criteria for conduct disorder, we did not analyse these results. The decrease in hyperactivity–inattention problems, measured on the

SDQ, was similar to the decrease on the ARS (webappendix p 3).

Prespecified IgE immunological analyses in responders (32 of 41) and non-responders (nine of 41) in the diet group showed no association between clinical response and increased IgE blood levels. Total IgE was increased in six of 30 responders (data missing for two children) and two of nine non-responders (p=1·0, Fisher's exact test). Food-specific IgE levels were increased in one of 31 responders (data missing for one child) and one of nine non-responders (p=0·41, Fisher's exact test).

Of the 32 children who were clinical responders, 30 proceeded to the challenge phase (figure 1). 19 of 30 showed a behavioural relapse after one or both challenges. The ACS (unmasked parent) and ARS (masked paediatrician) results in the children in the diet group who were included in the challenge phase (n=30) were compared with the results of the children in the control group who completed the trial (n=42; figure 3). The decrease in ARS total score in the clinical responders from baseline to the end of the first phase was 35·9 (95% CI 33·2–38·6; p<0·0001), which subsequently increased after the challenge by 20·8 (14·3–27·3; p<0·0001). The decrease in ACS score in the clinical responders from baseline to the end of the first phase was 18·3 (95% CI 16·7–19·9; p<0·0001), which increased after the challenge by 11·6 (7·7–15·4; p<0·0001). In the control group, the ARS score did not differ between the measurements at week 1 and week 9 (0·8, 95% CI −0·4 to 2·0; p=0·21) and week 9 and week 13 (0·8, −0·4 to 2·0; p=0·17). In the control group, the ACS score did not differ between week 1 and week 9 (0·2, 95% CI −0·8 to 0·4; p=0·5) and between week 9 and week 13 (0·2, −0·5 to 1·0; p=0·57). SDQ measurements showed similar results (webappendix p 4). Because only six of 30 teacher data were available at the end of the second phase, we did not analyse these results.

29 of 30 children were included in the IgG assessments (no suitable high-IgG foods were available for one responder; figure 1). 11 of 29 children were randomly assigned to start with the low-IgG challenge and 18 to the high-IgG challenge. Each challenge was followed by the other challenge. 13 of 29 low-IgG challenges and 13 of 29 high-IgG challenges resulted in a relapse of ADHD behaviour. No relapse was reported in 11 of 29 children, eight had relapses after both challenges, 15 had relapses after the first challenge, and 11 after the second challenge. The sequence of the challenges (low-IgG then high-IgG or high-IgG then low-IgG) was not significantly associated

	Diet group (parent n=50; teacher n=37)						Control group (parent n=50; teacher n=40)						End rating*	
	Start	End (week 9)	Difference (95% CI)	p value†	Scale reduction (%)	Cohen's d	Start	End (week 13)	Difference (95% CI)	p value†	Scale reduction (%)	Cohen's d	Difference (95% CI)	p value†
ADHD rating scale														
Parent total score (JT; 0–54)	45·3 (4·7)	21·1 (16·8)	24·2 (19·5–29·0)	<0·0001	53·4	2·0	47·6 (4·1)	46·2 (5·8)	1·3 (0·2 to 2·5)	0·023	2·7	0·28	23·7 (18·6–28·8)	<0·0001
Teacher total score (LP; 0–54)	34·4 (6·7)	20·1 (10·1)	14·3 (11·6–17·1)	<0·0001	41·6	1·67	39·2 (7·8)	39·6 (8·6)	−0·4 (−1·7 to 1·0)	0·580	−1·0	−0·05	15·3 (12·0–18·6)	<0·0001
Parent inattention score (JT; 0–27)	21·2 (4·1)	9·9 (9·0)	11·3 (8·9–13·8)	<0·0001	53·3	1·62	23·2 (3·5)	22·9 (3·6)	0·2 (−0·4 to 0·8)	0·433	0·9	0·09	11·8 (9·1–14·4)	<0·0001
Teacher inattention score (LP; 0–27)	15·1 (5·7)	8·6 (6·1)	6·5 (4·9–8·2)	<0·0001	43·0	1·10	19·5 (5·2)	19·3 (5·2)	0·3 (−0·6 to 1·1)	0·587	1·5	0·04	7·4 (5·4–9·4)	<0·0001
Parent hyperactivity and impulsivity score (JT; 0–27)	24·1 (3·5)	11·2 (8·6)	12·9 (10·5–15·3)	<0·0001	53·5	1·96	24·4 (3·1)	23·3 (4·5)	1·1 (0·2 to 2·0)	0·012	4·5	0·28	11·9 (9·3–14·5)	<0·0001
Teacher hyperactivity and impulsivity score (LP; 0–27)	19·3 (5·0)	11·5 (6·0)	7·8 (6·2–9·5)	<0·0001	40·4	1·41	19·7 (6·6)	20·3 (6·3)	−0·6 (−1·4 to 0·2)	0·128	−3·0	−0·09	8·5 (6·8–10·3)	<0·0001
Abbreviated Conners' scale														
Parent (LP; 0–30)	23·7 (3·4)	11·7 (8·7)	12·0 (9·4–14·6)	<0·0001	50·7	1·82	23·5 (3·9)	23·4 (4·7)	0·1 (−0·7 to 0·8)	0·828	0·3	0·02	11·8 (9·2–14·5)	<0·0001
Teacher (LP; 0–30)	18·5 (3·8)	11·9 (6·7)	6·6 (4·9–8·4)	<0·0001	35·9	1·22	19·1 (4·5)	19·9 (4·6)	−0·8 (−1·4 to −0·3)	0·003	−4·3	−0·18	7·5 (5·9–9·2)	<0·0001
Structured psychiatric interview														
Parent ODD score (JT; 0–8)‡	5·5 (1·1)	1·9 (2·3)	3·6 (2·5–4·6)	<0·0001	65·4	2·00	5·5 (1·2)	5·3 (1·4)	0·2 (−0·3 to 0·7)	0·488	3·6	0·15	3·6 (2·5–4·8)	<0·0001
Teacher ODD score (LP; 0–8)§	4·9 (1·1)	2·1 (2·9)	2·8 (1·5–4·0)	<0·0001	57·1	1·28	5·2 (1·1)	5·0 (1·7)	0·2 (−0·4 to 0·9)	0·501	3·8	0·14	2·0 (0·2–3·9)	0·0320

Data are mean (SD). All data are masked, except for the teacher ratings and the abbreviated Conners' scale ratings. ADHD=attention-deficit hyperactivity disorder. JT=masked paediatrician. LP=unmasked researcher. ODD=oppositional defiant disorder. *Adjusted for score at start and block. The interaction between block and group was not significant (generalised linear model) and the link test showed sufficient fit in all analyses. †Generalised linear model. ‡Diet group n=20, control group n=27. §Diet group n=8, control group n=13.

Table 3: ADHD rating scale, abbreviated Conners' scale, and structured psychiatric interview scores at start and end of the first phase

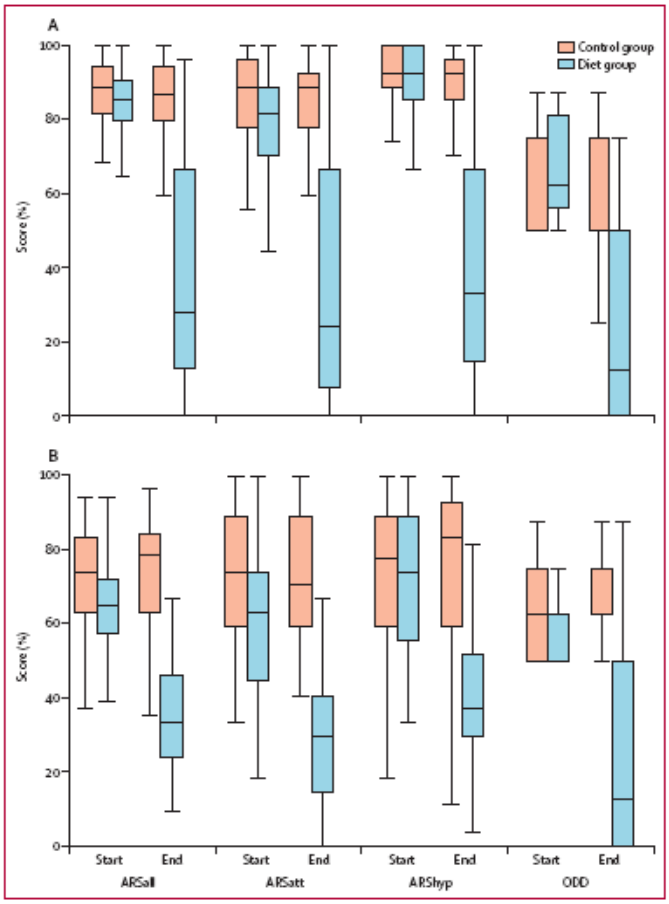

Figure 2: **Distribution of behaviour scores at start and end of the first phase**
Scores according to (A) masked paediatrician ratings and (B) unmasked teacher ratings. To facilitate comparison between the various measures, scores have been standardised as percentages of the maximum score per measure. Bars=maximum and minimum score. Shaded boxes=interquartile range. Horizontal bars within boxes=median. ADHD=attention-deficit hyperactivity disorder. ARSall=ADHD rating scale total score (maximum score 54). ARSatt=ADHD rating scale inattention score (maximum score 27). ARShyp=ADHD rating scale hyperactivity and impulsivity score (maximum score 27). ODD=oppositional defiant disorder (maximum score 8).

with the relapse of ADHD symptoms (Mainland-Gart p=1·0; Prescott p=0·38). The generalised estimated equations model showed no significant effects of IgG type (high-IgG *vs* low-IgG OR 0·86, 95% CI 0·36–2·09; p=0·75) or challenge period (first challenge *vs* second challenge 0·55, 0·23–1·33; p=0·26). Parents, teachers, and children reported no harms or adverse events in the first or second phase.

Discussion

In the INCA study, the restricted elimination diet had a significant beneficial effect on ADHD symptoms in 32 (64%) of 50 children, and reintroducing foods led to a significant behavioural relapse in clinical responders. Blood tests assessing IgG levels against foods did not predict which foods might have a deleterious behavioural effect. The effect of the diet was consistent and had a similar effect in reducing both ADHD and oppositional defiant disorder symptoms. Because of the worse prognosis of children with comorbid oppositional defiant disorder compared with those without comorbid disease, interventions that reduce oppositional defiant disorder symptoms have great clinical potential. The number of children with conduct disorder was, in accordance with the young age of the patients, too small to draw conclusions.

Total IgE levels were increased only in a few children, equally in responders and non-responders, suggesting that the underlying mechanism of food sensitivity in ADHD (which could be related to genetic factors[28]) is non-allergic, although we cannot rule out the involvement of a cell-mediated allergic response. In the second phase, some eliminated foods were added to the diet of the responders. Although the challenges consisted of only two groups of three different individually selected foods, there was a substantial relapse in behaviour in 63% of children. We recorded no difference in behavioural effects after challenge with high-IgG or low-IgG foods. These results suggest that use of IgG blood tests to identify which foods are triggering ADHD is not advisable. However, IgG blood tests might be useful in other diseases.[29,30]

Our results must be viewed in light of some limitations. First, in the first phase, we did an open-label randomised controlled trial with masked measurements by an independent paediatrician because parents, teachers, and researchers could not be masked. This method is generally accepted and applied when a double-blind randomised controlled trial cannot be done.[31–37] Nevertheless, expectations of the parents cannot be fully ruled out as a possible cause of the behavioural improvements. Theoretically, the fact that the second assessment was done by the paediatrician after 9 weeks in the diet group compared with after 13 weeks in the control group might have led to unmasking of the paediatrician. To prevent this from happening, the paediatrician was not informed about any previous assessments. Because of the number of children included, with new children starting every week, and some children from the diet and control groups returning every week for their second assessments, the paediatrician was unlikely to remember whether he had seen a particular child 9 or 13 weeks earlier. Parents were also instructed not to reveal any information about group assignment. Second, we cannot rule out that the behavioural improvements during the first phase might have been caused by increased attention for the child in the diet group. However, to avoid differences between groups the control group received healthy food advice and parents kept an extended diary of their child's

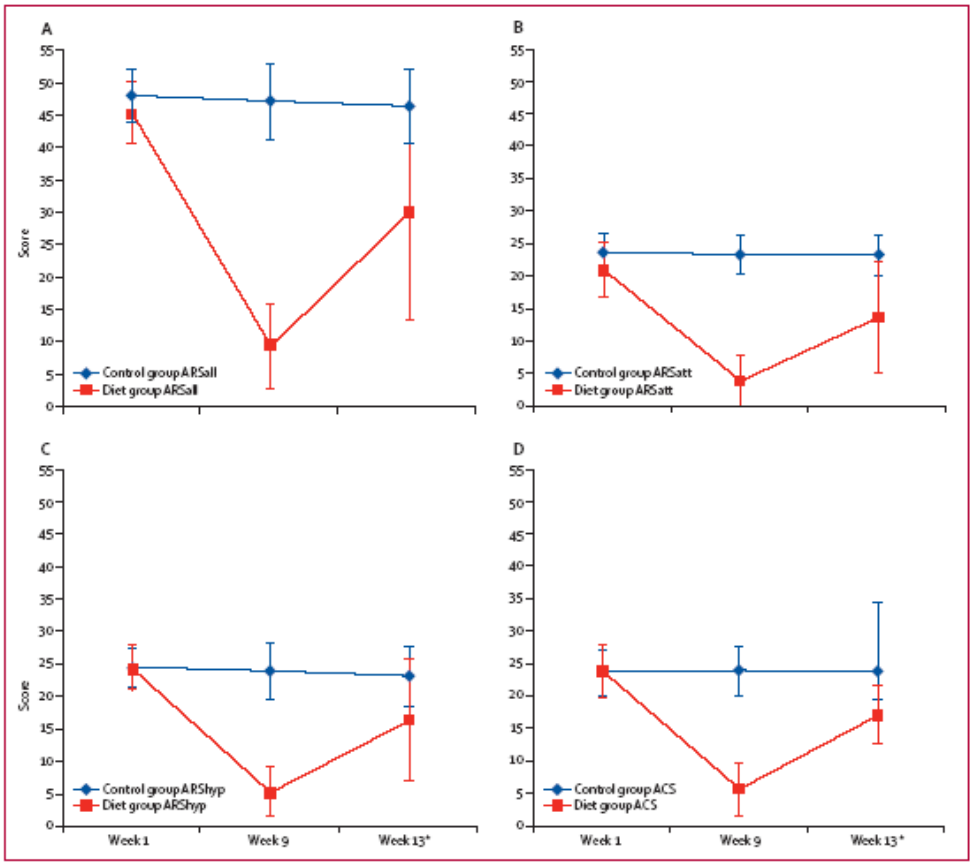

Figure 3: Behaviour scores at week 1, week 9, and week 13*

ARS total (A), inattention (B), and hyperactivity and impulsivity scores (C), and ACS scores (D) for the diet (n=30) and control (n=42) groups at week 1 (start), week 9 (end of the first phase in the diet group and during the first phase in the control group), and week 13 (end of the second phase in the diet group and end of the first phase in the control group). All ARS scores were masked paediatrician ratings except for the week 9 control group scores. All ACS scores were unmasked, except for the scores in the diet group at the end of the second phase. Error bars=SD. ADHD=attention-deficit hyperactivity disorder. ACS=abbreviated Conners' scale. ARSall=ADHD rating scale total score (maximum score 54). ARSatt=ADHD rating scale inattention score (maximum score 27). ARShyp=ADHD rating scale hyperactivity and impulsivity score (maximum score 27). *Week 11 in case of behavioural relapse in the diet group.

behaviour during the trial. Furthermore, the relapse in behaviour during the second phase, which required comparable parental attention as in the first phase, might be regarded as an internal replication of the effects of the diet. Third, we applied a tailor-made diet for each child to minimise the burden of the diet. In 24 (59%) of 41 children this individually composed diet proved to be sufficient.

A strength of the INCA study was its design, which included multiple ratings, its large sample size, and blood tests to investigate the existence of an immunological mechanism of action. Furthermore, the heterogeneous sample is representative of the general population of children with ADHD, and thus the results of our study are applicable to young children with ADHD whose parents are motivated to follow a 5-week dietary investigation period (panel). Another strength is the investigation of the effects of the diet on comorbid disorders such as oppositional defiant disorder. The results of the multiple ratings are consistent, which provides evidence for the clinically relevant beneficial effects of a restricted elimination diet on ADHD and oppositional defiant disorder.

The mechanisms and effects of food need to be investigated—eg, at a functional and structural brain level and in relation to genetic factors that increase the susceptibility to ADHD. Also, the challenge procedure, which is done to identify the incriminated foods in

Panel: Research in context

Systematic review

We first searched PubMed and the Cochrane Library with no date limits set (search terms "ADHD AND diet", "ADHD AND elimination diet" and "ADHD AND food") and then screened the references of relevant articles. Our search identified seven published randomised controlled trials[10,13,38–42] that applied some form of restricted elimination diet (ie, a diet that did not just focus on single foods such as additives or sugar) in children with ADHD.

Interpretation

The total number of children involved in these trials was 188 (age 2–15 years), and all trials showed evidence for the efficacy of a restricted elimination diet on ADHD. The overall weighted effect size of this group of heterogeneous studies was 1·6, but treatment groups were either small or only patients who had an allergic constitution were included, which thus impeded extrapolation of the results to the general population. Our study shows comparable effect sizes in patients who are representative of the general ADHD population, supporting the implementation of a dietary intervention in the standard of care for all children with ADHD.

clinical responders, should be made as easy as possible to follow, to increase the feasibility of the diet. Furthermore, the long-term effects of foods should be investigated; children might outgrow the sensitivity to the incriminating foods when they are avoided for a long period of time.

Our study shows considerable effects of a restricted elimination diet in an unselected group of children with ADHD, with equal effects on ADHD and oppositional defiant disorder. Therefore, we think that dietary intervention should be considered in all children with ADHD, provided parents are willing to follow a diagnostic restricted elimination diet for a 5-week period, and provided expert supervision is available. Children who react favourably to this diet should be diagnosed with food-induced ADHD and should enter a challenge procedure, to define which foods each child reacts to, and to increase the feasibility and to minimise the burden of the diet. In children who do not show behavioural improvements after following the diet, standard treatments such as drugs, behavioural treatments, or both should be considered.

Contributors

LMP wrote the proposal, was study coordinator, and wrote the final version of the manuscript. KF entered data and designed and undertook the data analysis. JT collected data, assessed patients, and edited earlier versions of the manuscript. RRP, TAH, NNR, and JKB provided advice on the field work. HFS and AED provided immunological advice. JKB also contributed to the development of the protocol and study design. All authors interpreted the data, commented on the manuscript, and approved the final version.

Conflicts of interest

LMP is franchiser of the ADHD Research Centre. In the past 4 years, TAH has been a speaker on symposia and courses organised by or subsidised by Janssen-Cilag and Eli Lilly. In the past 3 years, JKB has been a consultant, member of advisory board, speaker, or a combination thereof for Janssen Cilag, Eli Lilly, Bristol-Myers Squibb, Schering Plough, UCB, Shire, Medice, and Servier. All other authors declare that they have no conflicts of interest.

Acknowledgments

This study was supported by grants from the Foundation of Child and Behaviour, Foundation Nuts Ohra, Foundation for Children's Welfare Stamps Netherlands, and the KF Hein foundation. We thank Marjan de Boer (Dutch Food Allergy Organisation) for her contribution to the advisory board and expert advice; and Karin van Geene, Gerrie Raats, and Petrie van Meijel for their kind and valuable contributions. We thank the staff of Catharina Hospital Eindhoven for their commitment, and all parents, guardians, children, and teachers who participated in the INCA study.

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Restricted elimination diet for ADHD: the INCA study

See Articles page 494

Psychopharmacological and psychosocial treatments are evidence-based treatments for attention-deficit hyperactivity disorder (ADHD). However, concerns about side-effects of psychoactive drugs, and barriers to access to and commitment needed for psychosocial treatments, often lead to consideration of other interventions.[1] One such intervention relates to the tenet that hypersensitivity or intolerance to foods or additives is a risk factor for ADHD.[2]

In *The Lancet*, Lidy Pelsser and colleagues[3] report a two-phase randomised trial (INCA) with a control or a diet group in 100 children diagnosed with ADHD, who were aged 4–8 years and unselected for any food sensitivities. After a 2-week baseline period, controls were placed on a waiting list and continued normal eating, and their parents received healthy food advice and kept a diary of their child's behaviour. The diet group received a 5-week open trial with a restricted elimination diet of oligoantigenic few foods (rice, meat, vegetables, pears, water) complemented with specific foods such as potatoes, fruits, and wheat. Of the 41 diet-group children who completed phase 1, 17 (41·5%) had no behavioural response to the diet by the end of week 2 and their diet was further restricted to few foods only. At the end of phase 1, symptoms of ADHD and oppositional defiant disorder significantly improved in 64% children in the diet group compared with no improvement in the controls. Phase 1 clinical responders then had a double-blind crossover food challenge in random order with 2 weeks each of three high IgG and three low IgG foods added to the elimination diet or the few-foods diet. Selection of the high and low IgG foods was based on individual total IgG levels to 270 different foods. Relapse of ADHD symptoms occurred with the first, second, or both food challenges in 19 of the 30 children entering the crossover phase (phase 2). IgG levels against foods did not predict which foods might lead to a negative effect on behaviour because an equal number of low and high IgG food challenges resulted in relapse of ADHD symptoms.

Corbis

Studies with restricted elimination diets are complex and challenging. Pelsser and colleagues' study was well-designed and carefully done, showed benefit with a supervised elimination diet, and provides an additional treatment option for some young children with ADHD. The study also provides evidence against the benefit of using IgG blood levels (a common practice in complementary medicine) to determine which foods are triggering ADHD symptoms. However, it is important to note that 36% of children either did not respond to the elimination diet or were non-compliant in phase 1. Additionally, there were at least 16 other

eligible children who were not motivated to enter the study. To help provide guidance to practitioners and families about appropriate options for their child, it will be helpful to know which children can be predicted to respond to the diet.

The blinded assessments in Pelsser and colleagues' study were based on information provided by parents. However, the parents and teachers were aware whether the children received the elimination diet or not in phase 1, and that the children entering phase 2 received the challenge foods (the only information the parents and teachers were blind to pertained to whether the challenge foods were low or high IgG foods). Therefore, in both the control and diet groups, the beliefs and expectations of parents and teachers about changes in the ADHD symptoms could have been influenced by this knowledge. Hence, it is important to use more objective measures for treatment outcomes in these investigations.

In phase 2, ADHD symptoms relapsed in 19 of 30 (63%) children in response to the food challenge. We do not know which of the six foods in the food challenge caused the hypersensitivity, nor whether some of the other 264 remaining foods might also cause hypersensitivity in the 19 children who relapsed and 11 who did not relapse in phase 2. To provide guidance to families and to avoid unnecessary dietary restrictions over long periods, identifying the incriminated foods is important. Also, Pelsser and colleagues reported only short-term benefit from the dietary restriction; however, maintenance of benefits over time and any long-term effects of dietary elimination on the child's nutritional status are unknown.

Feingold[2] first introduced the idea that many children are sensitive to dietary salicylates and artificially added food colours, flavours, and preservatives, and that eliminating the offending substances could ameliorate learning and behavioural problems, including ADHD. Population-based studies have reported behavioural sensitivity to artificial food colours and preservatives in children with or without ADHD.[4,5] Food manufacturers are under increasing pressure from consumer groups and researchers to avoid these additives, to include a warning on the label about adverse effects on activity and attention of children, or both.[6]

Elimination diet studies suggest behavioural sensitivity to common salicylate and non-salicylate foods. Parents of children with ADHD should be made aware of the research about behavioural sensitivity to common foods and additives in some children. For interested parents, a careful dietary elimination strategy can be implemented especially in younger children, because dietary elimination can be more practical and more effective in younger children because of better control of the diet by the caregiver.[7,8] An elimination diet trial should be implemented only under the supervision of the child's primary health-care provider and a nutritionist to ensure that growing children do not suffer from nutritional deficiencies with the restricted diet.[7,8] On the basis of parental preference, dietary elimination can be done by itself or with standard recommended treatments for ADHD.

Diagnosing food sensitivity is complex, can take several weeks, and can be burdensome for families to implement. The restricted diet can be tried for 2–5 weeks.[3,8] If there is benefit, the restricted foods can be added back weekly, one food component at a time, to identify the problem foods to be excluded from a less restrictive permanent diet. In my opinion, a stringent elimination diet should not continue for more than 5 weeks without obvious benefit because of the time, effort, and resources required to implement the restricted diet and because long-term effects of dietary elimination on the child's nutritional status are not known.

To advance the field and provide clinical guidance to practitioners and parents, future studies should identify the specific incriminated foods responsible for the hypersensitivity reaction, include more objective and functional outcome measures, address predictors of response and non-response, address long-term effectiveness and tolerability of the dietary restriction, evaluate the nutritional composition of the elimination diet, investigate the impact of long-term dietary elimination on the child's nutritional status, and report on compliance, acceptance, and level of ease or difficulty in maintaining the dietary restriction.

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I declare that I have no conflicts of interest.

1 Dulcan MK, Benson RS. AACAP official action: summary of the practice parameters for the assessment and treatment of children, adolescents, and adults with ADHD. *J Am Acad Child Adolesc Psychiatry* 1997; 36: 1311–17.

Provincia di Milano

COD. 2680

AUTISMO: Corso di formazione teorico-pratico rivolto a dirigenti di servizi dedicati all'autismo

Titolo: Stato dell'arte e prospettive future per i servizi dedicati all'autismo

Premessa

Dal 2007 la Provincia di Milano, in collaborazione con il Coordinamento Autismo, ha progettato e realizzato moduli formativi teorico/pratici, rivolti agli operatori della rete di servizi, attivata inizialmente nell'ambito del Progetto Sperimentale Sindrome Autistica della Regione Lombardia (nel 2000-2003 sono stati coinvolti 8 servizi/polo autismo). Nella fase attuale del progetto *in service* risultano essere coinvolti 33 servizi. La formazione è stata definita in service, poiché si configura come prassi di confronto teorico-pratico fra operatori di servizi che si occupano di autismo. Il gruppo di lavoro è costituito da referenti della Provincia di Milano, dal Coordinamento Autismo, dall' Associazione genitori ANGSA Lombardia e dal Gruppo Asperger. Nel 2010 è stato realizzato un corso sperimentale dedicato a dirigenti e coordinatori di servizi dedicati parzialmente o totalmente all'autismo, che ha inoltre previsto l'avvio di una ricerca realizzata dal'università IULM, volta a valutare l'efficacia applicativa del modello formativo *in service.* La Provincia di Milano –Settore Formazione per operatori sociali – si è impegnata formalmente a sostenere (ottobre 2010-maggio 2011) la prosecuzione dell'esperienza in service: saranno pertanto realizzati tre moduli formativi- rivolti a famiglie, dirigenti-coordinatori e tecnici, operatori (nel periodo ottobre 2010-maggio 2011). Il presente modulo, che verrà realizzato nel periodo febbraio-marzo 2011, è rivolto a dirigenti, coordinatori, neuropsichiatri, psichiatri e psicologi che operano nei servizi della rete *in* service.

Obiettivi

- Il secondo modulo dell'in service *dirigent*i, prendendo spunto dalle riflessioni emerse nell'ambito della prima esperienza realizzata nel periodo febbraio-marzo 2010, si prefigge di mettere a confronto diversi modelli organizzativi e di presa in carico. Sempre più spesso all'interno della comunità scientifica internazionale e nazionale, delle associazioni di familiari di disabili e dei servizi dedicati alle persone disabili si assiste alla discussione sull'appropriatezza e efficacia dei diversi trattamenti, sui vantaggi di differenti modelli organizzativi e di presa in carico delle persone disabili e, ultimamente, sulla necessità o meno di individuare servizi "ad hoc" per categorie diagnostiche, ad esempio servizi ad hoc per autistici.
- Verrà ripreso e approfondito il tema dei Percorsi Diagnostici Terapeutici e Assistenziali (PDTA) per minori, adolescenti e adulti con autismo.

- Elemento di elevata criticità resta il passaggio dai servizi di neuropsichiatria a quelli della psichiatria: verrà affrontata la questione della Psicopatologia nell'ambito della disabilità intellettiva, della disabilità evolutiva e dell'autismo.

PROGRAMMA

- ✓ **Modello di presa in carico basato sul costrutto di qualità di vita elaborato da R. Schalock e A. Verdugo Alonso (2004): lavoro svolto dal 2006 ad oggi presso il Dipartimento Disabili dell'Istituto Ospedaliero di Sospiro.** Verranno trattati i seguenti argomenti:

  a. *priorità a progetti di vita in ottica esistenziale partendo dai bisogni di autodeterminazione delle persone con disabilità (M. Wehmeyer 2010);*
  b. *necessità di selezionare sistemi appropriati di identificazione dei bisogni di sostegno delle persone disabili (Support Intensity Scale, J. Thompson et alt. 2004);*
  c. *possibilità di individuare interventi appropriati partendo non tanto dalle categorie diagnostiche delle persone disabili, ma dal loro funzionamento e dai loro bisogni di sostegno.*

- ✓ **Percorsi Diagnostici Terapeutici e Assistenziali (PDTA) per minori, adolescenti e adulti con autismo: una possibile guida operativa per la contestualizzazione di principi e linee guida.**

- ✓ **Psicopatologia nell'ambito della disabilità intellettiva e delle disabilità evolutiva**. Tematiche che verranno affrontate:

  a. *la correttezza e la completezza della diagnosi sulla base dei sistemi attuali e futuri di codifica diagnostica (DSM-IV TR,DSM V, ICD 10, ICD 11, Sistema 0-3);*
  b. *la dicotomia tra psicopatologia e disturbi del comportamento da un punto di vista eziologico, clinico e funzionale;*
  c. *la fruibilità delle informazioni diagnostiche cliniche nella definizione degli obiettivi abilitativi, riabilitativi e educativi, in un' ottica ecologica e secondo modelli scientificamente fondati come AAIDD 11 edizione/Qualità di Vita;*
  d. *il superamento del concetto di doppia tripla...diagnosi verso la concettualizzazione di diagnosi complessa;*
  e. *la operazionalizzazione nelle procedure diagnostiche del contributo del paradigma della complessità in ambito clinico ed educativo, da allineare agli standard delle opportune e necessarie linee guida;*
  f. *l'integrazione tra strumenti e tecniche di tipo clinico come i manuali diagnostici e le interviste diagnostiche, con sistemi di classificazione del funzionamento umano (es.ICF e ICF CY) e di individuazione dei bisogni di sostegno (come la SIS);*
  g. *la specificazione delle stesse tematiche nel contesto dell'Autismo e nella fase critica del passaggio tra la gestione da parte dei servizi di Neuropsichiatria Infantile, e la problematica gestione della Psichiatria successivamente;*
  h. *la definizione di un razionale più convincente nelle prescrizioni psicofarmacologiche, sempre in una prospettiva integrata ed orientata al miglioramento della Qualità di Vita della Persona e dei suoi familiari.*

- ✓ **Strumenti che aiutano a valutare l'efficacia della formazione in service: ricerca realizzata dall'Università IULM di Milano.**

- ✓ **Sito esperienza in service: collaborazione con la Cooperativa LEM di Milano**

Metodologia

Il taglio dell'in service prevede un diretto e attivo coinvolgimento dei corsisti: pertanto agli interventi formativi frontali si alterneranno focus group, sottogruppi di confronto e elaborazione, restituzioni in sede plenaria.

Docenti

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GIUSEPPE CHIODELLI

Medico Psichiatra- Direttore Unità Operativa Medicina- Dipartimento Disabili -Fondazione Sospiro Cremona.

Destinatari

Dirigenti, coordinatori, psicologi, neuropsichiatri, psichiatri, assistenti sociali di servizi sanitari, educativi, scolastici, socio assistenziali della rete *in service*.

Periodo di realizzazione e orario

Il percorso formativo si svolgerà in tre giornate:

18 e 19 febbraio 2011
18 marzo 2011
dalle ore 9.00 alle ore 17.00

ECM

E' previsto l'accreditamento del percorso formativo per le seguenti figure professionali: psichiatri, neuropsichiatri, psicologi, medici, educatori professionali.

Sede e costi

- Provincia di Milano, Sala Guicciardini, Via Macedonio Melloni, 3 Milano.
- La partecipazione al corso prevede una quota d'iscrizione di 30 euro

Dati relativi ai conti correnti per effettuare il versamento:

- Intesa Sanpaolo - tesoreria provinciale Via Corridoni n. 45
  Conto corrente bancario n. 1009/22

IBAN IT86 D030 6901 7750 0000 0100 922

oppure

- Conto corrente postale intestato alla Provincia di Milano n. 52889201

Attestato frequenza

La Provincia di Milano rilascerà un attestato di frequenza ai corsisti che parteciperanno ad almeno il 75% del monte ore complessivo. Gli operatori che richiederanno gli ECM non avranno l'attestato della Provincia di Milano

Modalità e tempi d'iscrizione

E' possibile inviare la scheda d'iscrizione, tramite fax alla segreteria della coop. I Percorsi 02.89544742 o per e- mail a sportello@ipercorsicoop.org **entro il 27.01.2011.**

L'avvenuta iscrizione sarà confermata tramite comunicazione telefonica e/o e mail.

Per comunicazioni/informazioni

Segreteria I Percorsi tel 02.39198989 Signora Colombo o Signora Arias
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Per la Provincia di Milano: Coordinatrice Brunella Castelli tel 02.77403179 e mail
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ASSP ONLUS
Associazione Servizi Sociali Padova

CDA
Centro Diurno Archimede

L'ADHD DALL'INFANZIA ALL'ETA' ADULTA: NUOVE EVIDENZE

25 – 26 febbraio 2011
Centro Congressi Fiera di Vicenza

PROGRAMMA

Venerdì 25 febbraio 2011 – ore 14,30

ore 14,30	Registrazione partecipanti
ore 15,00	Apertura dei lavori Lauretta Furlan – Presidente ASSP – CDA Saluto delle Autorità
Modera e presiede:	Patrizia Bisiacchi
ore 15,30 – 17,10	Russell A. Barkley **L'ADHD dai primi contributi alla sua attuale definizione diagnostica**
ore 17,15 – 17,30	coffee – break
ore 17,30 – 18,15	Claudio Vio **Il contributo della neuropsicologia nell'interpretazione dell'ADHD**
ore 18,15 – 18,30	Discussione e chiusura lavori

Sabato 26 febbraio 2011 – ore 9,00

Modera e presiede:	Roberto Tombolato
ore 9,00 – 10,15	Russell A. Barkley **L'ADHD in una prospettiva evolutiva: dall'infanzia all'adolescenza**
ore 10,15 – 10,30	coffee – break
ore 10,30 – 11,15	Dino Maschietto **Percorso diagnostico e diagnosi differenziale**
ore 11,15 – 12,00	Stefano Vicari **Caratteristiche cognitive e comorbidità psichiatrica**
ore 12,15	Discussione
ore 12,30	Pranzo
Modera e presiede:	Stefano Vicari
ore 14,00 – 15,30	Russell A. Barkley **Nuove evidenze sull'intervento**
ore 15,30 – 15,45	coffee – break
ore 15,45 – 17,15	**Tavola Rotonda** con Dino Maschietto, Stefano Vicari e Anna Re **L'intervento per l'ADHD in ambito Italiano**
ore 17,15 – 17,30	Discussione, compilazione questionari di gradimento e apprendimento Chiusura lavori

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Per ricevere la newsletter iscriversi al seguente indirizzo:
http://crc.marionegri.it/bonati/adhdnews/subscribe.html

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'adolescenza
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G.R. n. 10804 del 16/12/2009)
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"
"*Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia*".

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