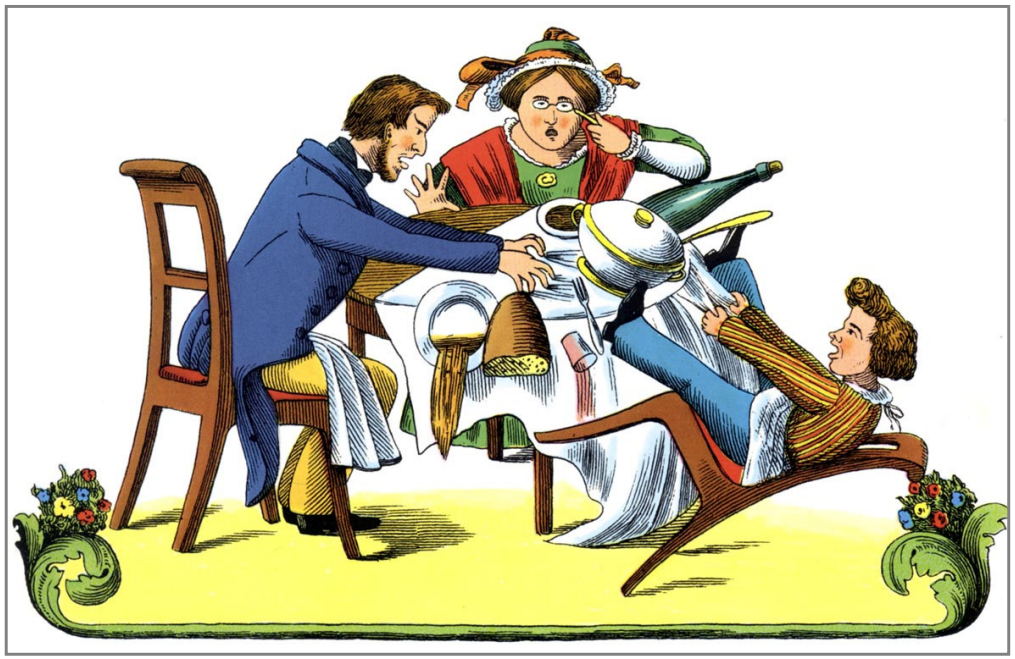
Aufmerksamkeitsdefizit-/Hyperaktivitätsstörungen - Update



Tobias Banaschewski

Klinik für Psychiatrie und Psychotherapie des Kindes- und Jugendalters,

Zentralinstitut für Seelische Gesundheit, Mannheim

Potentielle Interessenkonflikte

- Mitglied in Advisory Boards / Beratende Tätigkeit
  eyelevel, Infectopharm, Lundbeck, Medice, Neurim Pharmaceuticals, Oberberg GmbH, Roche, and Takeda
- Vortragshonorare
  Janssen, Medice, Takeda
- Forschungsförderung
  EU, DFG & BMBF

Definition

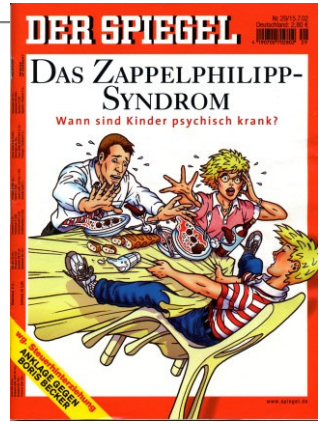
Kernsymptome

- Unaufmerksamkeit
- Motorische Hyperaktivität
- Mangelnde Impulskontrolle

- Beginn in Kindheit
- Nicht Alter, Intelligenz entsprechend
- Dauer (mindestens 6 Monate)
- Beeinträchtigungen in mind. 2 Lebensbereichen
- Nicht durch eine andere psychische Störung erklärbar

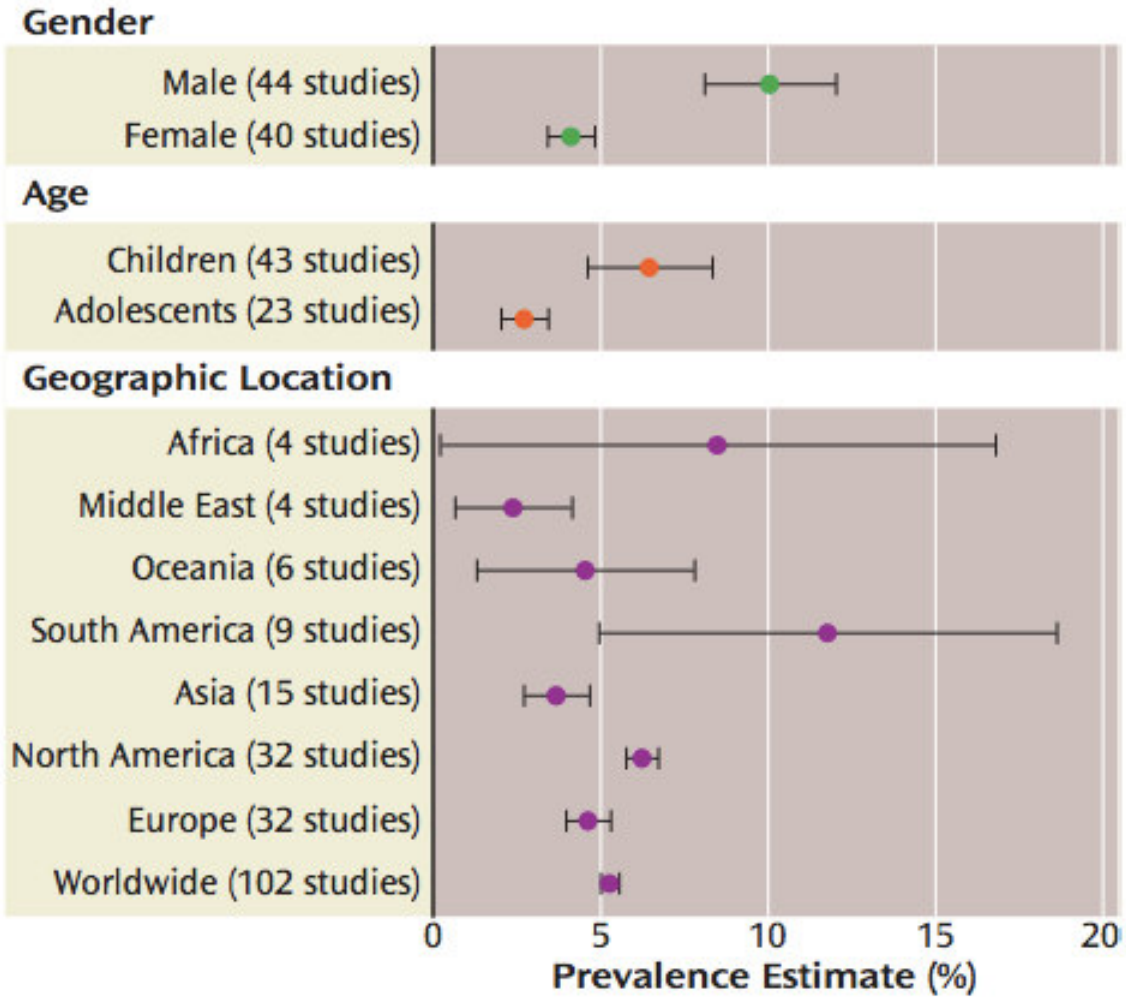
Klinische Relevanz

- ADHS ist eine häufige Störung: 3-6%
- ADHS ist eine chronische Störung
  - 30-60% Persistenz frühes Erwachsenenalter
- Assoziierte Störungen sind der Regelfall
  - Ca. 65-80 % mind. 1 assoziierte Störung
  - > 50 % mindestens 2 assoziierte Störungen
- ADHS führt oft zu psychosozialen Beeinträchtigungen
  - Z.B. schulische & berufliche Entwicklung, soziale Beziehungen, Unfallrisiko, Delinquenz



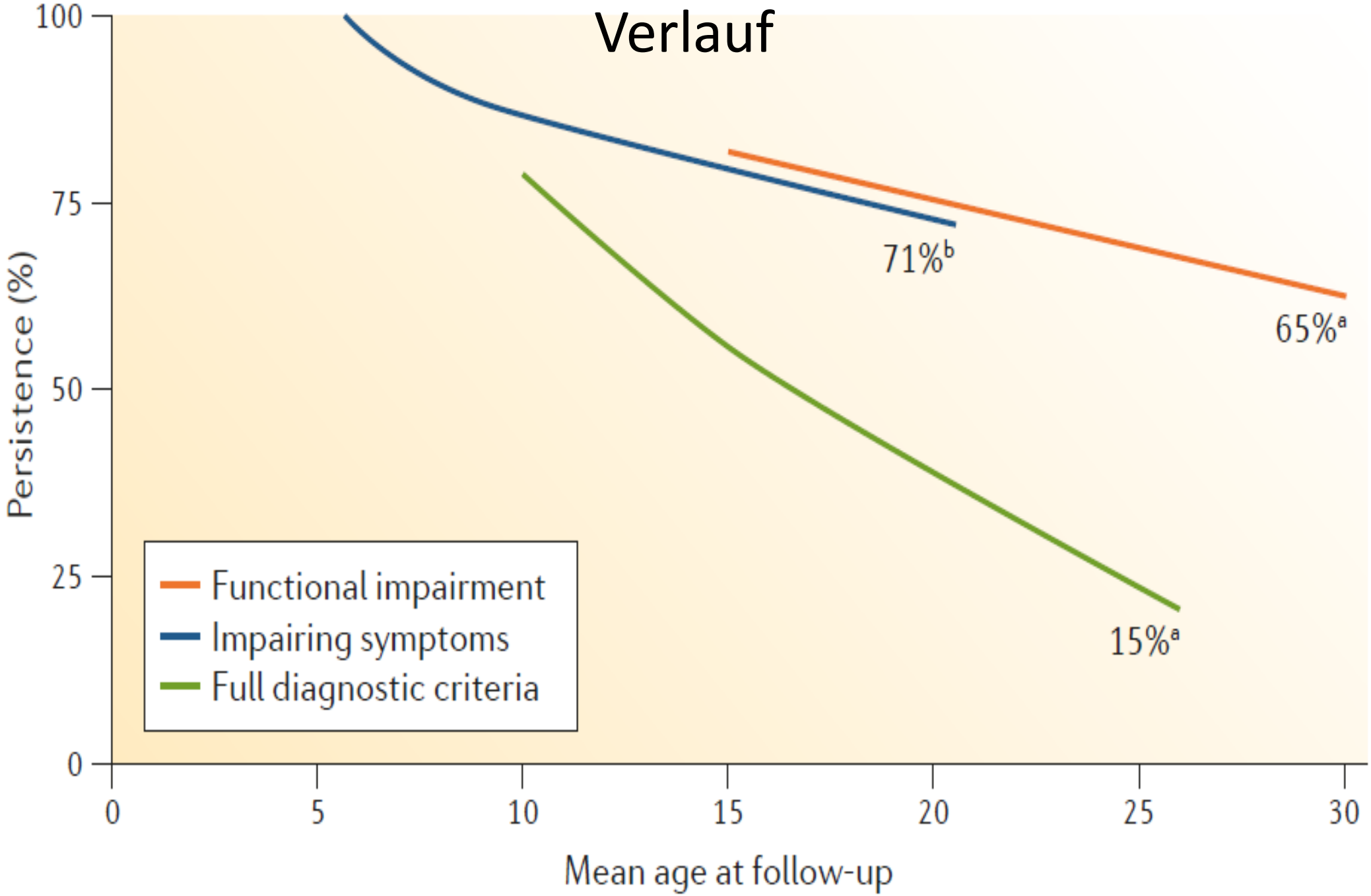
Epidemiologische Prävalenz

- ADHS ist eine häufige Störung: 3-6%



Polanczyk et al., 2007

Verlauf



Nature Reviews | Disease Primers

Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study

Am J Psychiatry 172:10, October 2015

Terrie E. Moffitt, Ph.D., Renate Houts, Ph.D., Philip Asherson, M.D., Daniel W. Belsky, Ph.D., David L. Corcoran, Ph.D., Maggie Hammerle, B.A., HonaLee Harrington, B.A., Sean Hogan, M.S.W., Madeline H. Meier, Ph.D., Guilherme V. Polanczyk, M.D., Richie Poulton, Ph.D., Sandhya Ramrakha, Ph.D., Karen Sugden, Ph.D., Benjamin Williams, B.A., Luis Augusto Rohde, M.D., Avshalom Caspi, Ph.D.

Objective: Despite a prevailing assumption that adult ADHD is a childhood-onset neurodevelopmental disorder, no prospective longitudinal study has described the childhoods of the adult ADHD population. The authors report follow-back analyses of ADHD cases diagnosed in adulthood, alongside follow-forward analyses of ADHD cases diagnosed in childhood, in one cohort.

Method: Participants belonged to a representative birth cohort of 1,037 individuals born in Dunedin, New Zealand, in 1972 and 1973 and followed to age 38, with 95% retention. Symptoms of ADHD, associated clinical features, comorbid disorders, neuropsychological deficits, genome-wide association study-derived polygenic risk, and life impairment indicators were assessed. Data sources were participants, parents, teachers, informants, neuropsychological test results, and administrative records. Adult ADHD diagnoses used DSM-5 criteria, apart from onset age and cross-setting corroboration, which were study outcome measures.

Results: As expected, childhood ADHD had a prevalence of 6% (predominantly male) and was associated with childhood comorbid disorders, neurocognitive deficits, polygenic risk, and residual adult life impairment. Also as expected, adult ADHD had a prevalence of 3% (gender balanced) and was associated with adult substance dependence, adult life impairment, and treatment contact. Unexpectedly, the childhood ADHD and adult ADHD groups comprised virtually nonoverlapping sets; 90% of adult ADHD cases lacked a history of childhood ADHD. Also unexpectedly, the adult ADHD group did not show tested neuropsychological deficits in childhood or adulthood, nor did they show polygenic risk for childhood ADHD.

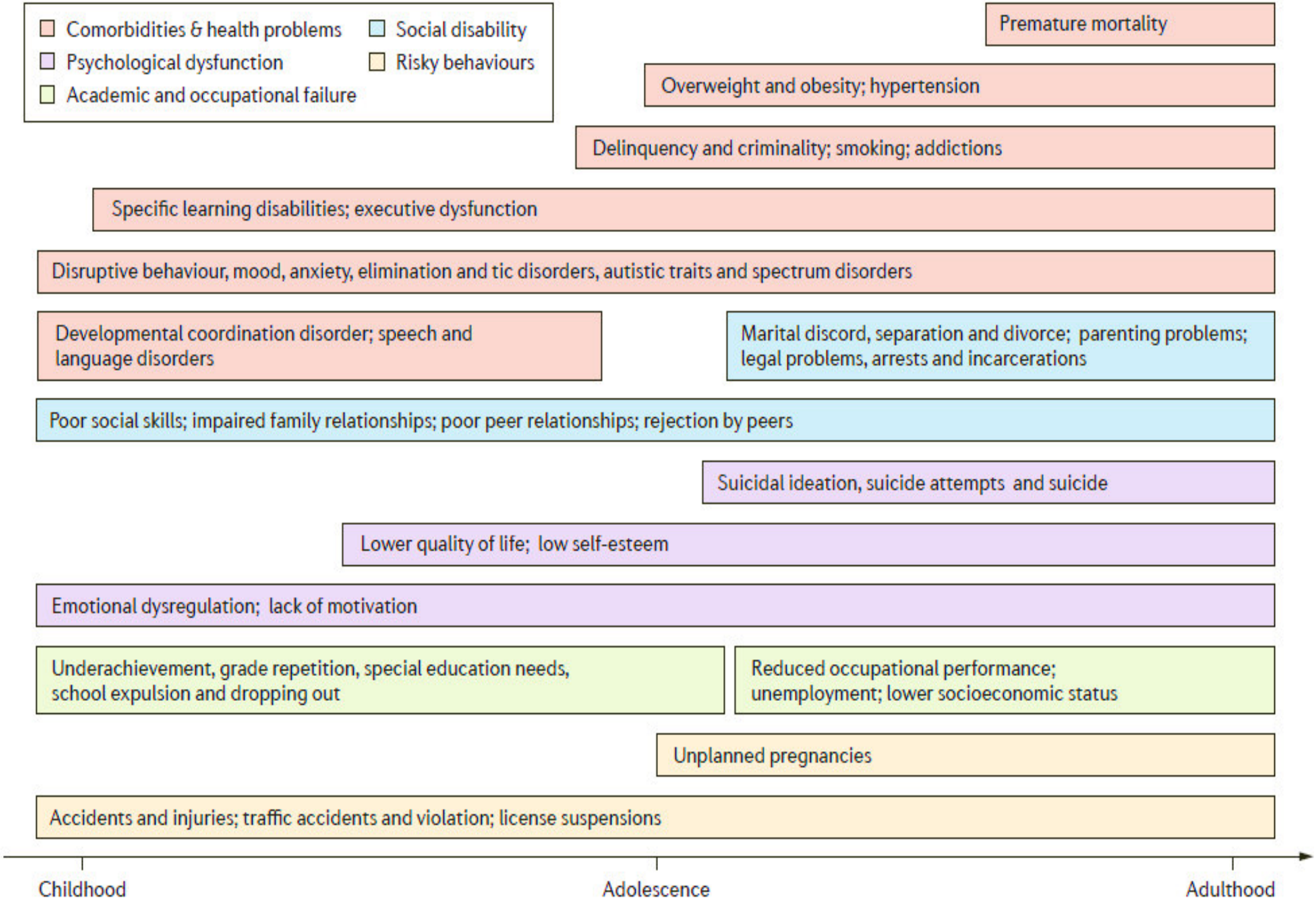
Conclusions: The findings raise the possibility that adults presenting with the ADHD symptom picture may not have a childhood-onset neurodevelopmental disorder. If this finding is replicated, then the disorder's place in the classification system must be reconsidered, and research must investigate the etiology of adult ADHD.

Am J Psychiatry 2015; 172:967–977; doi: 10.1176/appi.ajp.2015.14101266

Komorbide Störungen

Funktionelle Beeinträchtigungen

Gesundheitsbezogene Lebensqualität


Comorbidities & health problems
Social disability
Psychological dysfunction
Risky behaviours
Academic and occupational failure
Premature mortality
Overweight and obesity; hypertension
Delinquency and criminality; smoking; addictions
Specific learning disabilities; executive dysfunction
Disruptive behaviour, mood, anxiety, elimination and tic disorders, autistic traits and spectrum disorders
Developmental coordination disorder; speech and language disorders
Marital discord, separation and divorce; parenting problems; legal problems, arrests and incarcerations
Poor social skills; impaired family relationships; poor peer relationships; rejection by peers
Suicidal ideation, suicide attempts and suicide
Lower quality of life; low self-esteem
Emotional dysregulation; lack of motivation
Underachievement, grade repetition, special education needs, school expulsion and dropping out
Reduced occupational performance; unemployment; lower socioeconomic status
Unplanned pregnancies
Accidents and injuries; traffic accidents and violation; license suspensions
Childhood
Adolescence
Adulthood

Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study

Søren Dalsgaard, Søren Dinesen Østergaard, James F Leckman, Preben Bo Mortensen, Marianne Giørtz Pedersen 2015

	Number of deaths	Person-years	Mortality rate, per 10 000 person-years	Crude model MRR (95% CI)*	Partly adjusted model, MRR (95% CI)†	Fully adjusted model, MRR (95% CI)‡
Diagnosed with ADHD	47	138 198	3·40	1·70 (1·26–2·24)	1·55 (1·14–2·04)	1·50 (1·11–1·98)
Diagnosed with ADHD and oppositional defiant disorder or conduct disorder	19	31 177	6·09	2·56 (1·57–3·90)	2·26 (1·39–3·44)	2·17 (1·33–3·31)
Diagnosed with ADHD and substance use disorder	25	9722	25·71	7·01 (4·59–10·16)	5·91 (3·87–8·57)	5·63 (3·69–8·16)
Diagnosed with ADHD, oppositional defiant disorder or conduct disorder, and substance use disorder	16	3953	40·48	10·37 (6·07–16·36)	8·74 (5·12–13·80)	8·29 (4·85–13·09)
Diagnosed with oppositional defiant disorder, conduct disorder or substance use disorder	472	330 192	14·29	4·00 (3·62–4·41)	3·65 (3·30–4·02)	3·55 (3·21–3·92)
No diagnosis of ADHD, oppositional defiant disorder or conduct disorder, or substance use disorder	5001	24 394 318	2·05	1·00 (reference)	1·00 (reference)	1·00 (reference)
p value§	..	..	..	p<0·0001	p<0·0001	p<0·0001
Overall cohort	5580	24 907 560	2·24	..	..	..

Cohort consisted of 1·92 million children born 1981–2011. MRR=mortality rate ratio. ADHD=attention deficit hyperactivity disorder. ..=not applicable. *Crude model adjusted for age, calendar year, and sex. †Partly adjusted model adjusted for age, calendar year, sex, parental history of psychiatric disorders, and maternal and paternal age at time of delivery. ‡Fully adjusted model adjusted for age, calendar year, sex, parental history of psychiatric disorders, maternal and paternal age at time of delivery, parental education, and parental employment status. §p value measures the overall effect of being diagnosed with ADHD with and without the three comorbidities, compared with individuals without ADHD or any of the three comorbidities.

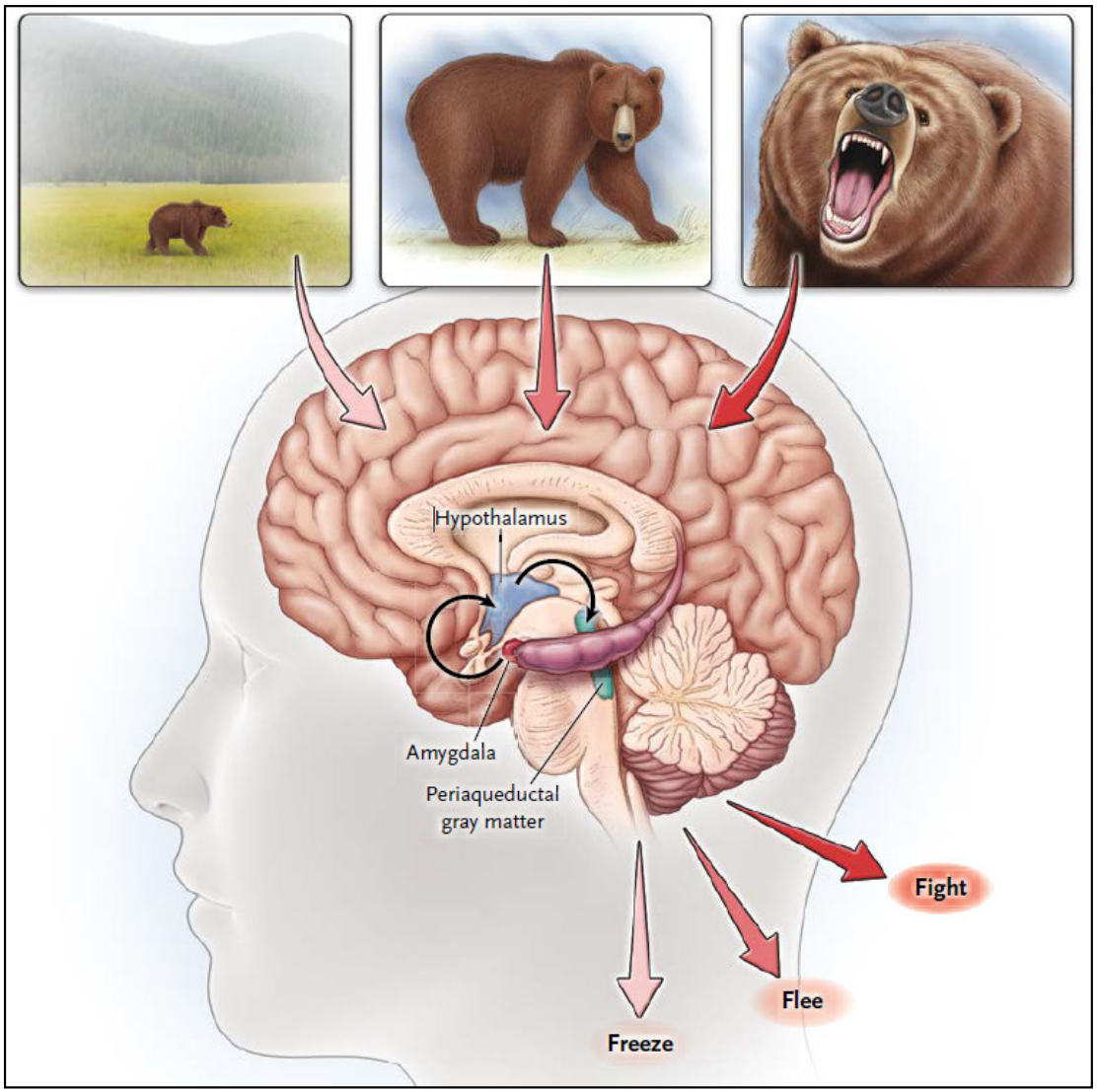
Table 3: Mortality rate ratios in individuals with ADHD in combination with oppositional defiant disorder, conduct disorder, or substance use disorder compared with individuals with none of the four disorders, in the overall cohort

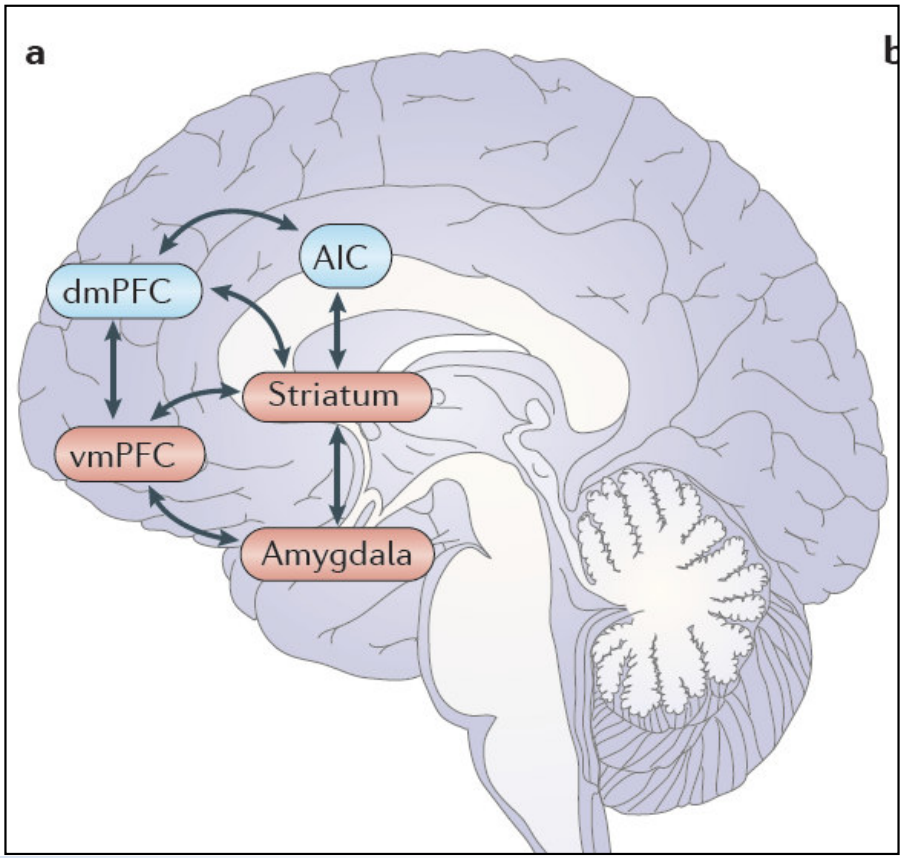
Assoziierte affektive Symptomatik

- Emotionale Dysregulation (ED)/Reizbarkeit & ADHS sind *häufig* assoziiert
- insbesondere
  - bei schwereren ADHS-Kernsymptomen & komorbiden Störungen
  - im Erwachsenenalter
- ED ist Prädiktor für stärkere klinische Beeinträchtigung und für Persistenz ins Erwachsenenalter
- ED bei ADHS nur teilweise vorhersagbar durch Schwere der Kernsymptome und assoziierte Psychopathologie
- ED im Kindesalter ist Prädiktor für spätere komorbide depressive Störung
- ADHS + Depression assoziiert mit:
  - höherem Risiko für Suchterkrankungen
  - höherer psychosozialer Beeinträchtigung

Sobanski et al., 2012; Banaschewski, Coghill & Zuddas, 2018

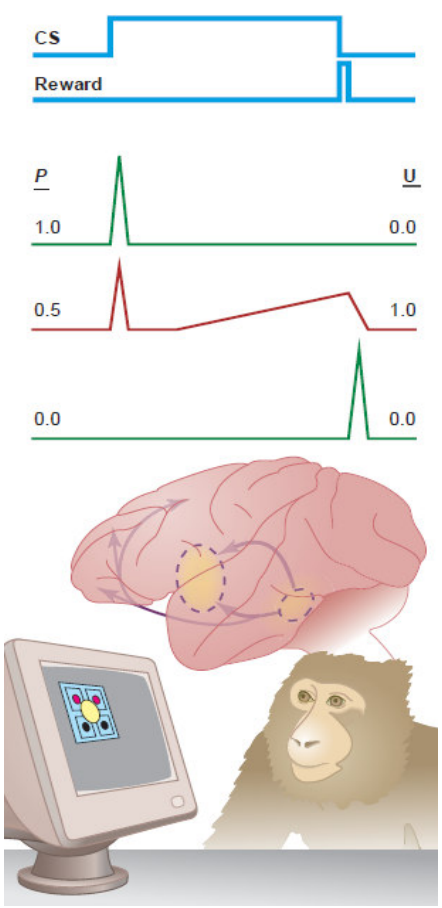
Thread Processing

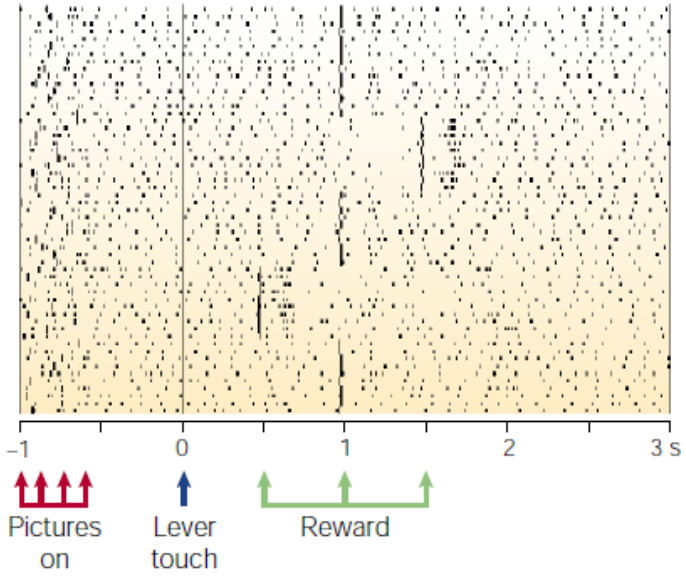


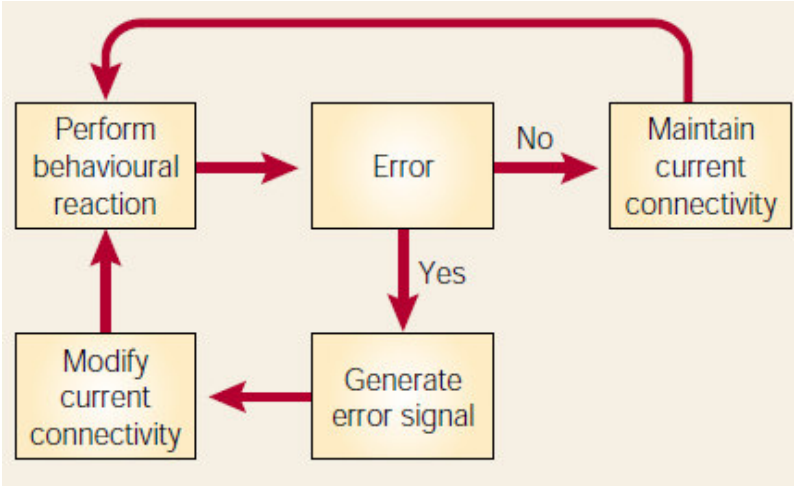


Blair, 2013; Blair et al. 2015

Reward Anticipation & Prediction Error







- Dopamine neurons encode an error in the temporal prediction of reward, i.e. difference between received and predicted reward value
- Firing rate is depressed when reward is delayed or omitted & enhanced when reward delivery is unpredicted
- If the prediction error falls to zero no new information about the consequences of the action is learned

Schultz et al., SCIENCE, 1997, Fiorillo et al., 2003

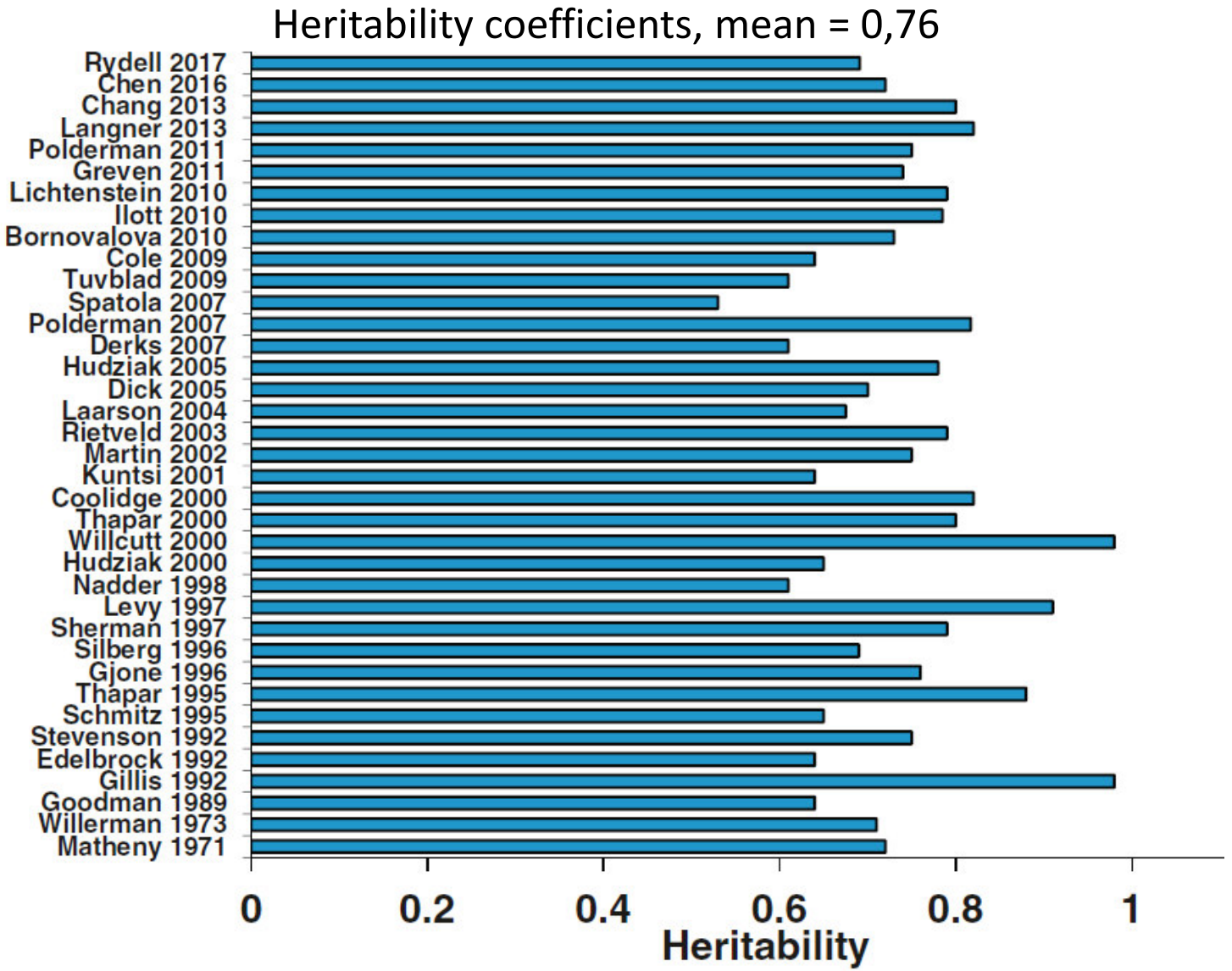
Pathophysiological Model of Irritability
Aberrant Reward and Threat Processing

- Aberrant Reward Processing
  - Reward learning & prediction error deficits (difficulties in appropriately updating changing reward and punishment contingencies)
  - Cognitive control deficits
  - Increased sensitivity to reward receipt and omission (receiving rewards more positive mood; higher levels of arousal, diminished ability to shift attention during frustrative nonreward)
- Aberrant Threat Processing /face emotion processing deficits associated with aberrant amygdala modulation
  - Increased orientation to threat
  - Tendency to interpret ambiguous or neutral social stimuli as threatening (hostile attribution bias)
  - Deficits in face emotion identification
  - Lower threshold for aggressive responses

Brotman et al., AJP, 2017

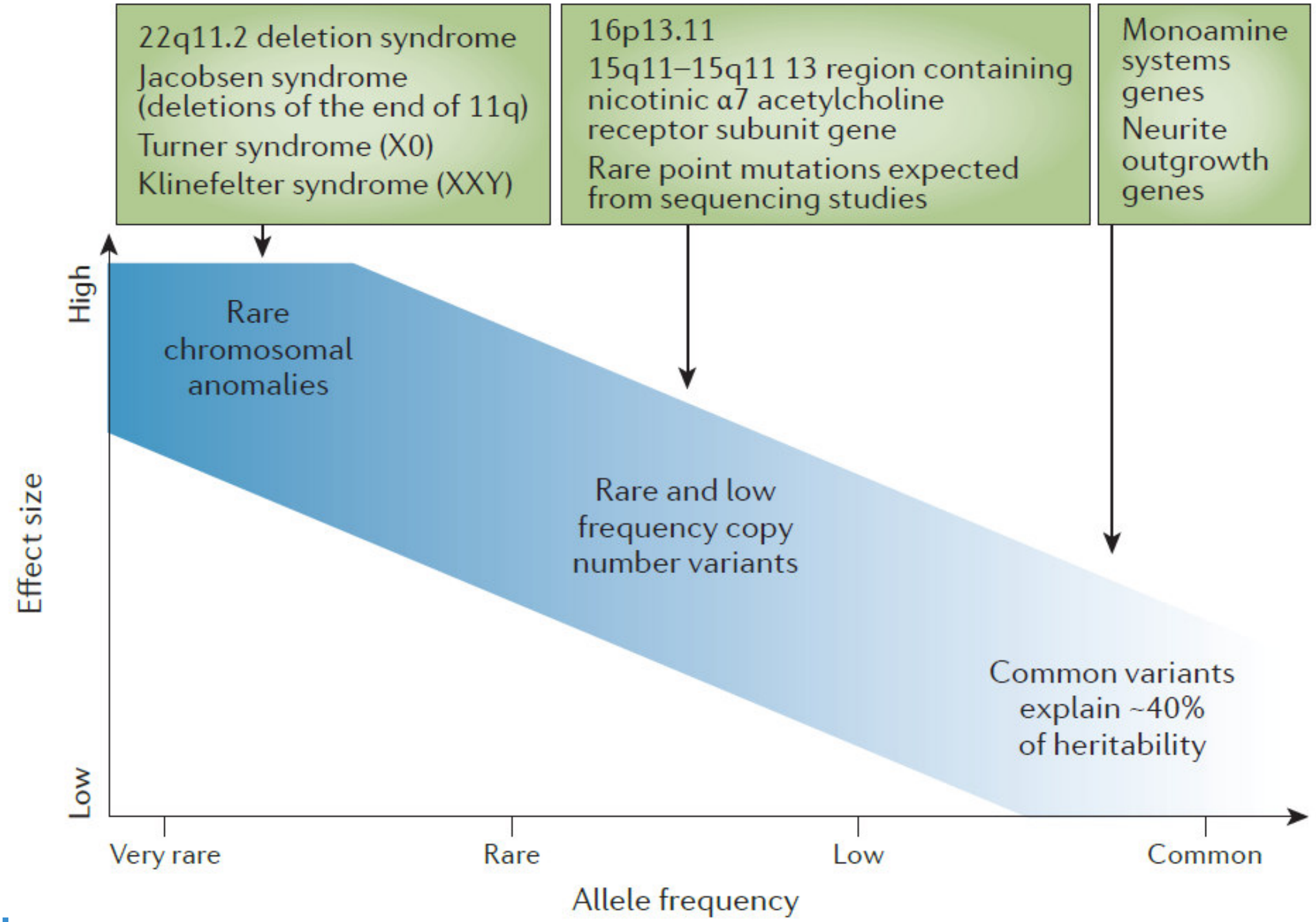
Risikofaktoren

Heritabilität



Genes are etiologically relevant

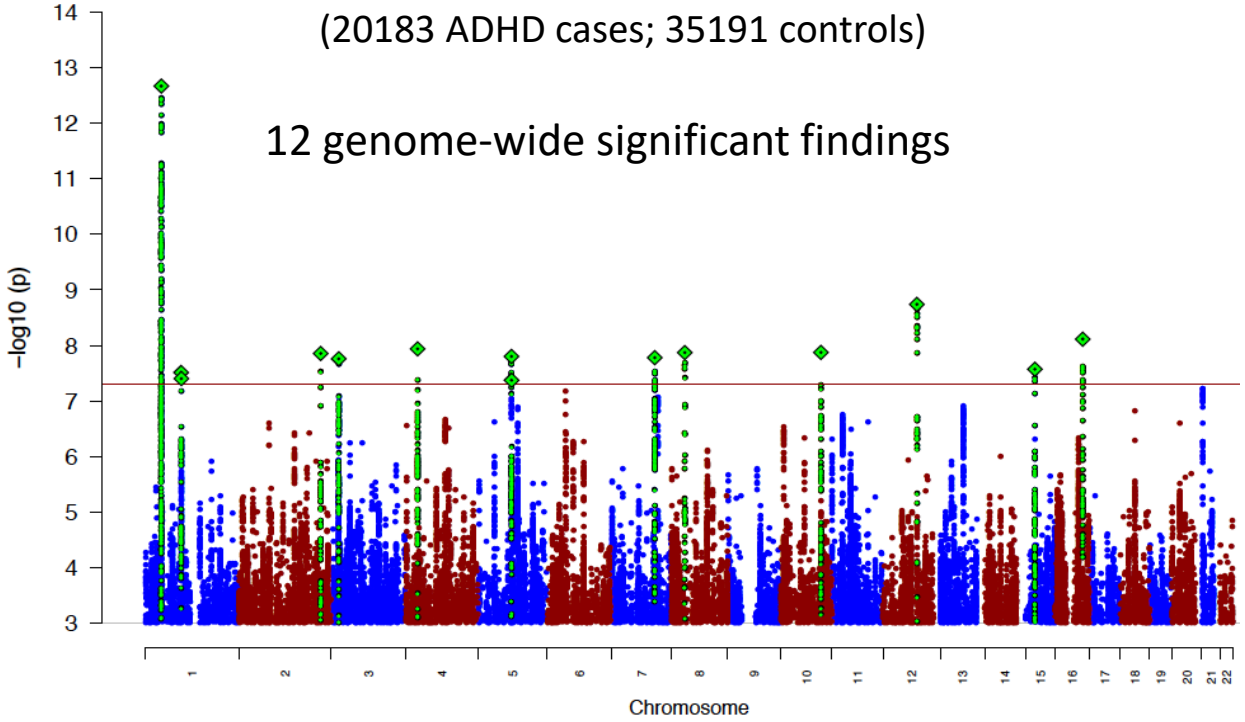
Faraone & Larsson, 2018

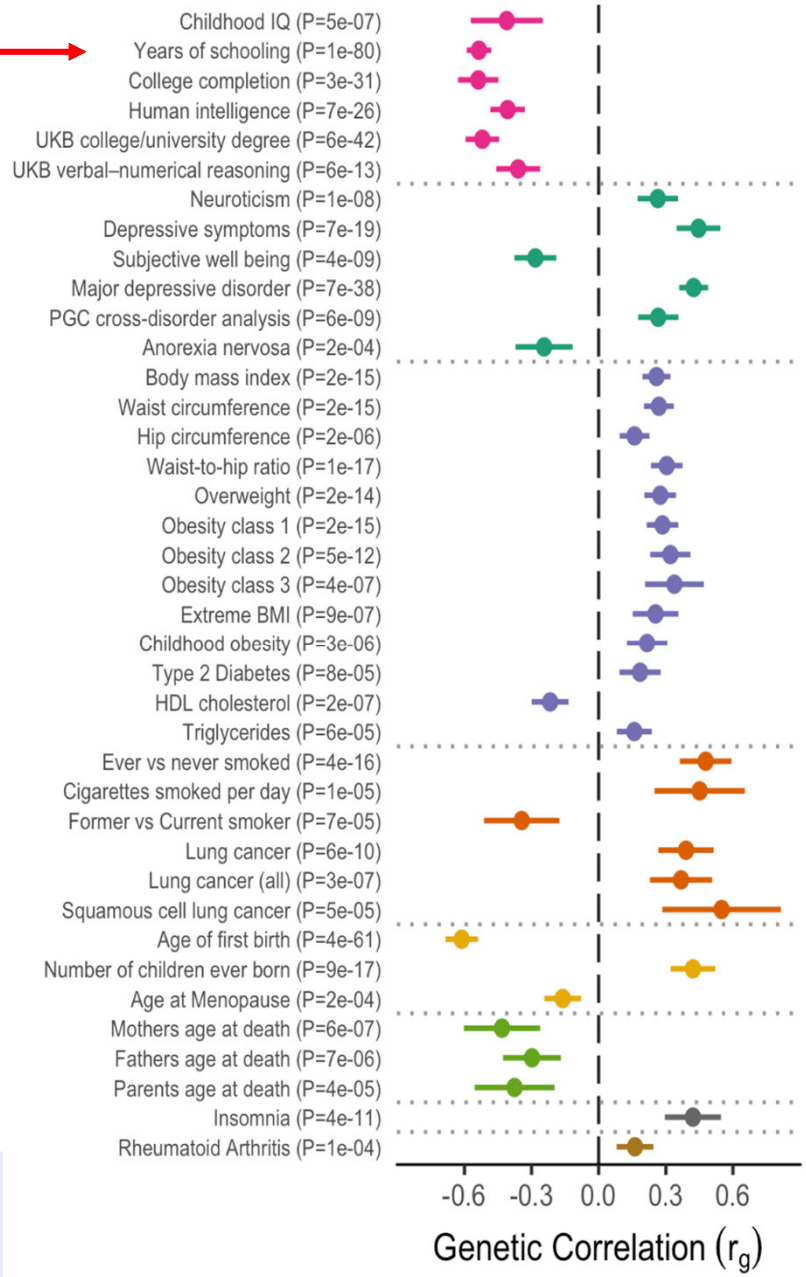

22q11.2 deletion syndrome
Jacobsen syndrome (deletions of the end of 11q)
Turner syndrome (X0)
Klinefelter syndrome (XXY)
16p13.11
15q11–15q11 13 region containing nicotinic α7 acetylcholine receptor subunit gene
Rare point mutations expected from sequencing studies
Monoamine systems genes
Neurite outgrowth genes
High
Low
Effect size
Rare chromosomal anomalies
Rare and low frequency copy number variants
Common variants explain ~40% of heritability
Very rare
Rare
Low
Common
Allele frequency

GWAS Befunde

Manhattan plot of GWAS meta-analysis
(20183 ADHD cases; 35191 controls)

12 genome-wide significant findings

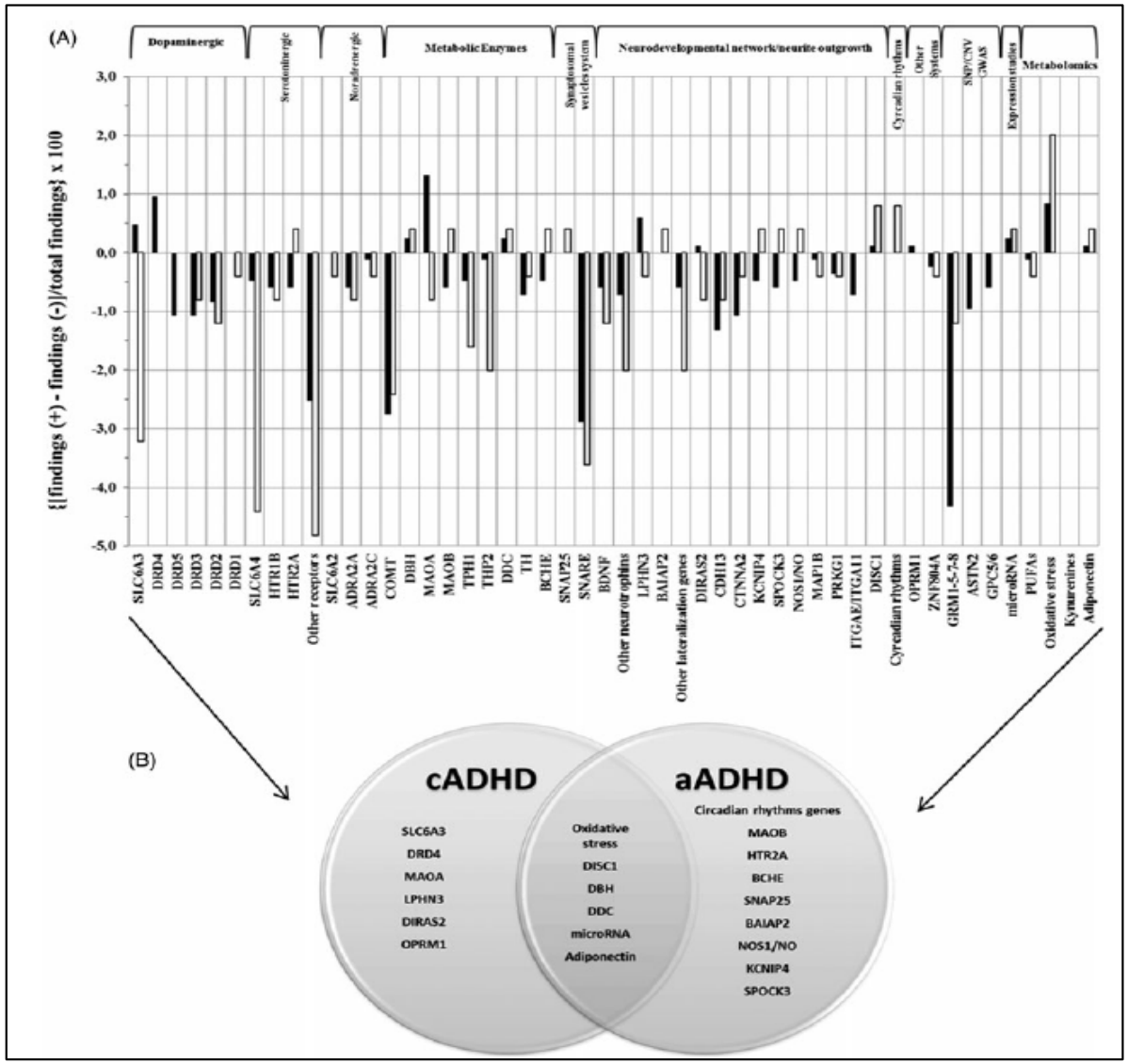




Demontis et al., Nature Genetics, 2019

Common and specific genes and peripheral biomarkers in children and adults with attention-deficit/hyperactivity disorder

Cristian Bonvicini[a], Stephen V. Faraone[b] and Catia Scassellati[a]



Practitioner Review: What have we learnt about the causes of ADHD?

Anita Thapar,[1,2] Miriam Cooper,[1,2] Olga Eyre,[1,2] and Kate Langley[1,2]

[1]Child & Adolescent Psychiatry Section, Institute of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, Cardiff; [2]MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University School of Medicine, Cardiff, UK

Umweltrisiken

Pre- and perinatal factors	Environmental toxins	Dietary factors	Psychosocial adversity
Maternal smoking, alcohol and substance misuse *Risk but not proven causal risk factor*	Organophosphate *pesticides* *Risk but not proven causal risk factor*	Nutritional deficiencies eg zinc, magnesium, polyunsaturated fatty acids *Correlate not yet proven risk factor*	Family adversity & low income *Correlate not yet proven risk factor*
Maternal stress *Risk but not proven causal risk factor*	Polychlorinated biphenyls *Risk but not proven causal risk factor*	Nutritional surpluses eg sugar, artificial food colourings *Correlate not yet proven risk factor*	Conflict/parent–child hostility *Correlate not yet proven risk factor*
Low birth weight and prematurity *Risk but not proven causal risk factor*	Lead *Risk but not proven causal risk factor*	Low/high IgG foods *Correlate not yet proven risk factor*	Severe early deprivation *Risk, likely causal risk factor*

Thapar et al., 2012

Gen – Umwelt Interaktionen

Psychosoziale Belastung & DAT

Interacting Effects of the Dopamine Transporter Gene and Psychosocial Adversity on Attention-Deficit/ Hyperactivity Disorder Symptoms Among 15-Year-Olds From a High-Risk Community Sample

Manfred Laucht, PhD; Markus H. Skowronek, PhD; Katja Becker, MD; Martin H. Schmidt, MD, PhD; Günter Esser, PhD; Thomas G. Schulze, MD; Marcella Rietschel, MD

Context: Recent evidence suggests that gene × environment interactions could explain the inconsistent findings of association studies relating the dopamine transporter (*DAT1*) gene with attention-deficit/hyperactivity disorder (ADHD).

Objective: To examine whether psychosocial adversity moderated the effect of genetic variation in *DAT1* on ADHD symptoms in adolescents from a high-risk community sample.

Design: Prospective cohort study.

Setting: Data were taken from the Mannheim Study of Children at Risk, an ongoing longitudinal study of the long-term outcomes of early risk factors followed up from birth on.

Participants: Three hundred five adolescents (146 boys, 159 girls) participated in a follow-up assessment at age 15 years.

Main Outcome Measures: Measures of ADHD symptoms according to *DSM-IV* were obtained using standardized structural interviews with adolescents and their parents. Psychosocial adversity was determined according to an "enriched" family adversity index as proposed by Rutter and Quinton. DNA was genotyped for the common *DAT1* 40–base pair (bp) variable number of tandem repeats (VNTR) polymorphism in the 3′ untranslated region; 3 previously described single nucleotide polymorphisms in exon 15, intron 9, and exon 9; and a novel 30-bp VNTR polymorphism in intron 8.

Results: Adolescents homozygous for the 10-repeat allele of the 40-bp VNTR polymorphism who grew up in greater psychosocial adversity exhibited significantly more inattention and hyperactivity-impulsivity than adolescents with other genotypes or who lived in less adverse family conditions (significant interaction, $P = .013$-$.017$). This gene × environment interaction was also observed in individuals homozygous for the 6-repeat allele of the 30-bp VNTR polymorphism and the haplotype comprising both markers.

Conclusions: These findings provide initial evidence that environmental risks as described by the Rutter Family Adversity Index moderate the impact of the *DAT1* gene on ADHD symptoms, suggesting a *DAT1* effect only in those individuals exposed to psychosocial adversity.

Arch Gen Psychiatry. 2007;64:585-590

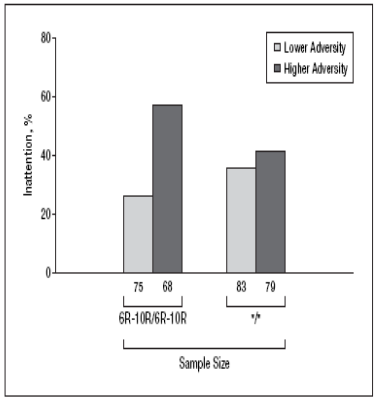


Figure 1. Percentage of inattention in adolescents grouped by the presence or absence of the *DAT1* 6-repeat allele–10-repeat allele (6R-10R) haplotype and exposure to psychosocial adversity. The 6R-10R/6R-10R haplotype exposed to higher adversity is significantly different from all other groups. */* indicates all other genotypes/haplotypes.

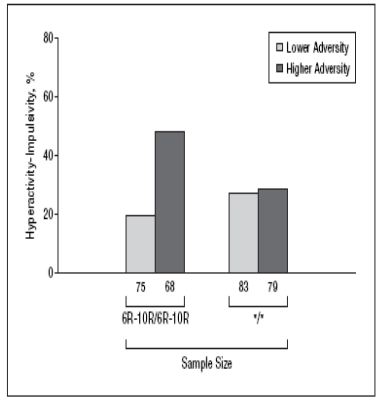
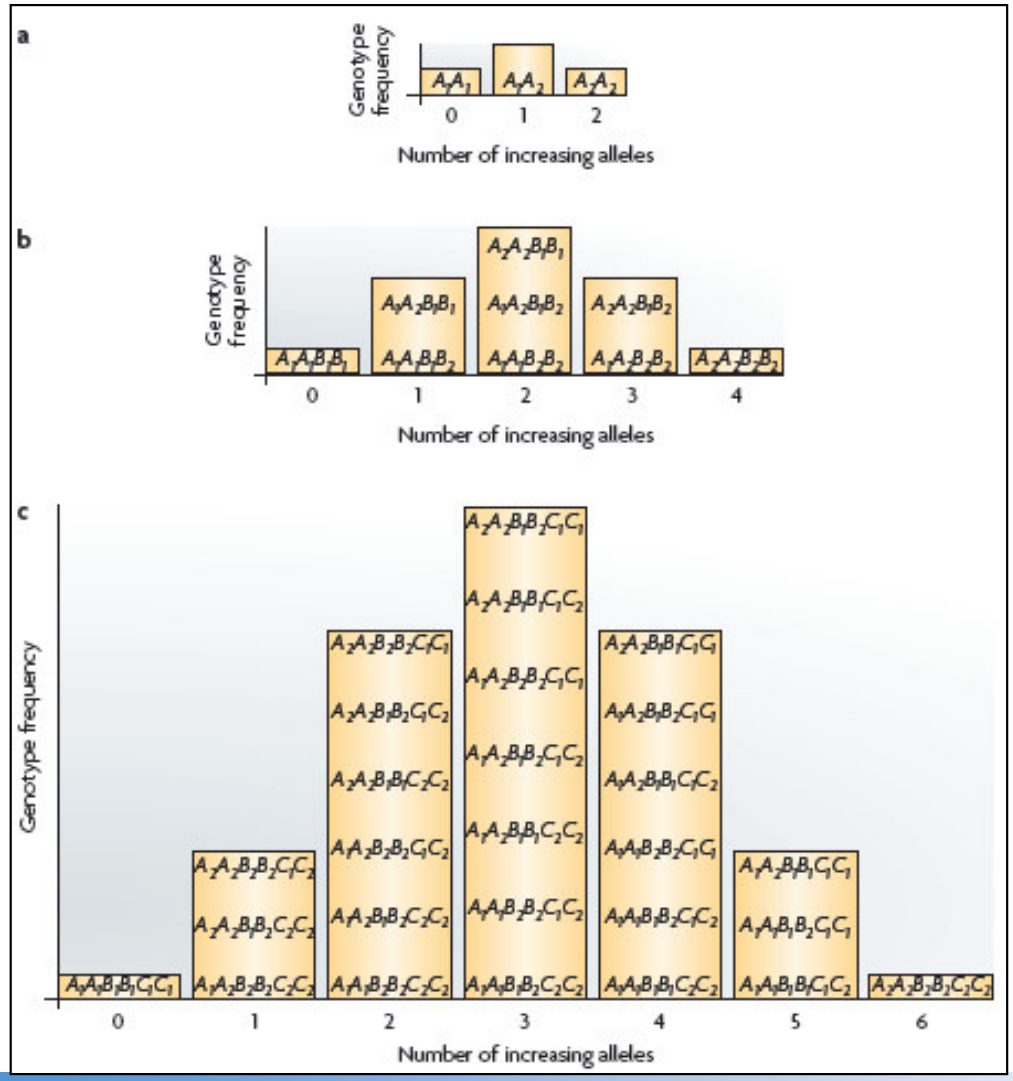


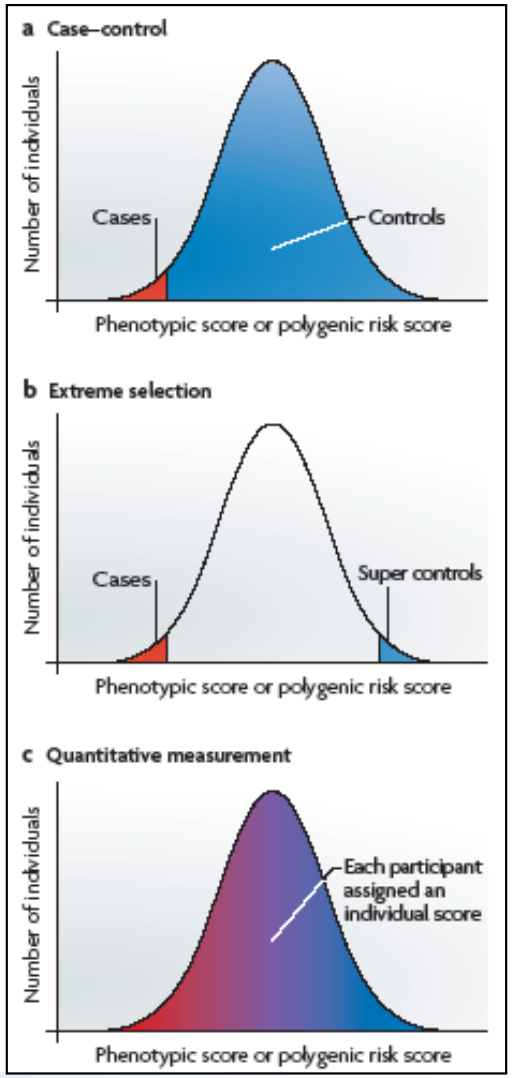
Figure 2. Percentage of hyperactivity-impulsivity in adolescents grouped by the presence or absence of the *DAT1* 6-repeat allele–10-repeat allele (6R-10R) haplotype and exposure to psychosocial adversity. The 6R-10R/6R-10R haplotype exposed to higher adversity is significantly different from all other groups. */* indicates all other genotypes/haplotypes.

Common disorders are quantitative traits

NATURE REVIEWS | GENETICS

Robert Plomin, Claire M. A. Haworth and Oliver S. P. Davis





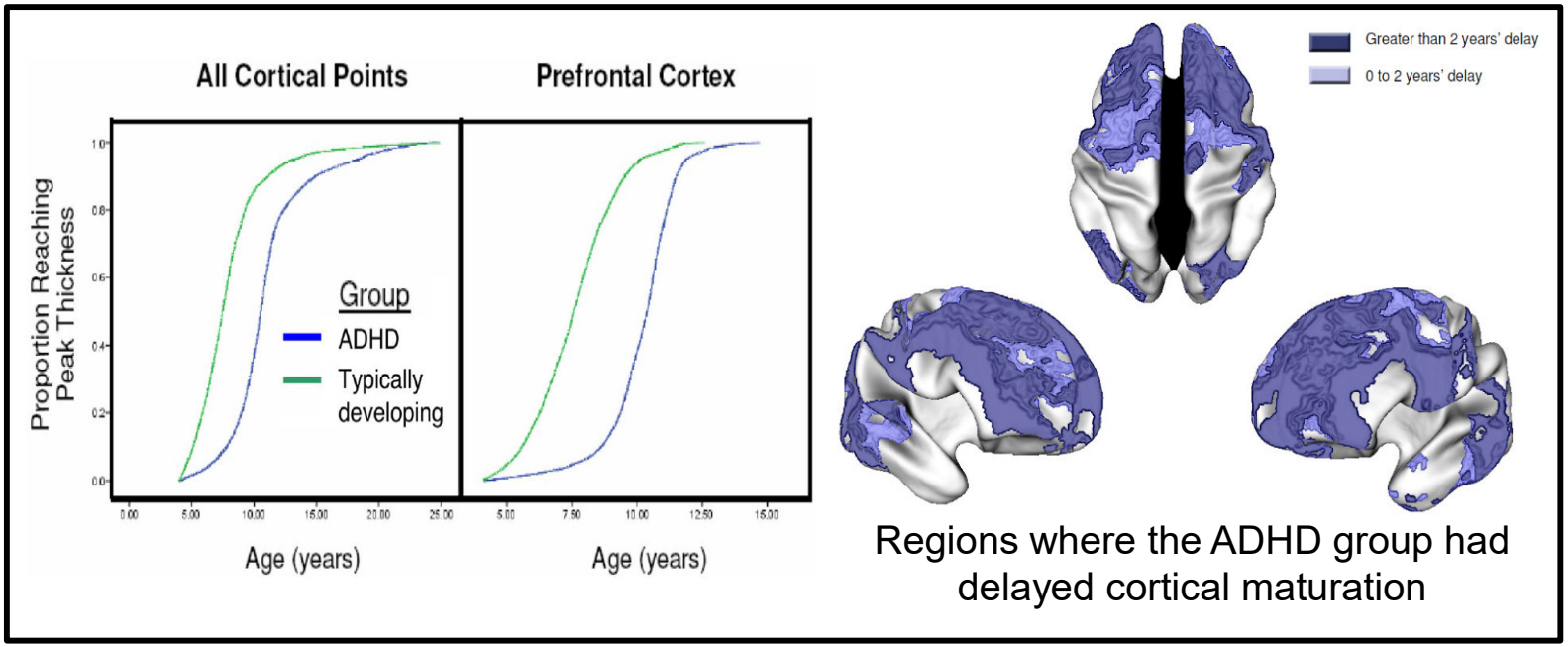
Plomin et al., 2009

Korrelate

Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation

P. Shaw[†‡], K. Eckstrand[†], W. Sharp[†], J. Blumenthal[†], J. P. Lerch[§], D. Greenstein[†], L. Clasen[†], A. Evans[§], J. Giedd[†], and J. L. Rapoport[†]

PNAS | December 4, 2007 | vol. 104 | no. 49 | 19649–19654



Regions where the ADHD group had delayed cortical maturation

Shaw et al., 2007

Neuroanatomische Entwicklung

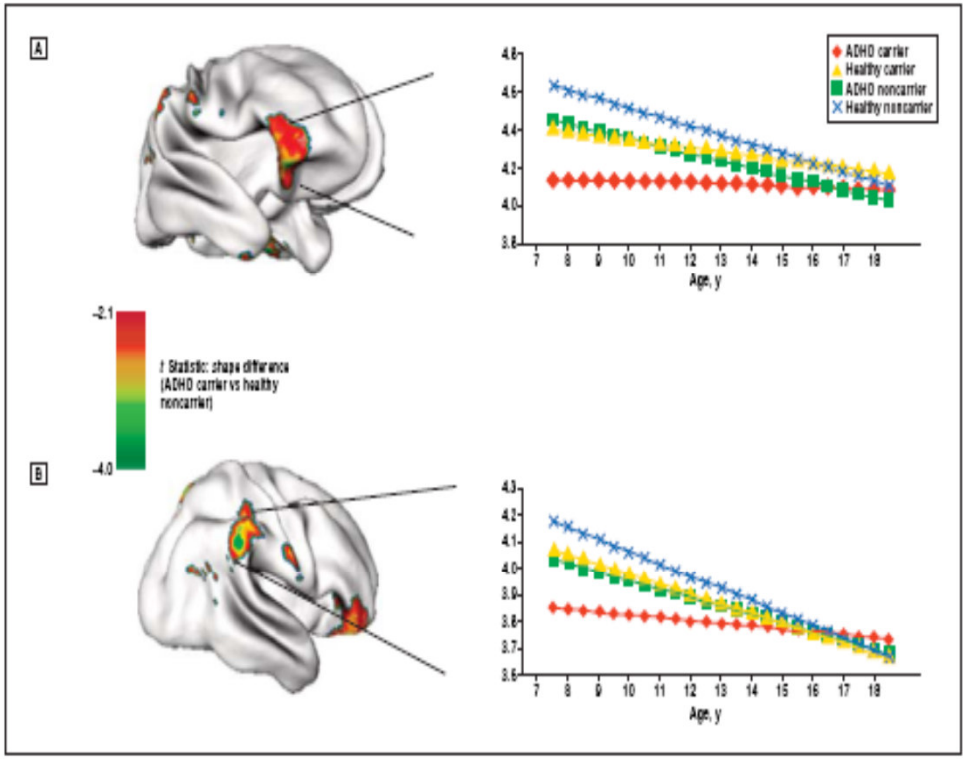


Figure 4. Brain maps of clusters where attention-deficit/hyperactivity disorder (ADHD) carriers of the 7-repeat allele differ in trajectory of cortical growth and graphs illustrating trajectories for these clusters. A, Right lateral orbitofrontal area, with a significant difference in shape between ADHD carriers and healthy noncarriers ($P = .01$). B, Right angular gyrus, with a significant difference between ADHD carriers and healthy noncarriers ($P = .007$).

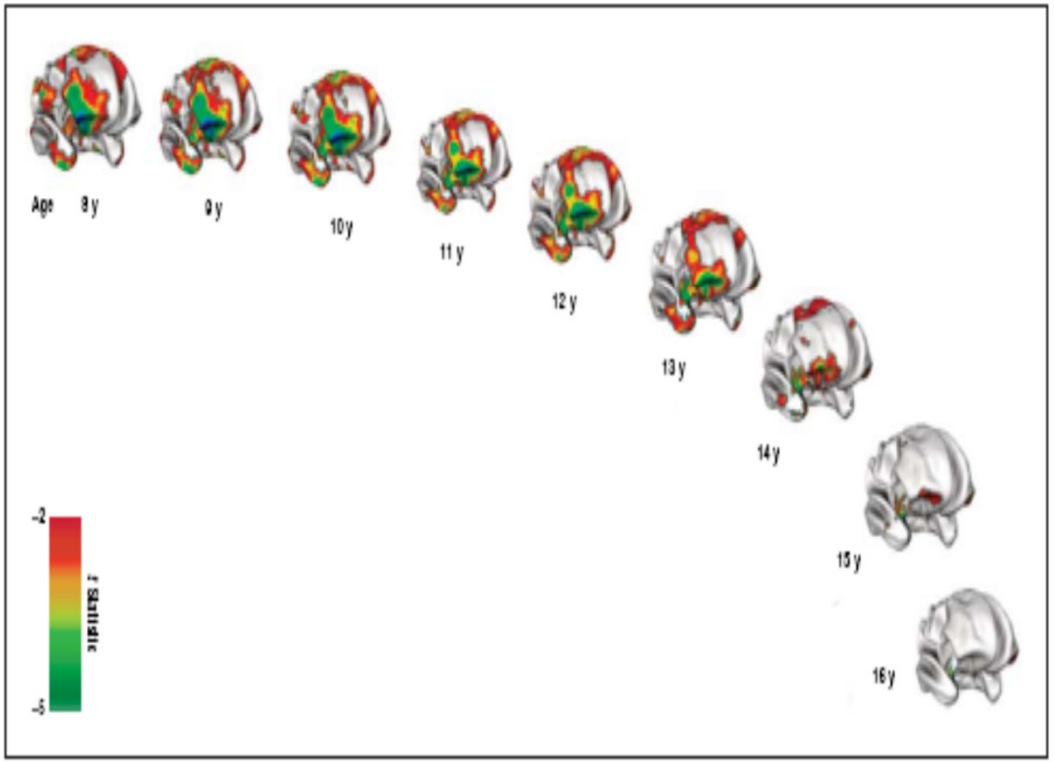
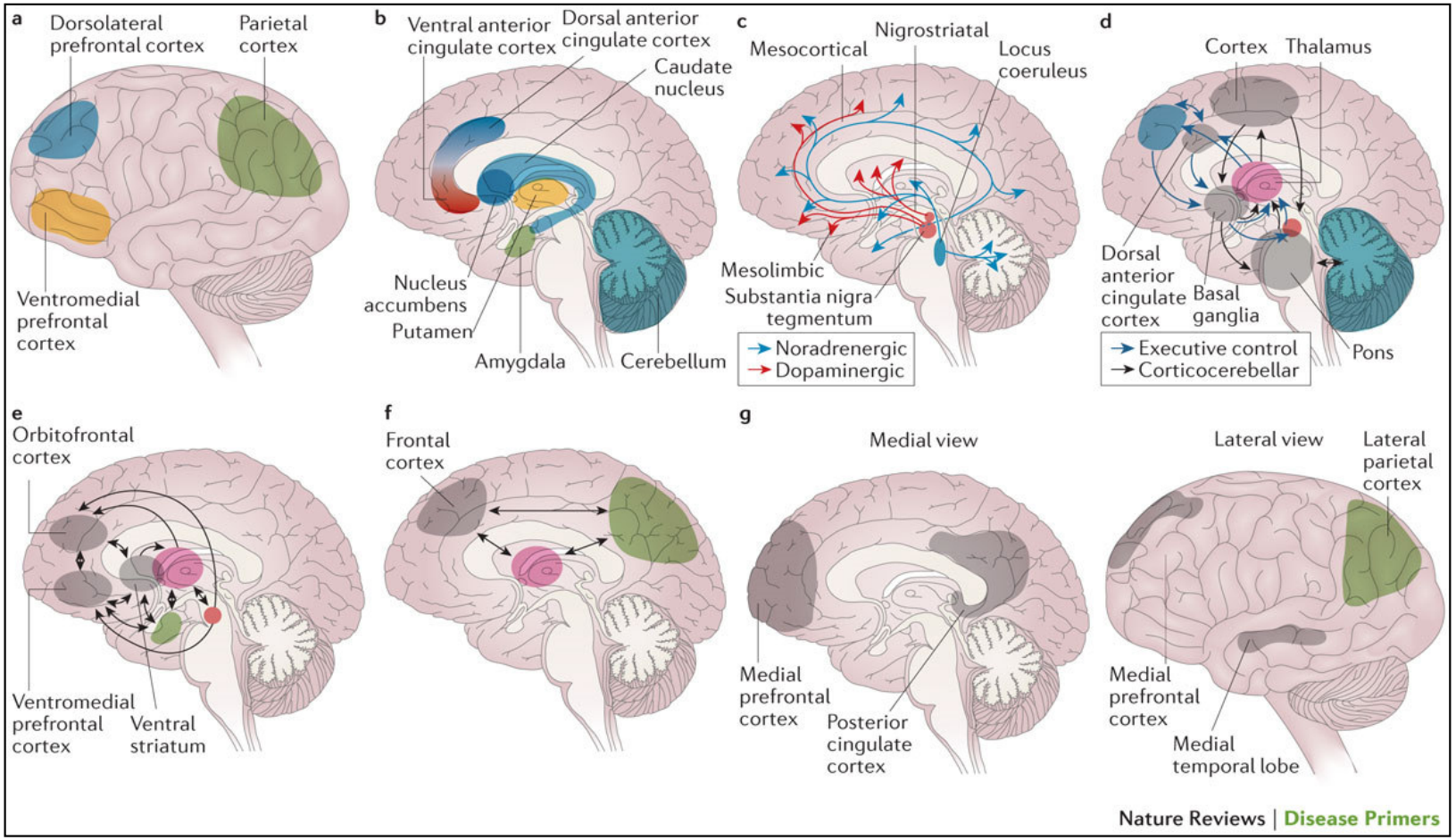


Figure 5. Cortical thinning at baseline in attention-deficit/hyperactivity disorder (ADHD) carriers of the 7-repeat allele corrects with age. Contrast between ADHD carriers and healthy controls without the 7-repeat allele from age 8 years through 16 years illustrating the resolution of regional cortical thinning with age (contrasts set at $t > 2$).

- Reduktion frontaler und parietaler Hirnregionen assoziiert mit ungünstigem Verlauf
- Besserer Verlauf => Normalisierung der (rechts-)parietalen Hirnregionen im Entwicklungsverlauf

Shaw et al. 2006

Heterogene hirnstrukturelle & -funktionelle Korrelate

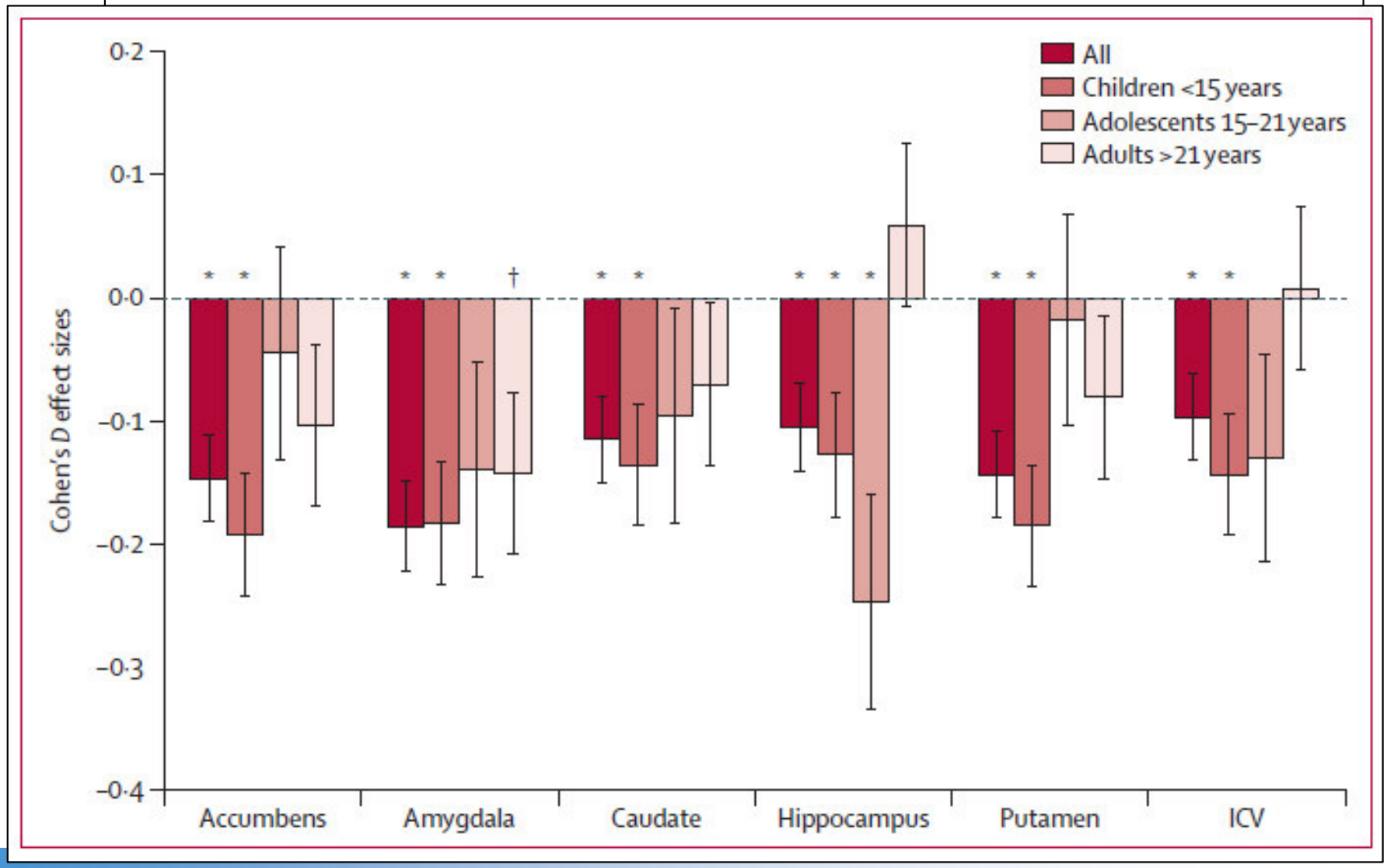


Multiple kognitive, motivationale, motorische Netzwerke involviert

Bush et al., 2011: “A single abnormality of any one region alone does not cause ADHD”

Faraone et al., 2015

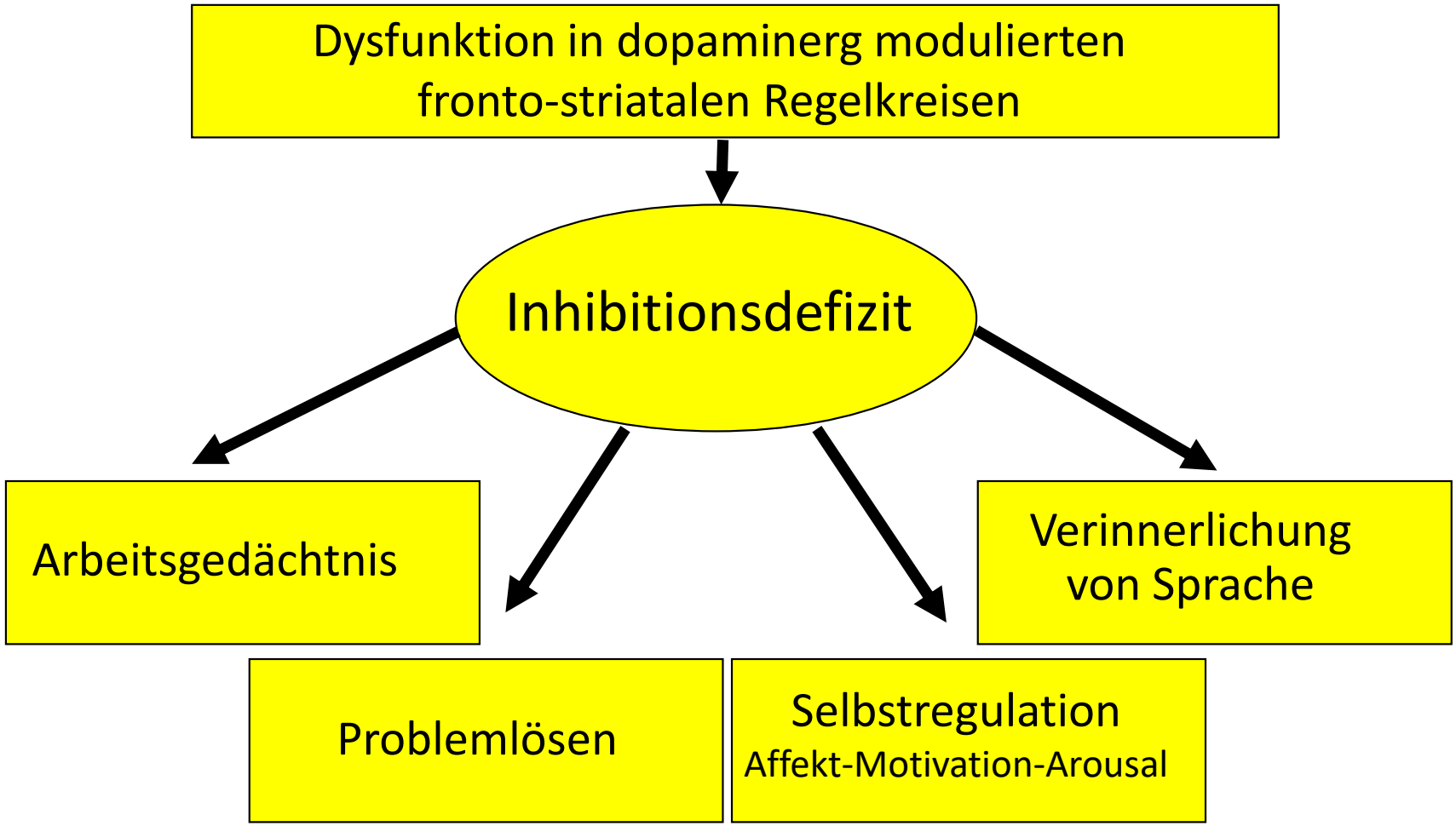
Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis



www.thelancet.com/psychiatry Published online February 15, 2017

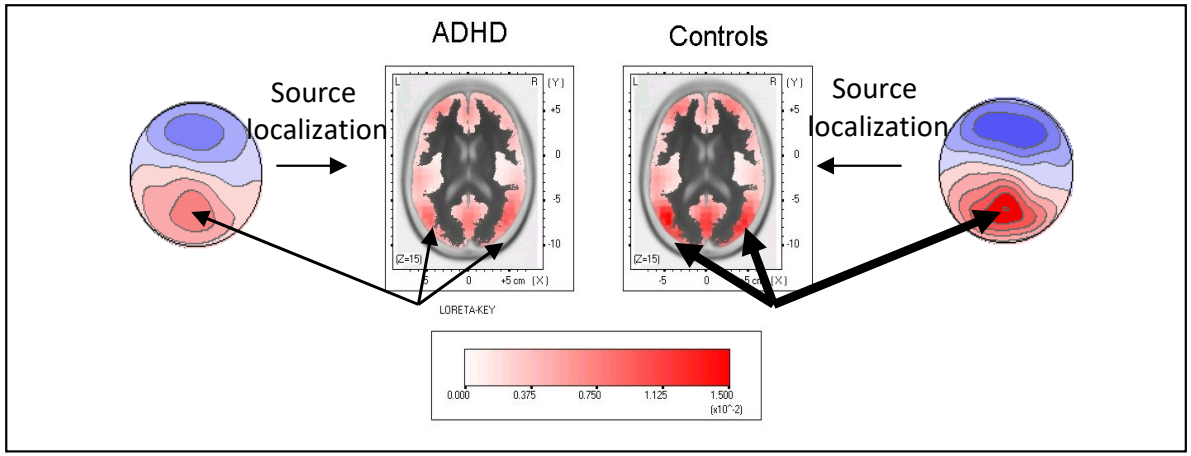
ADHS als Inhibitionsdefizit

(Barkley, 1997, 1998)



Abweichende Aufmerksamkeitsprozesse

Aktivierung nach Präsentation von A bei CPT A-X (P300)

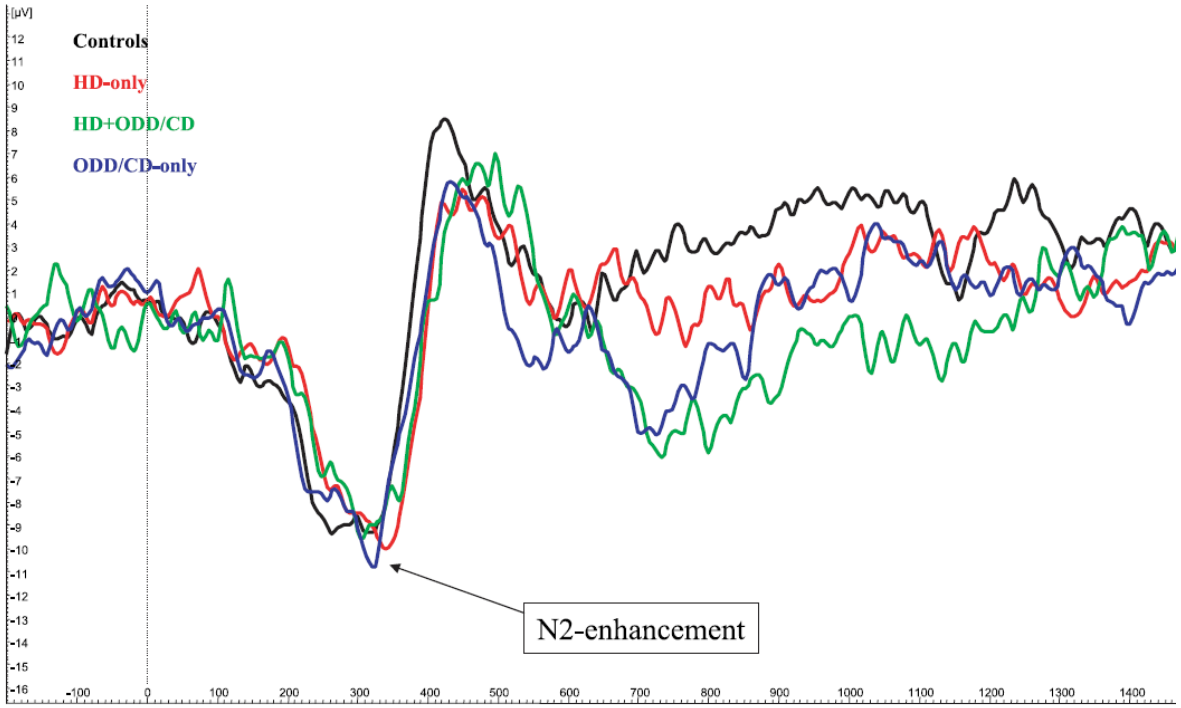


- Beeinträchtige Aufmerksamkeitsorientierung
- Posteriores Aufmerksamkeitssystem schwächer

Brandeis, Banaschewski et al., 2002: Multizenterstudie; Banaschewski, Brandeis et al., 2003

Questioning inhibitory control as the specific deficit of ADHD – evidence from brain electrical activity

T. Banaschewski[1], D. Brandeis[2], H. Heinrich[1,3], B. Albrecht[1], E. Brunner[4], and A. Rothenberger[1]

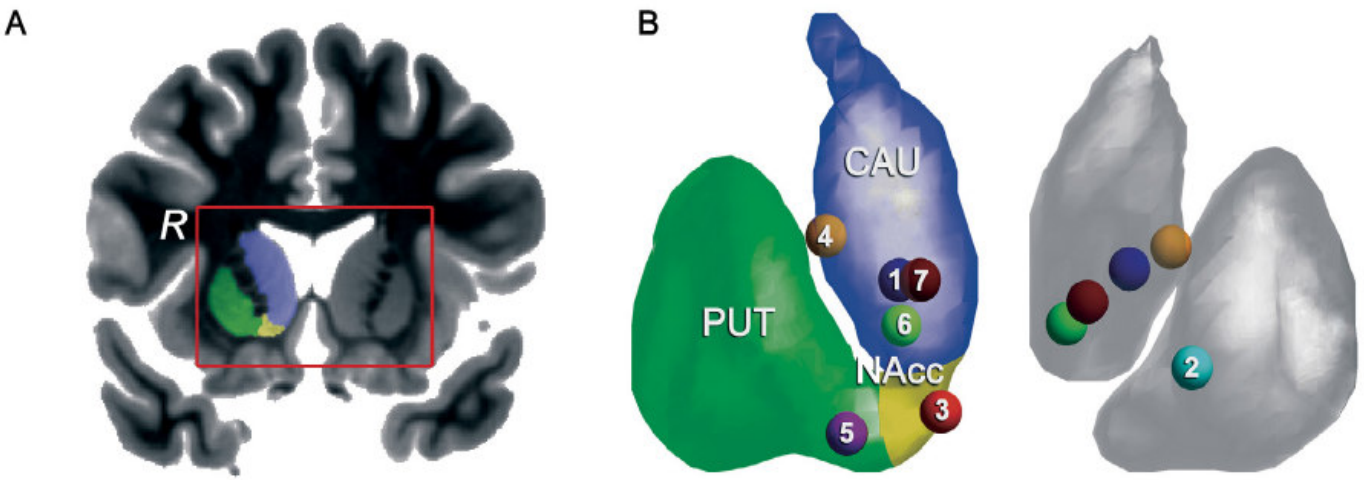


Kein ausschließliches Inhibitionsdefizit

Banaschewski, Brandeis et al., 2004

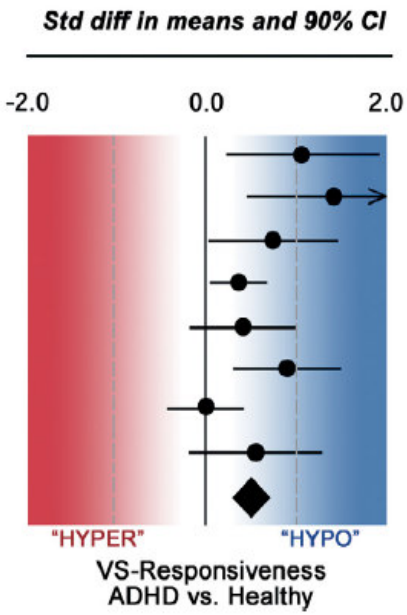
Ventral–striatal responsiveness during reward anticipation in ADHD and its relation to trait impulsivity in the healthy population: A meta-analytic review of the fMRI literature

Michael M. Plichta [a,*], Anouk Scheres [b]



C

Study	Year		Std diff in means	Standard error	Variance	Lower limit	Upper limit	z-value	Total N
Scheres	2007	1	1.060	0.519	0.270	0.205	1.914	2.041	22
Ströhle	2008	2	1.438	0.597	0.357	0.455	2.420	2.407	20
Plichta	2009	3	0.746	0.445	0.198	0.014	1.478	1.677	26
Hoogman	2011	4	0.368	0.202	0.041	0.035	0.701	1.819	104
Stoy	2011	5	0.418	0.361	0.130	-0.176	1.012	1.157	35
Camona	2012	6	0.906	0.371	0.138	0.296	1.517	2.442	38
Paloyelis[a]	2012	⊘	0.000	0.267	0.071	-0.440	0.440	0.000	59
Edel[b]	2013	7	0.563	0.468	0.220	-0.208	1.333	1.224	36
OVERALL			**0.476**	**0.120**	**0.014**	**0.279**	**0.673**	**3.974**	**340**



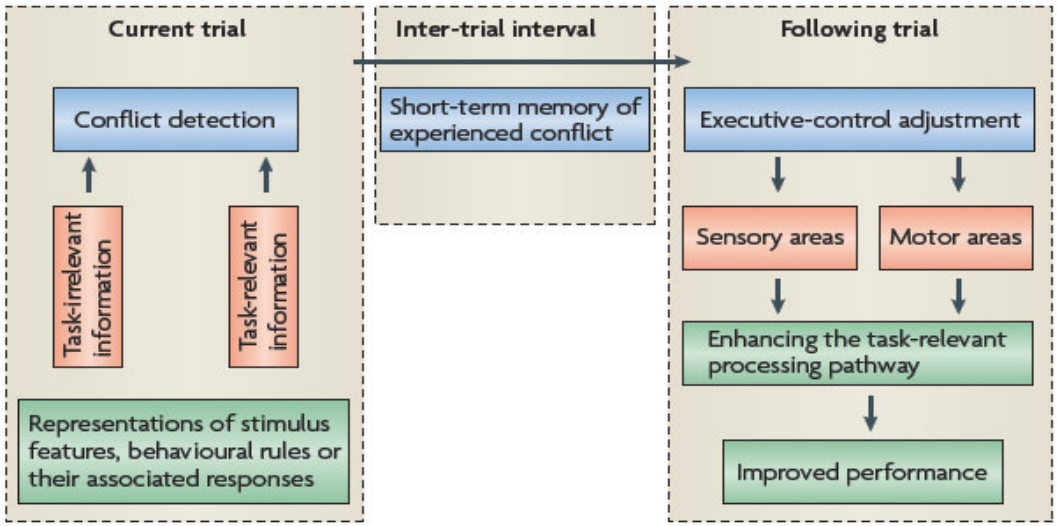
Decreased responses during anticipation (ES = 0.48)

Handlungskontrolle & Fehlerverarbeitung

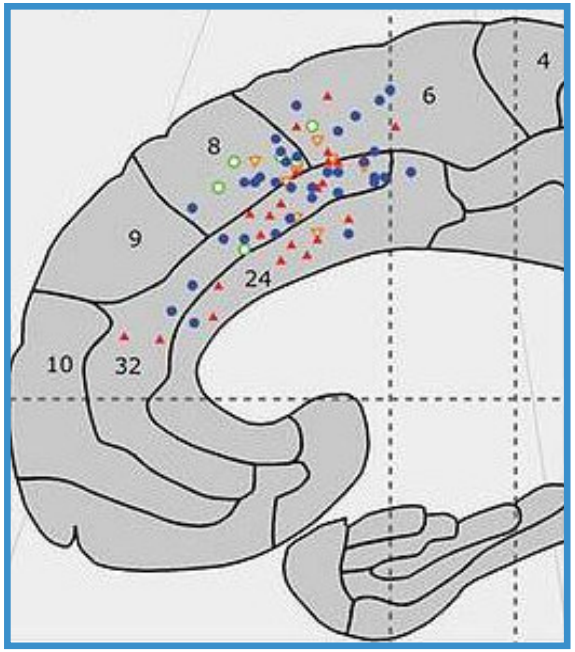
Conflict-induced behavioural adjustment: a clue to the executive functions of the prefrontal cortex

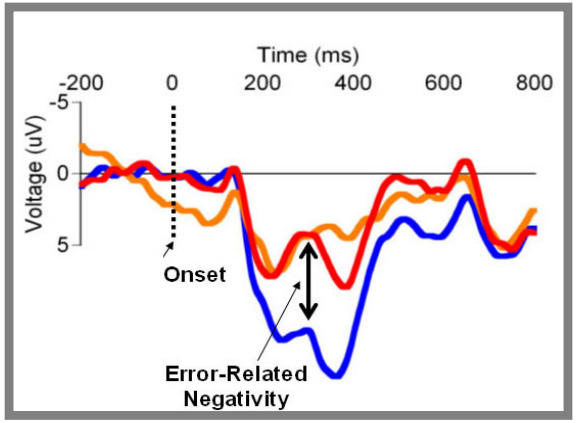
*Farshad A. Mansouri *§, Keiji Tanaka* and Mark J. Buckley‡§*

Abstract | The behavioural adjustment that follows the experience of conflict has been extensively studied in humans, leading to influential models of executive-control adjustment. Recent studies have revealed striking similarities in conflict-induced behavioural adjustment between humans and monkeys, indicating that monkeys can provide a model to study the underlying neural substrates and mechanisms of such behaviour. These studies have advanced our knowledge about the role of different prefrontal brain regions, including the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (DLPFC), in executive-control adjustment and suggest a pivotal role for the DLPFC in the dynamic tuning



NATURE REVIEWS | NEUROSCIENCE VOLUME 10 | FEBRUARY 2009





ADHS: Beeinträchtigte Antwortkontrolle aufgrund Funktionsstörung des anterioren cingulären Kortex

Action Monitoring in Boys With Attention-Deficit/ Hyperactivity Disorder, Their Nonaffected Siblings, and Normal Control Subjects: Evidence for an Endophenotype

Bjoern Albrecht, Daniel Brandeis, Henrik Uebel, Hartmut Heinrich, Ueli C. Mueller, Marcus Hasselhorn, Hans-Christoph Steinhausen, Aribert Rothenberger, and Tobias Banaschewski

Background: Attention-deficit/hyperactivity disorder (ADHD) is a very common and highly heritable child psychiatric disorder associated with dysfunctions in fronto-striatal networks that control attention and response organization. The aim of this study was to investigate whether features of action monitoring related to dopaminergic functions represent endophenotypes that are brain functions on the pathway from genes and environmental risk factors to behavior.

Methods: Action monitoring and error processing as indicated by behavioral and electrophysiological parameters during a flanker task were examined in boys with ADHD combined type according to DSM-IV (n = 68), their nonaffected siblings (n = 18), and healthy control subjects with no known family history of ADHD (n = 22).

Results: Boys with ADHD displayed slower and more variable reaction-times. Error negativity (Ne) was smaller in boys with ADHD compared with healthy control subjects, whereas nonaffected siblings displayed intermediate amplitudes following a linear model predicted by genetic concordance. The three groups did not differ on error positivity (Pe). The N2 amplitude enhancement due to conflict (incongruent flankers) was reduced in the ADHD group. Nonaffected siblings also displayed intermediate N2 enhancement.

Conclusions: Converging evidence from behavioral and event-related potential findings suggests that action monitoring and initial error processing, both related to dopaminergically modulated functions of anterior cingulate cortex, might be an endophenotype related to ADHD.

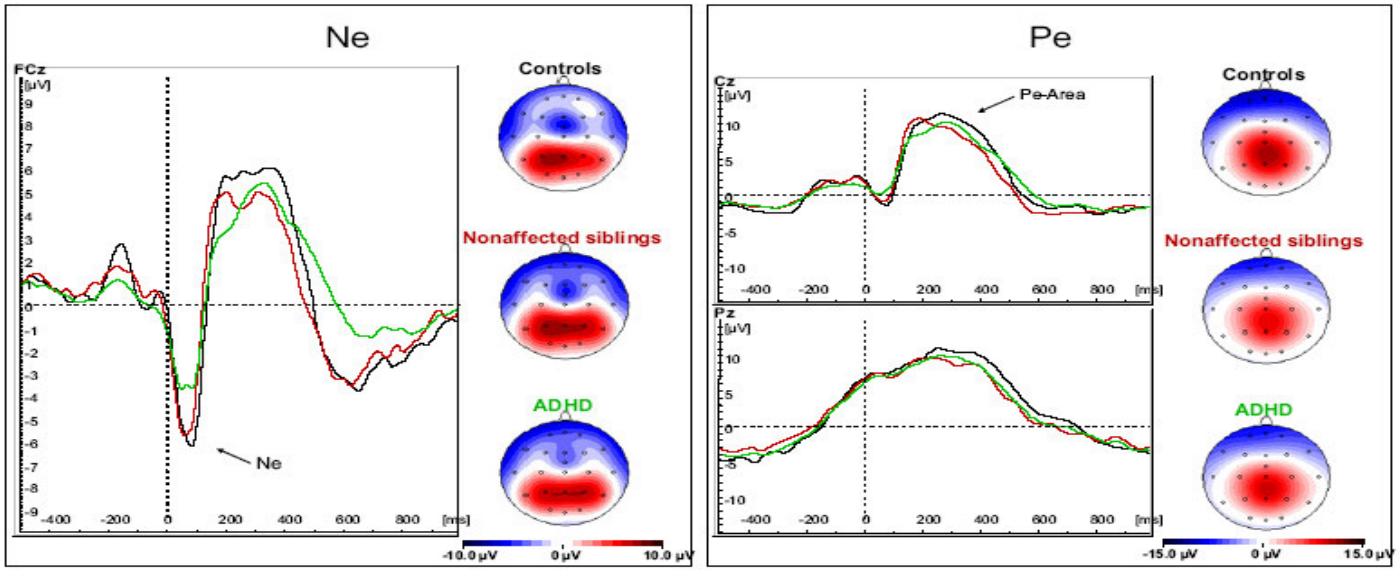
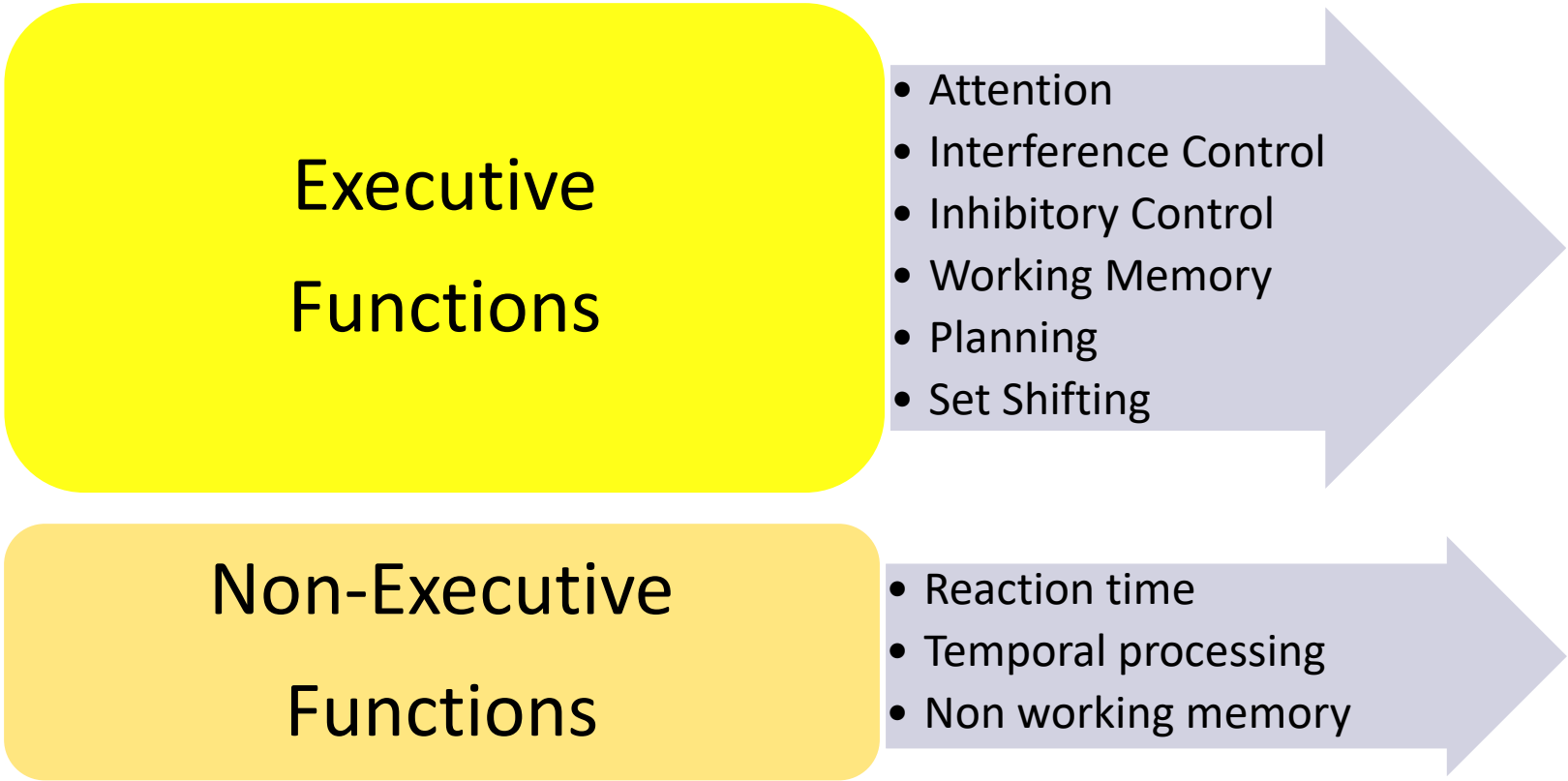


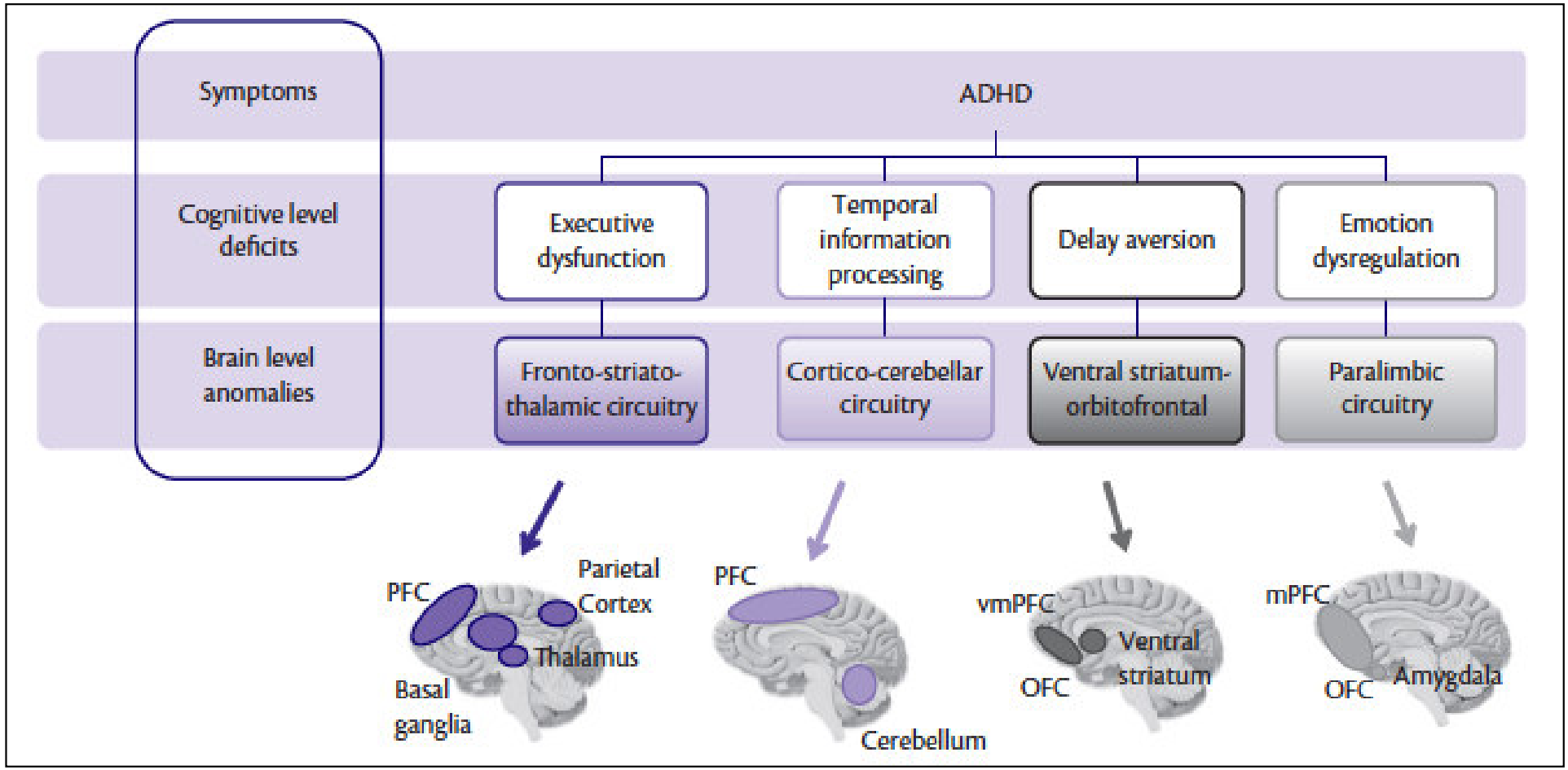
Figure 5. Response-locked error-related components. Response-locked grand average waves of control subjects (black), nonaffected siblings (red), and attention-deficit/hyperactivity disorder (ADHD) boys (green) with spline-interpolated maps of error negativity (Ne) at the respective group mean latency (left side) and error positivity (Pe) mean activity 200–500 msec after error response (right side). The response-locked Ne has its maximum at FCz (even more prominent when measured peak-to-peak), whereas Pe was maximal at centro-parietal electrodes.

Neuropsychologische Beeinträchtigungen



Coghill, 2018

From Simple Causal Models to Complex Development Pathways



Multiple Pathways – multiple markers?

Shaw & Szekely in: Banaschewski, Coghill & Zuddas OT-ADHD, 2018

Multifaktorielle Ätiologie

- Exakte pathophysiologischen Mechanismen noch unzureichend geklärt
  - 70–80% phänotypischer Varianz durch genetische Faktoren & GxE erklärbar
  - Ca. 40% genetisch bedingter Varianz durch häufige Varianten bedingt
  - assoziative Zusammenhänge mit verschiedenen Umweltfaktoren
    - prä- und perinatale Risiken (mütterlicher Stress, Nikotin- oder Alkoholkonsum während der Schwangerschaft, niedriges Geburtsgewicht, Frühgeburtlichkeit), Umwelttoxine (Organophosphate, polychlorierte Biphenyle, Blei), ungünstige psychosoziale Bedingungen, diätetische Faktoren: aber kausale Relevanz bislang nicht belegt (Ausnahme: schwere Formen frühkindlicher Deprivation)
- heterogene Profile hirnstruktureller und -funktioneller, neuropsychologischer und psychopathologischer Auffälligkeiten
  - multiple kognitive, motivationale, motorische Netzwerke involviert; keine ADHS-spezifischen Defizite
- ADHS: Extrembereiche kontinuierlich verteilter Merkmalsdimensionen

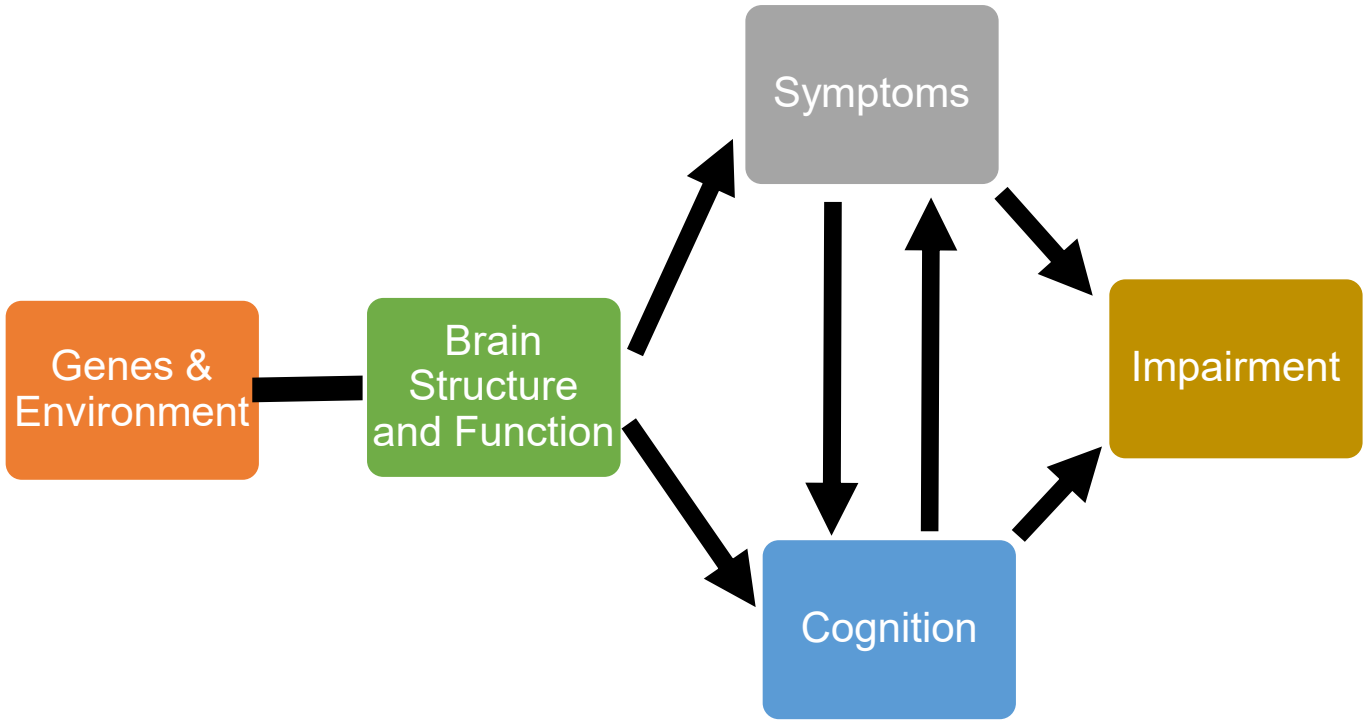
Faraone et al., 2015; Banaschewski, Coghill & Zuddas, 2018

A longitudinal examination of neuropsychological and clinical functioning in boys with attention deficit hyperactivity disorder (ADHD): improvements in executive functioning do not explain clinical improvement

Psychological Medicine (2014), 44, 1087–1099

D. R. Coghill[1*], D. Hayward[2], S. M. Rhodes[3], C. Grimmer[4] and K. Matthews[1]

No association between change in executive functioning and change in symptoms



Coghill et al., 2014

Pharmacological Treatment Options

Clinical Efficacy & Safety

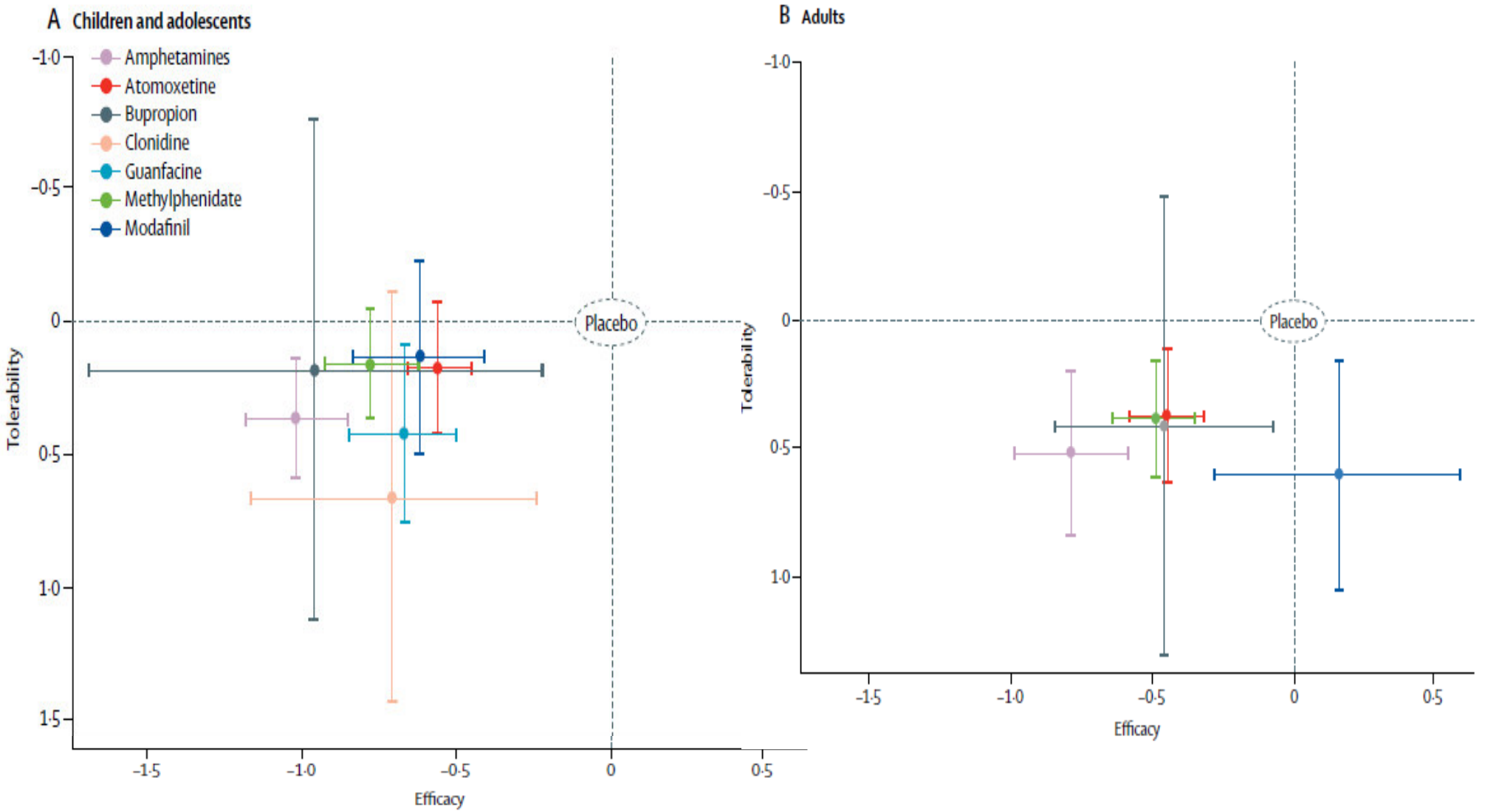
Effect Sizes for Classes of Psychiatric Medications

Medication	Condition	Effect size
Prodrug stimulant	ADHD	1.21
Long-acting stimulants	ADHD	0.95
IR stimulants	ADHD	0.90
Non-stimulants	ADHD	0.62
SSRIs	OCD / Depression	0.50
Atypical antipsychotics	Schizophrenia	0.25

Faraone et al. 2003; Gale et al. Clin Evid 2002; Geddes et al. Clin Evid 2002; Hay et al. Clin Evid 2002; Soomro, Clin Evid 2002; Leucht et al. Schizophr Res 1999; Biederman Clin Ther 2007

Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis

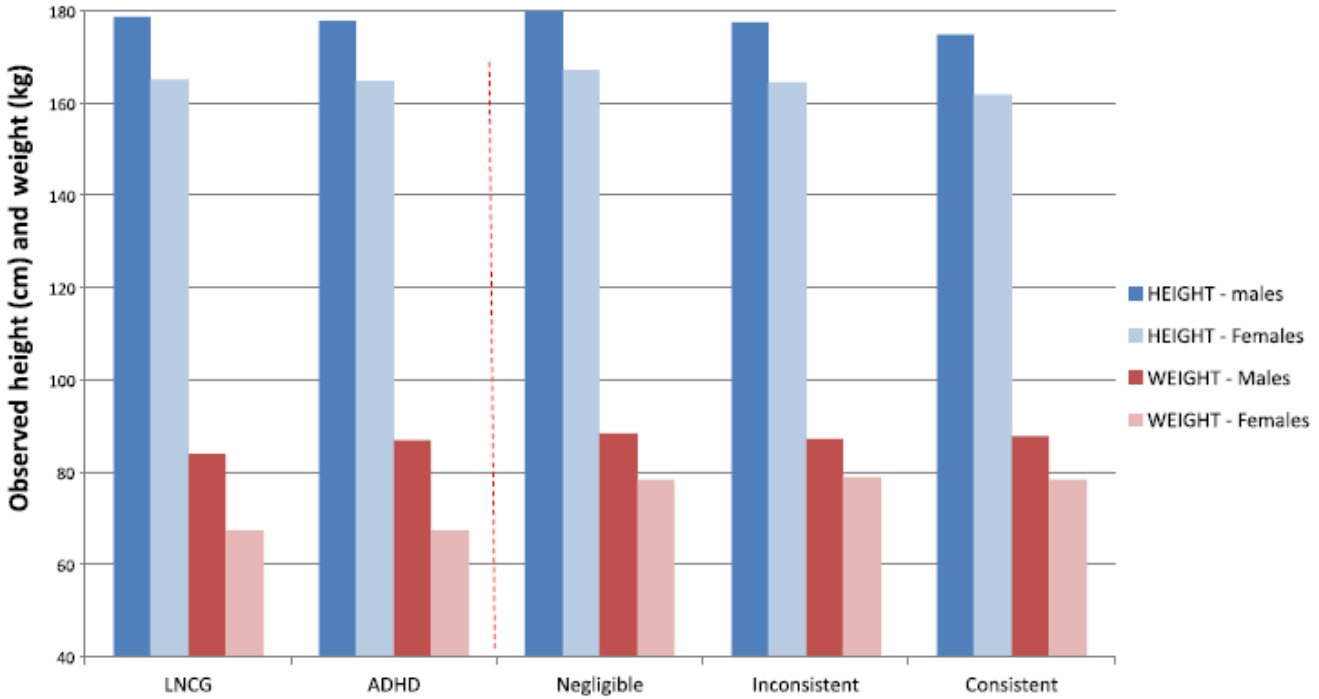
Samuele Cortese, Nicoletta Adamo, Cinzia Del Giovane, Christina Mohr-Jensen, Adrian J Hayes, Sara Carucci, Lauren Z Atkinson, Luca Tessari, Tobias Banaschewski, David Coghill, Chris Hollis, Emily Simonoff, Alessandro Zuddas, Corrado Barbui, Marianna Purgato, Hans-Christoph Steinhausen, Farhad Shokraneh, Jun Xia, Andrea Cipriani



Cortese et al., 2018

Young adult outcomes in the follow-up of the multimodal treatment study of attention-deficit/ hyperactivity disorder: symptom persistence, source discrepancy, and height suppression

James M. Swanson,[1] L. Eugene Arnold,[2] Brooke S.G. Molina,[3] Margaret H. Sibley,[4] Lily T. Hechtman,[5] Stephen P. Hinshaw,[6] Howard B. Abikoff,[7] Annamarie Stehli,[1] Elizabeth B. Owens,[8] John T. Mitchell,[9] Quyen Nichols,[10] Andrea Howard,[11] Laurence L. Greenhill,[12] Betsy Hoza,[10] Jeffrey H. Newcorn,[13] Peter S. Jensen,[14] Benedetto Vitiello,[15] Timothy Wigal,[16] Jeffery N. Epstein,[17] Leanne Tamm,[17] Kimberly D. Lakes,[1] James Waxmonsky,[18] Marc Lerner,[1] Joy Etcovitch,[19] Desiree W. Murray,[20] Maximilian Muenke,[21] Maria T. Acosta,[21] Mauricio Arcos-Burgos,[22] William E. Pelham,[23] and Helena C. Kraemer[24] for the MTA Cooperative Group



Journal of Child Psychology and Psychiatry 58:6 (2017), pp 663–678

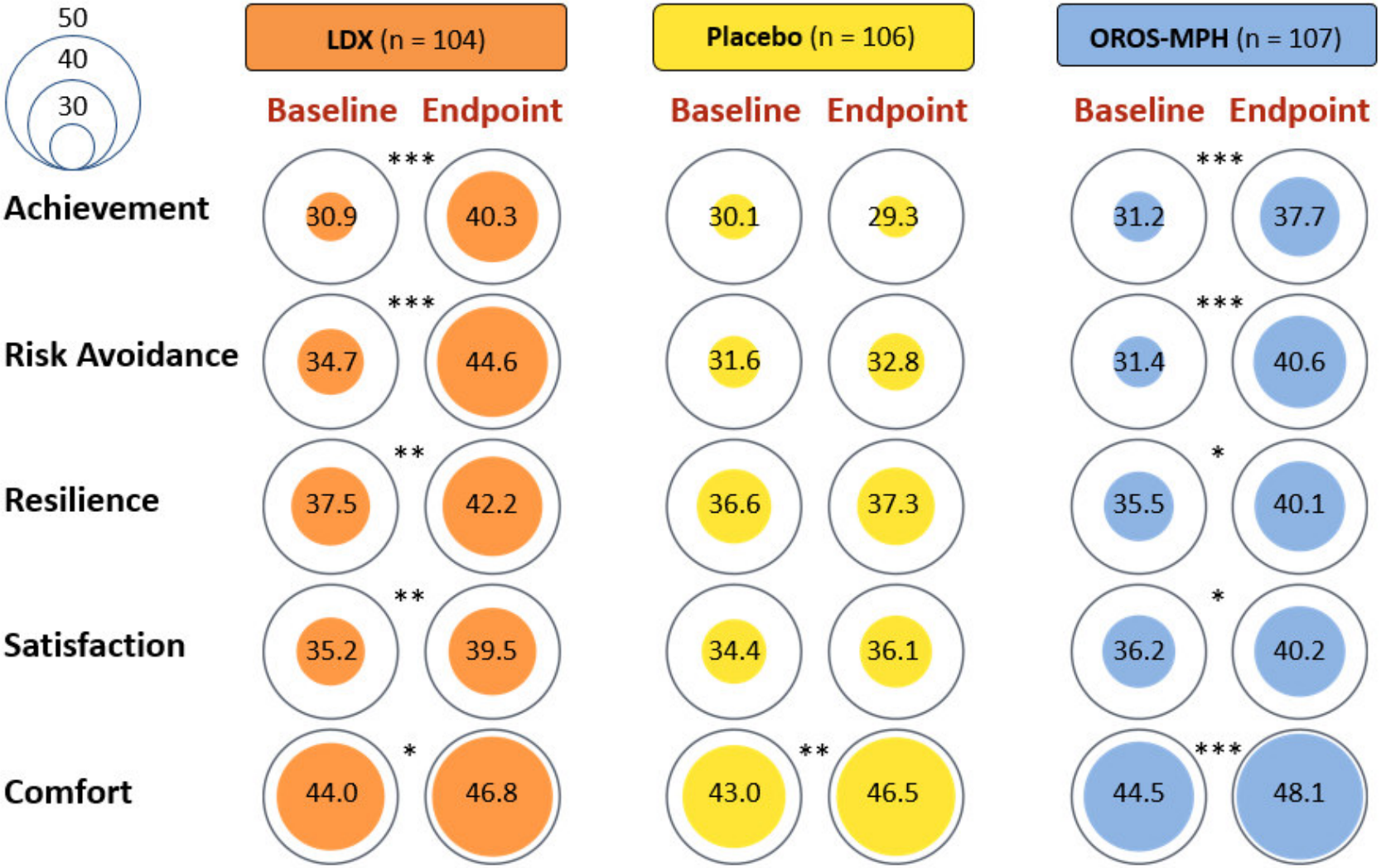
Cardiovascular Effects of Stimulant and Non-Stimulant Medication for Children and Adolescents with ADHD: A Systematic Review and Meta-Analysis of Trials of Methylphenidate, Amphetamines and Atomoxetine

Leonie Hennissen[1] · Mireille J. Bakker[1] · Tobias Banaschewski[3] · Sara Carucci[4] · David Coghill[5,14] · Marina Danckaerts[6] · Ralf W. Dittmann[3] · Chris Hollis[7] · Hanna Kovshoff[8] · Suzanne McCarthy[9] · Peter Nagy[10] · Edmund Sonuga-Barke[8] · Ian C. K. Wong[12,13] · Alessandro Zuddas[4] · Eric Rosenthal[11] · Jan K. Buitelaar[1,2] · The ADDUCE consortium

- Small but significant effect on systolic blood pressure
  - MPH 0.25 - AMP 0.09 - ATX 0.16
- Small but significant effect on diastolic blood pressure
  - AMP 0.16 - ATX 0.22 (no effect MPH)
- Small but significant effect on heart rate
  - AMP 0.37 - ATX 0.43 (no effect MPH)
- 12.6% reported cardiovascular effects
  - Hypertension, tachycardia, bradycardia, documented arrhythmia and changes in ECG intervals, morphology or repolarization.
- 2% discontinued medication treatment due to cardiovascular effects

CNS Drugs, 2017

Health-Related Quality of Life and Functional Outcomes from a Randomized, Controlled Study of Lisdexamfetamine Dimesylate in Children and Adolescents with Attention Deficit Hyperactivity Disorder



Banaschewski et al., CNS Drugs, 2013

JAMA Psychiatry | Original Investigation

Association Between Medication Use and Performance on Higher Education Entrance Tests in Individuals With Attention-Deficit/Hyperactivity Disorder

Yi Lu, PhD; Arvid Sjölander, PhD; Martin Cederlöf, PhD; Brian M. D'Onofrio, PhD; Catarina Almqvist, PhD; Henrik Larsson, PhD; Paul Lichtenstein, PhD

Table 3. Associations Between ADHD Medication Use and SweSAT Scores Using Definition of Medicated/Nonmedicated Periods

	Within-Patient Comparison[a]			
Patients	No. of Patients	No. of Tests (Medicated/Nonmedicated)[b]	Test Score Difference, Mean (95% CI)	*P* Value
Male[c]	493	1364 (325/1039)	5.69 (2.14-9.23)	.002
Female[c]	437	1160 (355/805)	3.60 (0.06-7.14)	.05
Overall	930	2524 (680/1844)	4.80 (2.26-7.34)	<.001

Original Investigation

Serious Transport Accidents in Adults With Attention-Deficit/Hyperactivity Disorder and the Effect of Medication

A Population-Based Study

JAMA Psychiatry March 2014 Volume 71, Number 3

Zheng Chang, PhD; Paul Lichtenstein, PhD; Brian M. D'Onofrio, PhD; Arvid Sjölander, PhD; Henrik Larsson, PhD

Table 2. Association Between ADHD and Serious Transport Accidents in Swedish Adults

Characteristic	Person-years at Risk	No. of Accidents	HR (95% CI)	
			Crude Association	Adjusted Association
Men				
ADHD	41 793	897	2.45 (2.27-2.65)	1.47 (1.32-1.63)
Non-ADHD	415 662	3217	1 [Reference]	1 [Reference]
Women				
ADHD	27 399	330	2.10 (1.86-2.38)	1.45 (1.24-1.71)
Non-ADHD	271 866	1417	1 [Reference]	1 [Reference]

Table 3. Rate of Serious Transport Accidents During Medication Periods Compared With Nonmedication Periods Among Swedish Adult Patients With ADHD

Characteristic	Person-years at Risk	No. of Accidents	HR (95% CI)	
			Between Individual	Within Individual
Men				
Medicated	8377	144	0.71 (0.57-0.89)	0.42 (0.23-0.75)
Nonmedicated	33 416	753	1 [Reference]	1 [Reference]
Women				
Medicated	6195	67	0.92 (0.78-1.23)	2.35 (0.83-6.64)
Nonmedicated	21 204	263	1 [Reference]	1 [Reference]

RESULTS Compared with individuals without ADHD, male patients with ADHD (adjusted hazard ratio 1.47; 95% CI, 1.32-1.63) and female patients with ADHD (1.45; 1.24-1.71) had an increased risk of serious transport accidents. In male patients with ADHD, medication was associated with a 58% risk reduction (hazard ratio, 0.42; 95% CI, 0.23-0.75), but there was no statistically significant association in female patients. Estimates of the population-attributable fractions suggested that 41% to 49% of the accidents in male patients with ADHD could have been avoided if they had been receiving treatment during the entire follow-up.

CONCLUSIONS AND RELEVANCE Attention-deficit/hyperactivity disorder is associated with an increased risk of serious transport accidents, and this risk seems to be possibly reduced by ADHD medication, at least among male patients. This should lead to increased awareness among clinicians and patients of the association between serious transport accidents and ADHD medication.

THE JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY

ACAMH THE ASSOCIATION FOR CHILD AND ADOLESCENT MENTAL HEALTH

Journal of Child Psychology and Psychiatry 55:8 (2014), pp 878–885 doi:10.1111/jcpp.12164

Stimulant ADHD medication and risk for substance abuse

Zheng Chang,[1] Paul Lichtenstein,[1] Linda Halldner,[1,2] Brian D'Onofrio,[3] Eva Serlachius,[4] Seena Fazel,[5] Niklas Långström,[1] and Henrik Larsson[1]

Table 3 Short-term associations: hazard ratios for substance abuse 2006–2009 during treatment periods compared with nontreatment periods in 38,941 patients with a diagnosis of ADHD

		Hazard ratio			
		Between-indivdual[a]		Within-individual[b]	
Medication	Number of substance abuse diagnoses	Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval
Stimulant ADHD medication	20,335	0.57	0.51–0.64	0.73	0.68–0.77

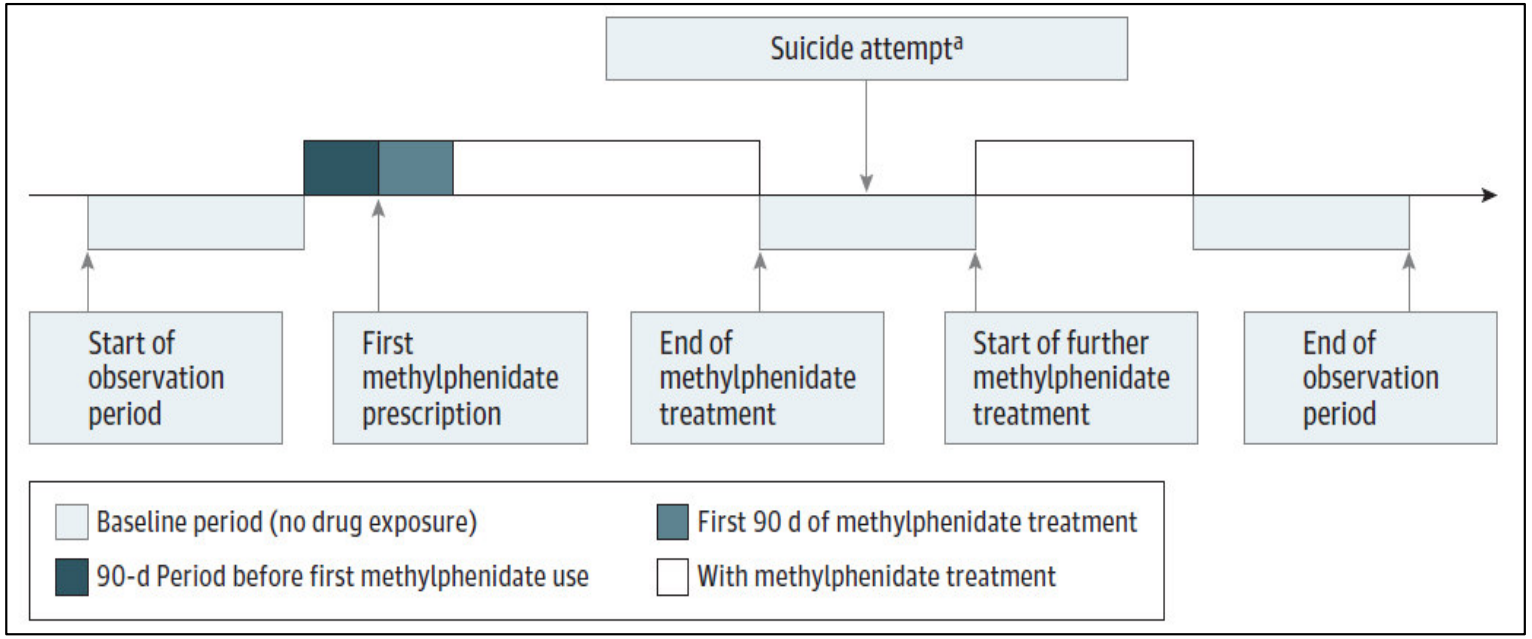
[a]Hazard ratios were calculated with Cox regression (comparing periods when patients received medication with periods when they did not).

[b]Hazard ratios were calculated with stratified Cox regression (comparing periods when patients received medication with periods they did not, within patients who changed their treatment status during follow-up).

JAMA Psychiatry | Original Investigation

Association of Risk of Suicide Attempts With Methylphenidate Treatment

Kenneth K. C. Man, MPH; David Coghill, MD; Esther W. Chan, PhD; Wallis C. Y. Lau, BSc; Chris Hollis, PhD; Elizabeth Liddle, PhD; Tobias Banaschewski, MD; Suzanne McCarthy, PhD; Antje Neubert, PhD; Kapil Sayal, PhD; Patrick Ip, MBBS; Martijn J. Schuemie, PhD; Miriam C. J. M. Sturkenboom, PhD; Edmund Sonuga-Barke, PhD; Jan Buitelaar, MD; Sara Carucci, MD; Alessandro Zuddas, MD; Hanna Kovshoff, PhD; Peter Garas, MD; Peter Nagy, MD; Sarah K. Inglis, PhD; Kerstin Konrad, PhD; Alexander Häge, MD; Eric Rosenthal, MD; Ian C. K. Wong, PhD



JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.2183
Published online July 26, 2017.

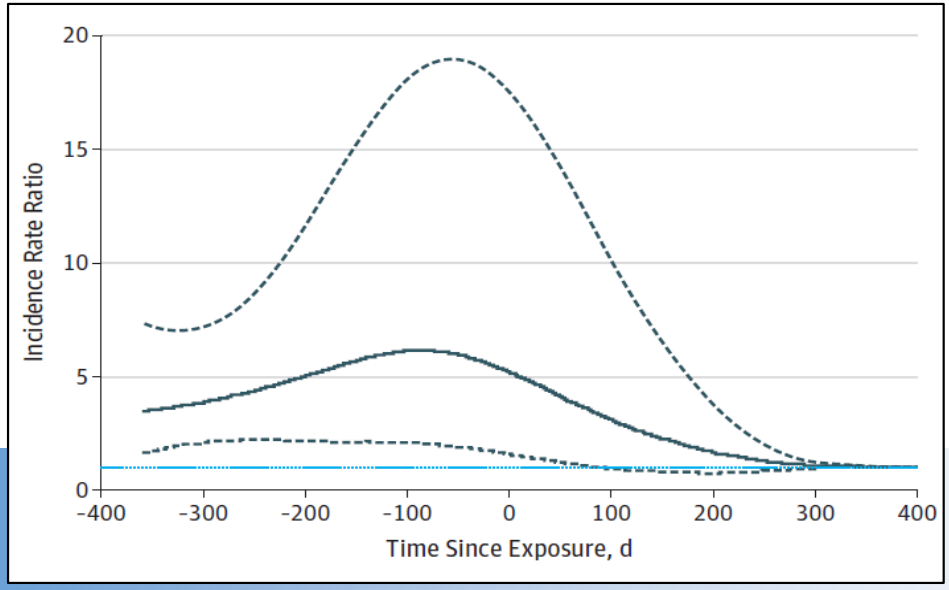
JAMA Psychiatry | Original Investigation

Association of Risk of Suicide Attempts With Methylphenidate Treatment

Kenneth K. C. Man, MPH; David Coghill, MD; Esther W. Chan, PhD; Wallis C. Y. Lau, BSc; Chris Hollis, PhD; Elizabeth Liddle, PhD; Tobias Banaschewski, MD; Suzanne McCarthy, PhD; Antje Neubert, PhD; Kapil Sayal, PhD; Patrick Ip, MBBS; Martijn J. Schuemie, PhD; Miriam C. J. M. Sturkenboom, PhD; Edmund Sonuga-Barke, PhD; Jan Buitelaar, MD; Sara Carucci, MD; Alessandro Zuddas, MD; Hanna Kovshoff, PhD; Peter Garas, MD; Peter Nagy, MD; Sarah K. Inglis, PhD; Kerstin Konrad, PhD; Alexander Häge, MD; Eric Rosenthal, MD; Ian C. K. Wong, PhD

Table 2. Incidence of Suicide Attempts Among Methylphenidate Users in Different Risk Windows

Risk Window	No. of Events	Patient-years	Incidence Per 10 000 Patient-years (95% CI)
Before prerisk	19	65 362	2.91 (1.86-4.54)
90 d Before first methylphenidate treatment	12	5594	21.45 (12.28-37.46)
First 90 d of methylphenidate treatment	6	4687	12.80 (5.87-27.90)
Subsequent methylphenidate treatment	36	42 728	8.43 (6.09-11.66)
After methylphenidate treatment	81	68 636	11.80 (9.50-14.66)



JAMA Psychiatry. doi:10.1001/jamapsychiatry.2017.2183
Published online July 26, 2017.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Medication for Attention Deficit–Hyperactivity Disorder and Criminality

Paul Lichtenstein, Ph.D., Linda Halldner, M.D., Ph.D., Johan Zetterqvist, M.Ed., Arvid Sjölander, Ph.D., Eva Serlachius, M.D., Ph.D., Seena Fazel, M.B., Ch.B., M.D., Niklas Långström, M.D., Ph.D., and Henrik Larsson, M.D., Ph.D.

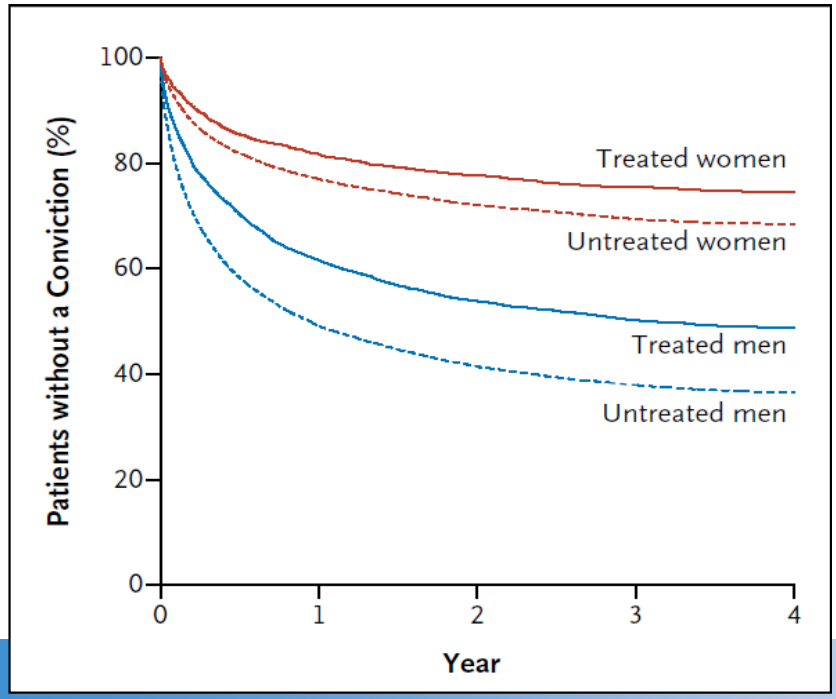


Table 2. Hazard Ratio for Conviction for Any Crime during a Period of Treatment with an ADHD Medication, as Compared with a Nontreatment Period (2006–2009).*

Sex	No. of Patients	No. of Crimes	Hazard Ratio (95% CI)	
			Cox Regression	Stratified Cox Regression
Men	16,087	23,693	0.70 (0.66–0.75)	0.68 (0.63–0.73)
Women	9,569	4,112	0.78 (0.68–0.90)	0.59 (0.50–0.70)

Non-pharmacological TX options

Article

Nonpharmacological Interventions for ADHD: Systematic Review and Meta-Analyses of Randomized Controlled Trials of Dietary and Psychological Treatments

Edmund J.S. Sonuga-Barke, Ph.D.
Daniel Brandeis, Ph.D.
Samuele Cortese, M.D., Ph.D.
David Daley, Ph.D.
Maite Ferrin, M.D., Ph.D.
Martin Holtmann, M.D.
Jim Stevenson, Ph.D.
Marina Danckaerts, M.D., Ph.D.
Saskia van der Oord, Ph.D.
Manfred Döpfner, Ph.D.
Ralf W. Dittmann, M.D., Ph.D.
Emily Simonoff, M.D.
Alessandro Zuddas, M.D.
Tobias Banaschewski, M.D., Ph.D.
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David Coghill, M.D.
Chris Hollis, M.D.
Eric Konofal, M.D., Ph.D.
Michel Lecendreux, M.D.
Ian C.K. Wong, Ph.D.
Joseph Sergeant, Ph.D.
European ADHD Guidelines Group

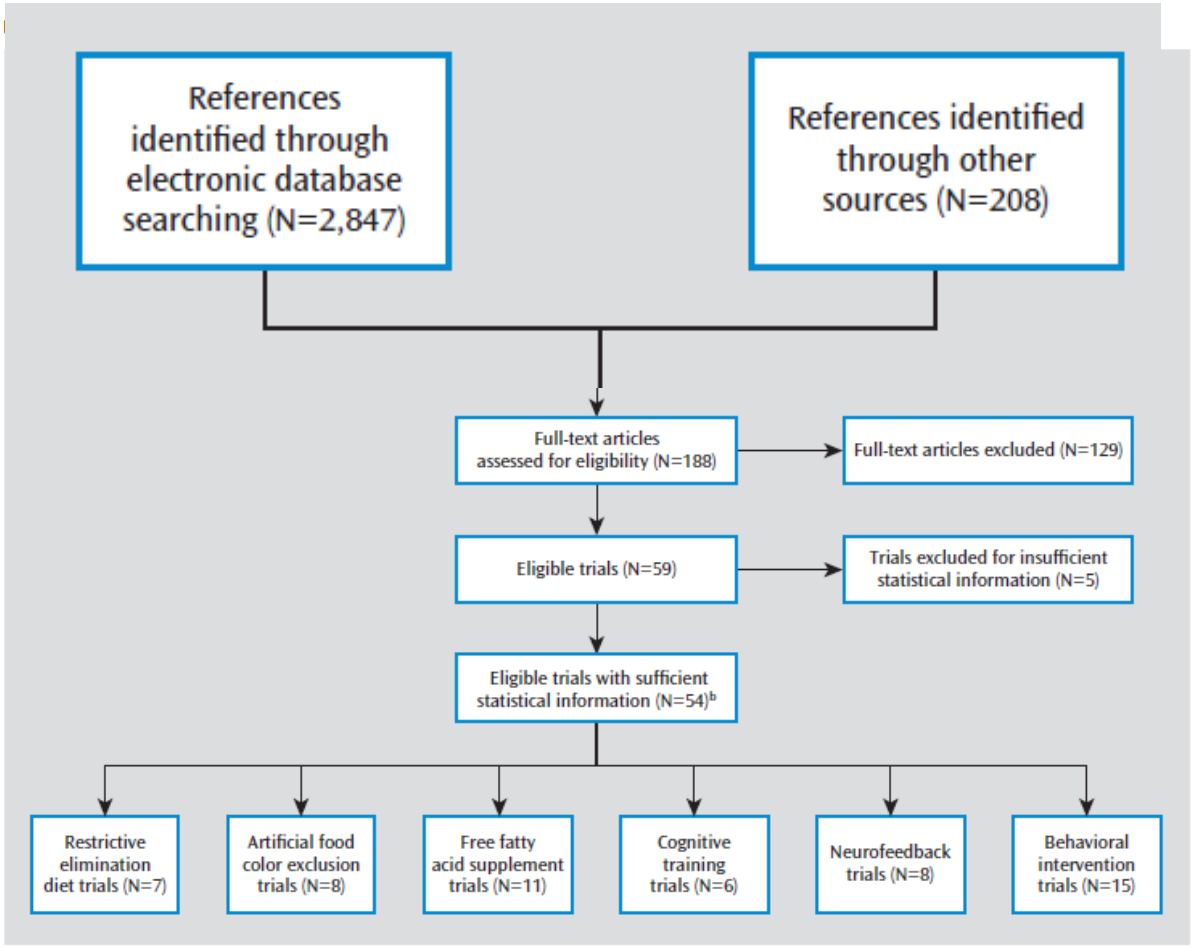
Objective: Nonpharmacological treatments are available for attention deficit hyperactivity disorder (ADHD), although their efficacy remains uncertain. The authors undertook meta-analyses of the efficacy of dietary (restricted elimination diets, artificial food color exclusions, and free fatty acid supplementation) and psychological (cognitive training, neurofeedback, and behavioral interventions) ADHD treatments.

Method: Using a common systematic search and a rigorous coding and data extraction strategy across domains, the authors searched electronic databases to identify published randomized controlled trials that involved individuals who were diagnosed with ADHD (or who met a validated cutoff on a recognized rating scale) and that included an ADHD outcome.

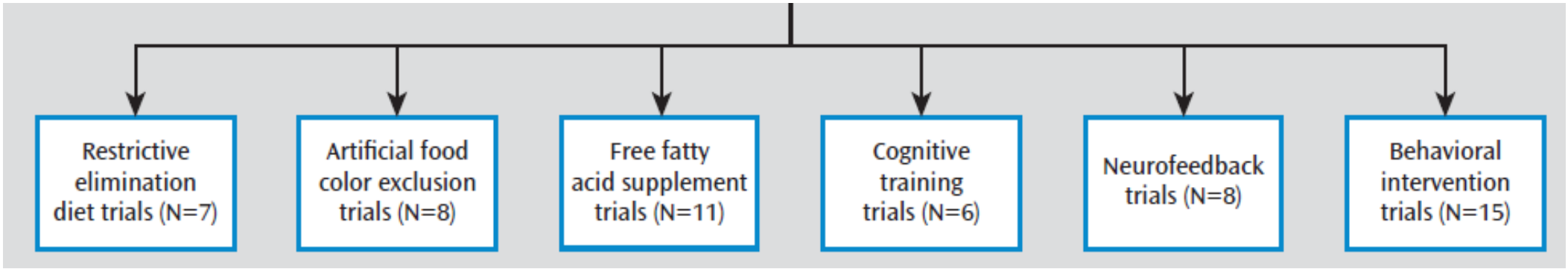
Results: Fifty-four of the 2,904 r
cate screened records were inc
the analyses. Two different anal
performed. When the outcome
was based on ADHD assessmen
ers closest to the therapeutic s
dietary (standardized mean diff
0.21–0.48) and psychological (
ized mean differences=0.40–0.
ments produced statistically s
effects. However, when the best
blinded assessment was employe
remained significant for free f
supplementation (standardized
ference=0.16) and artificial fo
exclusion (standardized mea
ence=0.42) but were substantiall
ated to nonsignificant levels f
treatments.

Conclusions: Free fatty acid sup
tation produced small but signi
ductions in ADHD symptoms e
probably blinded assessments,
the clinical significance of thes
remains to be determined. Artif
color exclusion produced large
but often in individuals selected
sensitivities. Better evidence fo
from blinded assessments is
for behavioral interventions, ne
back, cognitive training, and
elimination diets before they
supported as treatments for co
symptoms.

(Am J Psychiatry 2012;



[a] PRISMA=Preferred Reporting Items for Systematic Reviews and Meta-Analyses (www.prisma-statement.org).
[b] Data from one three-arm trial are included in both neurofeedback and cognitive training analyses.



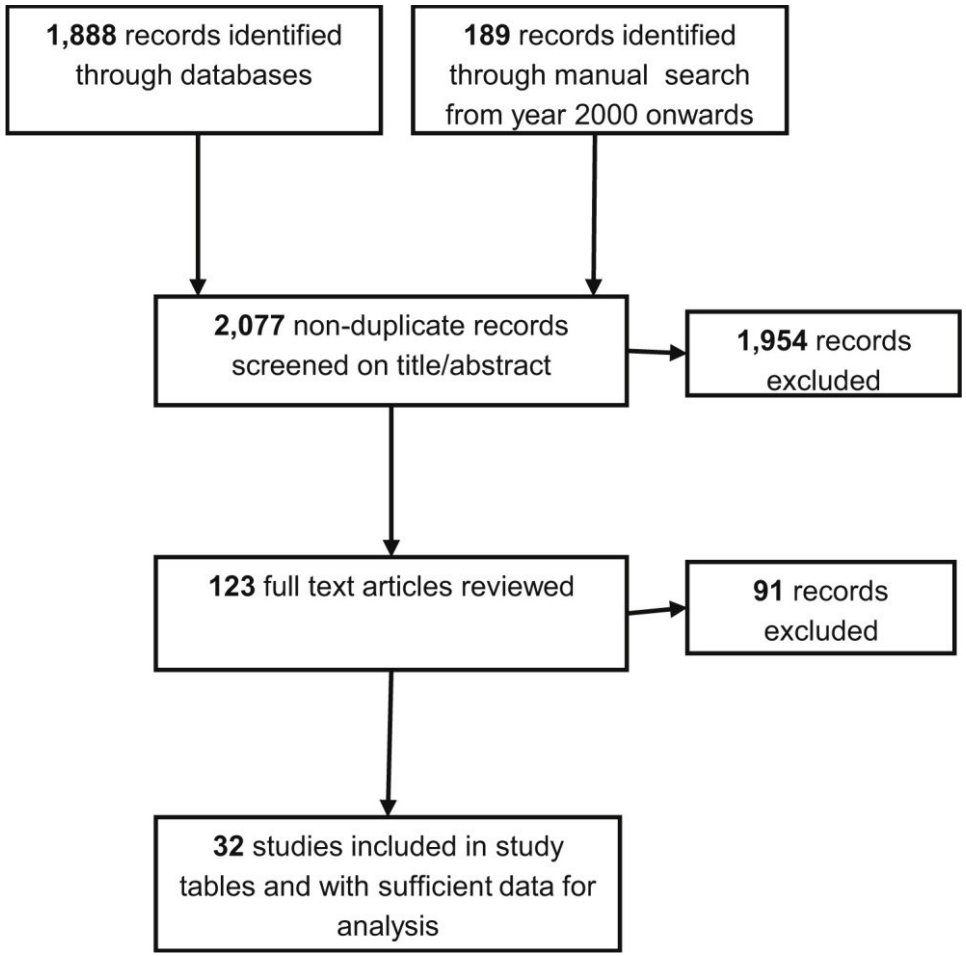
Intervention	Most proximal assessment	Probably blinding assessment (SMD)	
Restricted Elimination Diet	1.48	0.51	**n.s.**
Artificial food color exclusion	0.32	0.42	
Free fatty acid supplementation	0.21	0.16	
Cognitive training	0.64	0.24	**n.s.**
Neurofeedback	0.59	0.29	**n.s.**
Behavioral intervention	0.40	0.02	**n.s.**

But:

- Some patients and caregivers may wish to try non-pharmacological interventions, despite limited evidence of efficacy instead of medication
- Patients might be considered too young or to have an insufficiently severe presentation to warrant medication
- Some patients do not respond positively to medication
- Medication alone might not produce optimal results across all domains of ADHD-related impairment
- Some patients might not have access to medication

Behavioral Interventions in Attention-Deficit/ Hyperactivity Disorder: A Meta-Analysis of Randomized Controlled Trials Across Multiple Outcome Domains

David Daley, PhD, Saskia van der Oord, PhD, Maite Ferrin, MD, PhD, Marina Danckaerts, MD, PhD, Manfred Doepfner, PhD, Samuele Cortese, MD, PhD, Edmund J.S. Sonuga-Barke, PhD, on behalf of the European ADHD Guidelines Group



Dimension	MPROX	PBLIND
ADHD	0.35	0.02 **n.s.**
Conduct problem	0.26	0.31
Social skills	0.47	
Academic Achievement	0.28	

Dimension	MPROX	PBLIND
Positive parenting	0.68	0.63
Negative parenting	0.57	0.43
Parental self-concept	0.37	
Parental Mental Health	0.09	

Daley et al., JAACAP 2014

German Guidelines

- Psychoeducation +
- Children below age 6: first-line psychosocial treatment (parent training); pharmacotherapy only by a specialist, no pharmacotherapy in children below age 3
- Children (≥ 6 years) and adolescents (< age 18)
  - Mild/moderate ADHD: first-line psychosocial treatment
  - Moderate/severe ADHD: first-line pharmacological treatment
- Adults: first-line pharmacological treatment

[1] LDX is licensed in children (≥ 6 years) and adolescents (< age 18) if there is an insufficient clinical response to previous MPH therapy

Banaschewski et al. DGKJP, DGPPN & DGSPJ German guidelines, 2018

German Guidelines

- 1st line: psychostimulants (DEX, MPH and LDX [1])
  - if substance misuse: LA stimulants
  - If Tx is ineffective, change to second stimulant or ATX or GXR
  - If Tx is not tolerated, change to ATX or GXR
- 2nd line: non-stimulants (ATX; GXR)
  - ATX or GXR possible 1st line Tx if comorbidity with Tic disorder; substance misuse
  - ATX possible 1st line Tx if comorbidity with anxiety disorder

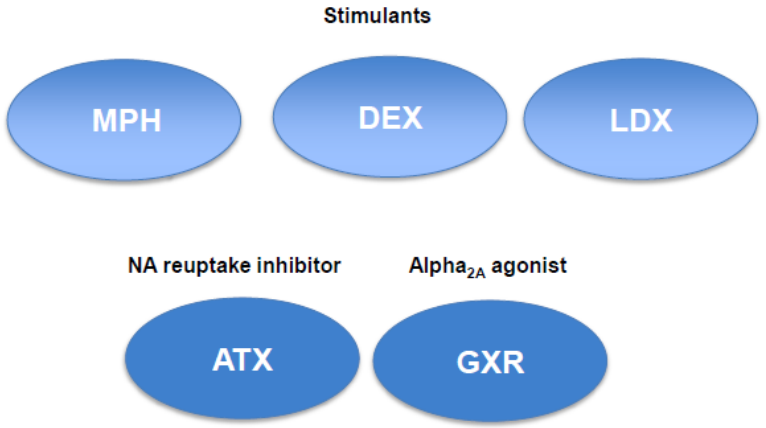
[1] LDX is licensed in children (≥ 6 years) and adolescents (< age 18) if there is an insufficient clinical response to previous MPH therapy

Banaschewski et al. DGKJP, DGPPN & DGSPJ German guidelines, 2018

Individualized pharmacotherapy

TX options for ADHD differ

- Modes of action
- Efficacy
- Pharmacokinetic profiles
- Tolerability profiles
- Mechanisms of delivery



Pharmacotherapy needs to be optimized individually

- Patients respond differently
- Patients show different comorbidities
- Unsatisfactory response occurs
- Patient's needs differ across the day
- Patient's needs change in the course of time

Trends in the Parent-Report of Health Care Provider-Diagnosed and Medicated Attention-Deficit/Hyperactivity Disorder: United States, 2003–2011

Susanna N. Visser, M.S., Melissa L. Danielson, M.S.P.H., Rebecca H. Bitsko, Ph.D., Joseph R. Holbrook, Ph.D., Michael D. Kogan, Ph.D., Reem M. Ghandour, Dr.P.H., Ruth Perou, Ph.D., Stephen J. Blumberg, Ph.D.

	Ever Diagnosed with ADHD							Current ADHD				Current ADHD and Current Medication for ADHD			
	2003	2007	2011	2003–2011		2007–2011		2007	2011	2007–2011		2007	2011	2007–2011	
	%	%	%	PR	95% CI	PR	95% CI	%	%	PR	95% CI	%	%	PR	95% CI
Overall	7.8	9.5	11.0	1.42	1.33–1.50	1.16	1.08–1.24	7.2	8.8	1.23	1.13–1.33	4.8	6.1	1.28	1.16–1.41
Sex															
Male	11.0	13.2	15.1	1.37	1.28–1.48	1.15	1.06–1.24	10.3	12.1	1.17	1.07–1.29	6.9	8.4	1.22	1.09–1.36
Female	4.4	5.6	6.7	1.52	1.36–1.71	1.19	1.04–1.37	4.0	5.5	1.38	1.19–1.59	2.5	3.7	1.46	1.24–1.72
Age															
4–10 y	5.7	6.6	7.7	1.35	1.22–1.50	1.17	1.03–1.31	5.5	6.8	1.24	1.09–1.41	3.7	4.9	1.33	1.15–1.55
11–14 y	9.8	11.2	14.3	1.46	1.32–1.61	1.28	1.14–1.43	8.6	11.4	1.33	1.17–1.51	6.3	8.0	1.26	1.08–1.47
15–17 y	9.6	13.6	14.0	1.46	1.31–1.63	1.03	0.91–1.17	9.3	10.2	1.10	0.94–1.29	5.2	6.5	1.24	1.02–1.50

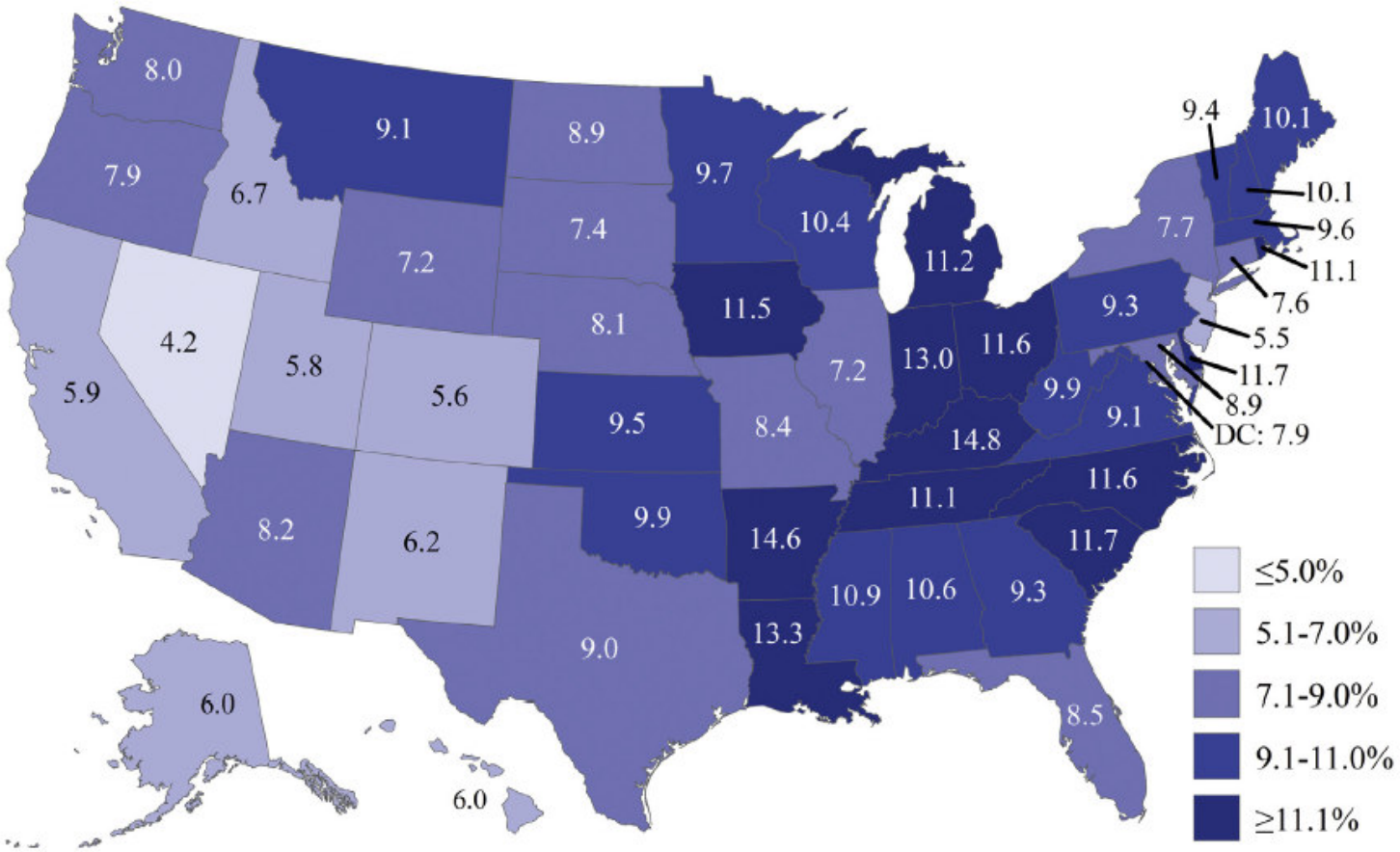
JAACAP, 2013

Trends in the Parent-Report of Health Care Provider-Diagnosed and Medicated Attention-Deficit/Hyperactivity Disorder: United States, 2003–2011

JAACAP, 2013

Susanna N. Visser, M.S., Melissa L. Danielson, M.S.P.H., Rebecca H. Bitsko, Ph.D., Joseph R. Holbrook, Ph.D., Michael D. Kogan, Ph.D., Reem M. Ghandour, Dr.P.H., Ruth Perou, Ph.D., Stephen J. Blumberg, Ph.D.

FIGURE 1 Weighted prevalence estimates of parent-reported current attention-deficit/hyperactivity disorder (ADHD) among children/adolescents 4 to 17 years of age, by state (United States, 2011).

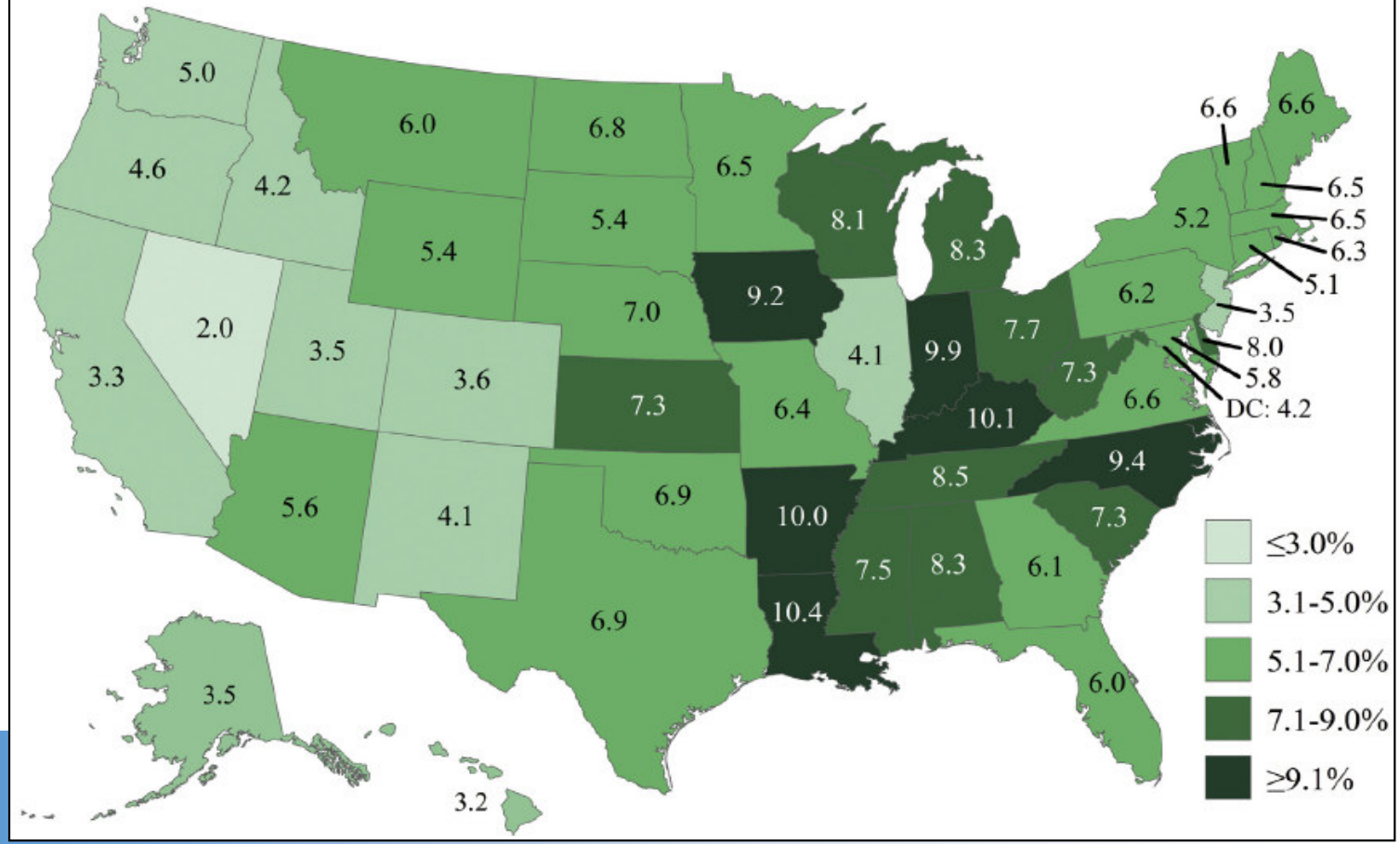


Trends in the Parent-Report of Health Care Provider-Diagnosed and Medicated Attention-Deficit/Hyperactivity Disorder: United States, 2003–2011

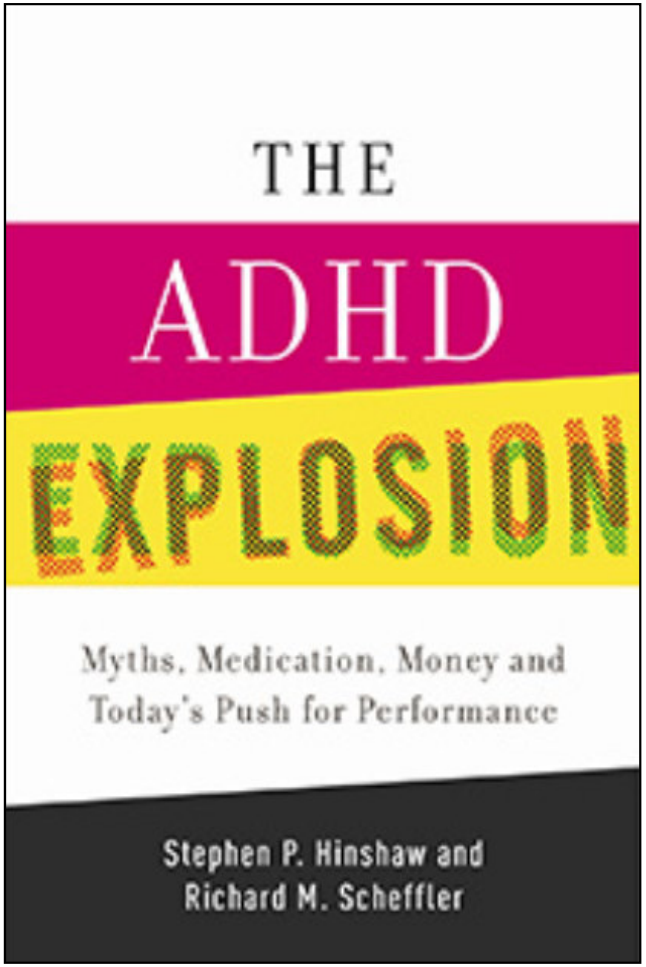
JAACAP, 2013

Susanna N. Visser, M.S., Melissa L. Danielson, M.S.P.H., Rebecca H. Bitsko, Ph.D., Joseph R. Holbrook, Ph.D., Michael D. Kogan, Ph.D., Reem M. Ghandour, Dr.P.H., Ruth Perou, Ph.D., Stephen J. Blumberg, Ph.D.

FIGURE 2 Weighted prevalence estimates of parent-reported current attention-deficit/hyperactivity disorder (ADHD) medication treatment among children/adolescents 4 to 17 years of age, by state (United States, 2011).



Administrative Prävalenz
Einflussfaktoren



- Definitionskriterien
- Behandlungsoptionen

- Gesundheitspolitik & Versorgungssystem
  - (Arztdichte, Versicherungssystem)

- Soziale Schicht
- Ethnische Zugehörigkeit
- Kulturelle Faktoren
- Stigmata, Medien, Werbung

- Schulpolitik

Hinshaw & Scheffler, 2014

THE JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY
ACAMH THE ASSOCIATION FOR CHILD AND ADOLESCENT MENTAL HEALTH
Journal of Child Psychology and Psychiatry 55:8 (2014), pp 897–904 doi:10.1111/jcpp.12229

Relative immaturity and ADHD: findings from nationwide registers, parent- and self-reports

Linda Halldner,[1,2] Annika Tillander,[1] Cecilia Lundholm,[1] Marcus Boman,[1] Niklas Långström,[1] Henrik Larsson,[1] and Paul Lichtenstein[1]

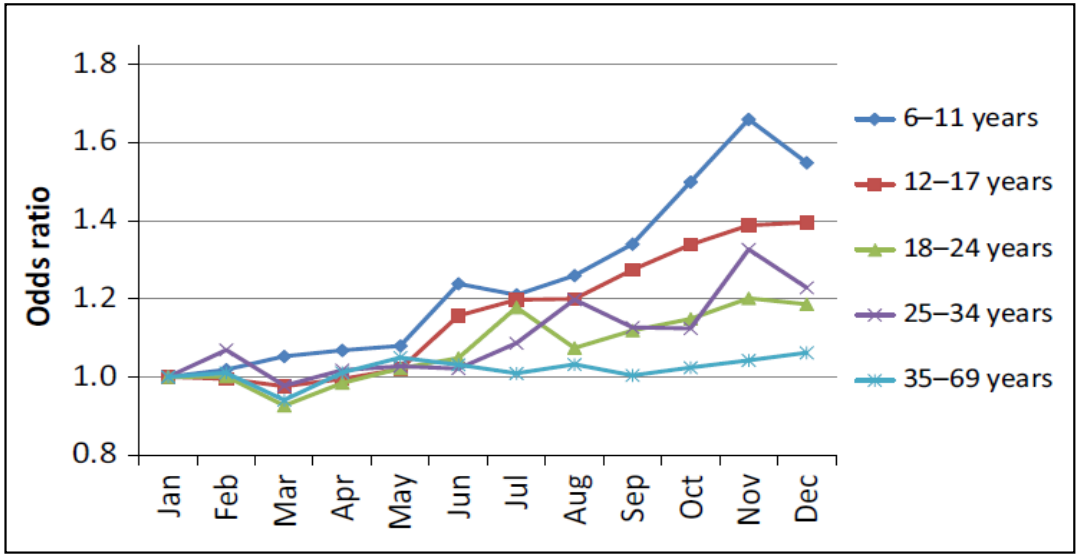


Table 1 Odds ratios for ADHD diagnosis and medication, respectively, at different ages as seen in data Swedish National Registries for individuals born in November/December compared withto individuals born in January/February the following year

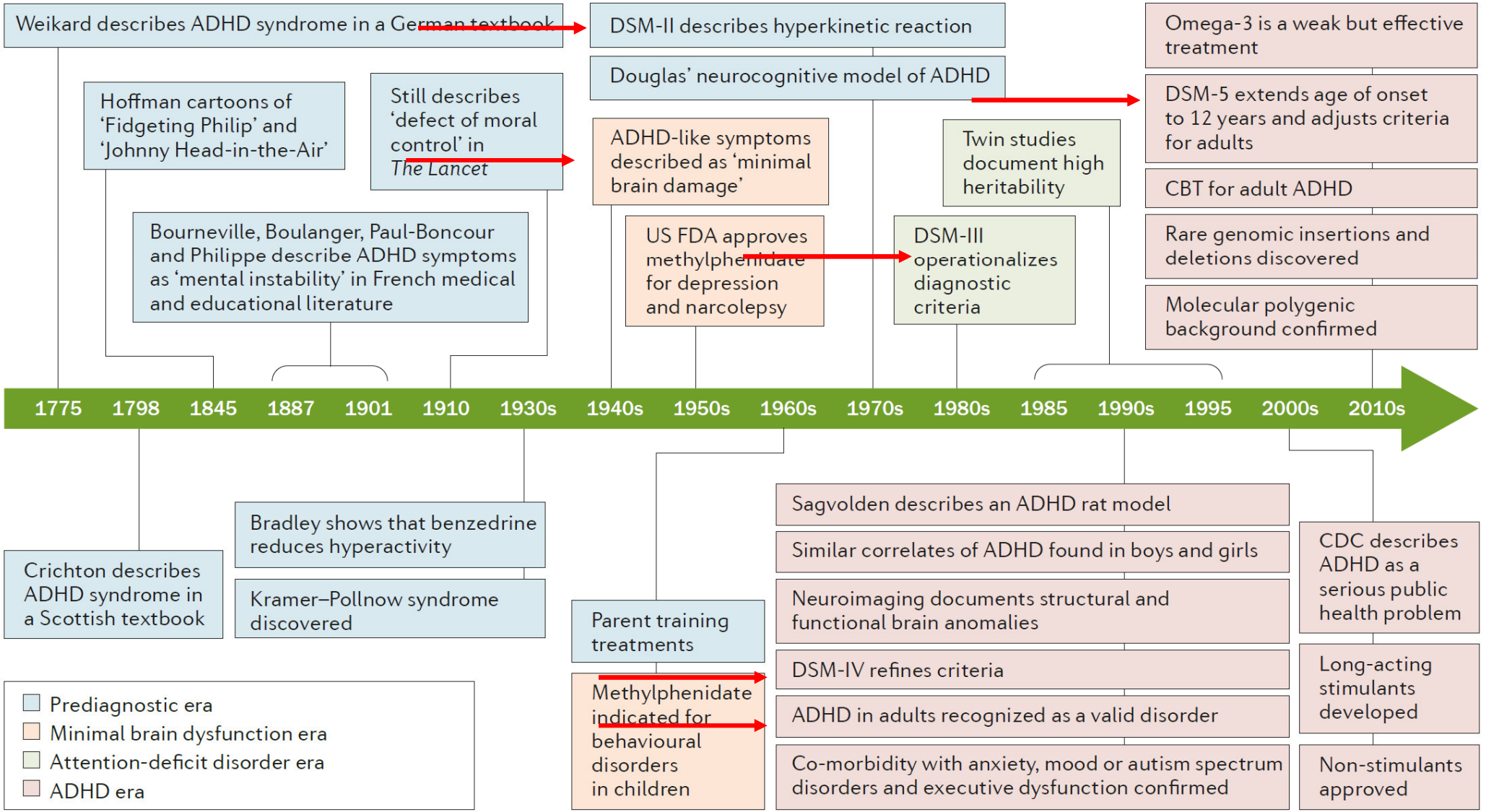
Birth month			ADHD diagnosis			ADHD medication		
Nov/Dec, years	Jan/Feb, years	Age	Yes	No	Odds Ratio (95% CI)	Yes	No	Odds Ratio (95% CI)
1998–2002	1999–2003	6	323	146,926	**1.3 (1.1, 1.6)**	392	146,857	**1.8 (1.5, 2.2)**
1997–2001	1998–2002	7	519	144,402	**1.5 (1.3, 1.8)**	699	144,222	**1.5 (1.3, 1.8)**
1996–2000	1997–2001	8	735	144,814	**1.5 (1.3, 1.8)**	1000	144,549	**1.5 (1.3, 1.7)**
1995–1999	1996–2000	9	864	146,534	**1.5 (1.3, 1.8)**	1300	146,098	**1.4 (1.3, 1.6)**
1994–1998	1995–1999	10	1017	152,294	**1.4 (1.2, 1.5)**	1587	151,724	**1.4 (1.3, 1.6)**
1993–1997	1994–1998	11	1109	160,372	**1.3 (1.2, 1.5)**	1811	159,670	**1.4 (1.3, 1.6)**
1992–1996	1993–1997	12	1219	169,596	**1.3 (1.1, 1.4)**	1989	168,826	**1.4 (1.3, 1.5)**
1991–1995	1992–1996	13	1255	180,519	**1.3 (1.2, 1.5)**	2145	179,629	**1.4 (1.2, 1.5)**
1990–1994	1991–1995	14	1332	190,135	**1.2 (1.1, 1.3)**	2346	189,121	**1.4 (1.3, 1.5)**
1989–1993	1990–1994	15	1389	195,495	**1.3 (1.1, 1.4)**	2285	194,599	**1.3 (1.2, 1.4)**
1988–1992	1989–1993	16	1325	197,330	1.1 (1.0, 1.3)	2011	196,644	**1.2 (1.1, 1.3)**
1987–1991	1988–1992	17	1146	196,602	1.1 (1.0, 1.3)	1698	196,050	**1.2 (1.1, 1.3)**
1980–1990	1981–1991	18–24	2625	406,101	**1.2 (1.1, 1.3)**	2595	406,131	1.1 (1.0, 1.2)
1970–1983	1971–1984	25–34	1854	535,897	**1.2 (1.1, 1.3)**	1987	535,764	1.1 (1.0, 1.2)
1940–1973	1941–1974	35–69	2239	1,342,425	1.1 (1.0, 1.1)	2862	1,341,802	1.0 (1.0, 1.2)

Figures in bold are significant at $p < .05$.

Attention-deficit/hyperactivity disorder

Stephen V. Faraone[1,2], Philip Asherson[3], Tobias Banaschewski[4], Joseph Biederman[5], Jan K. Buitelaar[6], Josep Antoni Ramos-Quiroga[7–9], Luis Augusto Rohde[10,11], Edmund J. S. Sonuga-Barke[12,13], Rosemary Tannock[14,15] and Barbara Franke[16]

NATURE REVIEWS | DISEASE PRIMERS



Faraone et al., 2015

ADHD (DSM-V)

Persistent & impairing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development

- Age of onset
  - Several symptoms present prior to age 12 y
- Duration
  - At least 6 months
- Significant degree of impairment
  - Interference with social, academic or occupational functioning
- Situational pervasiveness
  - Several symptoms present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities)
- Symptoms must not be solely attributable to other mental disorders

- Symptom threshold change for adults and older adolescents to 5 instead of 6 symptoms
- Comorbid diagnosis with ASD is now allowed

ADHD - Changes made in DSM-5

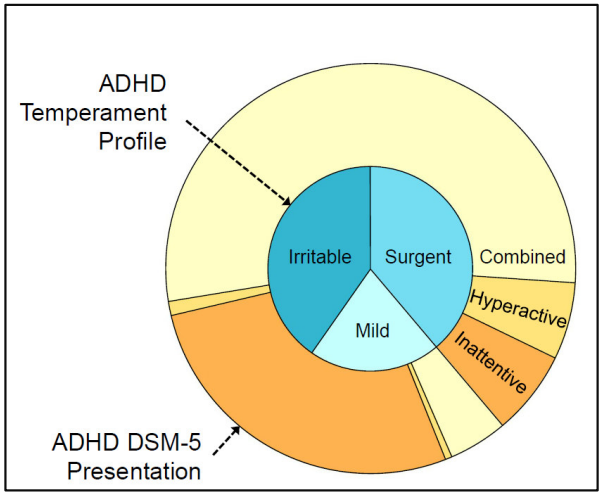
- Symptom threshold change for adults and older adolescents to 5 instead of 6 symptoms
- Comorbid diagnosis with ASD is now allowed
- Onset criterion changed to “several symptoms present prior to age 12”
- Cross-situational requirement strengthened to “several” symptoms in each setting
- Examples added to facilitate application across life span
- Subtypes replaced with presentation specifiers
- ADHD included in neurodevelopmental disorder chapter

Toward a Revised Nosology for Attention-Deficit/ Hyperactivity Disorder Heterogeneity

Joel T. Nigg, Sarah L. Karalunas, Eric Feczko, and Damien A. Fair

Table 1. A Selection of Proposals for Addressing ADHD Mechanistic Heterogeneity

Perspective	General Proposal for Heterogeneity
Clinical	Sluggish cognitive tempo
	Nonhyperactive/hypoactive
	Predominantly hyperactive, inattentive, combined
Neurobiological-Cognition	Executive dysfunction subtype
	Inhibition, working memory, time processing
	EF, time processing
Neurobiological-Motivation	EF vs. delay aversion
	EF, reward response/discounting
Emotion-Regulation/Temperament	Callous-unemotional
	Emotional dysregulation
	Irritability
	Surgent, negative affect, cognitive control
Neurobiology	Differential cortical-subcortical engagement
	Differential rates of neurodevelopment
Etiological	Perinatal exposure vs. genetic or G × E



Nigg et al., 2020

Mediale Kritik

"ADHD does not exist. ADHD is a diagnosis that lacks a clinical entity, and the medication, far from being a treatment itself, is actually a like doping in sports."

"(ADHD) it is not established on objective criteria that allow us to differentiate normal from supposedly pathological behavior, but rather it is based on subjective assessments."

ABC PADRES E HIJOS

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ABC FAMILIA Padres e hijos Parejas Educación Mayores Familia sana Planes con niños Mujeres Bebés

ENTREVISTA

«El TDAH no existe, y la medicación no es un tratamiento, sino un dopaje»

- El catedrático Marino Pérez, autor de «Volviendo a la normalidad», asegura que no hay biomarcador cerebral que justifique el Trastorno por Déficit de Atención

«Hay una patologización de problemas normales de la infancia», denuncia Marino - ernesto agudo

carlota fominaya

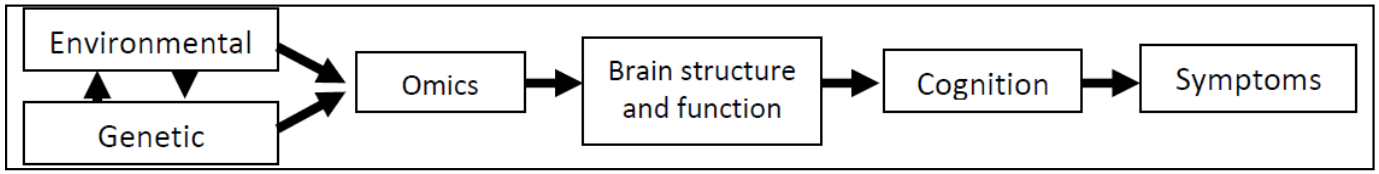
Actualizado:20/10/2014 03:31h

Available from https://www.abc.es/familia-padres-hijos/20141020/abci-trastorno-deficit-atencion-201410171200.html (accessed October 2020)

Image sourced by presenter

Should we aim at finding diagnostic biomarkers of ADHD?

Biomarker: “characteristic that can be objectively measured and evaluated as an indicator of normal biological processes, pathogenetic processes or pharmacologic responses to a therapeutic intervention” (Biomarkers Definitions Working Group 2001)

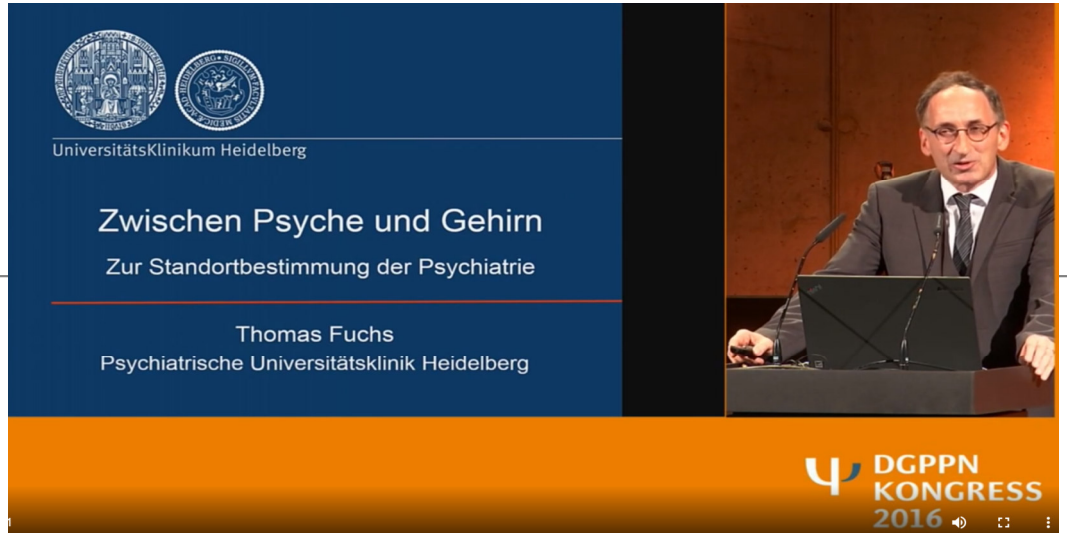


Biomarkers to predict

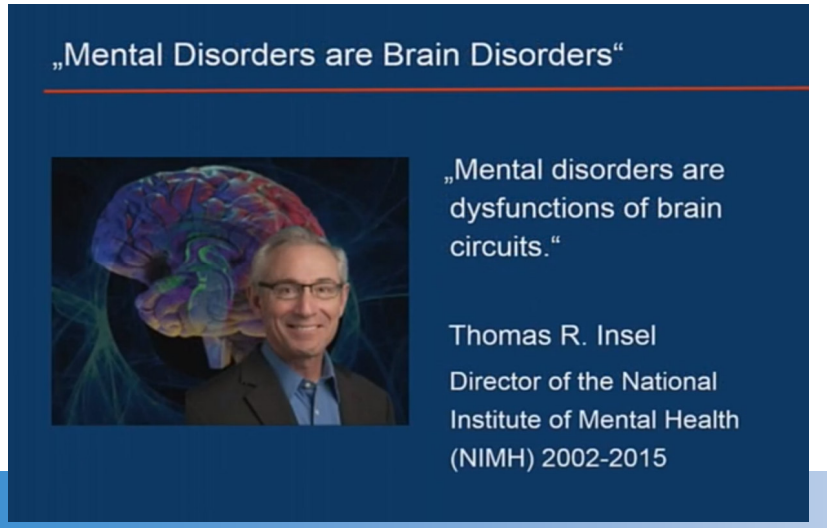
- (differential) diagnosis accuracy
- developmental outcomes
- treatment response

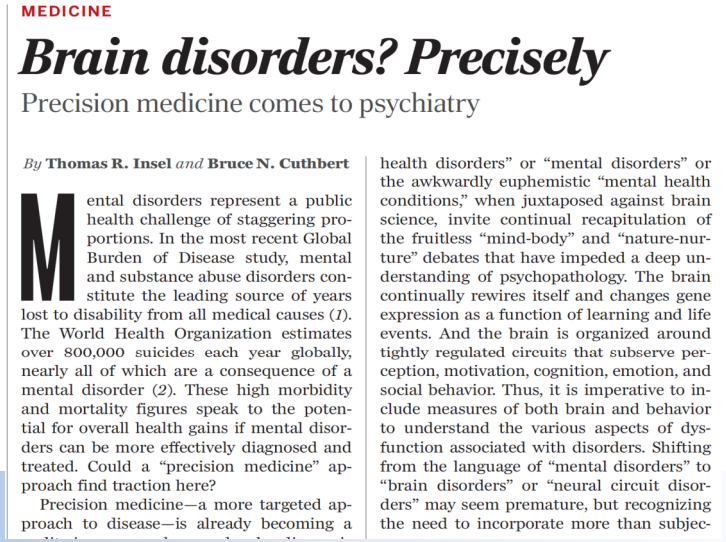
Biomarkers may even provide further insight into etiological mechanisms, but

- case – control differences could be markers of vulnerability, processes related to the onset, chronicity or treatment of ADHD, or reflect consequences or epiphenomena



- Fuchs warnte davor, psychische Erkrankungen angesichts der beeindruckenden Fortschritte neurowissenschaftlicher Grundlagenforschung zunehmend isoliert von den Beziehungen des Patienten zu seiner Umwelt zu betrachten
- Die Psychiatrie müsse ein integratives Rahmenmodell finden, das auch der Bedeutung der Subjektivität und Intersubjektivität für die Krankheit Rechnung trage





MEDICINE

Brain disorders? Precisely

Precision medicine comes to psychiatry

By **Thomas R. Insel** *and* **Bruce N. Cuthbert**

Mental disorders represent a public health challenge of staggering proportions. In the most recent Global Burden of Disease study, mental and substance abuse disorders constitute the leading source of years lost to disability from all medical causes (*1*). The World Health Organization estimates over 800,000 suicides each year globally, nearly all of which are a consequence of a mental disorder (*2*). These high morbidity and mortality figures speak to the potential for overall health gains if mental disorders can be more effectively diagnosed and treated. Could a “precision medicine” approach find traction here?

Precision medicine—a more targeted approach to disease—is already becoming a

health disorders” or “mental disorders” or the awkwardly euphemistic “mental health conditions,” when juxtaposed against brain science, invite continual recapitulation of the fruitless “mind-body” and “nature-nurture” debates that have impeded a deep understanding of psychopathology. The brain continually rewires itself and changes gene expression as a function of learning and life events. And the brain is organized around tightly regulated circuits that subserve perception, motivation, cognition, emotion, and social behavior. Thus, it is imperative to include measures of both brain and behavior to understand the various aspects of dysfunction associated with disorders. Shifting from the language of “mental disorders” to “brain disorders” or “neural circuit disorders” may seem premature, but recognizing the need to incorporate more than subjec-

Diagnosen als soziale Konstrukte

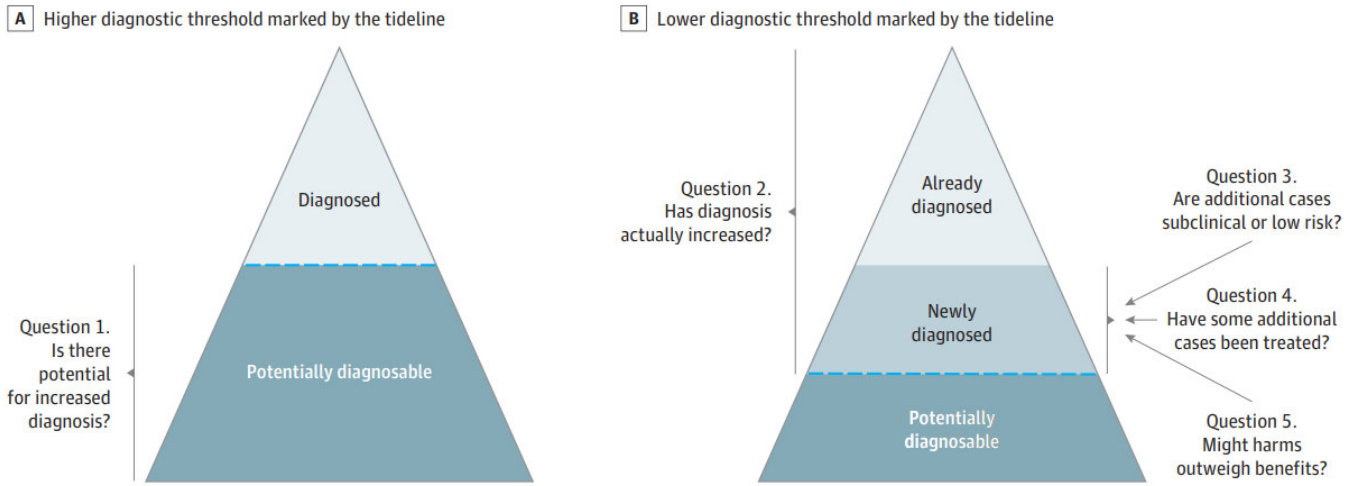
JAMA Network Open

Original Investigation | Pediatrics

Overdiagnosis of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents
A Systematic Scoping Review

Luise Kazda, MPH; Katy Bell, PhD; Rae Thomas, PhD; Kevin McGeechan, PhD; Rebecca Sims, MPsych(Clin); Alexandra Barratt, PhD

Figure 1. Five-Question Framework for Identifying Potential Attention-Deficit/Hyperactivity Disorder (ADHD) Overdiagnosis



- Only 5 studies evaluated the critical issue of benefits and harms among the additional, milder cases. These studies supported a hypothesis of diminishing returns in which the harms may outweigh the benefits for youths with milder symptoms

"Overdiagnosis is defined here as occurring when a person is clinically diagnosed with a condition, but the net effect of the diagnosis is unfavorable."

Stigmatisierung

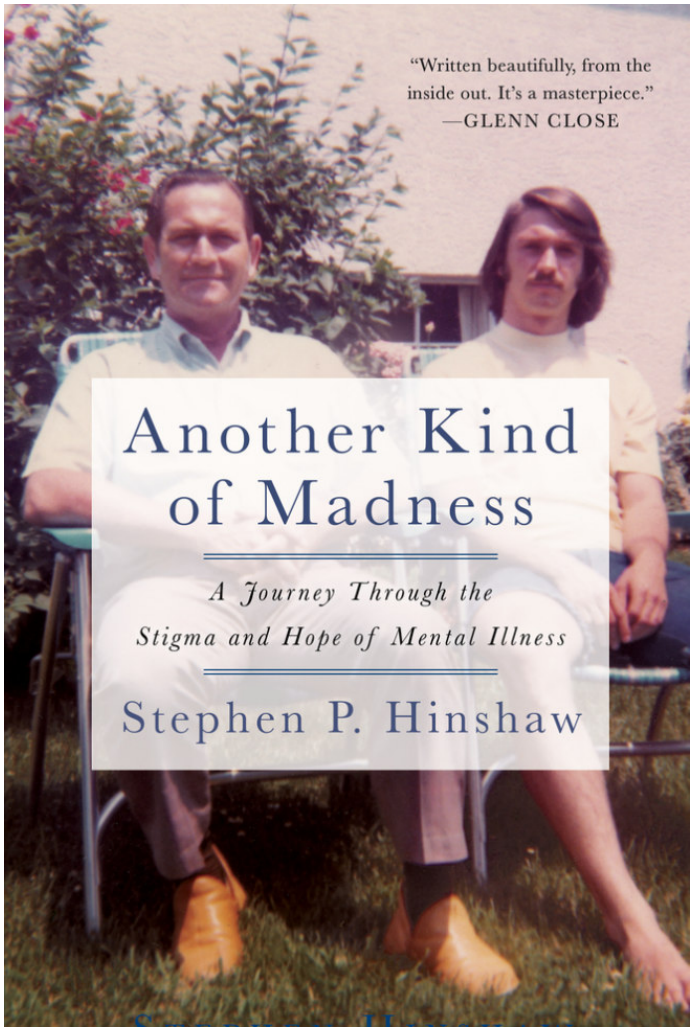


Foto: P. Navales

Stephen P. Hinshaw ist Professor für Psychologie und Psychiatrie in Kalifornien und Autor mehrerer Bücher zu psychischen Störungen wie ADHS und zur Stigmatisierung. Seine wissenschaftlichen Leistungen in den Bereichen Entwicklungs- und klinischer Psychologie wurden mehrfach mit Preisen ausgezeichnet.

Hinshaw betont, dass die öffentliche Aufklärung den Schwerpunkt auf die Behandelbarkeit psychischer Krankheiten und nicht auf ihre Ursachen legen sollte, da insbesondere eine reduktionistische und deterministische Konzeptualisierung der Entstehung und Aufrechterhaltung psychischer Erkrankungen tatsächlich eher Pessimismus schürt und den Wunsch nach sozialer Distanz erhöht. We-

Tobias Banaschewski,
Jörg M. Fegert
Andreas Meyer-Lindenberg

Stigmatization of ADHD: A Developmental Review

Journal of Attention Disorders
2016, Vol. 20(3) 199–205

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Abstract

Objective: In recent years, the stigmatization faced by people with mental disorders has received considerable attention in the empirical literature. However, individuals with different disorders are subject to distinct types of negative attitudes, necessitating examinations of stigma that treat specific disorders individually. **Method:** This article reviews recent empirical literature concerning the stigmatization of ADHD. Further specificity is achieved by taking a developmental perspective, reviewing studies of stigmatizing attitudes as a function of the age of the target and perceiver. **Results:** Findings from nationally representative data sets, experimental investigations, surveys, and qualitative studies indicate that individuals of all ages who exhibit symptoms of ADHD are the recipients of substantial stigmatization. **Conclusion:** Although the stigmatizing attitudes of children and adolescents appear to differ in some ways from those of adults, negative perceptions toward people with ADHD appear to generally be present at all stages of development. *(J. of Att. Dis. 2016; 20(3) 199-205)*

Heterogeneity and Subtyping in Attention-Deficit/ Hyperactivity Disorder—Considerations for Emerging Research Using Person-Centered Computational Approaches

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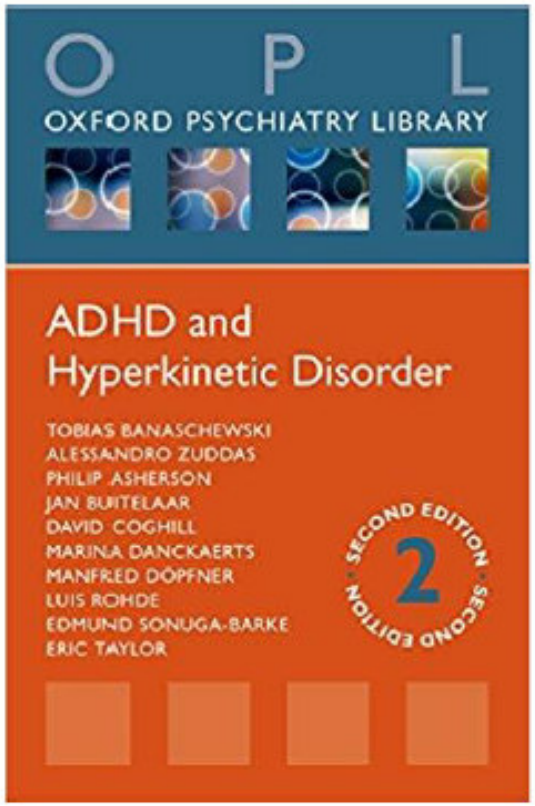
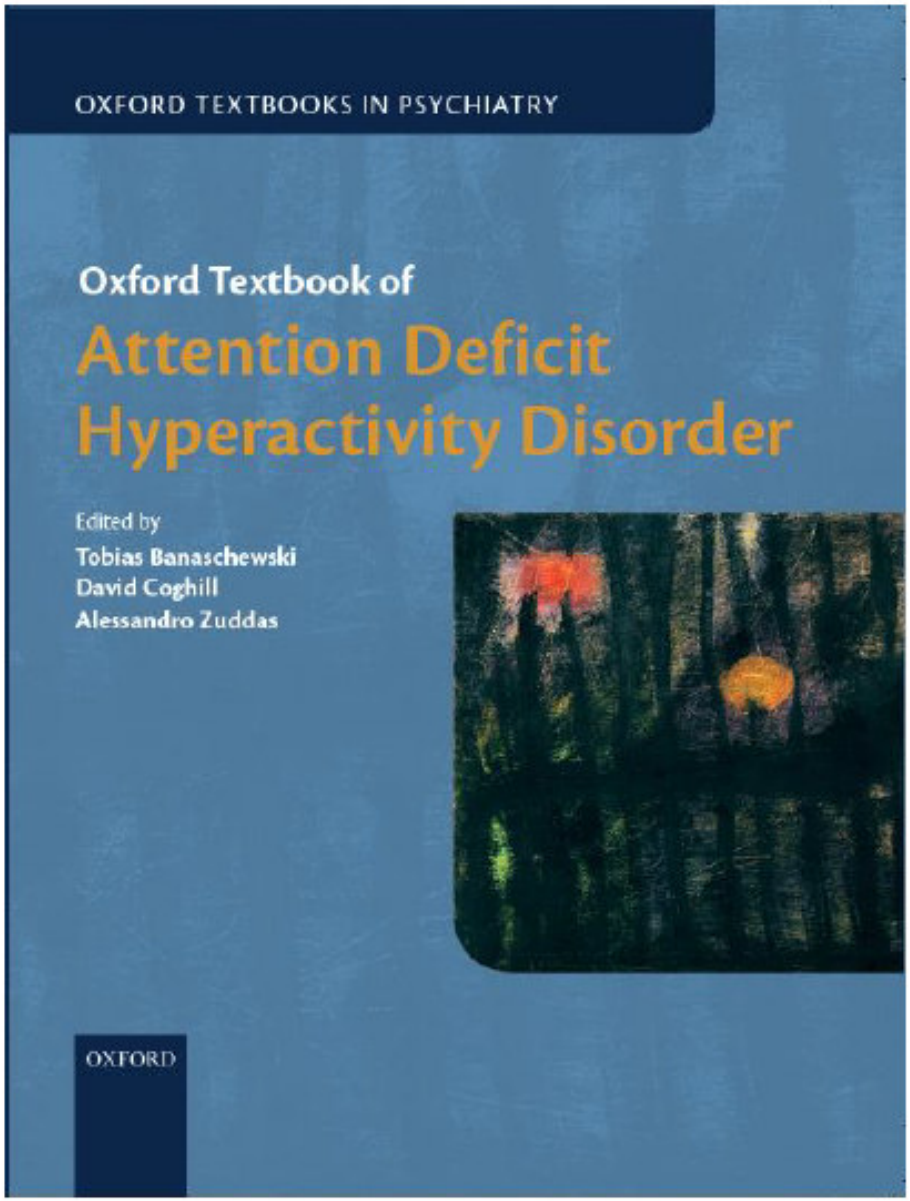
it may ultimately prove fruitful to shift away from studies seeking to identify markers or mechanisms for a putative discrete disease (ADHD) and toward studies identifying markers and mechanisms for specific subgroups or clinical outcomes.

While the presence of discrete taxa is possible, we emphasize that different observable features may cluster in ways that are informative without requiring the assumption of correspondence to a true or natural kind

- Man kann pragmatisch auf den Anspruch einer vollständigen Erklärungsmöglichkeit verzichten, ohne den Sinn neurowissenschaftlicher und medizinischer Forschung zu bestreiten
- Theorien sind Instrumente zur Systematisierung von Handlungswissen, praxiserprobtes Bewirkungs- und Prognosewissen, nicht um strukturisomorphe oder adäquate Abbilder einer natürlichen Welt

Karalunas & Nigg, 2019; Biological Psychiatry





OT-ADHD, Banaschewski, Coghill & Zuddas 2018

Vielen Dank für

Ihre Aufmerksamkeit !