Les rencontres de Biarritz

ATHS

BIARRITZ 2019

14e Colloque International

Addictions
Toxicomanie
Hépatites
SIDA

Comorbidités, dysfonctionnements et complications associés au TDAH tout au long de la vie. L´importance d´un troble sous-diagnostiqué

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Comorbidities, dysfunction and complications associated with ADHD along the lifespan. The importance of an underdiagnosed disorder

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14e Colloque International

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]

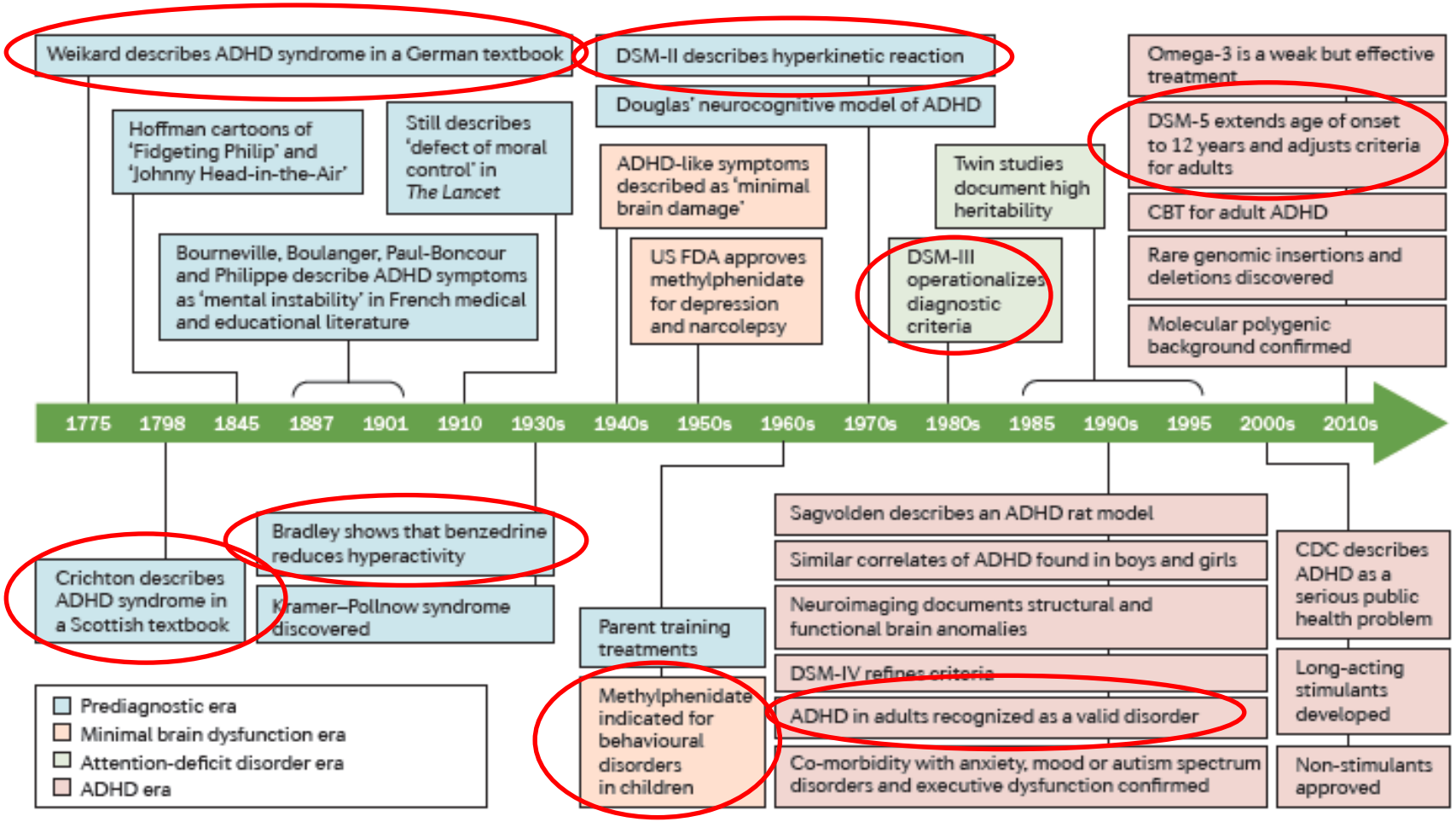


Figure 1 | **The history of attention-deficit/hyperactivity disorder.** Attention-deficit/hyperactivity disorder (ADHD) 'syndromes' have been described in the medical literature since the eighteenth century, but the growth of systematic research required the development of operational diagnostic criteria in the late twentieth century. This schematic outlines selected important developments in the history of ADHD research. CBT, cognitive–behavioural therapy; CDC, Centers for Disease Control and Prevention; DSM, *Diagnostic and Statistical Manual of Mental Disorders*.

TRASTORNO DÉFICIT

4 En el 76% ORIGEN

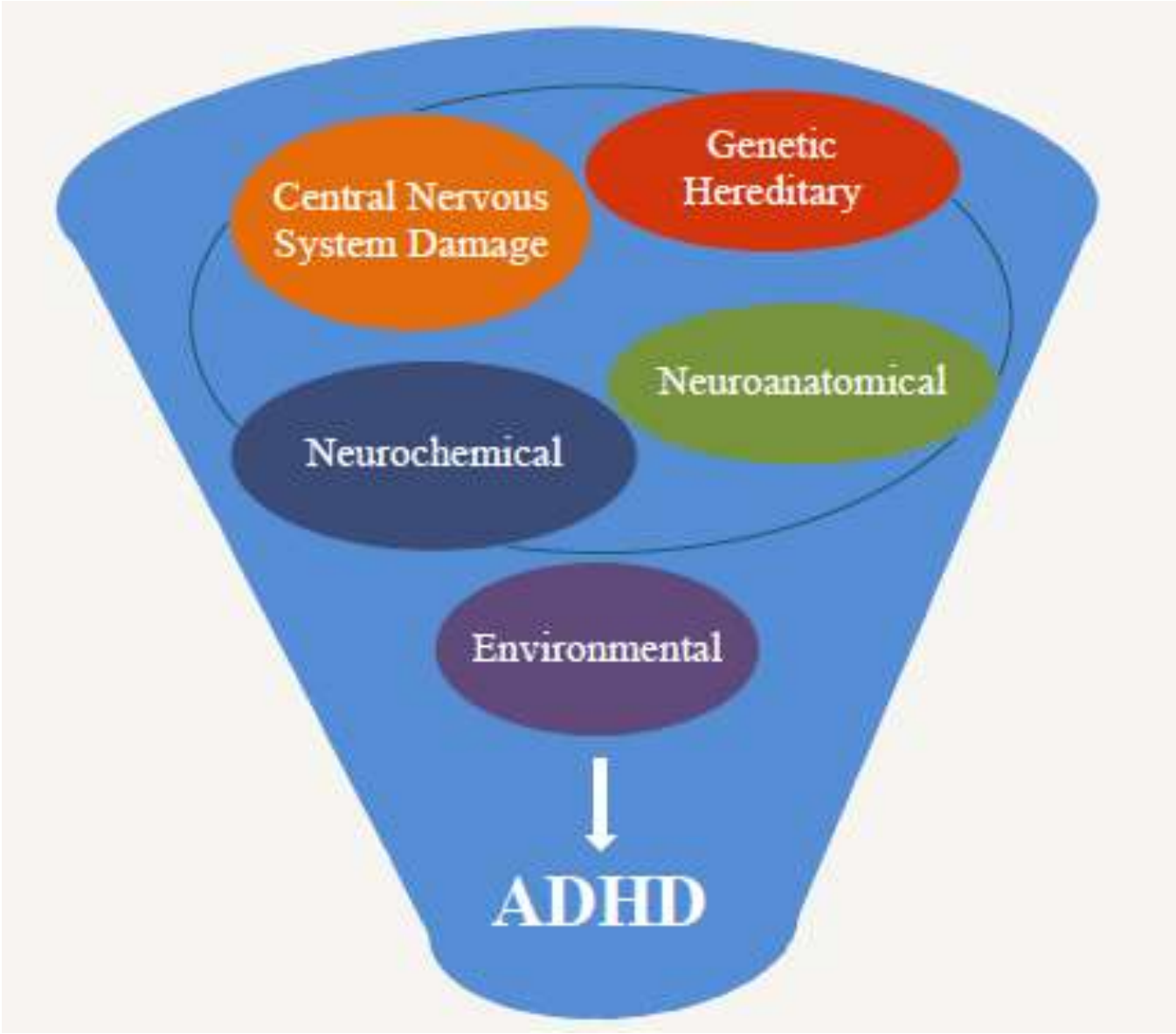
- ADHD is a **common**, **complex** and **multifactorial** neurodevelopmental disorder characterized by a *persistent pattern of inattention, hyperactivity and/or impulsivity*.

- ADHD is highly **heterogeneous** in its presentation and severity, partly as a result of the **very high comorbidity rates** with other mental disorders that often hinders its diagnosis, its treatment and the outcome.

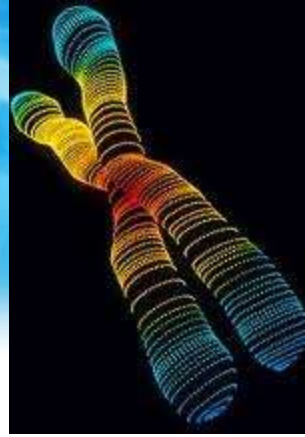
- **Substance use disorders (SUDs)** are **among the most frequent concurrent** psychiatric **disorders** in adolescent or adult patients with ADHD.

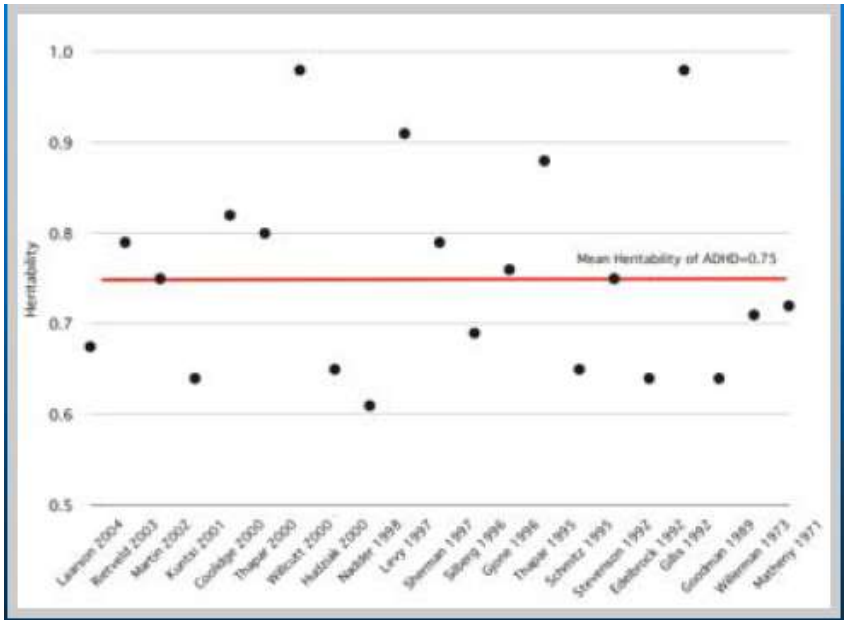
Referencias:
1. Polanczyk G et al. The worlwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry. 2007;164:942-8.
2. Faraone SV. et al. Molecular genetics of attention-deficit/hiperactivity disorder. Biol Psychiatry. 2005 Jun ;57(11):1313-23. Epub 2005 Jan 21.

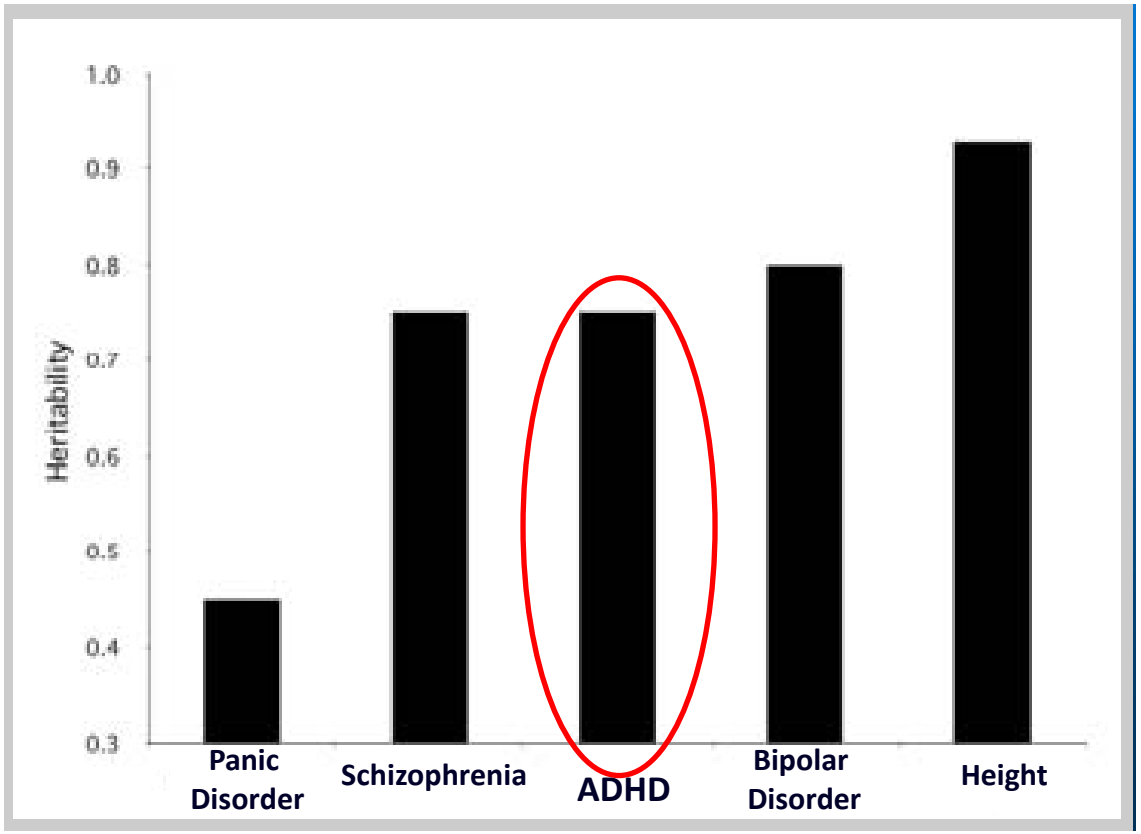
Etiological factors of ADHD



Heritability of ADHD







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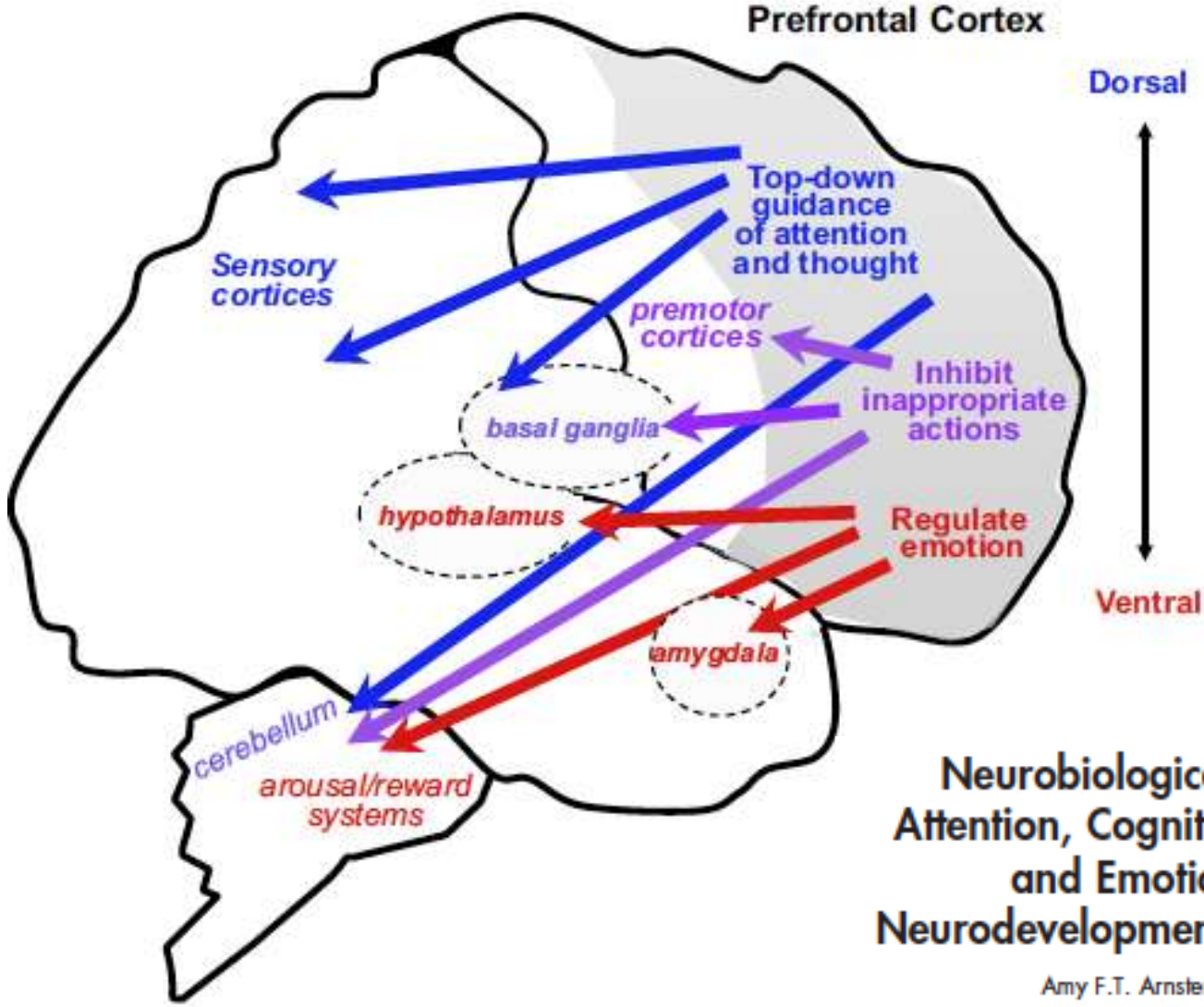
PFC connections in the regulation of attention, emotion and behavior

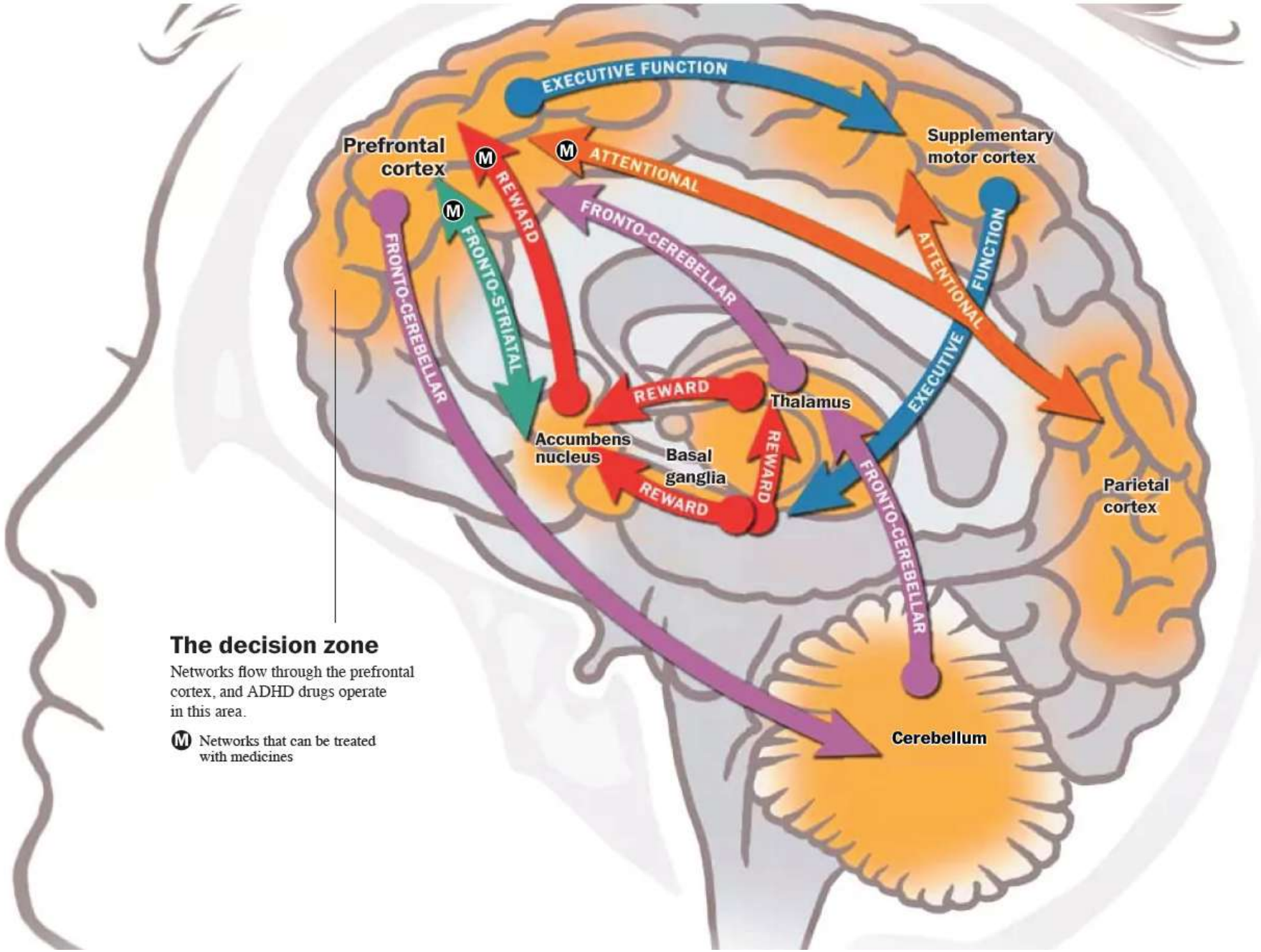


Neurobiological Circuits Regulating Attention, Cognitive Control, Motivation, and Emotion: Disruptions in Neurodevelopmental Psychiatric Disorders

Amy F.T. Arnsten, Ph.D., and Katya Rubia, Ph.D.

REVIEW

Journal of the American Academy of Child & Adolescent Psychiatry
VOLUME 51 NUMBER 4 APRIL 2012



The decision zone

Networks flow through the prefrontal cortex, and ADHD drugs operate in this area.

Ⓜ Networks that can be treated with medicines

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Neuropsychologia 49 (2011) 426–434

ADHD related behaviors are associated with brain activation in the reward system

R. Stark[a,*], E. Bauer[a,b], C.J. Merz[a,c], M. Zimmermann[a], M. Reuter[d], M.M. Plichta[e], P. Kirsch[f], K.P. Lesch[e], A.J. Fallgatter[g], D. Vaitl[a], M.J. Herrmann[e]

ARTICLE INFO

Article history:
Received 29 April 2010
Received in revised form
15 November 2010
Accepted 8 December 2010
Available online 14 December 2010

Keywords:
Attention-deficit/hyperactivity disorder (ADHD)
fMRI
Monetary reward anticipation
Nucleus accumbens
Punishment avoidance anticipation
Verbal feedback anticipation

ABSTRACT

Neuroimaging studies on attention-deficit/hyperactivity disorder (ADHD) suggest dysfunctional reward processing, with hypo-responsiveness during reward anticipation in the reward system including the nucleus accumbens (NAcc). In this study, we investigated the association between ADHD related behaviors and the reward system using functional magnetic resonance imaging in a non-clinical sample. Participants were 31 healthy, female undergraduate students with varying levels of self-reported ADHD related behaviors measured by the adult ADHD self-report scale. The anticipation of different types of reward was investigated: monetary reward, punishment avoidance, and verbal feedback.

All three reward anticipation conditions were found to be associated with increased brain activation in the reward system, with the highest activation in the monetary reward anticipation condition, followed by the punishment avoidance anticipation condition, and the lowest activation in the verbal feedback anticipation condition. Most interestingly, in all three conditions, NAcc activation was negatively correlated with ADHD related behaviors.

In conclusion, our results from a non-clinical sample are in accordance with reported deficits in the reward system in ADHD patients: the higher the number and severity of ADHD related behaviors, the lower the neural responses in the dopaminergic driven reward anticipation task. Thus, our data support current aetiological models of ADHD which assume that deficits in the reward system might be responsible for many of the ADHD related behaviors.

The Worldwide Prevalence of ADHD: A Systematic Review and Metaregression Analysis

Guilherme Polanczyk, M.D.
Maurício Silva de Lima, M.D., Ph.D.
Bernardo Lessa Horta, M.D., Ph.D.
Joseph Biederman, M.D.
Luis Augusto Rohde, M.D., Ph.D.

Objective: The worldwide prevalence estimates of attention deficit hyperactivity disorder (ADHD)/hyperkinetic disorder (HD) are highly heterogeneous. Presently, the reasons for this discrepancy remain poorly understood. The purpose of this study was to determine the possible causes of the varied worldwide estimates of the disorder and to compute its worldwide-pooled prevalence.

Method: The authors searched MEDLINE and PsycINFO databases from January 1978 to December 2005 and reviewed textbooks and reference lists of the studies selected. Authors of relevant articles from North America, South America, Europe, Africa, Asia, Oceania, and the Middle East and ADHD/HD experts were contacted. Surveys were included if they reported point prevalence of ADHD/HD for subjects 18 years of age or younger from the general population or schools according to DSM or ICD criteria.

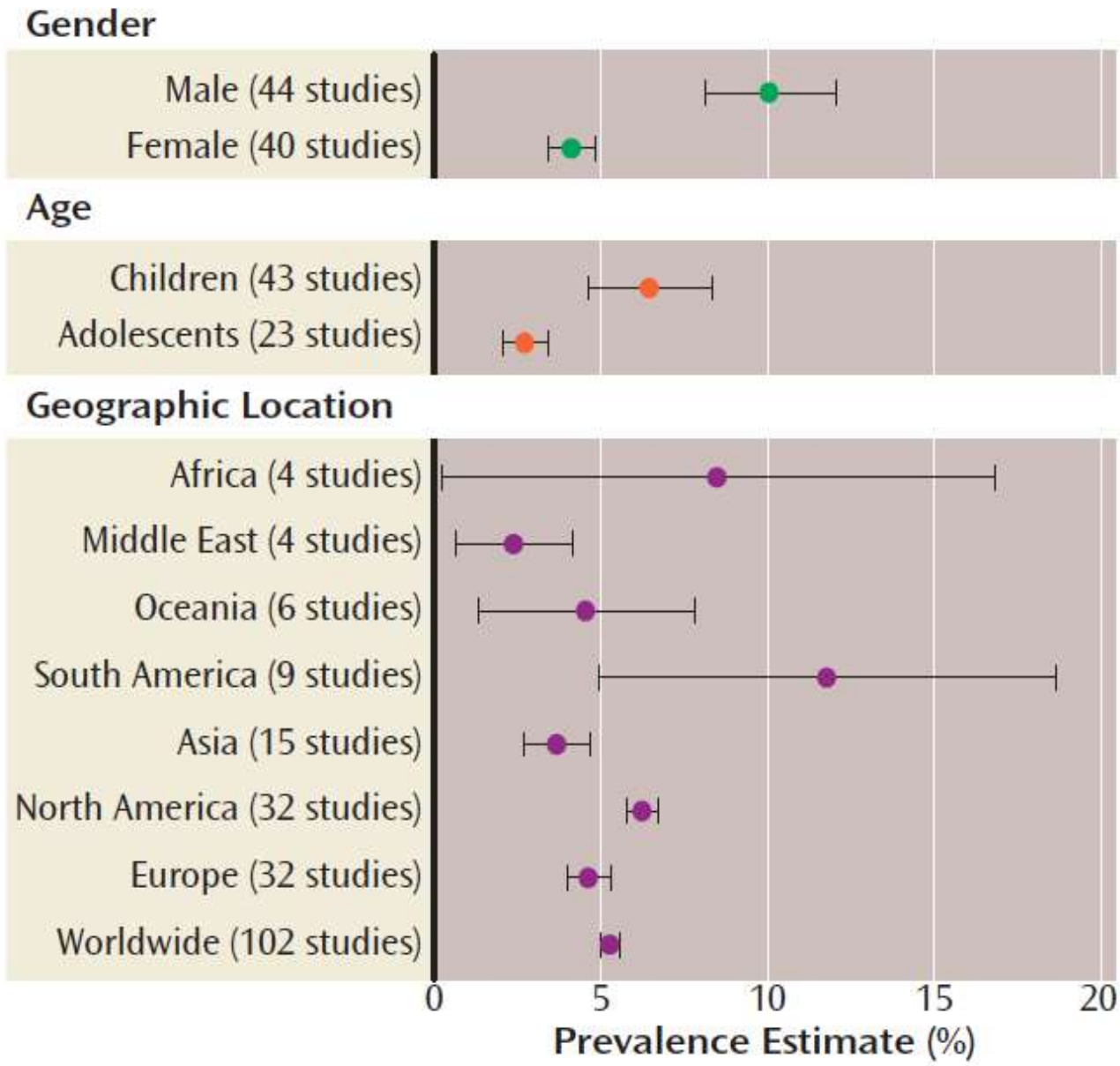
Results: The literature search generated 9,105 records, and 303 full-text articles were reviewed. One hundred and two studies comprising 171,756 subjects from all world regions were included. The ADHD/HD worldwide-pooled prevalence was 5.29%. This estimate was associated with significant variability. In the multivariate metaregression model, diagnostic criteria, source of information, requirement of impairment for diagnosis, and geographic origin of the studies were significantly associated with ADHD/HD prevalence rates. Geographic location was associated with significant variability only between estimates from North America and both Africa and the Middle East. No significant differences were found between Europe and North America.

Conclusions: Our findings suggest that geographic location plays a limited role in the reasons for the large variability of ADHD/HD prevalence estimates worldwide. Instead, this variability seems to be explained primarily by the methodological characteristics of studies.

(Am J Psychiatry 2007; 164:942–948)

ADHD is the most frequent psychiatric disorder of childhood onset, with a **worldwide prevalence in children and adolescence of 3.4-7.2%.**

FIGURE 2. ADHD/HD Pooled Prevalence According to Demographic Characteristics and Geographic Location



European Neuropsychopharmacology (2018) 28, 1059–1088

Live fast, die young? A review on the developmental trajectories of ADHD across the lifespan

ELSEVIER

www.elsevier.com/locate/euroneuro

Barbara Franke[a,b,*], Giorgia Michelini[c], Philip Asherson[c], Tobias Banaschewski[d], Andrea Bilbow[e,f], Jan K. Buitelaar[g], Bru Cormand[h,i,j,k], Stephen V. Faraone[l,m], Ylva Ginsberg[n,o], Jan Haavik[m,p], Jonna Kuntsi[c], Henrik Larsson[n,o], Klaus-Peter Lesch[q,r,s], J. Antoni Ramos-Quiroga[t,u,v,w], János M. Réthelyi[x,y], Marta Ribases[t,u,v], Andreas Reif[z]

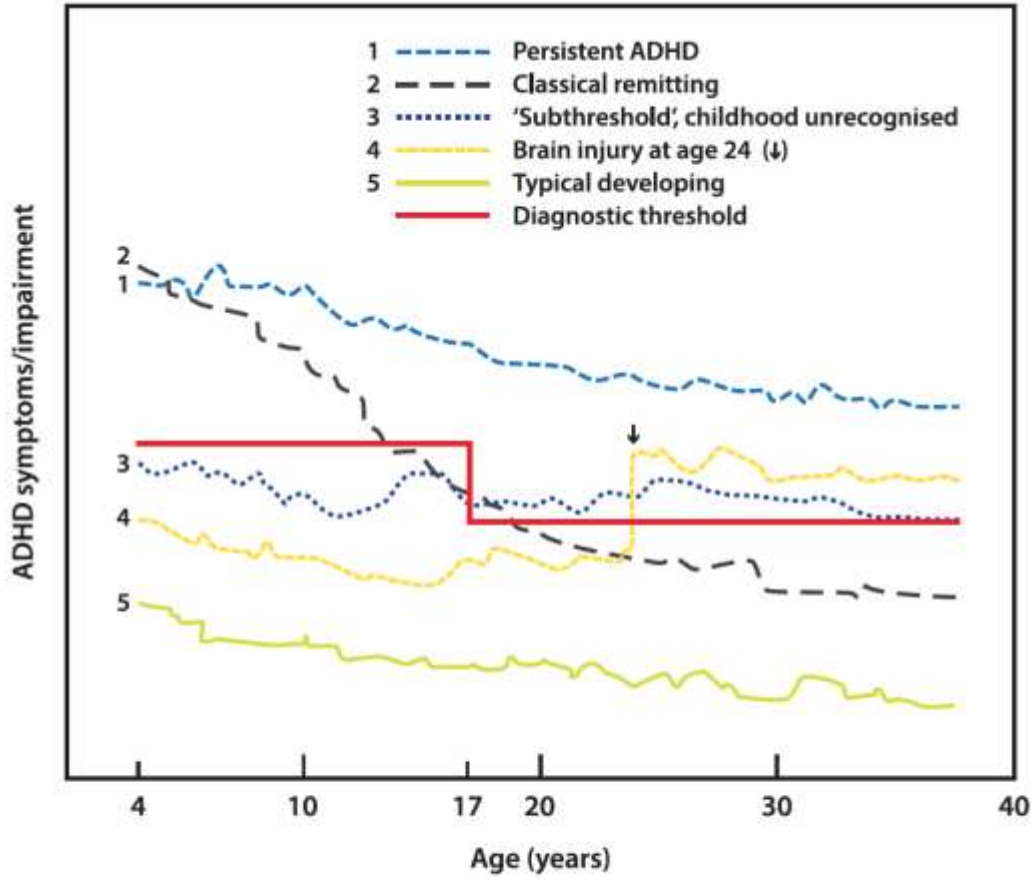


Fig. 1 Theoretical developmental trajectories of ADHD across the lifespan. Details are given in the text.

Studies show that about **two-thirds** of children diagnosed with ADHD continue with symptomatology in adulthood, so that it is estimated that **3-5% of the adult population** have the disorder.

Deberdt et al. BMC Psychiatry (2015) 15:242
DOI 10.1186/s12888-015-0624-5

BMC Psychiatry

RESEARCH ARTICLE Open Access

Prevalence of ADHD in nonpsychotic adult psychiatric care (ADPSYC): A multinational cross-sectional study in Europe

Walter Deberdt[1*], Johannes Thome[2], Jeremie Lebrec[3], Susanne Kraemer[3], Irene Fregenal[4], J. Antoni Ramos-Quiroga[5] and Muhammad Arif[6]

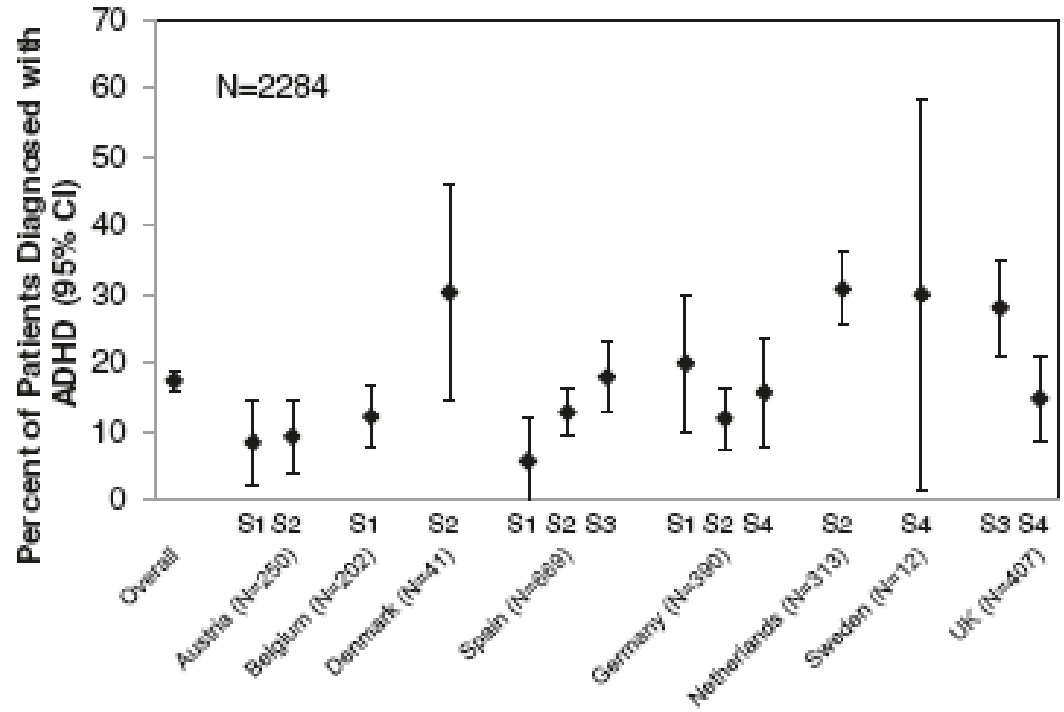


Fig. 2 ADHD prevalence in nonpsychotic psychiatric outpatients as determined by the DIVA according to criteria of the DSM-5, by country and setting. Abbreviations: ADHD = attention-deficit/hyperactivity disorder; CI = confidence interval; DIVA = Diagnostic Interview for ADHD in Adults; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; N = number of patients; S1 = general psychiatry outpatient clinics linked to general hospitals; S2 = private psychiatric practices; S3 = community mental health centers; S4 = outpatient clinics of psychiatric hospitals; UK = United Kingdom

NORDIC JOURNAL OF PSYCHIATRY

The clinical relevance of asking young psychiatric patients about childhood ADHD symptoms

M. Richter, H. Spangenberg, M. Ramklint & A. Ramirez

https://doi.org/10.1080/08039488.2019.1667427

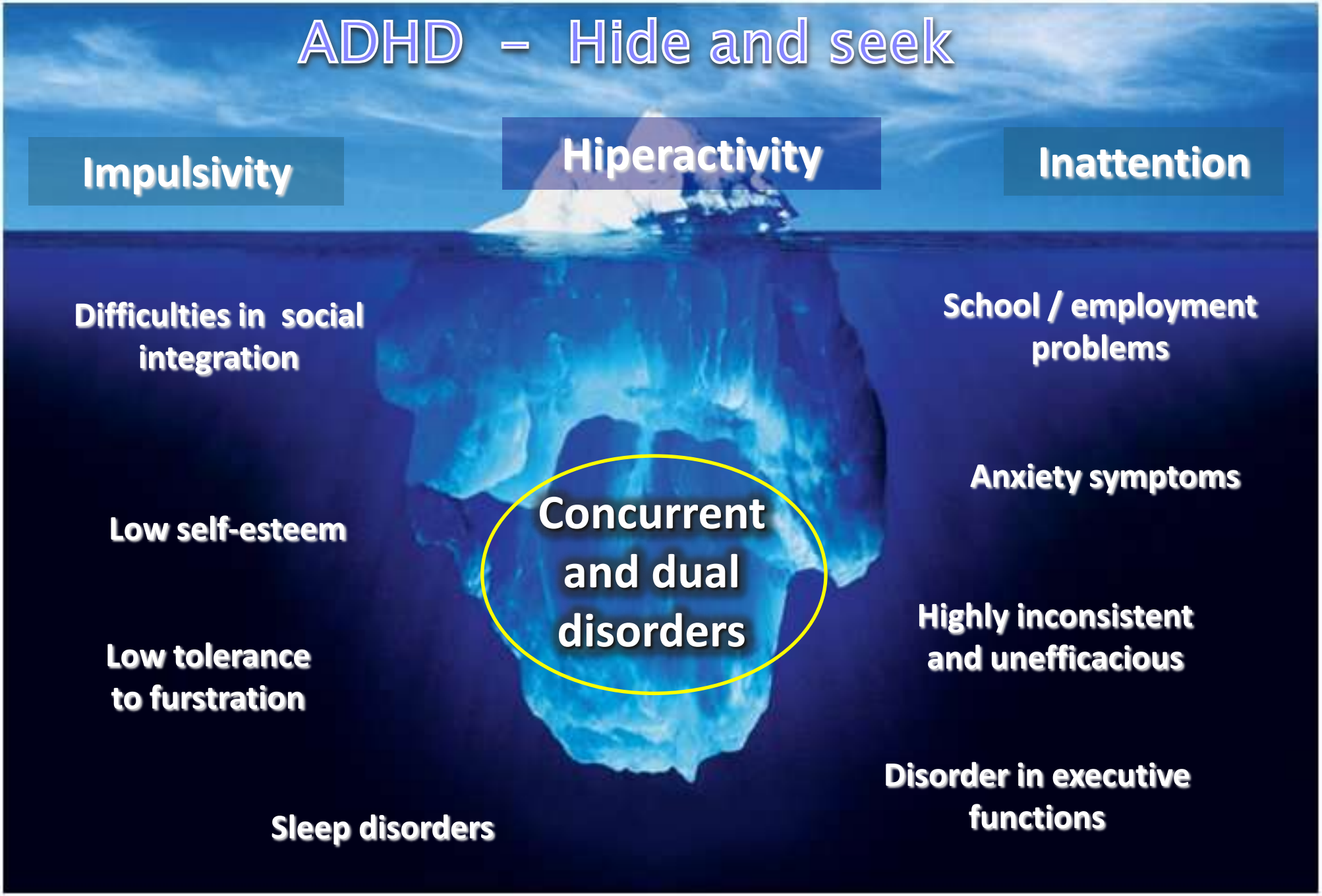
ABSTRACT

Aim: The aim of this study was to explore the relevance of asking young psychiatric patients about childhood symptoms of attention deficit hyperactivity disorder (ADHD).

Method: A total of 180 young adults (18–25 years of age) from a general psychiatric out-patient clinic in Uppsala filled in the Child and Adolescent Psychiatric Screening Inventory-Retrospect (CAPSI-R) as part of the diagnostic procedure. The study population was divided into groups based on number and subtype of reported ADHD symptoms, inattention (IN) or hyperactivity/impulsivity (HI). The clinical characteristics associated with different symptoms of ADHD were explored.

Results: The groups with five or more self-reported ADHD childhood symptoms, of either IN or HI, had more psychiatric comorbid conditions, a significantly higher co-occurrence of substance use disorders and personality disorders, and experienced more psychosocial and environmental problems.

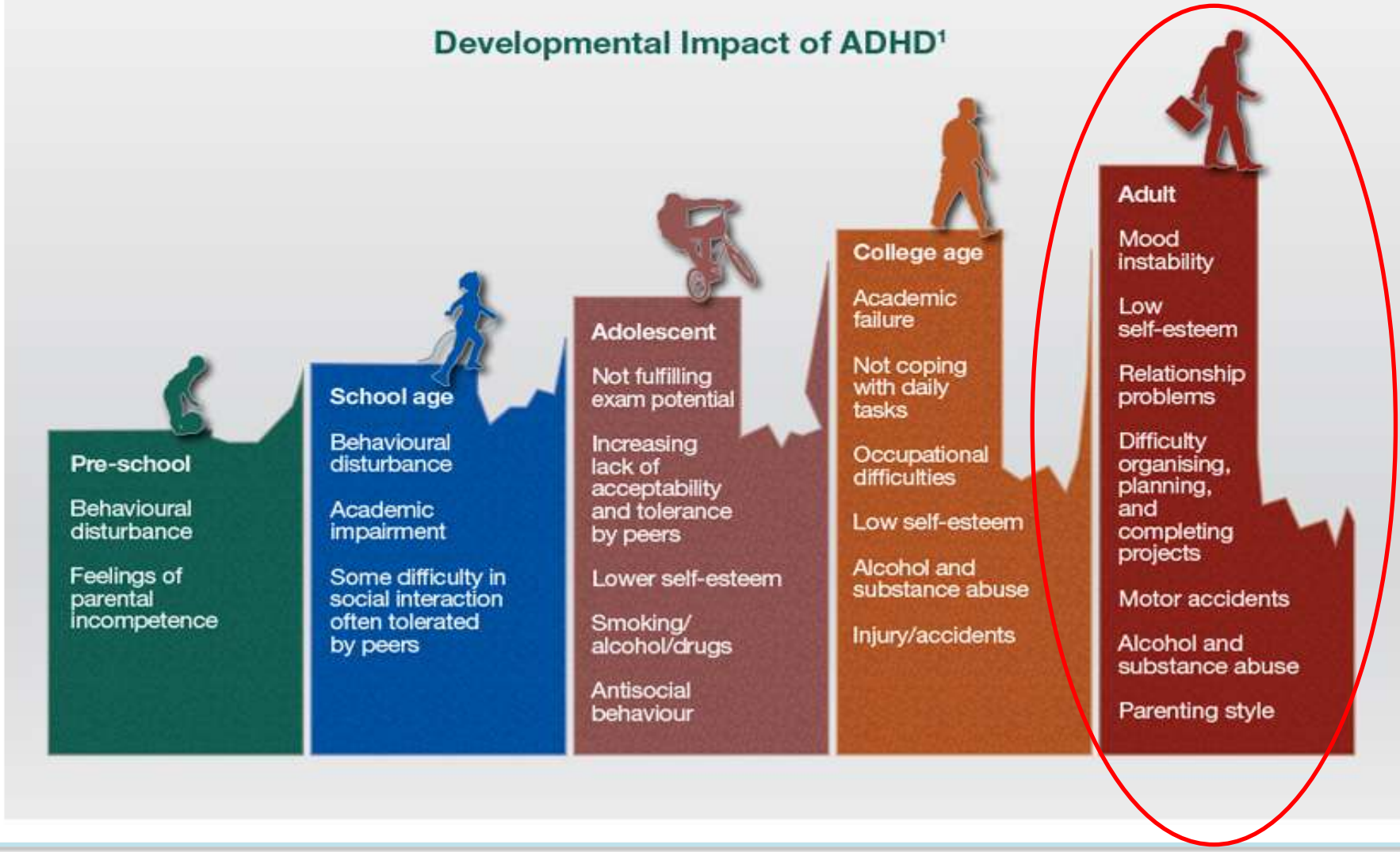
Conclusion: High level of self-reported ADHD childhood symptoms in young psychiatric patients identified a group more burdened with psychiatric comorbid conditions and more psychosocial problems. This group should be offered a thorough diagnostic assessment of ADHD.


ADHD – Hide and seek
Impulsivity
Hiperactivity
Inattention
Difficulties in social integration
School / employment problems
Anxiety symptoms
Low self-esteem
Concurrent and dual disorders
Highly inconsistent and unefficacious
Low tolerance to furstration
Disorder in executive functions
Sleep disorders

What is the impact of ADHD on the individual?

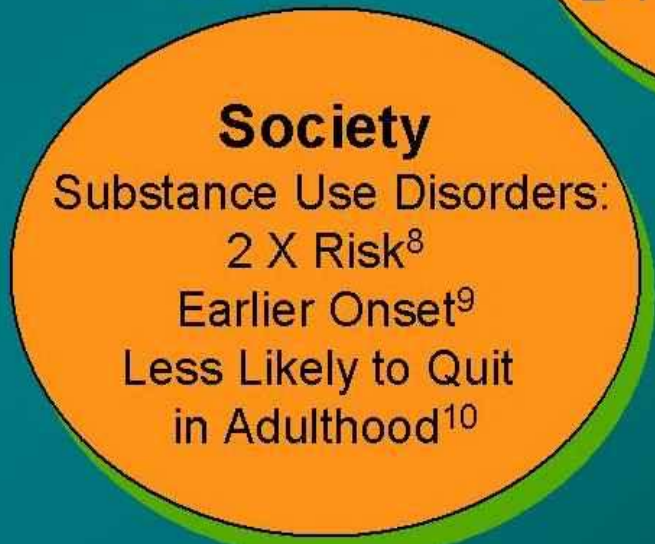
What is the impact of ADHD and a concurrent SUD on the individual?

Typical ADHD Trajectory Across the Ages



UK Adult ADHD Network (UKAAN). Handbook for Attention Deficit Hyperactivity Disorder in Adults. London, UK: Springer Healthcare Ltd; 2013.

ADHD: Impact of Untreated & Under-Treated ADHD



1. DiScala et al., 1998.
2. Liebson et al., 2001.
3. NHTSA, 1997.
4-5. Barkley et al., 1993; 1996.
6. Barkley, et al., 1990.
7. Mannuzza et al., 1997.
8. Biederman et al., 1997.
9. Pomerleau et al., 1995.
10. Wilens et al., 1995.
11. Barkley, Fischer et al., 1991.
12. Brown & Pacini, 1989.
13. Mash & Johnston, 1983.
14. Noe et al., 1999.

Economic impact of ADHD in children and adults

FIGURE 1 Annual national incremental costs of attention-deficit/hyperactivity disorder (ADHD) (in billions) by population groups. Note: The inner circle represents the lower end of the range of costs ($143B). The outer circle represents the higher end of the range of costs ($266B).

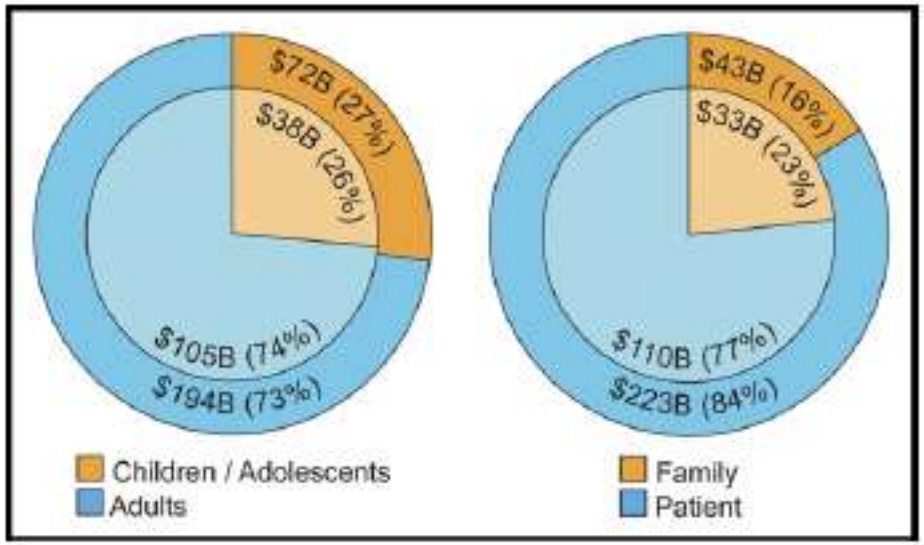
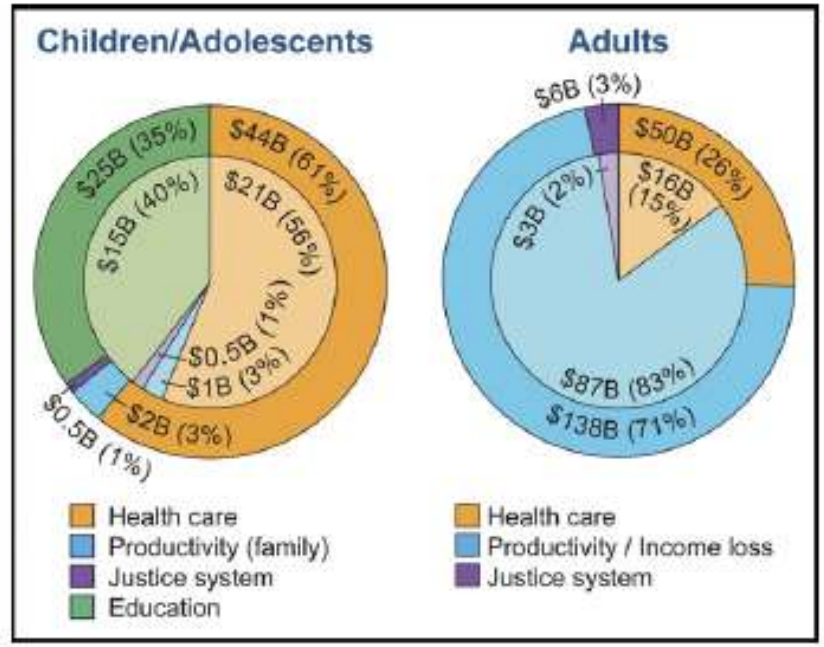


FIGURE 2 Annual national incremental costs of attention-deficit/hyperactivity disorder (ADHD) (in billions) by cost sectors within age groups. Note: The inner circle represents the lower end of the range of costs. The outer circle represents the higher end of the range of costs.



Economic Impact of Childhood and Adult Attention-Deficit/Hyperactivity Disorder in the United States

Jalpa A. Doshi, Ph.D., Paul Hodgkins, Ph.D., Jennifer Kahle, Ph.D., Vanja Sikirica, Pharm.D., Michael J. Cangelosi, M.P.H., Juliana Setyawan, Pharm.D., M. Haim Erder, Ph.D., Peter J. Neumann, Sc.D.

REVIEW
JOURNAL OF THE AMERICAN ACADEMY OF CHILD & ADOLESCENT PSYCHIATRY
VOLUME 51 NUMBER 10 OCTOBER 2012

The economic burden of adult attention deficit hyperactivity disorder: A sibling comparison cost analysis

D. Daley[a,*], R.H. Jacobsen[b], A.-M. Lange[c], A. Sørensen[d], J. Walldorf[d]

European Psychiatry 61 (2019) 41–48

Aim: Attention Deficit Hyperactivity Disorder (ADHD) is a lifespan disorder associated with considerable economic cost. While the economic burden of ADHD has been widely estimated, there is considerable variation in reported costs between studies, which typically focus on health outcomes only, lack adequate control and fail to correct for the influence of genetic and shared environmental factors. The aim of this study is to overcome these limitations to reach a fuller understanding of the economic burden of ADHD.
Method: Using the Danish National Registers 5269 adults with a diagnosis of ADHD in adulthood who had not received a diagnosis in childhood were identified. Excluding cases with missing data, comorbid diagnoses, and cases without a same sex sibling free of any diagnosed psychiatric diagnoses, a final cohort was formed consisting of 460 sibling dyads. Using a cross-sectional method focusing on the year 2010, cost differences between each adult with ADHD and their sibling were calculated from data retrieved from health, education, crime, employment and social care registers.
Results: Adults with ADHD had considerably lower disposable income and paid less tax than their siblings. They also received more state benefits, had higher costs for health, social care, and crime than their siblings. The total average costs difference for the year 2010 was 20,134 euros more than their sibling for each adult with ADHD.
Conclusion: ADHD is associated with considerable costs which are borne by both the individual and the state and underlines the need to consider the wider economic impact of ADHD beyond income and healthcare utilisation costs.

The economic burden of adult attention deficit hyperactivity disorder: A sibling comparison cost analysis

D. Daley[a,*], R.H. Jacobsen[b], A.-M. Lange[c], A. Sørensen[d], J. Walldorf[d]

European Psychiatry 61 (2019) 41–48

Table 3
Calculation of cost comparison using similar siblings, € per individual.

	Adults with ADHD	Siblings	Cost Difference €	Cost Difference %[c]
Individual or family borne costs				
Disposable income				
Total work income and public transfers	26,259	38,252	−11,992	−31%
Income tax payment[b]	6,887	11,406	4,519	40%
Other costs to the individual				
Patient cost of prescribed medication	313	68	−245	−360%
Costs of being a victim of a crime			0	N.A.
Total cost to the individual			**−7,718**	
Public costs				
Public transfers and income tax				
Income replacement transfers	7,476	1,917	−5,559	−290%
Income tax revenue to the state[b]	6,887	11,406	−4,519	−40%
Crime, traffic, foster care and education				
Costs of being in a traffic accident[a]			0	N.A.
Costs of crimes committed (investigation, sentencing)	1,361	349	−1,012	−290%
Education costs (direct costs)	367	711	344	48%
Adult continuation of foster care[a]			0	N.A.
Medical expenses				
Secondary health care	1,207	414	−794	−192%
Primary health care (GP and other primary care)	713	498	−215	−43%
Public subsidy to prescribed medication	764	103	−661	−642%
Total cost to the public sector			**−12,416**	
TOTAL COST (INDIVIDUAL + PUBLIC)			**−20,134**	

N.A.: Not applicable.

[a] We found no statistical significant differences for traffic accidents and continuation of foster care.

[b] The "income tax payment" listed under individual of family borne costs is repeated under "income tax revenue to the state" in the public costs part of the table (albeit with opposite signs). The lower "income tax payment" by "Adults with ADHD" reduces costs to the individual by €4,519, whereas the lower "income tax revenue to the state" by "Adults with ADHD" increases the public costs. The reason for this is that while "income tax payment" is a cost for the private individuals they represent a revenue of exactly the same magnitude to the public sector. Thus when aggregating, these two entries representing payment from one part of society to another cancels out and has no impact on the total costs, but needs to be included when looking at either the private individuals or the public sector separately.

[c] The cost difference in percent is calculated in relation to values for "Siblings".

The economic burden of adult attention deficit hyperactivity disorder: A sibling comparison cost analysis

D. Daley[a,*], R.H. Jacobsen[b], A.-M. Lange[c], A. Sørensen[d], J. Walldorf[d]

European Psychiatry 61 (2019) 41–48

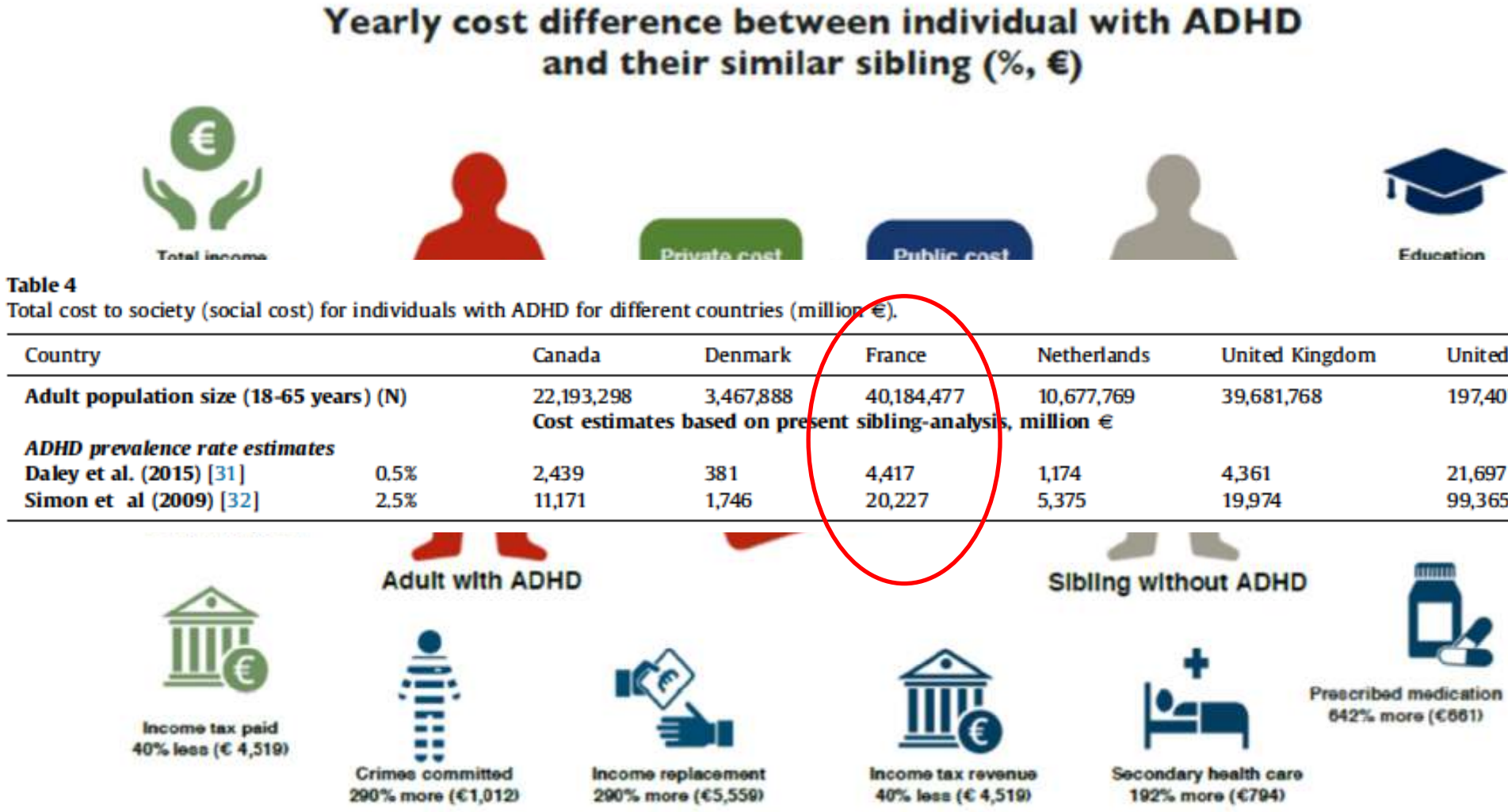


Table 4
Total cost to society (social cost) for individuals with ADHD for different countries (million €).

Country		Canada	Denmark	France	Netherlands	United Kingdom	United States
Adult population size (18-65 years) (N)		22,193,298	3,467,888	40,184,477	10,677,769	39,681,768	197,407,194
		Cost estimates based on present sibling-analysis, million €					
ADHD prevalence rate estimates							
Daley et al. (2015) [31]	0.5%	2,439	381	4,417	1,174	4,361	21,697
Simon et al (2009) [32]	2.5%	11,171	1,746	20,227	5,375	19,974	99,365

Fig. 2. Infographic demonstrating relative cost differences in percentages between Adults with ADHD and their similar siblings.

Prevalence of Attention Deficit Hyperactivity Disorder in Detention Settings: A Systematic Review and Meta-Analysis

Stéphanie Baggio[1,2], Ana Fructuoso[1], Marta Guimaraes[1], Eveline Fois[1], Diane Golay[1], Patrick Heller[1], Nader Perroud[3], Candy Aubry[4], Susan Young[5], Didier Delessert[6], Laurent Gétaz[1], Nguyen T. Tran[1,7] and Hans Wolff[1]*

frontiers in Psychiatry

SYSTEMATIC REVIEW
published: 02 August 2018
doi: 10.3389/fpsyt.2018.00331

Background: Previous studies have reported a high prevalence of attention deficit hyperactivity disorder (ADHD) among people living in detention (PLD) corresponding to a five- to ten-fold increase compared to the general population. Our main study objective was to provide an updated ADHD prevalence rate for PLD, including PLD in psychiatric units. Sub-objectives included (i) comparing different ways of assessing ADHD, including DSM-5 criteria and (ii) identifying which types of PLD are more likely to have ADHD.

Methods: We conducted a systematic review and meta-analysis following the PRISMA guidelines and the MOOSE checklist. PubMed/Medline, PsycINFO, and Web of Sciences were searched combining "ADHD" and "prison" keywords and synonyms for articles published between January 1, 1966 and January 2, 2018. Potential sources of variation to the meta-analytic ADHD prevalence rate were investigated using meta-regressions and subgroups analyses.

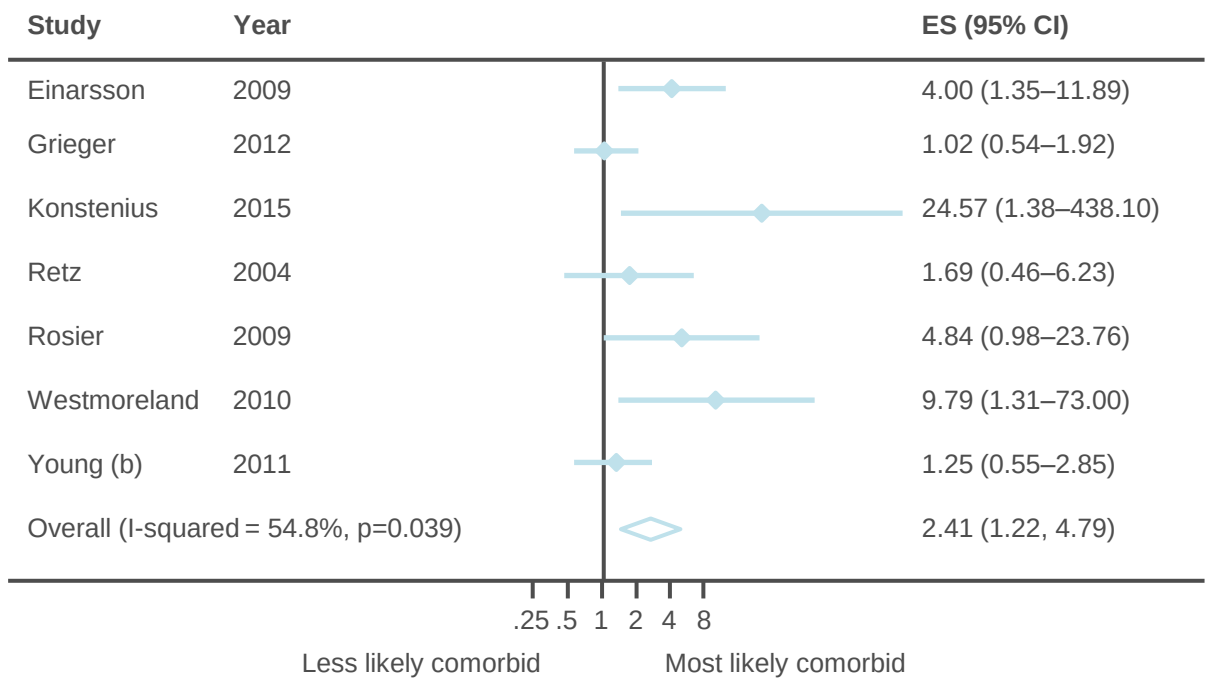
Results: The meta-analysis pooled 102 original studies including 69,997 participants. The adult ADHD prevalence rate was 26.2% (95% confidence interval: 22.7–29.6). Retrospective assessments of ADHD in childhood were associated with an increased prevalence estimate (41.1, 95% confidence interval: 34.9–47.2, $p < 0.001$). There was no significant difference in the prevalence estimate between screenings and clinical interviews in adulthood. Only three studies used the DSM-5 definition of ADHD and results were non-significantly different with other DSM versions. We found no difference according to participants' characteristics.

Conclusion: Our results confirmed the high prevalence rate of ADHD among PLD, corresponding to a five-fold increase compared to the general population. In light of such high ADHD prevalence, our results reinforce the importance of addressing this critical public health issue by (i) systematically offering ADHD screening and diagnosis to all individuals entering detention, and (ii) delivering treatment, monitoring, and care for ADHD during and after detention. These strategies may help reduce recidivism and reincarceration, as well as violence in detention settings, in addition to improving the health and wellbeing of people living in detention. Additionally, our study suggests that using screening scales may be a reliable way of assessing ADHD, although caution is needed because a complete evaluation by an experienced clinician is required to provide a formal diagnosis.

Substance-use disorder in incarcerated ADHD populations

Odds ratio [95% CI] of comorbid substance-use disorder in adult inmates with ADHD

2.41 [1.22–4.79]



In a systematic review and meta-analysis of 7 studies, which investigated the prevalence of psychiatric disorders in prison populations including individuals with ADHD (n=227) and without ADHD (n=934)[1]

CI, confidence interval

1. Young S et al 2015

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

www.thelancet.com Published online February 26, 2015 http://dx.doi.org/10.1016/S0140-6736(14)61684-6

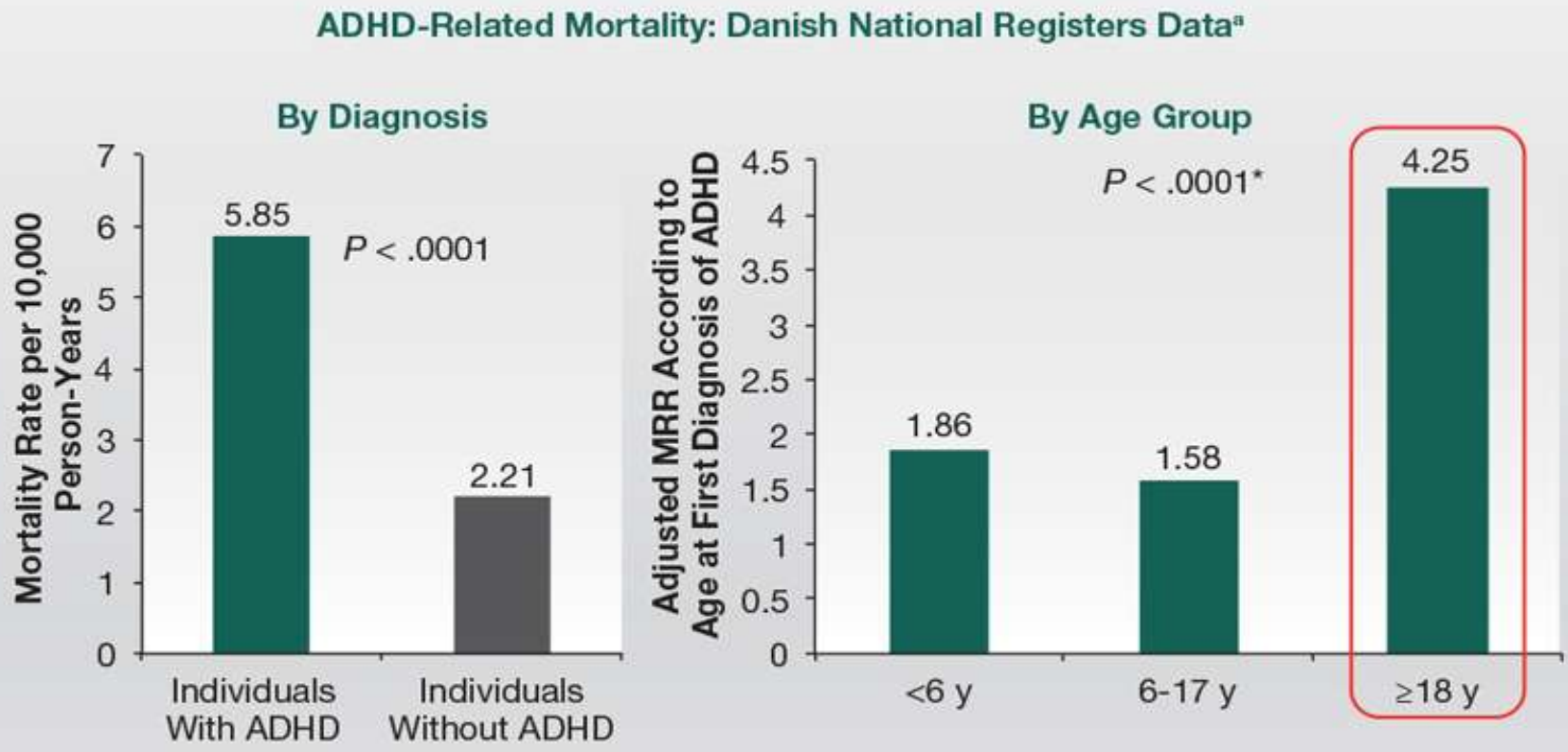
Summary

Background Attention deficit hyperactivity disorder (ADHD) is a common mental disorder associated with factors

- The study was a cohort study with over **32 years of follow-up** of **1,922,248 individuals** in the Danish national registers, including **32,061 with ADHD** (26% females).
- **ADHD** is associated with **significantly increased mortality rates (MR).**
- The authors calculated that **"all-cause MR"** (death from all causes) was:
  - **5.85 for every 10,000** person-years in people with **ADHD**
  - **2.21** per 10,000 in people without the disorder (**controls**).
- **Individuals diagnosed with ADHD in adulthood** had a **higher MR** than did those diagnosed in childhood and adolescence:
  - For individuals diagnosed in adulthood, there was an **MR: 4.25, compared with 1.58 for those people diagnosed in childhood**.

adulthood had a higher MRR than did those diagnosed in childhood and adolescence. Comorbid oppositional defiant disorder, conduct disorder, and substance use disorder increased the MRR even further. However, when adjusted for these comorbidities, ADHD remained associated with excess mortality, with higher MRRs in girls and women with ADHD than in boys and men with ADHD. The excess mortality in ADHD was mainly driven by deaths from unnatural causes, especially accidents.

Link Between ADHD and Increased Mortality Risk[1]

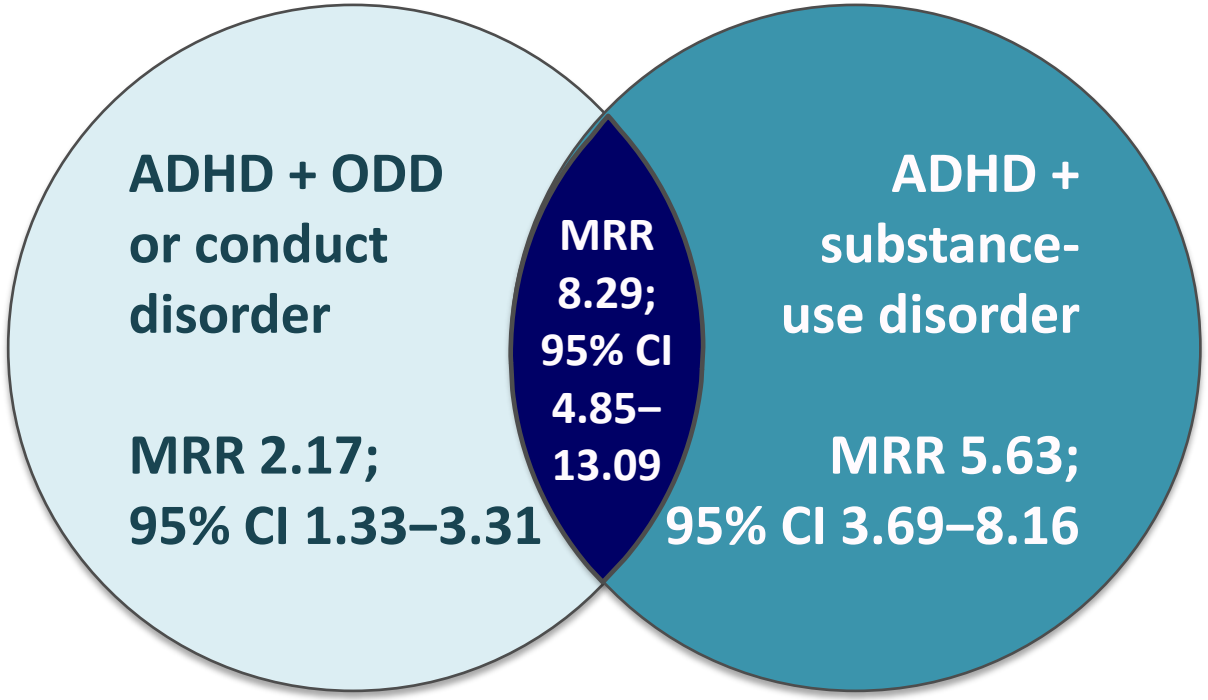


* *P* value is overall effect of being diagnosed with ADHD at different ages vs individuals without ADHD.
[a] Follow-up (24.9 million person-years) of 1.92 million individuals, including 32,061 with ADHD from first birthday through 2013 using the Danish National registers.

Dalsgaard et al. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. Lancet. 2015 Feb 26. pii: S0140-6736(14)61684-6. .

Untreated ADHD is associated with higher mortality rates

Factors associated with risk of death in ADHD included: antisocial disorders, **substance use**, symptoms of inattention and impulsivity, risky behaviors (i.e. comorbid disorders



Dalsgaard et al. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. Lancet. 2015 Feb 26. pii: S0140-6736(14)61684-6. .

Association between suicidal spectrum behaviors and Attention-Deficit/ Hyperactivity Disorder: A systematic review and meta-analysis

Mathilde Septier[a,b,1], Coline Stordeur[a,1], Junhua Zhang[c], Richard Delorme[a,d]
Samuele Cortese[e,f,g,h,i,*]

The relationship between ADHD and suicidal spectrum behaviors (SSBs) remains uncertain. We conducted the first meta-analysis on the association between ADHD and SSBs taking possible confounders into account. Based on a pre-registered protocol (PROSPERO-CRD42018093003), we searched Pubmed, Ovid and Web of Knowledge databases through April 6th, 2018, with no language/publication type restrictions, and contacted study authors for unpublished data/information. From a pool of 2798 references, we retained 57 studies. Random-effects models were performed. Study quality was rated using the Newcastle-Ottawa Scale. After pooling crude ORs, we found a significant association between ADHD and suicidal attempts (2.37, 95% CI = 1.64–3.43; I^2 = 98.21), suicidal ideations (3.53, 2.94–4.25; I^2 = 73.73), suicidal plans (4.54, 2.46–8.37; I^2 = 0), and completed suicide (6.69, 3.24–17.39; I^2 = 87.53). Results did not substantially change when pooling adjusted ORs. Findings were also in general robust to sensitivity analyses to assess possible moderators. Awareness of the association between ADHD and SSBs should contribute to more effectively prevent SSBs.

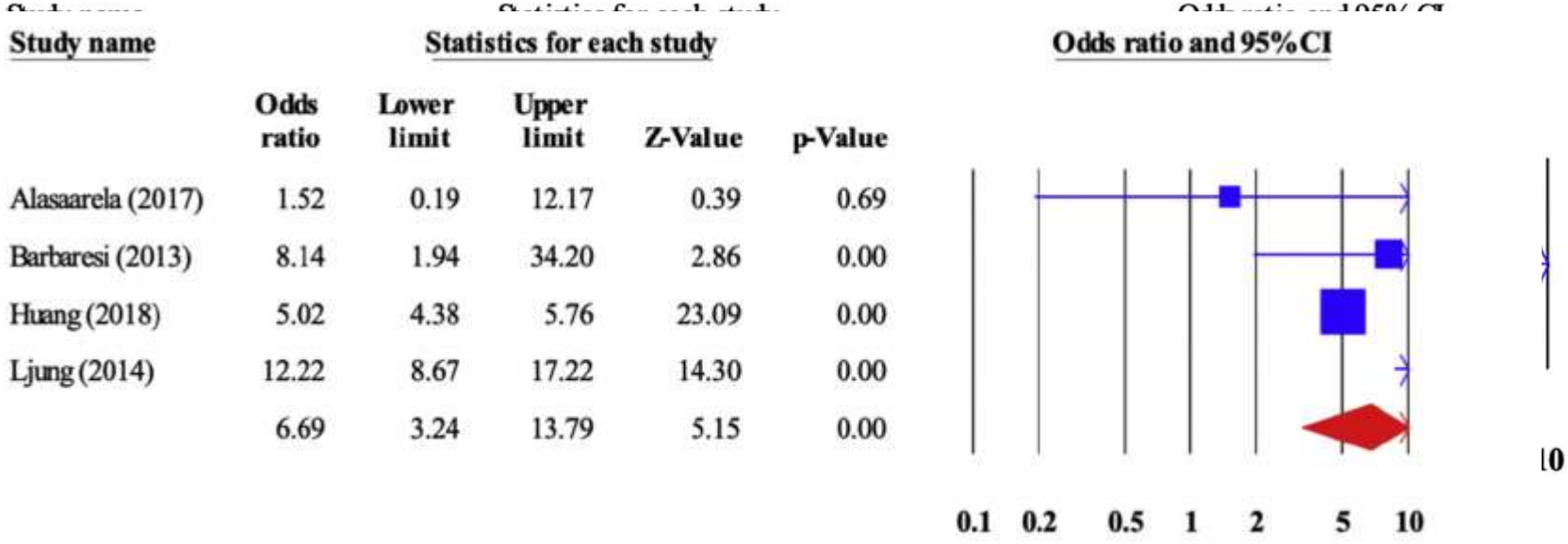
Neuroscience & Biobehavioral Reviews

Association between suicidal spectrum behaviors and Attention-Deficit/ Hyperactivity Disorder: A systematic review and meta-analysis

Mathilde Septier[a,b,1], Coline Stordeur[a,1], Junhua Zhang[c], Richard Delorme[a,d]
Samuele Cortese[e,f,g,h,i,*]

Neuroscience and Biobehavioral Reviews 103 (2019) 109–118

Study name	Subgroup within study	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Alasaarela (2017)	children	0.77	0.35	1.70	-0.64	0.52



OR = 6.69

Fig. 4. Forest plot. Unadjusted ORs for (completed) suicide.

OR = 3.53

Fig. 3. Forest plot. Unadjusted ORs for suicidal ideation (SI).

Fig. 2. Forest plot. Unadjusted ORs for suicidal attempts (SA).

Diagnosed Mental Health Conditions and Risk of Suicide Mortality

Hsueh-Han Yeh, Ph.D., Joslyn Westphal, M.P.H., Yong Hu, M.A., Edward L. Peterson, Ph.D., L. Keoki Williams, M.D., M.P.H., Deepak Prabhakar, M.D., M.P.H., Cathrine Frank, M.D., Kirsti Autio, M.S.W., Farah Elsiss, M.S., T.L.L.P., Gregory E. Simon, M.D., M.P.H., Arne Beck, Ph.D., Frances L. Lynch, Ph.D., M.S.P.H., Rebecca C. Rossom, M.D., M.S., Christine Y. Lu, Ph.D., M.Sc., Ashli A. Owen-Smith, Ph.D., S.M., Beth E. Waitzfelder, Ph.D., Brian K. Ahmedani, Ph.D.

Objective: Although mental health conditions are risk factors for suicide, limited data are available on suicide mortality associated with specific mental health conditions in the U.S. population. This study aimed to fill this gap.

Methods: This study used a case-control design. Patients in the case group were those who died by suicide between 2000 and 2013 and who were patients in eight health care systems in the Mental Health Research Network (N=2,674). Each was matched with 100 general population patients from the same system (N=267,400). Diagnostic codes for five mental health conditions in the year before death were obtained from medical records: anxiety disorders, attention deficit-hyperactivity disorder (ADHD), bipolar disorder, depressive disorders, and schizophrenia spectrum disorder.

Results: Among patients in the case group, 51.3% had a recorded psychiatric diagnosis in the year before death, compared with 12.7% of control group patients. Risk of suicide mortality was highest among those with schizophrenia spectrum disorder, after adjustment for age and sociodemographic characteristics (adjusted odds ratio [AOR]=15.0) followed by bipolar disorder (AOR=13.2), depressive disorders (AOR=7.2), anxiety disorders (AOR=5.8), and ADHD (AOR=2.4). The risk of suicide death among those with a diagnosed bipolar disorder was higher in women than men.

Conclusions: Half of those who died by suicide had at least one diagnosed mental health condition in the year before death, and most mental health conditions were associated with an increased risk of suicide. Findings suggest the importance of suicide screening and providing an approach to improve awareness of mental health conditions.

Psychiatric Services in Advance (doi: 10.1176/appi.ps.201800346)

Suicidal behaviour among persons with attention-deficit hyperactivity disorder

Cecilie Fitzgerald, Søren Dalsgaard, Merete Nordentoft and Annette Erlangsen

Background

Persons diagnosed with attention-deficit hyperactivity disorder (ADHD) have been found to have an increased risk of suicidal behaviour, but the pathway remains to be thoroughly explored.

Aims

To determine whether persons with ADHD are more likely to present with suicidal behaviour (i.e. suicide attempts and deaths by suicide) if they have a comorbid psychiatric disorder.

Method

Using nationwide registers covering the entire population of Denmark, this cohort study of 2.9 million individuals followed from 1 January 1995 until 31 December 2014, covers more than 46 million person-years. All persons aged ≥10 years with Danish-born parents were identified and persons with a diagnosis of ADHD were compared with persons without. Incidence rate ratios (IRRs) were calculated by Poisson regression, with adjustments for sociodemographics and parental suicidal behaviour.

Results

Persons with ADHD were followed for 164 113 person-years and 697 suicidal outcomes were observed. This group was found to have an IRR of suicidal behaviour of 4.7 (95% CI, 4.3–5.1) compared with those without ADHD. Persons with ADHD only had a 4.1-fold higher rate (95% CI, 3.5–4.7) when compared with those without any psychiatric diagnoses. For persons with ADHD and comorbid disorders the IRR was higher yet (IRR: 10.4; 95% CI, 9.5–11.4).

Conclusions

This study underlines the link between ADHD and an elevated rate of suicidal behaviour, which is significantly elevated by comorbid psychiatric disorders. In sum, these results suggest that persons with ADHD and comorbid psychiatric disorders are targets for suicide preventive interventions.

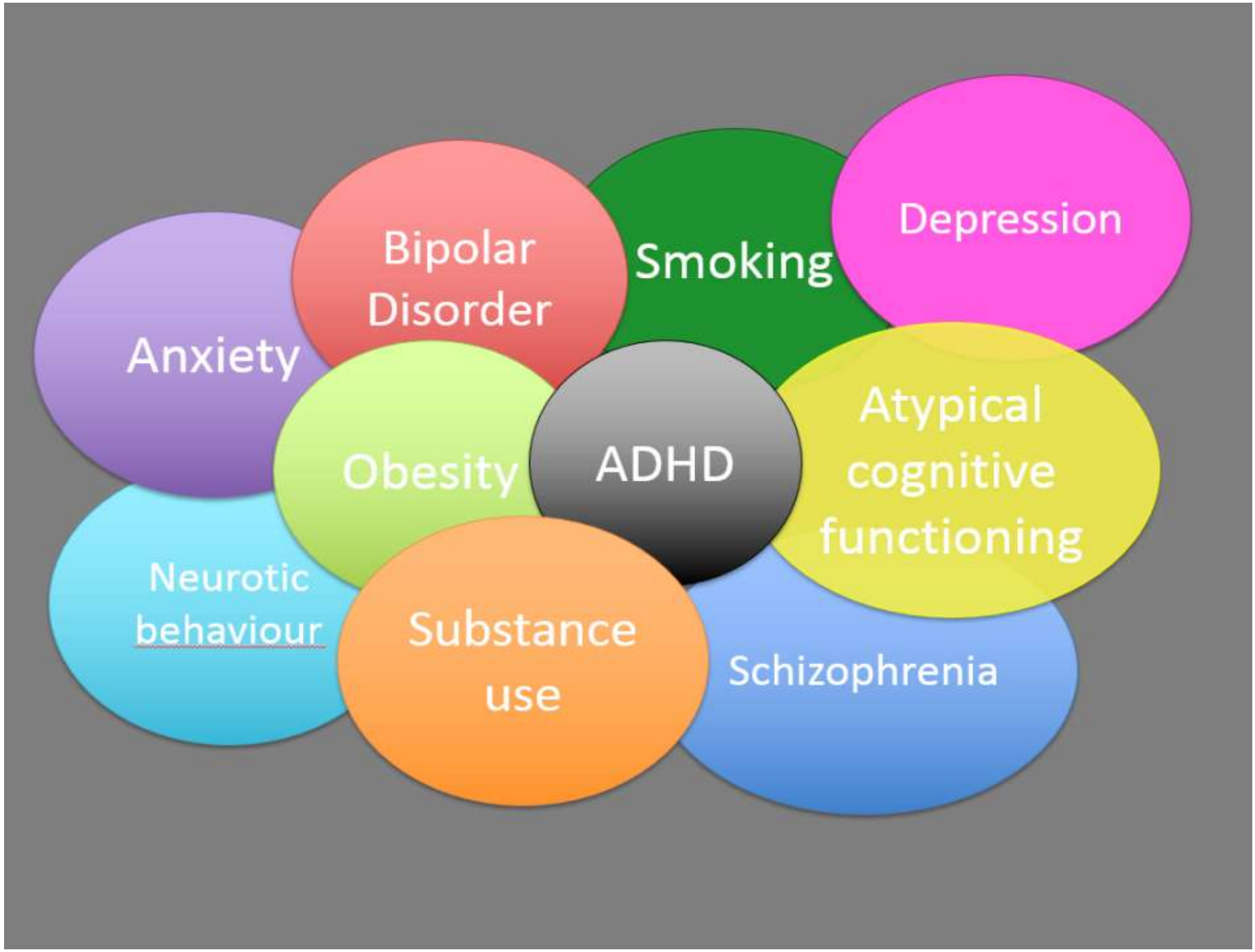
Declaration of interest

None.

Keywords

Suicide; attention-deficit hyperactivity disorders; epidemiology; statistical methodology; outcome studies.

BJPsych | The British Journal of Psychiatry (2019) 215, 615–620. doi: 10.1192/bjp.2019.128


Anxiety
Bipolar Disorder
Smoking
Depression
Obesity
ADHD
Atypical cognitive functioning
Neurotic behaviour
Substance use
Schizophrenia

Developmental trends in ADHD: psychiatric comorbidities

The majority of adults with ADHD have a comorbid psychiatric disorder, which can complicate diagnosis and treatment of ADHD[1-4]

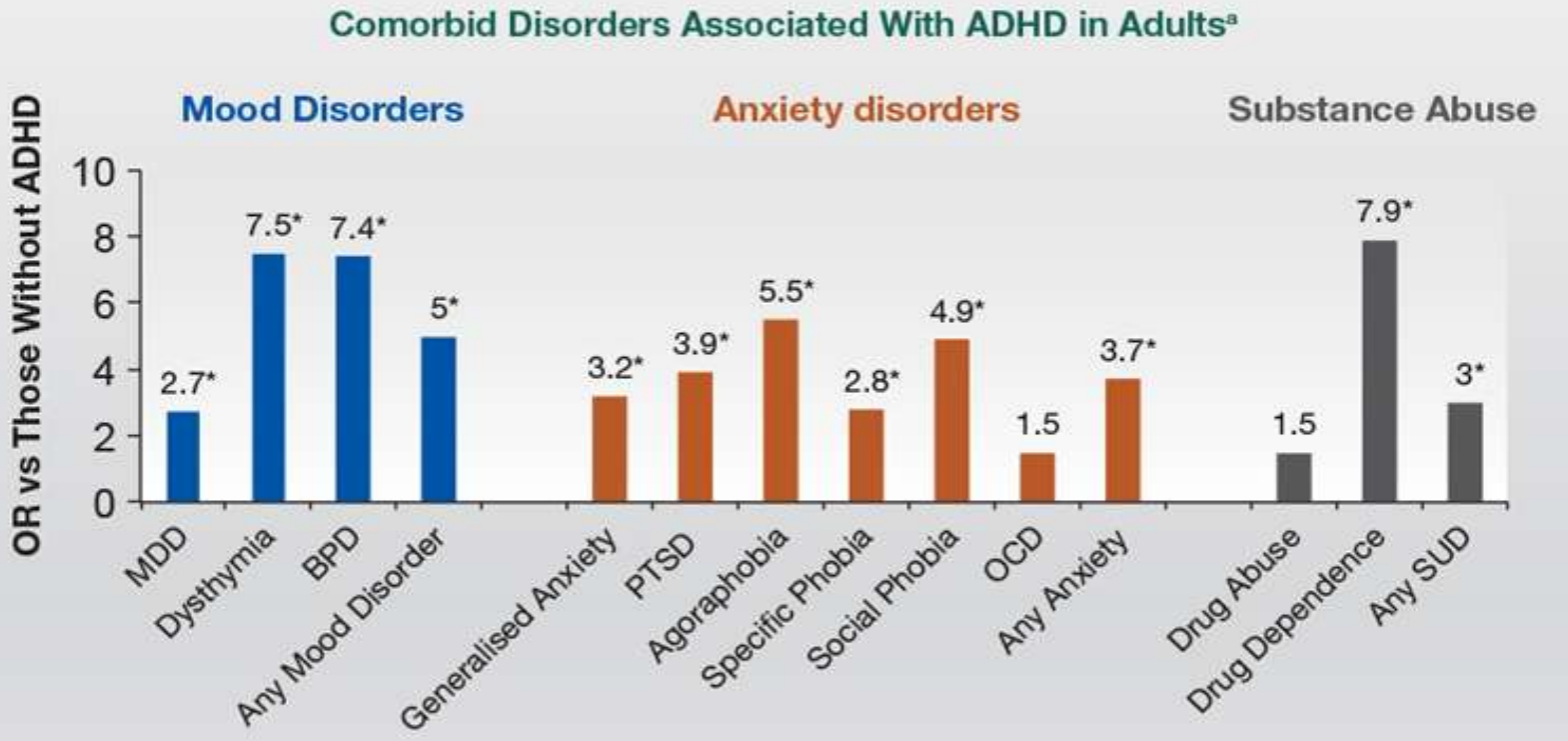
	<6 years	Children	Adolescents	Adults
ADHD / ADD[a]	ADHD>ADD	ADHD>ADD	ADHD=ADD	ADD>ADHD
Oppositional defiant disorder	+++	+++	++	+
Communication disorder	++	+	+	+
Conduct disorder	+	++	+++	Antisocial personality disorder
Anxiety disorder	±	++	+++	+++
Major depression	–	+	++	+++
Dysthymic disorder	–	+	++	+++
Substance-use disorder	–	–	+	++

[a]In this table,[5] ADHD means ADHD combined type and ADD means ADHD predominantly inattentive type Key: – = not diagnosed; + = rare; ++ = common; +++ = very common

Table adapted from Turgay A 2007

1. NCCMH 2008; 2. Kooij SJ et al 2010; 3. CADDRA 2011; 4. Kooij SJ et al 2012; 5. Turgay A 2007

Increased Prevalence of Comorbid Psychiatric Issues in Adults With ADHD[1]

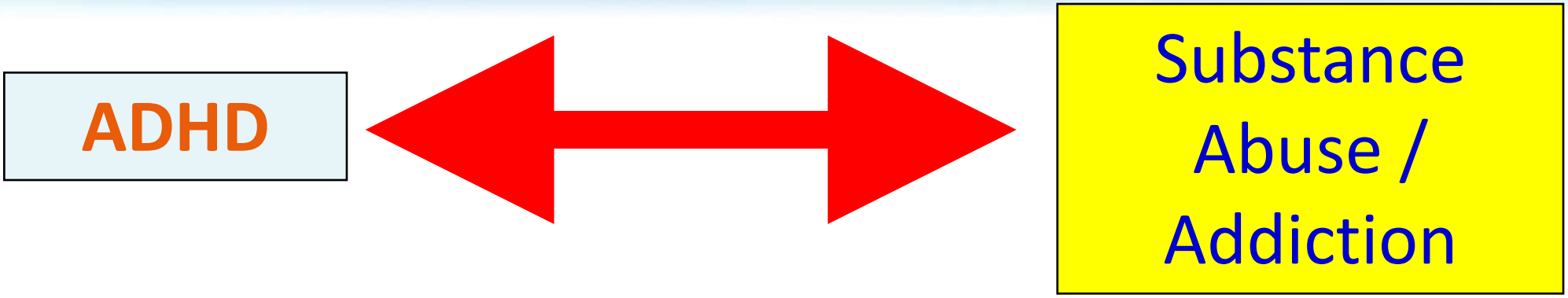


* $P < .05$.

[a] A screen for adult ADHD was included in a probability sub-sample (n = 3,199) of 18-44 y old respondents in the National Comorbidity Survey Replication (NCS-R), a nationally representative household survey assessing a wide range of DSM-IV disorders. Blinded clinical follow-up interviews of adult ADHD were carried out with 154 NCS-R respondents, over-sampling those with a positive screen.

Kessler et al. Am J Psychiatry 2006)

Overlap Between ADHD and Substance Use Disorders (SUD)



- SUD are particularly common in individuals with ADHD
- Excessive overlap of ADHD in Substance Abuse
- ADHD ± comorbidity is a risk factor for Substance Abuse
- Hyperactivity-impulsivity shmptoms appear to predict better the onset and maintenanece of the SUD *(Elkins et al, 2007)*

Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: A meta-analysis and meta-regression analysis

Katelijne van Emmerik-van Oortmerssen[a,b,*], Geurt van de Glind[c], Wim van den Brink[b], Filip Smit[c,d], Cleo L. Crunelle[b,e], Marije Swets[a], Robert A. Schoevers[f,a]

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ARTICLE INFO

Article history:
Received 10 October 2011
Received in revised form 4 December 2011
Accepted 6 December 2011
Available online xxx

Keywords:
Substance use disorders
ADHD
Prevalence
Meta-analysis

ABSTRACT

Context: Substance use disorders (SUD) are a major public health problem. Attention deficit hyperactivity disorder (ADHD) is a comorbid condition associated with both onset and prognosis of SUD. Prevalence estimates of ADHD in SUD vary significantly.
Objective: To obtain a best estimate of the prevalence of ADHD in SUD populations.
Data sources: A literature search was conducted using MEDLINE, PsycINFO and EMBASE. Search terms were ADHD, substance-related disorders, addiction, drug abuse, drug dependence, alcohol abuse, alcoholism, comorbidity, and prevalence. Results were limited to the English language.
Study selection: After assessing the quality of the retrieved studies, 29 studies were selected. Studies in which nicotine was the primary drug of abuse were not included.
Data extraction: All relevant data were extracted and analysed in a meta-analysis. A series of meta-regression analyses was performed to evaluate the effect of age, primary substance of abuse, setting and assessment procedure on the prevalence of ADHD in a variety of SUD populations.
Data synthesis: Overall, 23.1% (CI: 19.4–27.2%) of all SUD subjects met DSM-criteria for comorbid ADHD. Cocaine dependence was associated with lower ADHD prevalence than alcohol dependence, opioid dependence and other addictions. Studies using the DICA or the SADS-L for the diagnosis of ADHD showed significantly higher comorbidity rates than studies using the KSADS, DISC, DIS or other assessment instruments.
Conclusions: ADHD is present in almost one out of every four patients with SUD. The prevalence estimate is dependent on substance of abuse and assessment instrument.

Journal of Behavioral Addictions 7(3), pp. 743–751 (2018)

Attention-deficit hyperactivity disorder and addictions (substance and behavioral): Prevalence and characteristics in a multicenter study in France

LUCIA ROMO[1,2]*, JOEL LADNER[3,4,5], GAYATRI KOTBAGI[1,6], YANNICK MORVAN[1,7], DALIA SALEH[1,8], MARIE PIERRE TAVOLACCI[4,9] and LAURENCE KERN[1,10]

Aim: The aim of this study is to determine the possible links between attention-deficit hyperactivity disorder (ADHD) and the presence of concomitant addictions with or without substance use in a French student population. *Measures:* A battery of questionnaire measuring socioeconomic characteristics, university curriculum, ADHD (Wender Utah Rating Scale and Adult ADHD Self-Report Scale), substance consumptions (alcohol, tobacco, and cannabis), and behavioral addictions [(eating disorders (SCOFF)], Internet addiction (Internet Addiction Test), food addiction (Yale Food Addiction Scale), compulsive buying (Echeburua's), and problem gambling (The Canadian Problem Gambling Index)] and measures of physical activity (Godin's Leisure Time Exercise Questionnaire) was filled up by university students in Rouen and Nanterre in France. *Results:* A total of 1,517 students were included (472 from Paris Nanterre and 1,042 from Rouen). The mean age was 20.6 years ($SD = 3.6$) and the sex ratio male to female was 0.46. The prevalence of ADHD among the students (current ADHD with a history of ADHD in childhood) was 5.6%. A quarter (25.7%) of students had already repeated their university curriculum, compared to 42.2% among the students with ADHD. Students with possible ADHD had repeated classes more often and believed to have a lower academic level than the students without ADHD. Significant differences were found as students with ADHD were less likely to succeed in their studies (repeated classes more often) than non-ADHD students, and considered their academic level to be lower. They also had significantly higher scores on substance (alcohol, cannabis, and tobacco) as well as behavioral addictions (gambling, compulsive buying disorder, eating disorders, and Internet addiction). *Conclusion:* It seems essential to determine students' problems and propose interventions adapted to students' needs, in order to reduce the negative impact on their future academic and global successes.

Journal of Behavioral Addictions 7(3), pp. 743–751 (2018)

Attention-deficit hyperactivity disorder and addictions (substance and behavioral): Prevalence and characteristics in a multicenter study in France

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Table 2. Description of students' consumptions and the consumptions associated with ADHD ($N = 1,517$)

	ADHD− ($N = 1,432$)	ADHD+ ($N = 85$)	Total ($N = 1,517$)	p	AOR (95% CI)	p
Smoker (%)	25.5	38.1	26.2	.01	0.91 (0.52–1.57)	.73
Use of cannabis (%)				$<10^{-3}$		
No	70.6	50.6	69.5		Ref	
Occasional	25.3	40.2	26.2		1.59 (0.92–2.74)	.09
Regular	4.1	8.2	4.3		1.59 (0.61–4.14)	.34
Binge drinking (%)				.003		
Never	46.2	35.4	45.6		Ref	
Occasional	46.2	46.8	46.3		0.75 (0.41–1.39)	.37
Frequent	7.6	17.8	8.1		0.84 (0.33–2.14)	.72
Alcohol abuse problems				$<10^{-3}$		
No	76.3	50.6	74.9		Ref	
Hazardous drinking	15.2	23.5	15.6		2.47 (1.26–4.85)	.009
Risk of addiction	8.5	25.9	9.5		4.08 (1.26–4.86)	$<10^{-3}$

Note. Adjusted on universities, gender, cursus, and financial difficulties. ADHD: attention-deficit hyperactivity disorder; AOR: adjusted odds ratio; CI: confidence interval.

Table 3. Addictive behaviors associated with ADHD ($N = 1,517$)

	ADHD− ($N = 1,432$)	ADHD+ ($N = 85$)	Total ($N = 1,517$)	p	AOR (95% CI)	p
Physical activity (GLTEQ)				.30		
Insufficient	24.0	28.4	24.2			
Moderate	14.1	8.1	13.8			
Active	61.9	63.5	62.0			
Eating disorders (SCOFF)	17.4	32.9	18.3	$<10^{-3}$	1.33 (0.76–2.33)	.31
Internet Addiction Test (IAT)	8.4	34.5	9.9	$<10^{-3}$	3.87 (2.14–7.01)	$<10^{-4}$
Online compulsive buying (Echeburua's test)	11.8	40.0	13.4	$<10^{-3}$	3.38 (2.02–5.65)	$<10^{-4}$
Problem gambling (ICJE)	9.3	20.0	9.9	.001	1.76 (0.94–3.31)	.08
Food addiction (YFAS)	4.0	14.1	4.5	$<10^{-3}$	2.27 (1.05–4.88)	.04

Note. Adjusted on universities, gender, cursus, and financial difficulties. GLTEQ: Godin's Leisure Time Questionnaire; ADHD: attention-deficit hyperactivity disorder; AOR: adjusted odds ratio; CI: confidence interval; ICJE: Indice Canadian du Jeu excessif (Canadian Index of Excessive Gambling); YFAS: Yale Food Addiction Scale.

Clinical Psychology Review 31 (2011) 328–341

Clinical Psychology Review

Steve S. Lee [a,*], Kathryn L. Humphreys [a], Kate Flory [b], Rebecca Liu [a], Kerrie Glass [b]

Compared with control subjects without ADHD, children with ADHD were:

- 2x as likely to have a lifetime history of **nicotine** use (OR: 2.08, P < .001);
- nearly 3x more likely to report **nicotine** dependence in adolescence/adulthood (OR: 2.82, P < .001);
- almost 2x more likely to meet diagnostic criteria for **alcohol** use disorder (OR: 1.74, P < .001);
- approximately 1.5 times more likely to meet criteria for **cannabis** use disorder (OR: 1.58, P = .003);
- twice as likely to develop **cocaine** use disorder (OR: 2.05, P < .001); and
- more than 2.5 times more likely to develop an **SUD overall**.

Cigarette smoking as a risk factor for other substance misuse: 10-year study of individuals with and without attention-deficit hyperactivity disorder

Joseph Biederman, Carter R. Petty, Paul Hammerness, Holly Batchelder and Stephen V. Faraone

BJPsych
The British Journal of Psychiatry (2012)
201, 207–214. doi: 10.1192/bjp.bp.111.100339

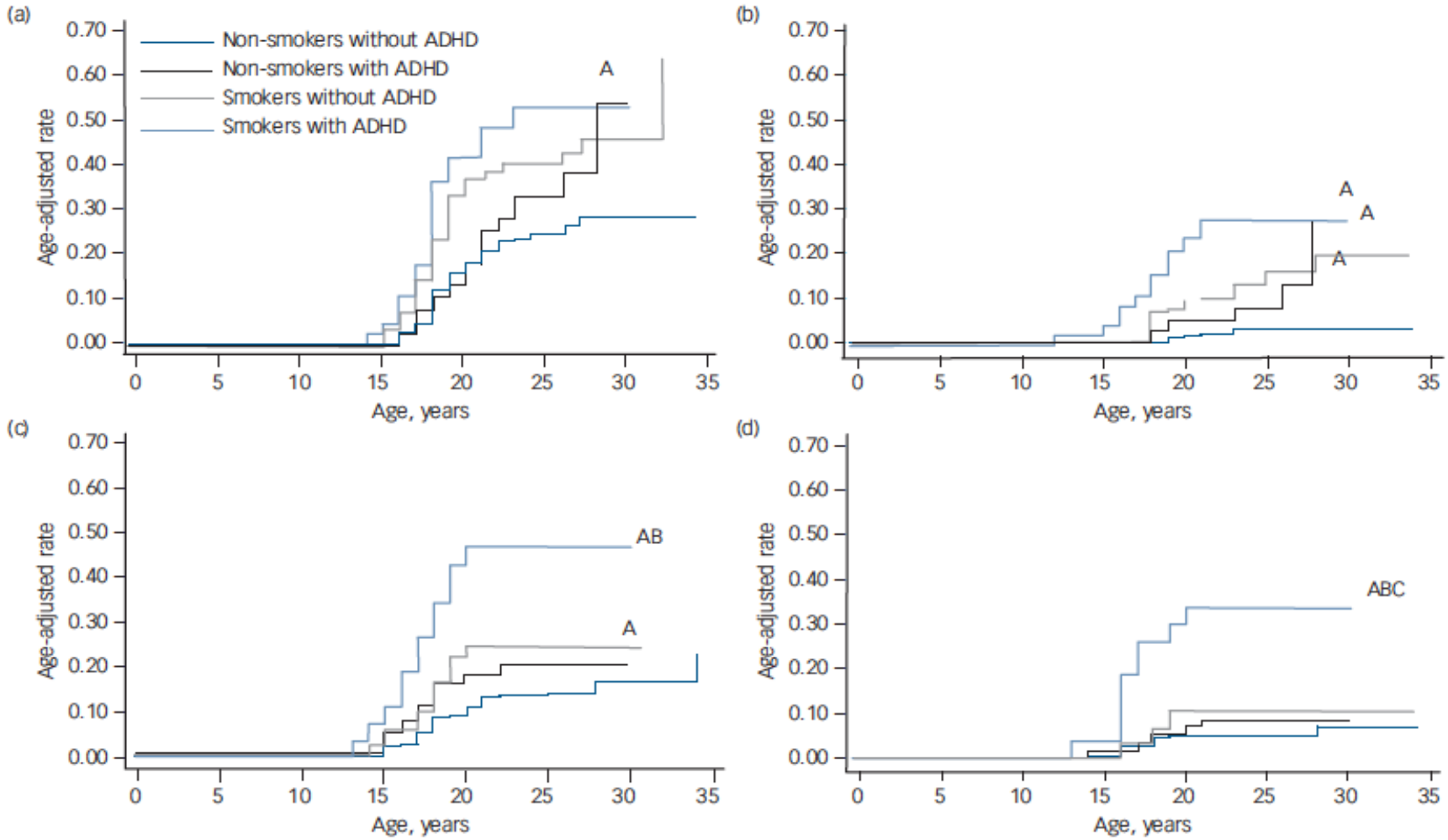

Fig. 2 Risk for psychoactive substance use disorder in smokers and non-smokers with and without attention-deficit hyperactivity disorder (ADHD): secondary analysis. (a) Risk for alcohol misuse, (b) risk for alcohol dependence, (c) risk for drug misuse, (d) risk for drug dependence.

A, $P<0.05$ *v.* non-smokers without ADHD; B, $P<0.05$ *v.* non-smokers with ADHD; C, $P<0.05$ *v.* smokers with ADHD.

Outcome of patients with ADHD + SUD vs. Patients with SUD or ADHD

Earlier onset of substance use and abuse [Arias et al, 2008; Carroll y Rounsaville, 1993; Gray and Upadhyaya, 2009; Johann et al, 2004; Ponce et al, 2000; Brinkman et al, 2015; Dunne et al, 2014]
Higher severity and chronicity of the addictive disorder [Arias et al, 2008; Carroll y Rounsaville, 1993; Carpentier et al, 2011; Dunne et al, 2014; Gray and Upadhyaya, 2009; Johann et al, 2004; Perez de los Cobos et al, 2011; Wilens y Upadhyaya, 2007; Marín-Navarrete, 2013; Peles et al, 2012]
Worse outcome of ADHD symptoms [Fergusson y Boden, 2008; Wilens y Upadhyaya, 2007]
More neuropsychological and cognitive impairment [Muld et al, 2013; Tamm et al, 2013]
Higher rates of poly-substance abuse [Arias et al, 2008; Carroll y Rounsaville, 1993; Gray and Upadhyaya, 2009; Marín-Navarrete, 2013]
Higher psychiatric comorbidity [Arias et al, 2008; Carpentier et al, 2011; Levin et al, 1998a; Wilens et al 2005b; Wilens et al, 1999; Peles et al, 2012]
Lower treatment retention rates [Schubiner, 2005; Wilens y Upadhyaya, 2007]

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Thanks for your attention!

NICE National Institute for Health and Care Excellence

NICE guideline

Attention deficit hyperactivity disorder: diagnosis and management

Adults

These recommendations are for healthcare professionals with training and expertise in diagnosing and managing ADHD. See recommendation 1.4.3 for details of ADHD-focused information.

1.5.15 Offer medication to adults with ADHD if their ADHD symptoms are still causing a significant impairment in at least one domain after environmental modifications have been implemented and reviewed. See the recommendations on medication choice. [2018]

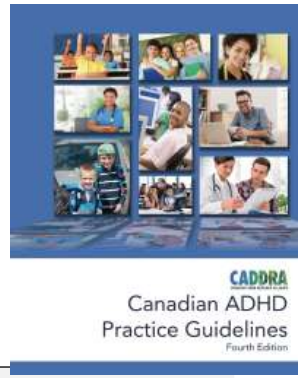
1.5.16 Consider non-pharmacological treatment for adults with ADHD who have:

- made an informed choice not to have medication
- difficulty adhering to medication
- found medication to be ineffective or cannot tolerate it. [2018]

1.5.17 Consider non-pharmacological treatment in combination with medication for adults with ADHD who have benefited from medication but whose symptoms are still causing a significant impairment in at least one domain. [2018]

NICE guideline
Published: 14 March 2018
nice.org.uk/guidance/ng87

CADDRA
CANADIAN ADHD RESOURCE ALLIANCE



SUBSTANCE USE DISORDER

Compared to typically developing individuals, people with ADHD have a two-fold risk for substance abuse and dependence [126, 127]. The literature suggests that one-quarter of adults with SUD [128] and one-half of adolescents with Substance Use Disorder (SUD) have ADHD [129]. Several studies suggest a higher rate of SUD in adults with ADHD than in the general population, and ADHD itself is a risk factor for SUD [130, 131]. Among ADHD patients with a comorbid behavior disorder, those with either comorbid CD or Bipolar Disorder have the greatest likelihood of developing SUD [114, 132-135].

Individuals with ADHD are at significant risk of using substances (e.g. nicotine, cocaine and cannabis) and of starting use earlier than the general population [134]. Moreover, the accompanying poor self-esteem and impulsivity associated with ADHD may be conducive to the development of SUD.

Marijuana continues to be the most commonly abused agent in individuals with ADHD [136]. Abuse can include alcoholism, smoking and other drugs [126]. Furthermore, substance use problems may increase the severity of ADHD symptoms. On the other hand, it is also true that patients with these substance use problems may present with attention, behaviour and self-control symptoms that can mimic ADHD. A referral to a specialist may be required before establishing an ADHD diagnosis when a patient is actively using illicit substances.

SUBSTANCE USE DISORDER

Treatment

The best approach to treatment sequencing in individuals with ADHD and comorbid substance use disorder is concurrent intervention with specific interventions for each disorder [125]. Some researchers suggest that ADHD and SUD-related craving share neurobiological similarities, and that treatment of ADHD may reduce craving for substances and subsequently reduce the risk for relapse to substance use [137]. An aggregate of the literature seems to suggest that early stimulant

Key Points

- In most cases, ADHD and SUD need to be treated concurrently and independently when comorbid.
- Psychostimulants taken orally do not have the same abuse liability as illicit stimulants (e.g. cocaine) due to slower dissociation from the site of action, slower uptake into the striatum, and slower binding and dissociation with the dopamine transporter protein.
- Non-stimulant and long-acting psychostimulants have less abuse potential than immediate-release preparations of psychostimulants.

issues [143].

Methylphenidate does not have the same abuse liability as cocaine due to slower dissociation from the site of action, slower uptake into the striatum, and slower binding and dissociation with the dopamine transporter protein relative to cocaine [144]. However, it is important to remember that the route of administration may alter the abuse liability of a substance. The oral administration of psychostimulants has been shown to decrease the likability of a substance while parenteral usage (IV, snorted) has been shown to be associated with euphoria [144]. Individuals with ADHD and either SUD or CD are at highest risk for diversion and misuse and are more likely to both misuse and divert their stimulant medication [145]. Both immediate-release and, to a lesser degree, extended-release preparations of stimulant medications can be diverted or misused, with extended release preparations having less potential for parenteral usage [55, 145]. Non-stimulants such as atomoxetine and guanfacine XR do not have abuse potential.

Addressing Dual Diagnosis Patients Suffering from Attention-Deficit Hyperactivity Disorders and Comorbid Substance Use Disorders: A Review of Treatment Considerations

Jose Martinez-Raga, MD, PhD,†‡ Carlos Knecht, MD,*§ Raquel de Alvaro, MD,‖ Nestor Szerman, MD,*¶ and Pedro Ruiz, MD#*

Original Article

ADDICTIVE DISORDERS & THEIR TREATMENT

Volume 12, Number 4
December 2013

Abstract

Objective:

To provide an updated, thorough, and critical review of the current status of the pharmacological and psychosocial treatments of patients with attention-deficit hyperactivity disorder (ADHD) and a comorbid substance use disorder (SUD).

Methods:

Comprehensive and systematic search of relevant databases (Medline, PubMed, Embase, and the Cochrane Library of systematic reviews and clinical trials) was carried out until January 31, 2012.

Results:

Treatment of patients with ADHD and a comorbid SUD is based on a multimodal and integrated approach, requiring the adequate management of the comorbid disorders, with psychosocial and pharmacological treatments. Regarding the pharmacotherapies for ADHD, prescription psychostimulants, particularly methylphenidate and atomoxetine, have all been assessed in dually diagnosed patients, for treating the symptoms of ADHD or for managing the comorbid SUD. Overall, medications are safe, well tolerated, and provide short-term and long-term benefits in patients with ADHD and comorbid SUD.

Conclusions:

Studies assessing the efficacy of pharmacotherapies for ADHD have shown that they are equally efficacious and well tolerated, generally in combination with psychological interventions, in patients with a comorbid SUD. In addition, psychostimulant treatment of children with ADHD appears to have a protective effect on the subsequent risk for SUD.

ELSEVIER

Updated European Consensus Statement on diagnosis and treatment of adult ADHD

European Psychiatry 56 (2019) 14–34

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7.5.2. ADHD with comorbid substance use

- In patients with ADHD and substance use disorder, to be effective, **treatment with stimulants may use higher dosages than normal**.
- **Immediate-release stimulants should be avoided** in patients with ADHD and SUD, whereas OROS-MPH and LDX have lower abuse potential.
- Based on data from large cohort studies**, following treatment, the negative outcomes associated with ADHD significantly diminish**, i.e. traffic accidents, mortality, criminality, depression and suicide, and substance abuse.

European Addiction Research

International Consensus Statement on Screening, Diagnosis and Treatment of Substance Use Disorder Patients with Comorbid Attention Deficit/Hyperactivity Disorder

Review

Eur Addict Res 2018;24:43–51
DOI: 10.1159/000487767

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- **Pharmacotherapy should not be avoided** and should be critically **encouraged** in patients with ADHD and SUD with a preference for high doses of **long-acting stimulants in ADHD patients with stimulant UD** or **atomoxetine in patients with alcohol use disorder**.

- Treatment of ADHD can be useful to reduce ADHD symptoms without worsening the SUD.

- **Treating both ADHD and SUD with their own medication simultaneously**, that is, for patients with ADHD and an alcohol use disorder, one may consider treatment with atomoxetine and with naltrexone, nalmefene, acamprosate or topiramate.

ANZJP 50 YEARS 1967-2017

Australian & New Zealand Journal of Psychiatry
1–10
DOI: 10.1177/0004867417714878

Managing attention deficit hyperactivity disorder in adults using illicit psychostimulants: A systematic review

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Abstract

Context: Attention deficit hyperactivity disorder and stimulant use disorder commonly co-exist, and appropriate treatments have not been well established.

Objective: To provide guidance for treatment of co-existing attention deficit hyperactivity disorder and stimulant use disorder.

Data sources: A systematic review of published English articles using MEDLINE, EMBASE, CINAHL, PsycINFO and Cochrane, utilising consistent search terms.

Study selection: Randomised controlled trials, comparing any treatment arm with a control group, for participants meeting *Diagnostic and Statistical Manual of Mental Disorders* or equivalent criteria for both attention deficit hyperactivity disorder and stimulant use disorder.

Results: Eight trials were identified for inclusion in this review. Four of eight studies showed improvement in attention deficit hyperactivity disorder outcome measures compared with placebo. Two of six studies that reported substance use outcomes showed improvement in treatment arms compared with placebo. Studies to show effect tended to be those with the highest treatment dosage.

Conclusion: Evidence for the efficacy of treatment of patients with comorbid stimulant use disorder and attention deficit hyperactivity disorder is limited. Promising outcomes need replication in further studies utilising higher treatment dosage.

EXPERT OPINION ON PHARMACOTHERAPY
https://doi.org/10.1080/14656566.2018.1551878

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REVIEW

Pharmacotherapeutic strategies for the treatment of attention-deficit hyperactivity (ADHD) disorder with comorbid substance-use disorder (SUD)

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ABSTRACT

Introduction: Substance use disorder (SUD) is very common amongst patients with attention deficit hyperactivity disorder (ADHD). The two disorders share partially overlapping features and SUD in ADHD is characterized by an early age of onset, high likelihood of poly-substance use, increased risk of suicide attempts, more hospitalizations, and scarce treatment adherence.

Areas covered: This paper reviews randomized active comparator-controlled or placebo-controlled trials evaluating the use of pharmacotherapy in patients with ADHD and SUD. The authors include open label and observational studies.

Expert opinion: Stimulant and non-stimulant treatments should be used to aid ADHD symptomatology in patients with SUD. SUD seems to be less responsive, suggesting a relative independence of the two conditions. For this reason, the association of ADHD-specific drugs and SUD-treatments should be recommended in a large proportion of patients suffering from both disorders. The rate and the quality of ADHD response to specific pharmacological treatments is highly variable, depending on the dose and the duration of the treatment, the age of the patient, and the severity and the chronicity of addiction. Further research is necessary to explore the divergences in treatment response of different ADHD subtypes in different subtypes of SUD.

ARTICLE HISTORY

Received 22 May 2018
Accepted 21 November 2018

KEYWORDS

Attention deficit hyperactivity disorder; substance use disorders; non stimulant drugs; simulant drugs

Tabla 11. Metilfenidato en el tratamiento de pacientes con TDAH y TCS dual

Autores y año	Tipo de estudio	Comparador	Terapia asociada	Dosis diaria	Muestra	Duración *	Hallazgos principales
Levin et al, 1998 [299]	Abierto	Ninguno	TPR	40-80 mg [a]	12 adultos con TDAH y dependencia de cocaína	12 semanas	8 sujetos completaron el estudio. Mejoría en síntomas de TDAH y reducción en el *craving* y en el consumo de cocaína
Castaneda et al, 1999 [298]	Abierto	FLX, BUP, MTF-LP, d-anfetamina, metanfetamina	Ninguna	20-120 mg	19 adultos con TDAH y dependencia de cocaína	52 semanas	El MTF-LP en monoterapia fue el tratamiento más eficaz en reducir los síntomas de TDAH, sin recaídas en la dependencia de cocaína
Schubiner et al, 2002 [308]	ECACP (doble ciego)	PBO	TCC grupal e individual semanal	30-90 mg [a]	48 adultos (18-55 años de edad) con TDAH y dependencia de cocaína	12 semanas	Mejoría en síntomas de TDAH con MTF vs PBO mediante escala de síntomas de TDAH tanto según el clínico (p<0,005) y según el sujeto (p<0,05). Sin diferencias en el consumo, urinoanálisis y *craving* de cocaína entre ambos tratamientos
Somoza et al, 2004 [300]	Abierto, multicéntrico	Ninguno	TPR	20-60 mg [a]	41 adultos (21-50 años de edad) con TDAH y dependencia de cocaína	10 semanas	70% completaron el estudio. Buena tolerabilidad del MTF, con mejoría de síntomas de TDAH evidenciado mediante la ICG y de la dependencia de cocaína
Carpentier et al, 2005 [303]	ECACP y cruzado (doble ciego)	PBO	Ninguna	15-45 mg [a] (dosis media: 34 mg/d)	25 adultos (em: 31,9 años) con TDAH y un TUS (ingresados en una unidad de adicciones)	8 semanas	19 sujetos completaron el estudio. Mejoría significativa en síntomas de TDAH en la AARS (P<0.01), la EOC (P<0,01) y la ICG (P<0,01) desde la primera semana, con MTF y con PBO. Más EAM con MTF que con PBO (p<0,05)
Levin et al, 2006 [306]	ECACP (doble ciego)	MTF-LP vs. BUP vs. PBO	TCC individual	10-80 mg (dosis media: 77 mg/d)	98 adultos (18-60 años de edad) con TDAH y dependencia de opiáceos en TMM	12 semanas	70% completaron el estudio. Mejoría general en los síntomas de TDAH (reducción del 30% en la AARS y ICG<3) sin diferencias significativos entre MTF, BUP o PBO (tasa de respuesta con PBO: 46%)
Levin et al, 2007 [307]	ECACP (doble ciego)	MTF-LP vs. PBO	TCC individual	10-60 mg	106 adultos (23-52 años de edad; em: 37 años) con TDAH y dependencia de cocaína	14 semanas	Mejoría >30% en síntomas de TDAH (reducción del 30% en la AARS y ICG<3) en mayoría de pacientes, similar en ambos grupos (55% MTF vs 47% PBO). La mejoría de síntomas de TDAH con el MTF, no así con PBO, se asoció con reducción en el consumo de cocaína.
Szobot et al, 2008 [302]	ECACP y cruzado	MTF-SODAS vs. PBO	Ninguna	0,3-1,2 mg/kg/día	16 adolescentes varones (15-21 años de edad; em:	6 semanas	Mejoría significativa en síntomas de TDAH (según la SNAP-IV y la ICG) con MPH-SODAS vs. PBO (p<0,001). Ausencia de efectos significativos

	(ciego simple)				17,5 años) con TDAH y TUS		sobre el consumo. Buena tolerabilidad de MTF-SODAS.
Konstenius et al, 2010 [304]	ECACP (doble ciego)	MTF-OROS vs. PBO	TPR	18-72 mg	24 pacientes adultos (18-65 años de edad; em: 37.4 años) con TDAH y dependencia de anfetaminas	13 semanas	Mejoría significativa en síntomas de TDAH según la CAARS-AA y CAARS-C, en el consumo de sustancias (objetivado por urinoanálisis), en tiempo hasta la recaída y en *craving;* similar en ambos grupos. Buena tolerabilidad de MTF-OROS.
Winhusen et al., 2010 [309]	ECACP (doble ciego), multicéntrico	MTF-OROS + TTN vs. PBO + TTN	TTN + TB para dejar de fumar	18-72 mg	255 adultos (18-55 años de edad; em: 38 años) con TDAH y dependencia de nicotina	15 semanas	Reducción de síntomas de TDAH (reducción 30% en la AARS, p<0,0001 y en la escala de gravedad de la ICG, p<0,01) con MTF-OROS vs. PBO. Tasas de abstinencia tabáquica prolongada similares con MTF-OROS (43.3%) y PBO (42.2%). Buena tolerabilidad de MTF-OROS. Mayor reducción en CPD con MTF-OROS vs. PBO (p<0,02).
Riggs et al., 2011 [301]	ECACP (doble ciego), multicéntrico	MTF-OROS + TCC vs. PBO + TCC	TCC	18-72 mg	303 adolescentes (13-18 años de edad) con TDAH + TUS	16 semanas	Reducción significativa en la AARS o en la ICG con MTF-OROS y PBO. Disminución significativa en el consumo con MTF-OROS y PBO. Significativamente mayor orinas negativas con MTF y PBO (p < 0,05). Buena tolerabilidad del MTF-OROS.
Konstenius et al., 2014 [305]	ECACP (doble ciego)	MTF-OROS vs. PBO	TCC individual	18-180 mg	54 adultos (18-65 años de edad; em: 42 años) con TDAH y dependencia de anfetaminas	24 semanas	Mayor mejoría en síntomas de TDAH con MTF vs. PBO mediante la CAARS-AA (p < 0,005). Reducción de al menos 30% en síntomas de inatención o hiperactividad en 17 pacientes del grupo MTF vs. 7 del grupo PBO (p < 0,05). Reducción significativa en ICG de gravedad con MTF, pero no con PBO. Mayor proporción de orinas negativas con MTF vs. PBO (p < 0,05); no hubieron diferencias en el *craving* entre los dos grupos. EAM leves a moderados.

* Indica duración del estudio; em: edad media

[a] Metilfenidato (MTF) de liberación inmediata;

ECACP: ensayo clínico aleatorizado y controlado con placebo

PBO: Placebo; FLX: Fluoxetina; BUP: Bupropion; TTN: Terapia transdérmica con nicotina; TMM: tratamiento de mantenimiento con metadona

MTF-LP: Metilfenidato de liberación prolongada; MTF- OROS: Metilfenidato de liberación controlada mediante sistema por presión osmótica (OROS)

MTF-SODAS: Metilfenidato de liberación prolongada mediante sistema de absorción de fármacos por vía oral en partículas esferoidales (SODAS)

CPD: Cigarrillos por día

TCC: Terapia cognitivo conductual; TPR: Terapia de prevención de recaídas; TB: Terapia breve

EAM: Efectos adversos medicamentosos

AARS: Adult ADHD rating scale; CAARS: Conners Adult ADHD Rating Scale (CAARS-AA: CAARS auto-aplicada; CAARS-C: CAARS administrada por el clínico); EOC: Escala de Observación Clínica; ICG: Escala de Impresión clínica global; SNAP-IV = Swanson, Nolan, and Pelham Scale, version IV.

Tabla 12. Ensayos clínicos de derivados anfetamínicos en el tratamiento de pacientes con TDAH y TCS dual

Autores y año	Tipo de estudio	Comparador	Terapia asociada	Dosis diaria	Muestra	Duración *	Hallazgos principales
Kollins et al, 2014 [310]	ECACP (doble ciego)	LDX vs PBO	Parche de nicotina	30-70 mg	32 adultos (18-50 años de edad media: 31,6 años) con TDAH y dependencia de nicotina	28 días	Reducción en el número de cigarillos/día con LDX y con PBO (p <0,0001). Mejoría significativa en síntomas de TDAH según la CAARS-C (p=0,01) y en la CAARS-AA (p=0,001) sólo con LDX. Buena tolerabilidad de la LDX.
Levin et al, 2015 [311]	ECACP (doble ciego),	SMA-LP vs PBO	TCC individual semanal	60 mg vs. 80 mg	126 adultos (18-60 años de edad) con TDAH y trastorno por consumo de cocaína	13 semanas	Se observó que comparado con el 39,5% en el grupo placebo, un Significativamente mayor número de pacientes en el grupo SMA-LP 60 mg (75,0%; OR=5,23) y en el grupo SMA-LP 80 mg (58,1%; OR=2,27) que en el grupo PBO alcanzaron al menos una reducción del 30% en la gravedad de los síntomas de TDAH (según la AISRS). Tasas de abstinencia continuada en las 3 semanas previas significativamente mayores con SMA-LP 80 mg (30,2%; OR=11,87) y con SMA-LP 60 mg (17,5%; OR=5,85) que con PBO (7,0%). Significativa mayor proporción de semanas con orinas negativas con SMA-LP 80 mg (OR=5,46) y con SMA-LP 60 mg (OR=2,92) que con PBO. Las sales de anfetamina fueron bien toleradas.

ECACP: ensayo clínico aleatorizado y controlado con placebo
PBO: Placebo; LDX: Lisdexanfetamina; SMA-LP: sales mixtas de anfetamina de liberación prolongada
AISRS: Adult ADHD Investigator Symptom Rating Scale; CAARS: Conners Adult ADHD Rating Scale (CAARS-AA: CAARS auto-aplicada; CAARS-C: CAARS administrada por el clínico).

Atomoxetine in the treatment of ADHD + SUD

Original Article | ADDICTIVE DISORDERS & THEIR TREATMENT

Addressing Dual Diagnosis Patients Suffering from Attention-Deficit Hyperactivity Disorders and Comorbid Substance Use Disorders: A Review of Treatment Considerations

Jose Martinez-Raga, MD, PhD,†‡ Carlos Knecht, MD,*§ Raquel de Alvaro, MD,‖ Nestor Szerman, MD,*¶ and Pedro Ruiz, MD#*

TABLE 2. Atomoxetine in the Treatment of Patients With ADHD and Comorbid SUD

References	Study Design	Comparison	Adjunctive Therapy	Dose	Sample	Duration (wk)*	Key Findings
Wilens et al[71]	RCT (double-blind)	PLC	None	100†	147 adults with ADHD+ alcohol abuse or dependence	12	Significant improvement of ADHD symptoms and significant reduction of heavy alcohol use in the ATMX cohort compared with placebo. Good tolerability of ATMX
Levin et al[72]	Open-label	None	CBT	100†	20 adult patients with ADHD+ cocaine dependence	12	Significant reduction in ADHD symptoms. No effects on cocaine use. 2 subjects discontinued ATMX because of MAE
McRae-Clark et al[73]	RCT (double-blind)	PLC	MI	100†	38 adults with ADHD + cannabis dependence	12	Significantly greater improvement of some ADHD symptoms with ATMX compared with PLC. No differences in marijuana use. The majority of MAE were mild to moderate in severity
Thurstone et al[74]	RCT (double-blind)	ATMX vs. PLC	MI/CBT	100†	70 adolescents (13-19 y of age) with ADHD+ comorbid SUD	16	No significant differences in ADHD scores or in substance use between ATMX and PLC. Rates of MAE were generally mild and short-lived
Adler et al[75]	Open-label	None	Residential rehab	120†	18 adult polysubstance users + ADHD	10	12 residents completed ≥2 wk of treatment. ATMX was well tolerated and associated with improvement of ADHD symptoms and in some measures of craving

* Indica duración del estudio

[a] dosis máxima de metilfenidato

ECACP: ensayo clínico aleatorizado y controlado con placebo

PLC: Placebo; ATMX: Atomoxetina; EAM: Efectos adversos de la medicación

EM: Entrevista Motivacional; TCC: Terapia cognitivo conductual; TPR: Terapia de prevención de recaídas

Addiction Biology

SSA SOCIETY FOR THE STUDY OF ADDICTION

Guanfacine decreases symptoms of cannabis withdrawal in daily cannabis smokers

Margaret Haney, Ziva D. Cooper, Gillinder Bedi, Evan Herrmann, Sandra D. Comer, Stephanie Collins Reed, Richard W. Foltin & Frances R. Levin

The α2a-adrenergic agonist, lofexidine, reduced cannabis withdrawal-related sleep disruption in the laboratory, but side effects (e.g. fatigue, hypotension) limit its utility as a treatment for cannabis use disorder. This study tested the potential efficacy and tolerability of a daily bedtime administration of the FDA-approved α2a-adrenergic agonist, guanfacine, in a human laboratory model of cannabis use disorder. Daily, nontreatment-seeking cannabis smokers (13M, 2F) completed a within-subject study comprising two 9-day inpatient study phases. Each phase tested the effects of daily placebo or immediate-release guanfacine (2 mg) on cannabis intoxication (5.6 percent THC; 2 days), withdrawal (4 days of abstinence) and subsequent 'relapse' (3 days of cannabis self-administration). Ratings of mood, sleep, cardiovascular effects, food intake, psychomotor performance and cannabis self-administration were assessed. An outpatient phase preceded each inpatient phase for medication clearance or dose induction. Under placebo medication conditions, cannabis abstinence produced significant withdrawal, including irritability, sleep disruption and anorexia. Guanfacine reduced ratings of irritability and improved objective measures of sleep during cannabis withdrawal relative to placebo but did not reduce cannabis self-administration. Guanfacine was well tolerated with little evidence of fatigue and only small decreases in blood pressure: no dose was held due to hypotension. Thus, a single daily administration of guanfacine at bedtime improved sleep and mood during cannabis withdrawal relative to placebo. This positive signal supports further studies varying the guanfacine dose, formulation or frequency of administration, or combining it with other medications to increase the likelihood of having an impact on cannabis use.

Final comments

- With greater emergence of adult ADHD its screening in SUD populations should become standard practice to establish data on multi-condition presentations with the ultimate goal of improving clinical outcomes.
- Careful and systematic evaluation of substance use in patients with ADHD is essential, particularly in adolescents or adults without previous diagnosis.
- It is also essential to evaluate the existence of ADHD in every patient, treatment and treatment for an addictive disorder.
- Stimulants are effective and safe medication in patients with and ADHD and with or without a concurrent SUD.

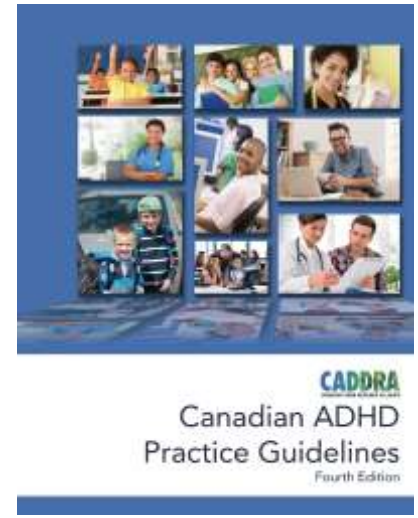
Review

Jose Martinez-Raga*, Nestor Szerman, Carlos Knecht and Raquel de Alvaro

Attention deficit hyperactivity disorder and dual disorders. Educational needs for an underdiagnosed condition

Abstract: A wide range of comorbid psychiatric disorders overlap with attention-deficit hyperactivity disorder (ADHD) across the life span. There is a robust and complex link between ADHD and substance use disorders (SUD). The aim of this report was to review the neurobiological and other vulnerability factors explaining the comorbidity of ADHD and an addictive disorder, as well as the key aspects of the assessment and diagnosis of dually diagnosed ADHD patients. A comprehensive and systematic search of relevant databases (PubMed, Embase, and PsychINFO) was conducted to identify studies published in peer-reviewed journals until July 31, 2012, with the aim of exploring the association of ADHD and SUD with postgraduate training and residency education. Across the life span, ADHD is associated with significant impairment and comorbidity. Data from epidemiological, clinical and epidemiological studies show a very solid link between ADHD and SUD. Therefore, it is very important to carefully and systematically assess for any substance use in patients with suspected ADHD coming to initial assessment, and vice versa. While there are various valid and reliable rating and screening scales, diagnosis cannot solely rely on any of the instruments available for both SUD and ADHD in adult patients with dual pathology. The most important and effective tool in the assessment of dually diagnosed patients with ADHD and SUD is a full and comprehensive clinical and psychosocial assessment. Hence, it is essential to actively incorporate training opportunities on the assessment, diagnosis, and management of adult ADHD and dually diagnosed ADHD patients during postgraduate education residency or specialist training.

MYTHS	FACTS
ADHD is not a real condition	ADHD is a neurobiological condition that can cause inattention, hyperactivity and/or impulsivity, along with several related difficulties, inappropriate for an individual's age.
ADHD is over-diagnosed	A US 2014 national survey found that healthcare practitioners are carefully diagnosing children. The vast majority (9 out of 10) of the 2,976 children diagnosed with ADHD had been diagnosed by practitioners using best practice guidelines [346]. Possible explanations for increased diagnosis of ADHD include improved healthcare practitioner and parental awareness; more screenings by pediatricians and other primary care givers; decreased stigma about ADHD; availability of better treatment options, and more cases arising from suspected environmental causes such prenatal exposure to toxins or high blood lead levels [347].



MYTHS	FACTS
ADHD results from ineffective teaching and/or poor parenting	ADHD is primarily biological and genetic in its origins. Environmental factors such as teaching and parenting quality, however, can minimize or intensify the difficulties experienced by an individual with ADHD [16].
Everyone has ADHD because everybody is inattentive sometimes, especially these days.	The core symptoms of ADHD can occur in everyone occasionally (e.g. forgetting items). People with ADHD, however, have significantly greater numbers of these symptoms (meeting a threshold of at least 6/9 symptoms for children, 5/9 for adults (17+)) occurring frequently and they experience more significant difficulties and impairment from them (e.g. job loss, academic underachievement).