NEWSLETTER







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BIBLIOGRAFIA ADHD GIUGNO 2019

Acta Paediatr Int J Paediatr. 2019.

ONE-THIRD OF SCHOOL-AGED CHILDREN WITH CEREBRAL PALSY HAVE NEUROPSYCHIATRIC IMPAIRMENTS IN A POPULATION-BASED STUDY.

Pahlman M, Gillberg C, Himmelmann K.

AIM: To describe motor function and associated impairments, particularly autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), in school-aged children with cerebral palsy (CP).

METHODS: Population-based study of all children with CP born 1999-2006 from the county of Västra Götaland, Sweden; 264 children (141 males, 123 females). Information was obtained from the CP Register of western Sweden (data collected at 4-8 years of age) and all medical records at 10-17 years of age.

RESULTS: Cerebral palsy was spastic in 76%, dyskinetic in 17% and ataxic in 7% of all children. Sixty-three per cent were independent walkers. Associated impairments were present in 75%. Vision was impaired in 19%, hearing in 8% and speech in 54%. Intellectual disability (ID) was present in 53% and epilepsy in 41%. ID had increased from 42% to 53% since preschool-age. Neuropsychiatric impairments were present in 32% of the children; ASD in 18%; and ADHD in 21%. All impairments, except for ASD and ADHD, increased with more severe motor impairment.

CONCLUSION: Three in four school-aged children with CP have associated impairments, underscoring the need to broadly assess every child. The high rate of ASD and ADHD points to the importance of in-depth studies of such impairments in CP.

Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

ADHD Atten Deficit Hyperact Disord. 2019.

DOES EXECUTIVE FUNCTION CAPACITY MODERATE THE OUTCOME OF EXECUTIVE FUNCTION TRAINING IN CHILDREN WITH ADHD?

Dovis S, Maric M, Prins PJM, et al.

Executive functioning (EF) training interventions aimed at ADHD-symptom reduction have limited results. However, EF training might only be effective for children with relatively poor EF capacity. This randomized double-blind placebo-controlled study examined whether pre-training EF capacity moderates the outcome of an EF-training intervention on measures of near transfer (EF performance) and far transfer (ADHD symptoms and parent-rated EF behavior) immediately after treatment and at 3-month follow-up. Sixty-one children with ADHD (aged 8-12) were randomized either to an EF-training condition where working memory, inhibition and cognitive flexibility were trained, or to a placebo condition. Single moderation models were used. All significant moderation outcomes had small effect sizes. After Bonferroni correction, there were no significant moderators of treatment outcome. Children with poor EF capacity do not benefit more from EF training than from placebo training. Training only EF-impaired children will probably not improve outcomes of EF training studies

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Alcohol Clin Exp Res. 2019;43:233A.

CHILDHOOD ADHD AND HEAVY ALCOHOL USE AT AGE 30: SHIFTING MEDIATORS WITH ADVANCING AGE.

Walther CAP, Pedersen SL, Wang FL, et al.

Childhood ADHD carries increased risk for substance use problems in adulthood (Lee et al., 2011). Previous research has described mediational pathways (e.g., through social impairment and delinquency) that partially explain this risk in adolescence and young adulthood (Molina et al., 2012; 2014), but prediction from these vulnerabilities to older-aged heavy drinking is under-researched. This study examined the extent to which previously established mediators were useful in predicting heavy alcohol use at age 30 from childhood ADHD. Participants were 272 adults (154 with, 118 without childhood ADHD) interviewed at age 30 for the Pittsburgh ADHD Longitudinal Study who also provided data in adolescence (ages 14-17), at age 20, and at age 25 (AA011873). Participants reported frequency of heavy drinking (average of binge drinking and drunkenness) and number of past year delinquent acts, and impairment in social relationships was parent-reported. Using Mplus 8.2 (Muthen &Muthen, 2017), adolescent, age 20, and age 25 social impairment and delinquency were tested as mediators of the childhood ADHD-age 30 heavy drinking association. Models were adjusted for race, age 17 alcohol use, and childhood socioeconomic advantage. Childhood ADHD was associated with adolescent social impairment (+i's = 0.60-0.61, p < 0.001) and delinquency (+i's = 0.27-0.28, p < 0.001) in both models but was only associated with age 20 social impairment (+| = 0.32, p < 0.001). Adolescent social impairment was associated with age 20 and 25 social impairment (+|'s = 0.46-0.56, p < 0.001), but adolescent delinquency was not associated with delinquency at either age (+| = 0.17-0.19, p = 0.06-0.57). Although we previously reported that social impairment and delinquency mediated the ADHD-heavy drinking association in adolescence, and delinquencymediated at age 20, these variables were not associated with heavy alcohol use at age 30 (+''s = -0.15-0.14, p's = 0.08-0.79). These findings suggest important changes with age in associations between established risk factors and heavy drinking for those with ADHD histories. Other indicators of vulnerability, such as emotional impulsivity, daily life functioning, and depression, may become increasingly relevant to heavy drinking risk with advancing age. These variables are being considered in additional analyses examining developmental shifting of reasons for alcohol problem vulnerability in ADHD

Alcohol Clin Exp Res. 2019;43:173A.

LONGITUDINAL TRAJECTORY GROUPS OF ALCOHOL OUTCOMES AND DEPRESSIVE SYMPTOMS IN ADULTHOOD: DIFFERENTIAL PREDICTION BY ADHD DIAGNOSES.

Wang FL, Pedersen SL, Devlin B, et al.

Alcohol problems and depressive symptoms frequently co-occur in adulthood, yet pathways to this joint outcome are little understood (Grant & Harford, 1995). Because children with ADHD are at greater risk for both problems in adulthood relative to those without (Biederman et al., 2006), ADHD may confer risk for their co-occurrence. Prior studies have not found that those with ADHD showed stronger associations between alcohol outcomes and depression cross-sectionally (Biederman et al., 1995) or between their slopes over time (Wang et al., in press), However, ADHDmay heighten risk for jointly increasing alcohol use and depression over time. We identified groups with unique trajectories of heavy drinking, alcohol problems, and depression from ages 21-29. We hypothesized that a group with worsening alcohol outcomes and depression over time would be associated with childhood and adulthood-persistent ADHD. Participants were from the Pittsburgh ADHD Longitudinal Study (n = 629; 60.3%ADHD; 39.7%non-ADHD; 81.9%White; 89.1%male). DSM criteria diagnosed childhood and adulthood-persistent ADHD. Participants self-reported depression (CES-D), heavy drinking (frequency 5 +), and alcohol problems at ages 21, 23, 25, 27, and 29. Multitrajectory models with one to eight independent groups were evaluated. Childhood or persistent ADHD were predictors of the posterior probability of groupmembership, adjusting for sex, race, childhood conduct disorder, parental education and parental ADHD. The six-groupmodel fit best. Persistent ADHD (b=0.11,p < 0.05) was overrepresented in a group with severe-stable alcohol outcomes and moderate-stable depression. Childhood (b=0.11,p < 0.05) and persistent (b=0.12,p < 0.05) ADHD were overrepresented in a group with moderate-stable alcohol outcomes and severe-stable depression. Childhood ADHD (b=0.13,p < 0.001) was also overrepresented in a group with virtually no heavy drinking or alcohol problems and low depression. Those with ADHD were less likely to belong to groups with high-decreasing alcohol outcomes and low depression (persistent: +| = -0.08,p < 0.05) or moderate-decreasing alcohol outcomes and low depression (childhood: $+\frac{1}{1} = -0.11$, p < 0.05; persistent: $+\frac{1}{1} = -0.09$, p < 0.05). A group low on all outcomes was not predicted by ADHD. Limitations included the small proportions of female and non-White participants, reducing generalizability. Parsing the heterogeneity in alcohol use and depression trajectories implicated ADHD as a risk factor in their co-occurrence. Research on factors that differentiate developmental pathways from childhood ADHD could uncover new treatment targets

Ann Trop Med Public Health. 2018;11:S702.

COMPARING THE EFFECTS OF CONSISTENT AND INCONSISTENT PHYSICAL ACTIVITIES ON DECREASING THE SYMPTOMS IN STUDENTS FEATURING ATTENTION DEFICIT/HYPERACTIVITY DISORDER SYNDROME.

Mehrabi-Taleghani S, Taheri H, Mashhadi A, et al.

This study was aimed at comparing the effectiveness of consistent versus inconsistent physical activities in patients with attention deficit/hyperactivity disorder syndrome for decreasing the symptoms of such a disorder. To do so, a sample consisting of 75 individuals who were assigned to three groups, and selected based on randomized clustering method involving students with attention deficit-hyperactivity disorder syndrome in the city of Tehran, one empirical group consisting of 25 individuals who were subjected to Pilates physical activities as well as 25-people group who was assigned the task of a highly dynamic game (football) and the third group included 25 individuals who were not subjected to any physical activity. The required information was collected by making use of SNAP-IV questionnaire and child behavior checklist (CBCL) administered to students ranging from 6 to 18 years. To analyze the data, besides the descriptive statistics, inferential statistics were used. These include multivariate covariance analysis (MANCOVA), the regression coefficients homogeneity default tests, intergroup variance homogeneity default test through taking advantage of the Levin test and Shapiro-Wilk test in order to evaluate the data distribution normality. The results indicated that there is a significant difference between the effects of consistent versus inconsistent physical activity in patients featuring attention deficit/hyperactivity disorder syndrome (a highly dynamic ball game and Pilates) regarding a secondary type of hyperactivity and a combined type of attention deficit/hyperactivity. Based on the results, although both physical activities are effective in improving the symptoms of disorder, the extent to which the symptoms are decreased in secondary type hyperactivity and the combined type of the disorder is found higher in inconsistent physical activity with disorder signs (Pilates) than in consistent physical activity with disorder signs (highly dynamic ball game). As for the attention problems, the reductions in the scores in consistent physical activity with disorder signs is higher than in inconsistent physical activity with disorder signs

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Arch Dis Child. 2019:104:A266-A267.

LOST IN TRANSITION? ADHD TRANSITION SERVICE AUDIT IN A DGH SETTING: A QUALITY IMPROVEMENT PROJECT. Pulla V, Nelapatla S, Brown C.

Background ADHD is now well recognized to be a chronic neurodevelopmental disorder that persists well into adulthood. A previous clinical audit in a NW district showed that 73% of adolescents were either discharged or lost to follow up. An ADHD surveillance study run by BPSU and CAPSS showed that less than 25% clinicians were holding a transition planning meeting or having a hand over period and less than 50% out of 90 eligible adolescents needing transition were referred to AMHS. We have set up transition service 5 years ago young people who continue to need medication beyond the paediatric age group 16 to adult psychiatric service.

Aim We aim to report the outcome of a Quality Improvement Project (QIP) and to share our experience and our practice against guidelines on transition services.

Methods A retrospective review of 30 case notes was carried out between 2016 and 2018, using the NICE Clinical Guideline (2008) as benchmark standards. Patient information recoded included common comorbidities, medications used and age at transition.

Results We have been delivering acute paediatric services to children in Lincolnshire for several years but due to lack of comprehensive mental health services we set up ADHD clinics with a small team of 4 about 19 years ago and now actively manage over 200 children per year with ADHD and co morbid Neurodevelopmental problems. Demand for transition services for young people leaving paediatric service was recognized by local PCT in 2011 and was commissioned in 2012. A transition document was specifically designed. This led to an opportunity to set up 6 joint clinics a year with adult Psychiatric colleagues. 137 patients have so far transitioned till 2018. The initial problems identified with the service and solutions discovered are discussed. We will be presenting the findings from a random sample of our ADHD patients and recommendations from this QIP.

Conclusion NICE guidelines are now a decade old and RCPCH expects the next epidemic affecting children to be mental health problems. Services around the UK are still quite poor. Further improve our services based on audit findings

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Arch Dis Child. 2019;104:A268-A269.

Understanding the new nice guidelines for ADHD in Children.

Perera SJ.

Background The current ADHD NICE Guideline (NG87) includes new and amended recommendations that reflect the latest evidence for best practice. It updates and replaces Clinical Guideline (CG72) from 2008. It provides recommendations on: recognition, information and support, managing ADHD, medication, including monitoring and review of adherence to treatment.

Aim To review the New ADHD 2018 guideline, new recommendations and compare against the previous guidelines, clinical guidelines and quality standards.

Methods Literature review was done using search terms' ADHD NICE guidelines, NICE technology appraisals on ADHD, conduct disorder, transition of care and ADHD NICE quality standards'. NICE research questions, the resources and the published information was reviewed.

Results The presentation includes Impact of New Guidelines and other guidelines on current practice, Transition to adult care, Guidelines on Medication prescription, titration and follow up will reviewed during the presentation. The Role of Primary care in Identification and referral is clarified. It highlights groups of people who have increased risk of developing ADHD compared with the general population. Females are

more likely to have undiagnosed ADHD and may be more likely to receive an incorrect diagnosis of another mental health or neurodevelopmental condition. NICE recommends management of ADHD within Multi Disciplinary/Multi Agency Teams with representatives from Paediatrics, Forensic services, Child and adolescent mental health services (CAMHS), services for education and social services, Parent support groups and others with a significant local involvement in the lives of CYP with ADHD, such as Youth offending services. This team should also oversee local ADHD-specific training of parents and teachers.

Conclusion The learning objective to the participants is to gain sufficient information to discuss practice implications of NICE recommendations and management of ADHD beyond NICE guidelines. The guideline also includes recommendations on: service organisation and training, identification and referral, diagnosis and dietary advice. It provides guidance for clinicians about what principles to follow when discussing decisions to start, adjust, or discontinue pharmacological treatment for people with ADHD. The diagnosis of ADHD must be associated with at least moderate psychological, social and/or educational or occupational impairment based on interview and/or direct observation in multiple settings. It should not be made solely on the basis of rating scale or observational data

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Arch Dis Child. 2019;104:A210-A211.

NURSE-LED OUT OF HOURS CLINICS FOR ADHD.

Street H, Corker E, Walker V.

For children and young people (CYP), attending medical appointments can lead to missing school affecting educational attainment; isolation from social activity and friendship groups. In neurodevelopmental conditions there is often increased anxiety about missing activities or change of routineand hospital settings can be distressing. Specialist nurses are in a better positon to offer clinics outside of 9-5 Mon to Fri in settings away from the hospital, and offer quality intervention at a comparative reduced cost. This flexibility improves service user experience which supports medication compliance, reduces DNA rates and promotes inclusivity of patient led care. NICE guidance and best practice supports nurse-led clinics as a means of improving service user outcomes. Aims Gain opinions of service users regarding clinic times and venues Evaluate evening and weekend clinics - DNA, user feedback, staff activity Methods Families attending specialist nurse clinics for ADHD review were asked if they would attend an evening or Saturday clinic if available Simple feedback forms were used to record service user feedback following appointments Results Of 52 families, 34 (65%) preferred out of hours and 18 (35%) expressed no preference Of a sample of 48 OPAs. 42 attended, 5 DNA and 1 cancelled Conclusion There was good attendance at both Saturday and evening clinics, with a reduced DNA rate, which was also affected by adverse weather conditions. Very good feedback was received, e.g. not having to miss school, supporting working parents. Families appreciated flexibility of venue and being seen away from the hospital setting. Clinics were held where CYP may also attend for support groups and childrens centres introducing families to other means of support at the same time. This enhances outcomes for our cohort of families. Out of hours clinics were built into nursing job plans and did not attract overtime or additional payment, thus were cost negative to the service. The Community Paediatric workforce is recognised to be at crisis point with capacity and lack of qualified doctors; this report demonstrates a viable alternative which not only meets but adds to current provision. The project has also led to a Trust-wide Standard Operating Procedure to support out of hours-loffsite clinics for any speciality

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Arch Dis Child. 2019;104:A267-A268.

A REVIEW OF THE EVIDENCE FOR THE DIAGNOSIS AND MANAGEMENT OF PRE-SCHOOL ADHD.

Upadhyay D.

Background NICE guidelines (NG87)1 recognises the under 5 or pre-school ADHD and recommends ADHD-focused groupbased parent-training programme as the first-line treatment and taking advice from a specialist ADHD service/or tertiary service if above fails. NICE also reported that there was limited evidence on the efficacy of medication, with concerns and lack of evidence about the long-term effects of medication, in terms of growth and development among pre-school ADHD children. However, NICE also commented that

untreated ADHD can have far-reaching, long-lasting negative impacts on a child's life and further specialist advice, ideally from a tertiary service should be sought if Parent-training programme and environmental modifications are not effective. The recommendations from the American Academy of Child and Adolescent Psychiatrist (AACP) and the The American Academy of pediatrics (AAP)2 are slightly different. The AAP recommends that the primary care clinician should prescribe evidence-based parent-and/or teacher-administered behavior therapy as first line treatment and may prescribe Methylphenidate if the behavior therapy does not provide significant improvement. They recommend that in areas where evidence-based behavioral therapy is not available, the clinician needs to weigh the risks of starting medication at an early age against the harm of delaying diagnosis and treatment.

Methods A review of recently published literature was conducted, including meta-analyses and national guidelines. A survey of clinical experience among a cohort of ADHD specialists across the UK was also conducted. Three illustrative cases of preschool ADHD is presented to highlight the variable management approaches used.

Results The literature review showed few studies on preschool ADHD from Europe/UK. A review of 'Pre School ADHD Treatment Study (PATS)'3 on Efficacy and safety of immediate release Methylphenidate in preschool children (Greenhill et al 2006) suggested that Methylphenidate in 2.5-, 5-, and 7.5 mg doses three times daily, produced significant reductions on ADHD symptom scales compared to placebo, although effect sizes (0.4-0.8) were smaller than those cited for school-age children on the same medication. The follow up study by Vitiello et al (2015), showed about 2/3rd of participants from original PATS study were still on the medication andthe long-term pharmacotherapy of preschoolers with ADHD was heterogeneous.

Conclusion Pre-school ADHD studies are predominantly from the USA. NICE guidelines tend to take a more conservative approach. Medication should be considered only if others measures have failed and after a tertiary specialist opinion. We need more UK/European studies to measure how prevalent is ADHD in pre-schoolers. Also in the UK, ADHD specific Parental training programmes are patchy which can encourage pharmacotherapy. More investment on ADHD specific parental intervention/Parental training programme is needed

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Arch Dis Child. 2019;104:A266.

DEVELOPMENT OF A FORMAL CLINICAL SUPERVISION POLICY FOR **ADHD** SPECIALIST NURSES WORKING IN A CHILD DEVELOPMENT CENTRE.

Ozer S, Takon I, Atherton M, et al.

Introduction Clinical Supervision is a formal process of professional support and learning enabling individual practitioners to develop knowledge and competence assume responsibility for their own practice and enhance consumer protection and safety of care in complex clinical situations. Following a CQC inspection of our Trust, poor documentation of nursing competencies was highlighted in their report. It is recommended by the Care Quality Commission (CQC) that in services for people with a learning disability or autism, staff caring for the people using the services should have access to appropriate forms of support including Clinical supervision.2

Aim/objectives Provide a safe and confidential environment for ADHD nurse to reflect on and discuss their work and personal and professional responses to their work. Support ADHD Nurse Specialists in their personal and professional development and in reflecting on their practice. Facilitate new learning opportunities, identify training needs and ensure availability of ADHD and neurodevelopmental related CPD opportunities for continuous improvement. Support elements of clinical governance including quality improvement and risk management.

Methodology ADHD Lead Clinicians engaged over a 3 month period (April-June 2018) with the Lead nurses in Acute/Community Paediatrics and ADHD Nurse Specialists to review the CQC recommendation above and explore the need for a formal clinical supervision protocol that could be replicated across other Nurse Specialist areas. ADHD Lead Clinicians also reviewed academic literature on the benefits of clinical supervision incorporating this into the discussions with lead nurses and final document. Following discussions, the purpose, scope of supervision and expectations for effective and successful supervision were agreed and documented in the policy. The final document was ratified by the Trust's quality and patient safety committee and then circulated to the Team.

Results The ratified clinical supervision policy includes an agreement between the supervisees (ADHD Nurse Specialists) and clinical supervisors (ADHD Lead Clinicians). Date, time and frequency of the supervision event are clearly documented in the policy. Agenda items circulated ahead of the supervision meeting include clinical/prescribing issues, leadership, clinical governance, learning, teaching and support. The supervisee (ADHD Nurse) is expected to record all discussions and make this available to their line manager. Clinical supervisors (ADHD Lead Clinicians) and ADHD Nurse Specialists are expected to ensure all agreed goals and actions are SMART. The first supervision meeting was rated very useful by the Specialist nurses

Conclusion Following the development of the clinical supervision protocol, work is in progress to develop the first formal national clinical supervision competency framework for ADHD Nurses. The clinical supervision protocol has also been adopted by other specialist nursing areas locally

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Arch Dis Child Educ Pract Ed. 2019.

FIFTEEN-MINUTE CONSULTATION: MANAGING SLEEP PROBLEMS IN CHILDREN AND YOUNG PEOPLE WITH ADHD. Hobson S, Davie M, Farquhar M.

Sleep difficulties are common in children and young people presenting with features of attention-deficit/hyperactivity disorder (ADHD). Sleep problems may be both an effect of and a contributor to ADHD symptomatology, as well as having a significant impact on both individual and family functioning and well-being. There are often complex interacting contributing factors. Assessment of children presenting with symptoms suggestive of possible ADHD should include routine enquiry about sleep. Ongoing management of children with diagnosed ADHD should include regular reassessment and review of sleep. When sleep difficulties are present, we discuss how to further assess these, including the role of investigations, and a structured management strategy

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Archives of Gynecology and Obstetrics. 2019.

LOW MODERATE PRENATAL ALCOHOL EXPOSURE AND OFFSPRING ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): SYSTEMATIC REVIEW AND META-ANALYSIS.

San Martin PM, Maravilla JC, Betts KS, et al.

Purpose: To evaluate the available evidence on the association between low-to-moderate prenatal alcohol exposure (PAE) and the development of attention-deficit hyperactivity disorder (ADHD) symptoms in the offspring.

Methods: We systematically reviewed and meta-analysed studies reporting an association between low and/or moderate PAE and offspring ADHD symptoms (attention and/or hyperactivity). Systematic searches were performed in EMBASE, Pubmed, Medline, and PsycINFO and reviewed from selected references. Random effects modelling was conducted to pool adjusted odds ratios (OR) in different alcohol consumption levels (20-g/week, 50-g/week, and 70-g/week). Stratified analysis by sex per alcohol level was conducted to investigate the difference on OR and the magnitude between-study heterogeneity.

Results: Ten studies were included in the systematic review and six in the meta-analysis. Eight studies found no association and two studies suggested an apparent protective effect of low PAE in hyperactivity/inattention symptoms in boys. These results were confirmed by the meta-analysis showing no association between 20-g/week [OR 1.01 (0.68-1.49)], 50-g/week [OR 0.94 (0.85-1.03)] and 70-g/week [OR 0.94 (0.86-1.02)] and ADHD symptoms, with no evidence of publication bias. Stratified analysis by sex for a PAE 50-g/week exposed less risk of ADHD symptoms in boys compared to girls [OR 0.89 (0.83-0.96)].

Conclusions: We found no increased risk of ADHD symptoms in offspring born to mothers who drank alcohol up to 70-g/week

Biol Psychiatry. 2019.

RISKS AND BENEFITS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATION ON BEHAVIORAL AND NEUROPSYCHIATRIC OUTCOMES: A QUALITATIVE REVIEW OF PHARMACOEPIDEMIOLOGY STUDIES USING LINKED PRESCRIPTION DATABASES.

Chang Z, Ghirardi L, Quinn PD, et al.

Attention-deficit/hyperactivity disorder (ADHD) medication is one of the most commonly prescribed medication classes in child and adolescent psychiatry, and its use is increasing rapidly in adult psychiatry. However, major questions and concerns remain regarding the benefits and risks of ADHD medication, especially in real-world settings. We conducted a qualitative systematic review of studies that investigated the effects of ADHD medication on behavioral and neuropsychiatric outcomes using linked prescription databases from the last 10 years and identified 40 studies from Europe, North America, and Asia. Among them, 18 used within-individual designs to account for confounding by indication. These studies suggested short-term beneficial effects of ADHD medication on several behavioral or neuropsychiatric outcomes (i.e., injuries, motor vehicle accidents, education, substance use disorder), with estimates suggesting relative risk reduction of 9% to 58% for these outcomes. The within-individual studies found no evidence of increased risks for suicidality and seizures. Replication studies are needed for several other important outcomes (i.e., criminality, depression, mania, psychosis). The available evidence from pharmacoepidemiology studies on long-term effects of ADHD medication was less clear. We discuss time-varying confounding and other limitations that should be considered when interpreting results from pharmacoepidemiology studies. Furthermore, we highlight several knowledge gaps to be addressed in future research and implications for research on mechanisms of outcomes of ADHD medications

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Birth Defects Research. 2019;111:531.

PREVALENCE AND PREDICTORS OF ADHD MEDICATION USE IN A COHORT OF PREGNANT WOMEN.

Lemelin M, Boukhris T, Sheehy O, et al.

Attention deficit with or without hyperactivity disorder (ADHD) is common. Increased prevalence of ADHD medication use has been reported in adults. Thus, its utilization in pregnancy has become a concern. We sought to determine the 1) prevalence/ trends of ADHD medication use before and during pregnancy; 2) ADHD medication mean dosages by class, prevalence of medication switches; and 3) determinants of ADHD medication use during pregnancy. A longitudinal cohort study was performed, using data from the Quebec Pregnancy Cohort (QPC), which includes data on all pregnancies of mothers covered by Quebec's prescription drug insurance from 1998, to 2015. Cohort entry date was the first day of gestation. Women aged 15-45 years old at cohort entry covered by the RAMQ prescription drug plan for at least 12 months before and during pregnancy were eligible. ADHD medication users were defined as those having at least one ADHD medication filling before or during pregnancy overall and stratified by trimester. Generalized estimating equations were used to estimate crude and adjusted odds ratios (OR) with 95% confidence intervals (CIs) to identify determinants associated with ADHD medication use during pregnancy. 428,479 pregnant women were included in the study. A significant increase in the prevalence of ADHD medication use in pregnant women was observed (0.08% in 1998 to 1.2% in 2015 (p<0.01)). Methylphenidate, a stimulant, was the most used (70.1% of ADHD medication users). ADHD medication fillings were at optimal dosages 91.8% of the time; 28.1% of women switched to another ADHD medication class or had concomitant multiple ADHD medications use during gestation. Main determinants associated with ADHD medication use during pregnancy were being on welfare (aOR 1.27; 95%CI 1.06-1.52), hypertension (aOR 1.85; 95%CI 1.31-2.62), antidepressant/depression (aOR 3.18; 95%Cl 2.58-3.93), or other medication use (aOR 3.26; 95%CI 2.36-4.49) in the year before pregnancy; pregnant women were also at increased risk of using ADHD medications during gestation with increasing calendar year (aOR 1.33; 95%CI 1.26-1.41). Our findings show an increasing trend in ADHD medication use during pregnancy over the past 20 years. Our results are suggestive of a detection bias given the increase in use associated with increasing calendar year

Birth Defects Research. 2019;111:555.

MATERNAL USE OF SEROTONERGIC ANTIDEPRESSANTS DURING PREGNANCY AND RISK OF ADHD DIAGNOSIS AND SYMPTOMS IN OFFSPRING.

Lupattelli A, Mahic M, Handal M, et al.

The time-dependent effect of prenatal exposure to serotonergic antidepressants on attention deficit hyperactive disorder (ADHD) risk remains unresolved. This study sought to quantify the effect of time-varying prenatal exposure to serotonergic antidepressants on ADHD risk in childhood, as clinical diagnosis and parent-reported symptoms. We used data from the Norwegian Mother and Child Cohort Study, the Medical Birth Registry, the Prescription Database, and the Patient Registry of Norway, limited to women with depressive/anxiety disorders in pregnancy. The windows of drug of self-reported exposure were mid (week 16-28) and late pregnancy (> week 28). Symptoms of ADHD symptoms at 5 years were parent-reported via the Conners' Parent Rating Scale-Revised; ADHD diagnoses were retrieved from the specialist health care system, the Patient Registry (ICD-10 F90). We fit general linear and Cox marginal structural models (MSM) to account for time-varying exposure and confounders (depressive/anxiety symptoms as measured by SCL, co-medication with other psychotropics and analgesics), and time-fixed confounders. We included 3232 pregnancychild dyads within women with self-reported depressive/ anxiety disorders in pregnancy. Overall, 481 (14.9%) children had been prenatally exposed to serotonergic antidepressants and 90 children (2.8%) had a clinical diagnosis for ADHD. Relative to children born to women with non-medicated depression/anxiety (n=2751), those exposed to serotonergic antidepressants in mid (weighted HR: 1.74, 95% CI: 0.41-7.15) or late pregnancy (weighted HR: 1.66, (0.41-6.82)) did not have an increased risk for an ADHD diagnosis. Likewise, there were no differences on symptoms of ADHD according to timing of exposure (midpregnancy: weighted +|:-0.02, 95% CI:-0.30, 0.34; late pregnancy: weighted +|:-0.04, (-0.32, 0.25)). In a population of children born to women with depressive/anxiety disorders in pregnancy, there was no evidence for a substantial association between prenatal exposure to serotonergic antidepressants at different timings in pregnancy, and risk for ADHD symptoms and diagnosis. However, we were unable to confirm or refute whether a smaller increased risk exists

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BMC Psychiatry. 2019;19.

EVALUATION OF A STRUCTURED SKILLS TRAINING GROUP FOR ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD) - STUDY PROTOCOL OF A RANDOMISED CONTROLLED TRIAL.

Meyer J, Ramklint M, et al.

Background: Attention deficit/hyperactivity disorder (ADHD) has a negative impact on several domains of life. However, there is a shortage of evidence-based non-pharmacological treatments for adolescents with ADHD. A structured skills training group (SSTG) based on dialectical behaviour therapy (DBT) has been used in adult patients with ADHD with some promising results, although the treatment has not yet been adapted or evaluated for adolescents with ADHD. This study protocol describes how this treatment was adapted for an adolescent population and how the efficacy of the SSTG will be evaluated using a randomised controlled trial (RCT) design.

Methods: A sample of 184 adolescents (15-18 years of age) with a diagnosis of ADHD has been recruited from seven child and adolescent psychiatric outpatient units and randomised to either the SSTG or an active control group based on psychoeducation. Measures are conducted weekly during the treatment, as well as 2 weeks before treatment and 2 weeks and 6 months after treatment. The primary outcome measures are ADHD symptoms, functional impairment, quality of life and mindfulness. Secondary outcome measures are symptoms of comorbid psychopathology, perceived stress and sleep problems. This article describes the design, methods and analysis plan for evaluating the efficacy of the SSTG.

Discussion: The study will be the first RCT to examine the acceptability and efficacy of a SSTG based on DBT adapted for adolescents with ADHD. We believe that the study will extend the current knowledge base about psychological treatment for adolescents with ADHD.

Trial registration: ISRCTN registry (ISRCTN17366720). Retrospectively registered May 112,016

BMC Psychiatry. 2019 May;19.

DOES THE EDUCATION SYSTEM SERVE AS A PERSUASION AGENT FOR RECOMMENDING ADHD DIAGNOSIS AND MEDICATION UPTAKE? A QUALITATIVE CASE STUDY TO IDENTIFY AND CHARACTERIZE THE PERSUASION STRATEGIES OF ISRAELI TEACHERS AND SCHOOL COUNSELORS.

Gesser-Edelsburg A, Hamade Boukai R.

Background: There has been a steady rise in the use of medication by Israeli school children to treat ADHD, partly due to what seems like school teachers' and counselors' tendency to express positive attitudes towards its use. Therfore it is important to examine the involvement of the school teachers and counselors in the parents' decision-making about giving their children medication.

Methods: This study used a qualitative constructivist research method of semi-structured interviews. It included individual interviews with 36 teachers and school counselors and 11 parents of students ages 9–14 from the Jewish and Arab populations.

Results: Teachers and school counselors use different strategies to encourage parents to have their children diagnosed for ADHD and medicated. First they suggest diagnosis as a necessary step in the best interest of the child, distinguishing between diagnosis and medication to mitigate parents' concerns. In the second stage, teachers normalize the use of medication, as well as framing it as a drug that provides not only a medical treatment but also emotional wellbeing.

Conclusions: Teachers and counselors are involved in parents' decision-making process about medicating their children to treat ADHD, which contradicts the education system's guidelines. It is necessary to set clear and explicit limits and guidelines for education system employees so that they do not cross professional and ethical limits

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BMJ Open. 2018;8.

HUMAN EARLY LIFE EXPOSOME (HELIX) STUDY: A EUROPEAN POPULATION-BASED EXPOSOME COHORT.

Maitre L, De BJ, Casas M, et al.

Purpose Essential to exposome research is the collection of data on many environmental exposures from different domains in the same subjects. The aim of the Human Early Life Exposome (HELIX) study was to measure and describe multiple environmental exposures during early life (pregnancy and childhood) in a prospective cohort and associate these exposures with molecular omics signatures and child health outcomes. Here, we describe recruitment, measurements available and baseline data of the HELIX study populations.

Participants The HELIX study represents a collaborative project across six established and ongoing longitudinal population-based birth cohort studies in six European countries (France, Greece, Lithuania, Norway, Spain and the UK). HELIX used a multilevel study design with the entire study population totalling 31 472 mother-child pairs, recruited during pregnancy, in the six existing cohorts (first level); a subcohort of 1301 mother-child pairs where biomarkers, omics signatures and child health outcomes were measured at age 6-11 years (second level) and repeat-sampling panel studies with around 150 children and 150 pregnant women aimed at collecting personal exposure data (third level).

Findings to date Cohort data include urban environment, hazardous substances and lifestyle-related exposures for women during pregnancy and their offspring from birth until 6-11 years. Common, standardised protocols were used to collect biological samples, measure exposure biomarkers and omics signatures and assess child health across the six cohorts. Baseline data of the cohort show substantial variation in health outcomes and determinants between the six countries, for example, in family affluence levels, tobacco smoking, physical activity, dietary habits and prevalence of childhood obesity, asthma, allergies and attention deficit hyperactivity disorder. Future plans HELIX study results will inform on the early life exposome and its association with molecular omics signatures and child health outcomes. Cohort data are accessible for future research involving researchers external to the project

Brain Dev. 2019.

ASSOCIATION OF INATTENTION WITH SLOW-SPINDLE DENSITY IN SLEEP **EEG** OF CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER.

Saito Y, Kaga Y, Nakagawa E, et al.

Objective: We evaluated the power of slow sleep spindles during sleep stage 2 to clarify their relationship with executive function, especially with attention, in children with attention deficit-hyperactivity disorder (ADHD).

Methods: Subjects were 21 children with ADHD and 18 aged-matched, typically developing children (TDC). ADHD subjects were divided into groups of only ADHD and ADHD + autism spectrum disorder (ASD). We employed the Continuous Performance Test (CPT) to measure attention. We focused on sleep spindle frequencies (12ΓÇô14 Hz) in sleep stage 2 and performed a power spectral analysis using fast Fourier transform techniques and compared sleep spindles with the variability of reaction time in CPT.

Results: In the CPT, reaction variabilities in ADHD and ADHD + ASD significantly differed from those in TDC. Twelve-hertz spindles were mainly distributed in the frontal pole and frontal area and 14-Hz spindles in the central area. The ratio of 12-Hz frontal spindle power was higher in ADHD than in TDC, especially in ADHD + ASD. Significant correlation between the ratio of 12-Hz spindles and reaction time variability was observed.

Conclusions: Twelve-hertz frontal spindle EEG activity may have positive associations with sustained attention function. Slow frontal spindles may be useful as a biomarker of inattention in children with ADHD

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Brain Connectivity. 2019;9:437-50.

ELECTROENCEPHALOGRAPHY FUNCTIONAL NETWORKS REVEAL GLOBAL EFFECTS OF METHYLPHENIDATE IN YOUTH WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Rubinson M, Horowitz I, Naim-Feil J, et al.

Methylphenidate (MPH) is the leading drug for treatment of attention deficit/hyperactivity disorder (ADHD), yet its underlying neuronal mechanisms are still unclear. Here, we use a dynamical brain networks approach to explore the effects of cognitive effort and MPH on ADHD subjects. Electroencephalography data were recorded from 19 ADHD subjects and 18 controls during a Go/No-Go Task. ADHD subjects completed the task twice a day over 2 days. The second session was administered post-ingestion of placebo/MPH (alternately). Controls performed two tasks in 1 day. The data were divided into 300 ms windows from -300 pre-stimulus until 1200 ms post-stimulus. Brain networks were constructed per subject and window, from which network metrics were extracted and compared across the experimental conditions. We identified an immediate shift of global connectivity and of network segregation after the stimulus for both groups, followed by a gradual return to baseline. Decreased global connectivity was found to be 400-700 ms post-stimulus in ADHD compared with controls, and it was normalized post-MPH. An increase of the networks' segregation occurred post-placebo at 100-400 and 400-700 ms post-stimulus, yet it was inhibited post-MPH. These global alterations resulted mainly from changes in task-relevant frontal and parietal regions. The networks of medicated ADHD subjects and controls exhibited a more significant and lasting change, relative to baseline, compared with those of nonmedicated ADHD. These results suggest impaired network flexibility in ADHD, corrected by MPH

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Brain, Behavior, and Immunity. 2019.

ANTENATAL ACTIVE MATERNAL ASTHMA AND OTHER ATOPIC DISORDERS IS ASSOCIATED WITH ADHD BEHAVIORS AMONG SCHOOL-AGED CHILDREN.

Cowell WJ, Bellinger DC, Wright RO, et al.

Background: Identifying modifiable risk factors for neuropsychological correlates of attention deficit hyperactivity disorder (ADHD) in early childhood can inform prevention strategies. Prenatal inflammatory states, such as maternal asthma and other atopic disorders, have been increasingly linked to enhanced risk for neurobehavioral disorders in children, with some studies suggesting sex-specific effects.

Objectives: To assess the association between maternal active asthma and/or atopy in the antenatal period and child symptoms of ADHD during mid-childhood and, given the male-bias in ADHD prevalence, to examine modifying effects of child sex.

Study design: The study sample includes 250 maternal-child pairs enrolled in the Boston-based Asthma Coalition on Community, Environment and Social Stress (ACCESS) pregnancy cohort. We defined antenatal active atopy based on maternal report of current asthma, allergic rhinitis or atopic dermatitis during and/or in the year before pregnancy. When children were approximately 6 years old, mothers completed a battery of standardized child behavior rating scales designed for evaluating symptoms of ADHD. We used multivariable quantile regression to assess the relations between maternal antenatal atopy and symptoms of ADHD among children.

Results: In adjusted models, maternal atopy was significantly associated with greater risk for ADHD behaviors, as indicated by scores on the ConnersΓÇÖ Parent Rating Scale-Revised ADHD index (+! = 3.32, 95% CI: 0.33, 6.32). In sex-stratified models this association was stronger among girls (5.96, 95% CI = 0.95, 10.96) compared to boys (2.14, 95% CI = 5.75, 1.45, p-interaction = 0.01). Among girls, we observed a similar finding for the Behavior Assessment System for Children 2nd Edition Parent Rating Scale Attention Problems subscale (+! = 7.77, 95% CI = 1.57, 13.97). Results from other outcome subscales were similar in magnitude and direction, however, associations did not reach statistical significance at the p = 0.05 level.

Conclusions: Maternal antenatal active atopy may be a risk factor for the development of ADHD-like symptoms, especially among girls

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Child Dev. 2019 May;90:e339-e355.

PEER PROBLEMS AMONG POSTINSTITUTIONALIZED, INTERNATIONALLY ADOPTED CHILDREN: RELATIONS TO HYPOCORTISOLISM, PARENTING QUALITY, AND ADHD SYMPTOMS.

Pitula CE, DePasquale CE, Mliner SB, et al.

Seventy-eight postinstitutionalized (PI) children adopted at ages 17–36 months were assessed 2, 8, 16, and 24 months postadoption on measures of cortisol and parenting quality, and compared to same-aged children adopted from foster care (FC, n = 45) and nonadopted children (NA, n = 45). In kindergarten (Mage = 6.0 years), teachers, parents, and trained observers completed measures of peer relationships and attention deficit hyperactivity disorder (ADHD) symptoms. PI children had more peer problems and ADHD symptoms according to teachers and observers than NA children with FC children in between, whereas both PI and FC children were at significantly greater risk of hypocortisolism (i.e., blunted cortisol diurnal rhythm and reactivity). Hypocortisolism and ADHD symptoms mediated the association between preadoption adversity and peer difficulties. Higher postadoption parenting quality was protective

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Child Psychiatry Hum Dev. 2019 Apr;50:308-20.

SHOULD WE SUBTYPE ADHD ACCORDING TO THE CONTEXT IN WHICH SYMPTOMS OCCUR? CRITERION VALIDITY OF RECOGNISING CONTEXT-BASED ADHD PRESENTATIONS.

Murray AL, Ribeaud D, Eisner M, et al.

ADHD symptoms show considerable individual variation in the contexts in which they are expressed. It has previously been proposed that subtyping individuals according to the contexts in which symptoms are expressed may be clinically useful. We examined context-based patterns of ADHD symptoms in a longitudinal cohort study of n = 1388 children, as well as context-specific and context-general predictors of symptoms. Participants were community-ascertained and provided ADHD symptom data at ages 7, 9, and 11. Using growth mixture modelling we identified five inattention and five hyperactivity/ impulsivity categories that differed in the developmental patterns of symptoms reported by parent and teacher informants. We found some evidence that context-specific predictors were related to context-specific expressions. Specifically, after controlling for other risk factors for ADHD symptoms, relationships with teachers predicted school-specific (teacher-reported) but not home-specific (parent-reported) symptom levels. However, no subtypes defined by exclusively home-based symptoms emerged, suggesting that while symptoms may sometimes

be specific to the school context, they are only rarely confined to the home context. Subtyping by context could be informative; however, further work will required to uncover the nature of any etiological, functional, or outcome differences between those who show symptom expression in different contexts.

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Clin Neuropharmacol. 2019;42:105-07.

CESSATION OF SKIN PICKING SYMPTOMS WITH METHYLPHENIDATE TREATMENT IN A CHILD WITH COMORBID SKIN PICKING AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Colak SR. Colak B.

Skin picking disorder includes behaviors such as picking, scratching, and squeezing of the normal skin in an impulsive, repetitive manner despite the fact that no dermatological condition is detected. Skin picking disorder may also be comorbid in children with attention-deficit/hyperactivity disorder (ADHD) and vice versa. There is a great deal of data regarding the efficacy and safety of methylphenidate (MPH) treatment of ADHD. In this article, we report the cessation of skin picking behaviors in a 10-year-old girl diagnosed as having skin picking disorder and ADHD after modified-release MPH treatment. To our knowledge, this is the first case report that shows the cessation of skin picking behavior after MPH treatment in a child with ADHD

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Clin Neurophysiol. 2019.

IS THERE A CLUSTER OF HIGH THETA-BETA RATIO PATIENTS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER? Bussalb A, Collin S, Barth+®lemy Q, et al.

Objective: It has been suggested that there exists a subgroup of ADHD patients that have a high theta-beta ratio (TBR). The aim of this study was to analyze the distribution of TBR values in ADHD patients and validate the presence of a high-TBR cluster using objective metrics.

Methods: The TBR was extracted from eyes-open resting state EEG recordings of 363 ADHD patients, aged 5ΓÇô21 years. The TBR distribution was estimated with three Bayesian Gaussian Mixture Models (BGMMs) with one, two, and three components, respectively. The pairwise comparison of BGMMs was carried out with deviance tests to identify the number of components that best represented the data.

Results: The two-component BGMM modeled the TBR values significantly better than the one-component BGMM (p-value = 0.005). No significant difference was observed between the two-component and three-component BGMM (p-value = 0.850).

Conclusion: These results suggest that there exist indeed two TBR clusters within the ADHD population.

Significance: This work offers a global framework to understanding values found in the literature and suggest guidelines on how to compute theta-beta ratio values. Moreover, using objective data-driven method we confirm the existence of a high theta-beta ratio cluster

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Clin Neurophysiol. 2019;130:1256-62.

EEG DEVELOPMENT IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: FROM CHILD TO ADULT.

Clarke AR, Barry RJ, Johnstone SJ, et al.

Objective: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common psychiatric disorders found in children. While an extensive literature has documented the EEG in this clinical population, few studies have investigated EEG throughout the lifespan in ADHD. This study aimed to investigate EEG maturational changes, in subjects with ADHD combined type, that spanned from childhood into adulthood.

Method: Twenty five male adults with ADHD were assessed between the ages of 8\(\Gamma\)Cô12 years and again as adults. At both ages, an EEG was recorded during an eyes-closed resting period, and power estimates were calculated for relative delta, theta, alpha and beta.

Results: At the childhood assessment, the ADHD subjects had elevated posterior delta. Relative theta was elevated, with diminished alpha activity across all sites. Significant maturational changes were observed,

with reductions in the delta and theta bands, and increases in the alpha and beta bands across all electrodes. In adulthood, relative to controls, diminished frontal delta and elevated global theta activity were apparent. **Conclusions**: Substantial developmental changes occurred in the EEG of these subjects. These results identify important issues when using EEG as part of the diagnosis for ADHD.

Significance: This study is the first to explore EEG changes from childhood to adulthood over an 11 year period in the same subjects with ADHD

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Current Hypertension Reports. 2019;21.

EVALUATION AND MANAGEMENT OF ELEVATED BLOOD PRESSURE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Yamaguchi I, Hanevold C.

Purpose of Review: To understand the impact of attention deficit hyperactivity disorder (ADHD) and its medications on blood pressure (BP) in children and adolescents and provide recommendations for management of elevated BP in children and adolescents with ADHD.

Recent Findings: ADHD medications have cardiovascular effects including elevated BP. However, the bulk of the evidence indicates that stimulants and other ADHD medications are safe and do not cause severe cardiovascular diseases. BP should be assessed carefully at the time of ADHD diagnosis, because some behavioral changes similar to ADHD may be associated with hypertension.

Summary: ADHD medications appear to be safe. However, their long-term impact on the cardiovascular system is not clearly understood and needs further investigation. BP should be monitored regularly during ADHD pharmacotherapy in order to optimize the management of both conditions

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Deutsches Arzteblatt International. 2019;116:A945.

FDA: TRIGEMINAL NERVE STIMULATION IS APPROVED FOR THE TREATMENT OF ADHD IN CHILDREN IN THE US. Meyer R.

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Dev Med Child Neurol. 2019;61:40-41.

AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER IN CHILDREN WITH CEREBRAL PALSY - MORE COMMON THAN WE THINK?

Pahlman M, Himmelmann K, Gillberg C.

Introduction: Associated impairments are common in children with cerebral palsy (CP) and can sometimes be more limiting than the motor disorder. There is a growing awareness that autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are more common in CP than in the general population. We described the occurrence of ASD and ADHD, and the associations with CP type, gross motor function, and intellectual level in children with CP.

Patients and Methods: A population-based group of 264 children, born 1999 to 2006, from the CP Register of western Sweden, were studied at the age of 10 to 17 years. 40 Abstracts Information from all available records were retrieved regarding ASD, ADHD, intellectual level, and other associated impairments. Parents were asked to fill a comprehensive combined screening questionnaire for ASD and ADHD, and responded in 230 of 264 cases. But 19 in the most disabled group could not be assessed, resulting in 211 analyzed questionnaires.

Results: ASD was diagnosed in 18% (47/264) and ADHD in 21% (55/264). Positive screening for ASD was found in 35% (74/211) and ADHD in 50% (105/211); of which 29% (61/211) for both disorders. Positive screening was found in children with all CP types, and at all levels of gross motor function, and more likely with increasing intellectual disability (except for profound intellectual disability).

Conclusion: ASD and ADHD are common in children with CP, and may still be underdiagnosed. Assessment of ASD and ADHD is needed in all types of CP and functional levels

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Emot Behav Difficulties. 2019.

ADHD AS A CLASSROOM DIAGNOSIS. AN EXPLORATORY STUDY OF TEACHERS' STRATEGIES FOR ADDRESSING 'ADHD CLASSROOM BEHAVIOUR'.

Teatmeier T.

This study scrutinizes strategies that teachers deploy when confronted by behaviour related to the diagnosis of attention-deficit/hyperactivity disorder (ADHD). Over two years, ethnographic fieldwork was conducted in two inclusive classrooms in Denmark, and all instances of teacher initiatives addressing ADHD-related classroom behaviour were recorded. Six basic strategies recurred across teachers and classrooms. To maintain the instructional flow with the rest of the students and not continually stop, the strategy of ignoring the disruptive conduct of a diagnosed child is often used. This strategy has not previously been explored in classroom research on ADHD. This is probably because previous research has primarily focused on the singular child and the singular teacher, thus leaving the whole-class interplay and complex orientations of teachers unexplored

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Emot Behav Difficulties. 2019.

THE CONSEQUENCES OF ADHD DIAGNOSIS: INTEGRATING SCAFFOLDING AND PEREZHIVANIE TO REDESIGN PEDAGOGY FOR ADHD-DIAGNOSED CHILDREN.

Renshaw PD.

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Encephale. 2019;45:S80.

EFFECTIVE NEUROFEEDBACK APPLICATIONS IN ANXIETY AND ATTENTION SYMPTOMATOLOGY IN ADOLESCENTS.

Tsatali M, Sidiropoulos S, Bamidis P.

Objectives: It is expected that Alpha and SMR activity would be enhanced (Vernon et al., 2003), whereas Theta activity would be diminished (Hammond, 2005) in adolescents in line with previous studies on this population.

Methods: Ten adolescents from 11 to 18 years old came to the Northern Greece Neurofeedback Centre because they had problems about their self-reported attention, as well as having anxiety symptoms, including daydreaming, loss of concentration during reading, and thoughts of worry. Neurofeedback training consisted of 10 sessions, 20 minutes each. Participants EEG records were evaluated pre and post the Neurofeedback training in eyes-opened resting-state by Nexus-10. In continuation, they were trained on Alpha, Theta and Beta bands through specific protocols. The active electrode was placed to the Cz point with frequency rate two times/week. Additionally, individuals completed two Visual Analogue Scales (VAS), scored from 0-100, before each Neurofeedback session regarding to whether they felt anxiety and felt absent- minded during the previous days.

Results: Non parametric Wilcoxon signed-rank test was used in order to identify possible differences between the post amplitude of the EEG brain rhythms, especially Alpha, Theta and SMR. After attending the Neurofeedback sessions, participants Alpha and SMR bands were enhanced. Specifically, significant differences were found in Alpha mean amplitude (z = 2.366; P = .018), as well as SMR activity (z = 2.666; P = .008). Furthermore, no significant differences were found for Theta. VAS for attention was significantly increased (z = 2.197; P = .030), whereas VAS for anxiety was statistically decreased (z = 2.265; P = .023).

Conclusion: Neurofeedback can be regarded as a promising therapeutic technique at reducing anxiety symptoms and attention deficits in adolescents. However, future research should be conducted in order to investigate the effectiveness of Neurofeedback in alleviating anxiety and attention deficits in adolescents by recruiting a larger number of individuals and over a longer period of time

Environ Int. 2019.

MANGANESE TRANSPORTER GENETICS AND SEX MODIFY THE ASSOCIATION BETWEEN ENVIRONMENTAL MANGANESE EXPOSURE AND NEUROBEHAVIORAL OUTCOMES IN CHILDREN.

Broberg K, Taj T, Guazzetti S, et al.

There is increasing evidence that environmental manganese (Mn) exposure early in life can have negative effects on children's neurodevelopment and increase the risk of behavioral problems, including attention deficit hyperactivity disorder (ADHD). Factors that may contribute to differences in sensitivity to Mn exposure are sex and genetic variation of proteins involved in the regulation of Mn concentrations. Here we investigate if sex and polymorphisms in Mn transporter genes SLC30A10 and SLC39A8 influence the association between Mn exposure and ADHD-related behavioral problems in children. The SNPs rs1776029 and rs12064812 in SLC30A10, and rs13107325 in SLC39A8 were genotyped by TaqMan PCR or pyrosequencing in a population of Italian children (aged 11Γ Cô14 years; n = 645) with a wide range of environmental Mn exposure. Mn in surface soil was measured in situ using XRF technology or modeled by geospatial analysis. Linear regression models or generalized additive models (GAM) were used for analyzing associations between soil Mn and neurobehavioral problems assessed by the Conners' behavior rating scales (self-, and parent-reported). Gene-environment interactions (Mn transporter genotype x soil Mn) were evaluated using a genetic score in which genotypes for the three SNPs were combined based on their association with blood Mn, as an indication of their influence on Mn regulation. We observed differences in associations between soil Mn and neurobehavior between sexes. For several self-reported Conners' scales, girls showed U-shaped relationships with higher (worse) Conners' scoring at higher soil Mn levels, and several parent-reported scales showed positive linear relationships between increasing soil Mn and higher Conner's scores. For boys, we observed a positive linear relationship with soil Mn for one Conner's outcome only (hyperactivity, parent-reported). We also observed some interactions between soil Mn and the genetic score on Conner's scales in girls and girls with genotypes linked to high blood Mn showed particularly strong positive associations between soil Mn and parent-reported Conners' scales. Our results indicate that sex and polymorphisms in Mn transporter genes contribute to differences in sensitivity to Mn exposure from the environment and that girls that are genetically less efficient at regulating Mn, may be a particularly vulnerable group

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Environ Res. 2019.

MATERNAL URINARY CONCENTRATIONS OF PYRETHROID AND CHLORPYRIFOS METABOLITES AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) SYMPTOMS IN 2-4-YEAR-OLD CHILDREN FROM THE ODENSE CHILD COHORT.

Dalsager L. Fage-Larsen B, Bilenberg N, et al.

Background: Pyrethroids and chlorpyrifos are widely used insecticides, but the potential impact of prenatal exposure on child neurodevelopment has only been addressed in few longitudinal studies.

Objectives: To investigate associations between prenatal exposure to pyrethroids and chlorpyrifos and traits of ADHD in 2-4-year-old children.

Methods: Metabolites of chlorpyrifos and pyrethroids were measured in maternal urine collected at gestational week 28 among 1207 women from the Odense Child Cohort. Of these, 948 completed the Child Behavior Check List for ages 1.5ΓÇô5 years (CBCL: 1-¢-5). Negative binomial and logistic regression models were used to estimate relative differences in ADHD problem scores (CBCL: 1-¢-5 subscale) expressed as the ratio of expected scores between exposure groups and the odds (OR) of scoring equal to or above the 90th percentile in relation to maternal urinary metabolite concentrations (continuous In2-transformed or categorized into tertiles). The analyses were adjusted for maternal education level, parental psychiatric diagnosis, child age and sex.

Results: The chlorpyrifos metabolite, 3,5,6-trichloro-2-pyridinol (TCPY), the generic pyrethroid metabolite, 3-phenoxybenzoic acid (3-PBA), and the metabolite of trans-isomers of permethrin, cypermethrin, and cyfluthrin, trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (trans-DCCA), were detected in 90%, 94%, and 11%, respectively, of the urine samples. Each doubling in maternel 3-PBA concentration was associated with a 3% increase in the ADHD score (Ratio: 1.03 (95% CI: 1.00,1.07)) and a 13% higher odds of having a ADHD score the 90th percentile (OR: 1.13 (1.04,1.38)). Similar associations were seen for 3-PBA as categorical variable (p-trend=0.052 in negative binimoal regression, p-trend=0.007

in logistic regression). Furthermore, concurrent concentrations of 3-PBA and TCPY above their medians were associated with higher ADHD score (Ratio: 1.20 (1.04, 1.38)) and higher odds of scoring the 90th percentile (OR: 1.98 (1.26, 3.11)). Maternal trans-DCCA above the detection level increased the odds of ADHD symptoms (OR: 1.76 (1.08, 2.86)). The associations were not modified by sex.

Conclusions: Prenatal exposure to pyrethroids was associated with ADHD related traits at 2-4 years of age. Considering the widespread use of pyrethroids these results are of concern

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Epilepsy Behav. 2019.

SOCIAL COGNITION AND PSYCHOPATHOLOGY IN CHILDHOOD AND ADOLESCENCE.

Besag FMC, Vasey MJ.

There is a substantial body of research on social cognition in adults with epilepsy, and in broad categories such as focal and generalized epilepsies, but much less has been written about social cognition in children with epilepsy (CWE), and in childhood-onset epilepsy syndromes specifically. In several of these syndromes, autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD), two disorders with social cognitive impairments, are reported. There is strong evidence for social cognitive deficits in juvenile myoclonic epilepsy (JME). There is also a considerable amount of evidence for such deficits in a number of syndromes that may be associated with ASD or ADHD, including West syndrome (WS), Dravet syndrome (DS), and the Landau-Kleffner syndrome (LKS). However, the evidence is of variable quality and incomplete across the range of childhood epilepsy syndromes. In some syndromes, childhood epilepsy substantially increases the risk of severe social cognitive impairment, which may persist after the seizures remit. This paper presents an overview of current research on social cognition in childhood epilepsy, with a particular focus on syndromes with a high prevalence of autistic and behavioral comorbidities. Social cognitive impairments represent a considerable additional challenge for patients and caregivers. Early diagnosis and intervention might significantly improve long-term social cognitive outcomes, highlighting the need for greater awareness among clinicians of this important topic. This article is part of the Special Issue Epilepsy and social cognition across the lifespan

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Eur Child Adolesc Psychiatry. 2019.

SUGGESTIVE DIAGNOSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN INDIGENOUS CHILDREN AND ADOLESCENTS FROM THE BRAZILIAN AMAZON.

Azevedo PVB, Caixeta LF, Taveira DLR, et al.

The prevalence of attention-deficit/hyperactivity disorder (ADHD) symptoms has been scarcely studied in indigenous cultures that preserve ancestral cultural characteristics. The objective of the study is to estimate the prevalence of suggestive diagnosis of ADHD among indigenous children and adolescents from villages in the Amazon. This is an analytical cross-sectional study using instruments to track ADHD symptoms (the Child Behaviour Checklist for ages 6-18: CBCL/6-18 and the teacher report form for ages 6-18: TRF/6-18) and to investigate their negative impact on the patients (using the Strengths and Difficulties Questionnaire-SDQ). The prevalence of a suggestive ADHD diagnosis according to the CBCL/TRF DSM-IV ADHD subscale without and with negative impact as assessed by the SDQ was 4.3% and 1.1%, respectively. Comorbid oppositional-defiant, conduct problems and anxious symptoms were present in all cases screening positive for ADHD. We also presented a case report as an illustration of the observed clinical presentation. ADHD is a recognizable disorder even in a culture that preserves millennial characteristics. Furthermore, the presence of ADHD symptoms was associated with significant impairment

European Journal of Clinical Pharmacology. Online 4June2019

PRESCRIPTION PREVALENCE OF PSYCHOTROPIC DRUGS IN CHILDREN AND ADOLESCENTS: AN ANALYSIS OF INTERNATIONAL DATA

Piovani D, Clavenna A, Bonati M.

Purpose We conducted a review and meta-analysis to establish the international pooled prevalence of psychotropic drugs in children and adolescents, and comment on recent trends.

Methods Medline, Embase, and PsycINFO were searched for studies with annual prevalence estimates of attention deficit hyperactivity disorder (ADHD) medications, antidepressants, antipsychotics, sedative/hypnotics and anxiolytics in outpatient children and adolescents. Data were extracted regarding the representativeness, sampling frame, and the quality of reporting.

Results A total of 59 studies reporting prevalence data for 23 countries were collected. Most studies were conducted in Europe (42) and were at high or moderate risk of bias (35). The global random-effect pooled prevalence was 15.3‰(95% confidence interval [CI], 7.6–25.7‰) for ADHD medications, 6.4‰ (95%CI 4.3–8.7) for antidepressants, and 5.5‰ (95%CI 3.6–7.8) for antipsychotics. Heterogeneity was extremely high (I2 > 99%). Large increases were found in the prevalence of ADHD medications in most countries, particularly up until 2010. The antidepressants' trend was U-shaped in most countries with the lowest prevalence in 2007–2009 and rise more recently. Large to weak increases in the prevalence of antipsychotics were seen until 2011, and contrasting data were found more recently. Data on anxiolytics and sedative/hypnotics were limited.

Conclusions The study provides global estimates of paediatric psychotropic drug prevalence and its trends. Systematic monitoring is lacking in most countries, and very heterogeneous reporting is common across studies

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Eur J Psychiatry. 2019.

EVIDENCE FOR SHARED ENVIRONMENTAL CONTRIBUTIONS TO ATTENTION-DEFICIT/HYPERACTIVITY TRAITS. A TWIN STUDY.

Iranzo-Tatay C, Rojo-Moreno L, Rojo-Bofill L, et al.

Background and objectives: Behavior-genetic analyses have shown that measurements of inattention and hyperactivity-impulsivity are genetically-influenced. In view of limited studies on ADHD (Attention deficit hyperactivity disorder) in Spanish samples, this study aims to explore the genetic architecture of ADHD symptoms; inattention and hyperactivity-impulsivity in a Spanish twin schoolchildren sample.

Methods: Participants were 258 pairs of adolescent Spanish twins. Symptoms of ADHD, inattention and hyperactivity-impulsivity were assessed by means of a sub-scale of the Strengths and Difficulties Questionnaire. Univariate twin models, according to sex, were run to assess the heritability of ADHD symptoms.

Results: Heritability of hyperactivity was 55% in girls, 57% in boys. Inattention showed a heritability of 26% in girls, and no genetic factors influence was found in boys. Environmental factors are prominent influences among these traits.

Conclusion: Our results highlight the magnitude of environmental effects among ADHD symptoms and therefore the importance of preventive programs that may modify the expression of these traits

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Front Behav Neurosci. 2019;13.

EFFECT OF METHYLPHENIDATE ON STATE ANXIETY IN CHILDREN WITH ADHD-A SINGLE DOSE, PLACEBO CONTROLLED, CROSSOVER STUDY.

Kritchman M, Koubi M, Bloch AM, et al.

Introduction: Non-adherence to efficacious pharmacotherapy is a major obstacle in the treatment of children suffering from attention deficit hyperactive disorder (ADHD). Some hold the position that pharmacotherapy induces anxiety, and that this is one of the reasons for this non-adherence. Previous studies have pointed to the opposite, a moderating effect of methylphenidate (MPH) on state anxiety in patients with ADHD. This has

been shown in continuous treatment in children, but not on a single dose. We hypothesized that a single dose might have a different effect.

Method: Twenty children with ADHD were given single doses of MPH in a randomized, controlled, crossover, double blind study. State anxiety using The Spielberger State-Trait Anxiety Inventory (STAI) and a continuous performance test were assessed.

Results: As a group, no change was detected in state anxiety with MPH or placebo. However, children who were given MPH during the first session as opposed to those who received placebo first, demonstrated deterioration in baseline state anxiety in the second session [t(2.485), p < 0.05].

Conclusion: Our findings show a possible delayed anxiety-provoking effect of a single dose of MPH. This may be relevant to the understanding of difficulties in adherence with MPH treatment in children with ADHD

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Front Psychiatry. 2019;10.

EFFECT MODIFICATION BY ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) SYMPTOMS ON THE ASSOCIATION OF PSYCHOSOCIAL WORK ENVIRONMENTS WITH PSYCHOLOGICAL DISTRESS AND WORK ENGAGEMENT.

Nagata M, Nagata T, Inoue A, et al.

Objective: The aim of this study was to examine how attention-deficit hyperactivity disorder (ADHD) symptoms play an interaction effect on the association between psychosocial work environments and health (psychological distress/work engagement) among workers.

Methods: This is a cross-sectional study of 2,693 employees at a pharmaceutical company using a self-administered questionnaire evaluating ADHD symptoms (Adult ADHD Self-Report Scale Screener), psychosocial work environments (job demands, job control and social support), and health outcomes (psychological distress; K6, and work engagement; Utrecht Work Engagement Scale). Multiple regression analyses were applied to assess the interaction between ADHD symptoms and psychosocial work environments on health outcomes.

Results: The prevalence of workers with ADHD symptoms was 5.9% (n = 159). Significant interaction effects of ADHD symptoms $+\dot{u}$ job control and ADHD symptoms $+\dot{u}$ social support were observed ($+\dot{l}$ = 0.067, p < 0.01 and $+\dot{l}$ = 0.052, p < 0.01, respectively) on psychological distress after adjustment of age, sex, occupation and education. The interaction effect of ADHD symptoms each psychosocial work environment was not observed on work engagement.

Conclusions: Job control and social support were more influential factors that were related to psychological distress in accordance with ADHD symptoms. This study also found no difference of the interaction between psychosocial work environments and ADHD symptoms on work engagement. To the best of our knowledge, this study was first to clarify the effect of ADHD symptoms on the association between psychosocial work environments and health outcomes (psychological distress/work engagement). These findings can aid employers how to arrange better work environments for workers with ADHD symptoms

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Indian J Pediatr. 2019.

PREVALENCE OF EPILEPSY AND INTER-ICTAL EPILEPTIFORM DISCHARGES IN CHILDREN WITH AUTISM AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Anukirthiga B, Mishra D, Pandey S, et al.

Objective: To study the prevalence of epilepsy and Inter-ictal epileptiform discharges (IED) in children with Autism spectrum disorder (ASD) and Attention-deficit hyperactivity disorder (ADHD), and the factors associated with occurrence of epilepsy in these children.

Methods: Children between 6 and 12 y attending the Child Development Centre of a tertiary-care institute in India were evaluated for ASD and ADHD as per Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). Childhood Autism Rating Scale was used to assess ASD severity,-áand Conner's Rating Scales were used to sub-classify children with ADHD. Intelligence quotient was assessed if not assessed in the previous 1 y. History of seizures was taken, and electroencephalography was done in all children. Epilepsy was diagnosed and classified according to International League Against Epilepsy.

Results: Of the 130 children enrolled (90 ASD, 40 ADHD), 56 (43%) had epilepsy and 55 (42.3%) had IED. The proportion of both epilepsy and IED was higher among ASD (both 45.5%) as compared to ADHD (37.5% and 35%), although not statistically significant. Among children with ASD, epilepsy was common in those with severe ASD (P < 0.001), and IED were more common in those with IQ <80 (P = 0.047). There were no significant differences between occurrence of epilepsy/IED and subtypes of ADHD.

Conclusions: The high prevalence of epilepsy and IED among children with ASD and ADHD emphasizes the need for guidelines for identifying and diagnosing epilepsy in this group. This will-áensure appropriate management and improve patient outcomes

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Indian J Psychiatry. 2019;61:232-37.

ASSESSMENT OF PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG SCHOOLCHILDREN IN SELECTED SCHOOLS.

Catherine TG, Robert N, Mala KK, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is considered the most common neurodevelopmental disorder of childhood and can continue through adolescence and adulthood. Global impairment in children with ADHD increases with increasing number of concurrent disorders. The presence of ADHD in childhood increases the likelihood of additional difficulties in academic performance, social interactions, and low self-esteem developing into adolescents and young adults.

Aims: The study aims to (i) to determine the prevalence of ADHD among schoolchildren at selected schools in Kancheepuram district, (ii) to find the agreement between parent and teacher reports, and (iii) to associate the prevalence of ADHD among schoolchildren with their selected demographic variables.

Settings and Design: A quantitative research approach with cross-sectional research design was adopted for the study. The study focused on primary schoolchildren from the selected schools in Kancheepuram district. Materials and Methods: Totally 3253 children aged between 8 and 11 years were enumerated from the selected six schools in Kancheepuram district after obtaining informed consent from their caregivers. The presence of ADHD was assessed using Conners' Teacher-Parent Rating Scale given to caregivers and teachers and confirmed with the Diagnostic and Statistical Manual of Mental Disorders-5 criteria for ADHD. **Paguits:** The analysis revealed the overall prevalence of ADHD to be 8.8%. The subtypes of ADHD were

Results: The analysis revealed the overall prevalence of ADHD to be 8.8%. The subtypes of ADHD were categorized as 124 (43.3%) for inattentive type, 124 (43.3%) for hyperactive type, and 38 (13.2%) for combined type of ADHD.

Conclusion: The present study shows a high prevalence of ADHD among primary schoolchildren

Int J Hum Comput Stud. 2019 Jun;126:26-43.

GUIDELINES TO DESIGN TANGIBLE TABLETOP ACTIVITIES FOR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Cerezo E. Coma T. Blasco-Serrano AC. et al.

Attention deficit hyperactivity disorder is one of the most frequent neurodevelopmental disorders among children. In spite of this, there is a lack of HCI research specifically devoted to these children. This paper describes efforts to transfer previous experience with other neurodiverse children in the field of tangible tabletops to ADHD children. The results of evaluation sessions carried out in conjunction with an ADHD association, complemented with an in-depth study of their special characteristics and needs, have led to a set of guidelines oriented to the design of tangible tabletop activities. These guidelines are mostly general and applicable to the design of any interactive application oriented to ADHD children. They are also appropriate for applications for other neurodiverse children or, in fact, any child from a more inclusive perspective

Iran J Psychiatry. 2019;14:154-59.

CAN PARENTS IMPROVE THE QUALITY OF LIFE OF THEIR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER?

Kousha M, Kakrodi MA.

Objective: The aim of this study was to evaluate the effectiveness of mothers Group psychoeducation on Quality of Life (QoL) of children with Attention Deficit Hyperactivity Disorder.

Method: In this clinical trial, 60 mothers of ADHD children were randomly divided into two groups (30 participants in each group). An educational program based on Positive Parenting Program (Triple P) was performed for the intervention group, while only pharmacotherapy was provided for the control group. Pediatric Quality of Life Inventory (Peds QL) was completed by all 60 mothers before, eight week, and three months after intervention. Data were analyzed using mean and standard deviation, and K-square or paired t test were used for data analysis.

Results: A total of 60 mothers participated in this study. Of their children, 80% were boys and 20% were girls. The mean of the total score of QoL increased significantly in the intervention group at week eight and three months after the intervention. Also, the mean scores of emotional, social, school and psychosocial domains, but not physical domain of QoL, found to be higher in ADHD children after intervention (p< 0.05). The total score of QoL and mean scores of domains increased in the posttest in the control group, but it was not significant (p> 0.05).

Conclusion: A significant increase in the total score of QoL was reported by mothers in the posttest compared to the pretest in the experimental group, which showed that educating parents can improve the QoL of their ADHD children

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Ir J Med Sci. 2019.

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN WITH EPILEPSY.

Wang M, Zhao Q, Kang H, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a common comorbidity of childhood epilepsy. ADHD symptoms in children with epilepsy have been studied since 1970s in western countries. However, relative studies are still rather limited in China.

Aims: To study the incidence rate of ADHD in children with epilepsy, and further analyze the relationship of epilepsy and ADHD in China. Materials and methods: 206 children (age 6ΓÇô16) with epilepsy and 58 healthy controls underwent assessment instruments (DSM-IV ADHD, ADHD Rating Scale-IV, and SNAP-IV Rating Scale).

Results: The prevalence of comorbid ADHD was significantly higher in children with epilepsy (24.76%) than that in controls (5.17%), and inattentive subtype (ADHD-I, 14.1%) was the most prevalent. ADHD in childhood epilepsy was associated with younger age, early first onset age, and high frequency of epileptic seizures. There was no significant difference of ADHD incidence rate regarding the seizure type and abnormal electroencephalogram (EEG) discharges. The ADHD comorbidity rate in children treated with antiepileptic drugs (AEDs) (27.6%) was higher than that without AEDs therapy (14.0%); multiple AEDs were associated with a higher rate of ADHD comorbidity as compared with single AEDs. The incidence of comorbid ADHD in epileptic children treated with traditional single AEDs was significantly higher than those treated with novel single AEDs.

Conclusion: Children with epilepsy have more attention problems as compared with healthy controls. ADHD in childhood epilepsy is associated with male sex, younger age, early first onset age, high frequency of epileptic seizures, and multiple AEDs

JAMA Pediatr. 2019.

EVALUATION OF METHYLPHENIDATE SAFETY AND MAXIMUM-DOSE TITRATION RATIONALE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A META-ANALYSIS.

Ching C, Eslick GD, Poulton AS.

Importance: Evidence on the titration of stimulant medications for attention-deficit/hyperactivity disorder (ADHD) is lacking. However, this lack of evidence has not prevented medication guidelines from specifying apparently arbitrary dose limitations, which could discourage clinicians from titrating methylphenidate to higher and, perhaps for some patients, more efficacious doses.

Objective: To determine the evidence on dose titration and adverse events associated with dose titration of stimulants for ADHD.

Data Sources: MEDLINE from 1946, Embase from 1974, and PsycINFO from 1806 through April 1, 2019, were searched to identify relevant articles. Study Selection: The inclusion criteria were that (1) the study was conducted on children up to 18 years of age; (2) children had a diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, or hyperkinetic disorder according to the International Classification of Diseases codes; and (3) the dose of methylphenidate was determined by titration.

Data Extraction and Synthesis: The PRISMA guidelines for abstracting data and assessing data quality and validity were followed. Quality assessment was undertaken using the Jadad scoring system. Statistical analysis was undertaken using a random-effects model.

Main Outcomes and Measures: The outcomes of interest were (1) the doses used in published clinical trials, (2) the clinical justification given by researchers for their selected dose range, and (3) the adverse effects associated with methylphenidate when the dose is established by titration.

Results: A total of 11 randomized clinical trials and 38 cohort studies were analyzed. The randomized clinical trials involved 1304 participants treated with methylphenidate and 887 controls; the 38 cohort studies included 5524 participants. Maximum doses of methylphenidate ranged from 0.8 to 1.8 mg/kg/d. Some studies detailed their method of titration, including starting dose, titration interval, increment dose, and maximum dose. Not all of these studies reported justification for the chosen dose range. Common adverse effects of methylphenidate included insomnia (odds ratio, 4.66; 95% CI, 1.99-10.92; P <.001), anorexia (5.11 higher than for those who took placebo; 95% CI, 1.99-13.14; P <.001), abdominal pain (1.9 times more likely; 95% CI, 0.77-4.77; P =.16), and headache (14% of participants; 95% CI, 10%-20%; P <.001).

Conclusions and Relevance: A range of maximum doses for methylphenidate was recommended in clinical studies; no discernable scientific justification for any particular dose was given. Reports of life-threatening adverse events were absent; further studies of the efficacy, tolerability, and safety of methylphenidate titrated purely on clinical grounds, without reference to any set maximum dose, are needed

JAMA Psychiatry. 2019;76:624-33.

ASSOCIATION BETWEEN CHILDHOOD ANHEDONIA AND ALTERATIONS IN LARGE-SCALE RESTING-STATE NETWORKS AND TASK-EVOKED ACTIVATION.

Pornpattananangkul N, Leibenluft E, Pine DS, et al.

Importance: Anhedonia can present in children and predict detrimental clinical outcomes.

Objective: To map anhedonia in children onto changes in intrinsic large-scale connectivity and task-evoked activation and to probe the specificity of these changes in anhedonia against other clinical phenotypes (low mood, anxiety, and attention-deficit/hyperactivity disorder ADHD).

Design, Setting, and Participants: Functional magnetic resonance imaging (fMRI) data were from the first annual release of the Adolescent Brain Cognitive Development study, collected between September 2016 and September 2017 and analyzed between April and September 2018. Cross-sectional data of children aged 9 to 10 years from unreferred, community samples during rest (n = 2878) and during reward anticipation (n = 2874) and working memory (n = 2745) were analyzed.

Main Outcomes and Measures: Alterations in fMRI data during rest, reward anticipation, and working memory were examined, using both frequentist and Bayesian approaches. Functional MRI connectivity within large-scale networks, between networks, and between networks and subcortical regions were examined during rest. Functional MRI activation were examined during reward anticipation and working memory using the monetary incentive delayed and N-back tasks, respectively. Results: Among 2878 children with

adequate-quality resting-state fMRI data (mean SD age, 10.03 0.62 years; 1400 girls 48.6%), children with anhedonia (261 9.1%), compared with those without anhedonia (2617 90.9%), showed hypoconnectivity among various large-scale networks and subcortical regions, including between the arousal-related cingulo-opercular network and reward-related ventral striatum area (mean SD with anhedonia, 0.08 0.10 vs without anhedonia, 0.10 0.10; t2,876 = 3.33; P <.001; qfalse discovery rate = 0.03; InBayes factor10 = 2.85). Such hypoconnectivity did not manifest among children with low mood (277 of 2878 9.62%), anxiety (109 of 2878 3.79%), or ADHD (459 of 2878 15.95%), suggesting specificity. Similarly, among 2874 children (mean SD age, 10.03 0.62 years; 1414 girls 49.2%) with high-quality task-evoked fMRI data, children with anhedonia (248 of 2874 8.63%) demonstrated hypoactivation during reward anticipation in various areas, including the dorsal striatum and areas of the cingulo-opercular network. This hypoactivity was not found among children with low mood (268 of 2874 9.32%), anxiety (90 of 2874 3.13%), or ADHD (473 of 2874 16.46%). Moreover, we also found context- and phenotype-specific double dissociations; while children with anhedonia showed altered activation during reward anticipation (but not working memory), those with ADHD showed altered activation during working memory (but not reward anticipation).

Conclusions and Relevance: Using the Adolescent Brain Cognitive Development study data set, phenotype-specific alterations were found in intrinsic large-scale connectivity and task-evoked activation in children with anhedonia. The hypoconnectivity at rest and hypoactivation during reward anticipation complementarily map anhedonia onto aberrations in neural-cognitive processes: lack of intrinsic reward-arousal integration during rest and diminishment of extrinsic reward-arousal activity during reward anticipation. These findings help delineate the pathophysiological underpinnings of anhedonia in children

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J Abnorm Child Psychol. 2019 Jun;47:975-87.

EXAMINATION OF THE STRUCTURE AND MEASUREMENT OF INATTENTIVE, HYPERACTIVE, AND IMPULSIVE BEHAVIORS FROM PRESCHOOL TO GRADE 4.

Allan DM, Lonigan CJ.

Attention Deficit/Hyperactivity Disorder (ADHD) is a complex and heterogeneous disorder consisting of inattentive and hyperactive/impulsive behaviors. Although, the multidimensionality of ADHD is widely accepted, questions remain regarding the extent to which the components of this disorder are overlapping or distinct. Further, although the same measures are generally used to assess inattentive, hyperactive, and impulsive behaviors across childhood, it has been argued that the structure and measurement of inattentive, hyperactive, and impulsive behaviors may be susceptible to developmental influences. The purpose of this study was to examine the factor structure and measurement invariance of inattentive and hyperactive/impulsive behaviors in a large group of children (N = 10,047) ranging in grade level from preschool to grade 4. A bifactor model with a general factor and two specific factors of inattention and hyperactivity/impulsivity fit the data best. This finding held across all groups and all grade levels. In general, the bifactor model demonstrated measurement invariance from kindergarten through grade 4 but not for preschool. Implications for the understanding and measurement of inattentive, hyperactive, and impulsive behaviors across early and middle childhood are discussed

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J Abnorm Child Psychol. 2019 Apr;47:589-603.

RESPONSE INHIBITION, RESPONSE EXECUTION, AND EMOTION REGULATION AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tenenbaum RB, Musser ED, Morris S, et al.

Attention-deficit/hyperactivity disorder (ADHD) is associated with deficits in response inhibition, response execution, and emotion regulation. However, the nature of the associations among these deficits remains unclear. Thus, this study examines these associations using a multi-method design. One hundred sixty-six children (aged 5–13 years; 66.3% male; 75 with ADHD) completed two conditions (i.e., neutral and fear) of an emotional go/no-go task. Parasympathetic-based regulation was indexed via respiratory sinus arrhythmia (RSA), and sympathetic-based reactivity was indexed via cardiac pre-ejection period (PEP). Overall, children

exhibited more difficulty with response execution (i.e., more omission errors, fewer correct go responses) and less difficulty with response inhibition (i.e., fewer commission errors, more correct no-go responses) during the fear condition than the neutral condition. Children with ADHD displayed more difficulty with response execution during the fear condition compared to typically developing youth. Additionally, children with ADHD displayed parasympathetic-based dysregulation (i.e., RSA increase from baseline) and reduced sympathetic-based reactivity (i.e., PEP lengthening) compared to typically developing youth across task conditions. In sum, children with ADHD demonstrate greater difficulty with response execution during emotionally salient contexts, as well as parasympathetic-based emotion dysregulation. Future work should examine these associations longitudinally with the aim of predicting impairment and treatment response in youth with ADHD

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J Abnorm Child Psychol. 2019 May;47:755-64.

THE LONGITUDINAL RELATION BETWEEN OBSERVED MATERNAL PARENTING IN THE PRESCHOOL PERIOD AND THE OCCURRENCE OF CHILD ADHD SYMPTOMS IN MIDDLE CHILDHOOD.

Choenni V, Lambregtse-van den Berg M, Verhulst FC, et al.

In this longitudinal population-based cohort (N = 547) we examined the relation between maternal discipline and sensitivity in the preschool period and the occurrence of attention-deficit hyperactivity disorder (ADHD) symptoms in middle childhood, taking into account pre-existing child attention and executive function (EF) problems, and oppositional defiant disorder (ODD) symptom comorbidity. Maternal parenting was observed during a 'do not touch task' (positive and negative discipline) and a teaching task (sensitivity) at age 3. Parents reported on the occurrence of ADHD and ODD symptoms at age 8 using the Conners' Parent Rating Scale. Attention and executive function problems were assessed using parent questionnaires at age 4. Important covariates such as harsh discipline and maternal depression were also taken into account. Maternal sensitivity significantly predicted later ADHD symptoms beyond pre-existing child attention and EF problems, and comorbid ODD symptoms over and above these covariates. This study demonstrates the importance of maternal sensitivity in the etiology of core ADHD symptoms above and beyond pre-existing child attention and EF problems, and comorbid ODD symptoms

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J Abnorm Child Psychol. 2019 Jun;47:961-74.

INHIBITORY CONTROL AND INFORMATION PROCESSING IN ADHD: COMPARING THE DUAL TASK AND PERFORMANCE ADJUSTMENT HYPOTHESES.

Fosco WD, Kofler MJ, Alderson RM, et al.

Inhibition is a key neurocognitive domain in ADHD that is commonly assessed with the stop-signal task. The stop-signal involves both 'go' and 'stop' trials; previous research indicates that response times are reliably slower to 'go' trials during tasks with vs. without intermittent 'stop' trials. However, it is unclear whether this pattern reflects deliberate slowing to maximize inhibitory success (performance adjustment hypothesis) and/or disrupted bottom-up information processing due to increased cognitive demands (dual-task hypothesis). Given the centrality of 'go' responding for estimating children's inhibitory speed, finding that children with ADHD slow differently -or for different reasons- has the potential to inform cognitive and selfregulatory theories of ADHD. The current study used a carefully-controlled experimental design to assess the mechanisms underlying stop signal-related slowing in ADHD. Children ages 8-13 with (n = 81) and without ADHD (n = 63) completed the stop-signal task and a control task that differed only in the presence/absence of 'stop' trials. Using drift-diffusion modeling, Bayesian repeated-measures ANOVAs revealed a pattern consistent with the performance adjustment hypothesis, such that children adopted more cautious response strategies (BF10 = 6221.78; d = 0.38) but did not show changes in processing speed (BF01 = 3.08; d = 0.12) or encoding/motor speed (BF01 = 5.73; d = 0.07) when inhibition demands were introduced. Importantly, the ADHD/Non-ADHD groups showed equivalent effects of intermittent 'stop' trials (BF01 = 4.30-5.56). These findings suggest intact self-regulation/performance monitoring in the context of adapting to increased inhibitory demands in ADHD, which has important implications for the continued isolation of potential mechanisms associated with ADHD symptoms and impairment

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J Autism Dev Disord. 2019.

INTEREST IN RESEARCH PARTICIPATION AMONG CAREGIVERS OF CHILDREN WITH NEURODEVELOPMENTAL DISORDERS.

Kalb L, Jacobson L, Zisman C, et al.

The goal of this study was to examine caregiver agreement to hear about local research opportunities by joining a clinical research registry. Data from this cross-sectional study were gathered, between 2014 and 2017, across two outpatient clinics: (1) a multidisciplinary Autism Spectrum Disorder (ASD) clinic (N = 5228) and (2) a general psychology clinic serving youth with, or at risk for, a neurodevelopmental disorder (NDD; N = 5040). Overall, more than 8 in 10 caregivers agreed to join the registry. Several child clinical characteristics, as well as racial and sociodemographic factors, were predictive of parental agreement. Findings suggest caregivers of youth with ASD and NDD are amenable to joining the local research enterprise, however further work is needed to understand why some caregivers decline

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J Child Psychol Psychiatry. 2019 Jun;60:630-37.

DOES A SOCIAL SELF-PERCEPTUAL BIAS MASK INTERNALIZING SYMPTOMS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

Martin CP, Peisch V, Shoulberg EK, et al.

Background Children with attention-deficit/hyperactivity disorder (ADHD) often present with additional psychiatric conditions. Comorbidity is associated with poorer long-term outcomes, highlighting the need for effective assessment and intervention. However, self-perceptual biases may mask the presence of symptoms for a subgroup of children with ADHD. This study examined the role of social self-perceptual biases in children with ADHD versus control children on self-reports of loneliness, and depressive and anxious symptoms.

Methods The research question was examined in two samples. Sample 1 consisted of 7.7-12.8-year-old boys with ADHD (n = 199) and control boys (n = 74); Sample 2 consisted of 7.7-11.4-year-old boys and girls with ADHD (n = 178) and control children (n = 86). Across samples, children reported social competence and symptoms of anxiety and depression. Child-reported loneliness was examined in Sample 1. A social competence discrepancy score (difference between self-report and teacher-report) was used as an indicator of social self-perceptual bias.

Results Hierarchical multiple regression analyses tested social self-perceptual bias as a suppressor variable. The magnitude of the associations between ADHD and self-reported feelings of depression, anxiety and loneliness was greater when social self-perceptual bias was included in models as compared to models that did not include social self-perceptual bias (?R2s range = 0.04–0.19).

Conclusions Findings across both samples suggest that social self-perceptual biases may mask internalizing symptom severity on self-reports for individuals who overestimate their social competence. More research is needed to determine the best approach to assessing internalizing problems among children with ADHD

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J Child Psychol Psychiatry. 2019 Jun;60:665-75.

ADVERSE FAMILY LIFE EVENTS DURING PREGNANCY AND ADHD SYMPTOMS IN FIVE-YEAR-OLD OFFSPRING.

Rosenqvist MA, Sjölander A, Ystrom E, et al.

Background: Prenatal exposure to maternal adverse life events has been associated with offspring ADHD, but the role of familial confounding is unclear. We aimed to clarify if adverse life events during pregnancy are related to ADHD symptoms in offspring, taking shared familial factors into account.

Method: Data were collected on 34,751 children (including 6,427 siblings) participating in the population-based Norwegian Mother and Child Cohort Study. During pregnancy, mothers reported whether they had experienced specific life events. We assessed ADHD symptoms in five-year- old children with the Conners' Parent Rating Scale—Revised: short form. We modeled the associations between life events and mean ADHD scores with ordinary linear regression in the full cohort, and with fixed-effect linear regression in sibling comparisons to adjust for familial confounding.

Results: Children exposed to adverse life events had higher ADHD scores at age 5, with the strongest effect observed for financial problems (mean differences 0.10 [95% CI: 0.09, 0.11] in adjusted model), and the weakest for having lost someone close (0.02 [95% CI 0.01, 0.04] in adjusted model). Comparing exposure-discordant siblings resulted in attenuated estimates that were no longer statistically significant (e.g. mean difference for financial problems 0.03 [95% CI 0.07, 0.02]). ADHD scores increased if the mother had experienced the event as painful or difficult, and with the number of events, whereas sibling-comparison analyses resulted in estimates attenuated toward the null.

Conclusions: These results suggest that the association between adverse life events during pregnancy and offspring ADHD symptoms is largely explained by familial factors

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J Clin Child Adolesc Psychol. 2019 May;48:440-54.

TRAIT-BASED PROFILES OF ADHD IN ADOLESCENTS AND YOUNG ADULTS.

Smith TE. Martel MM.

Empirical work has examined the utility of using person-centered statistical approaches emphasizing traits to parsing attention deficit/hyperactivity disorder (ADHD) heterogeneity in preschool and school-age children. However, trait-based profiles have not yet been examined in other age ranges, specifically adolescence and young adulthood. Therefore, the goal of the present study is to examine trait-based profiles in adolescents and young adults with ADHD to evaluate their similarity with trait-based profiles in preschoolers and children with ADHD and through comparison with external correlates (e.g., comorbidity). One hundred eighty-two adolescents and 287 young adults completed measures of ADHD symptoms, personality and temperament traits, and comorbid internalizing and externalizing problems. Latent profile analysis suggested at least 3 consistent trait-based profiles related to ADHD within adolescents and young adults: low extraversion, high extraversion, and high neuroticism. These profiles were largely similar to those found in preschool and middle childhood and demonstrated similar comorbidity patterns, namely, the low-extraversion profile exhibited higher internalizing problems, the high-extraversion profile exhibited higher externalizing problems. Such profiles may have utility for personalization of intervention based on trait profiles and comorbidity patterns, as well as—more speculatively—possible prognostic utility

J Clin Child Adolesc Psychol. 2019 May:48:455-68.

SYMPTOMS OF ADHD AFFECT INTRASUBJECT VARIABILITY IN YOUTHS WITH AUTISM SPECTRUM DISORDER: AN EXGAUSSIAN ANALYSIS.

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Hwang-Gu SL, Lin HY, Chen YC, et al.

Increased intrasubject variability in reaction times (RT-ISV) is frequently found in individuals with autism spectrum disorder (ASD). However, how dimensional attention deficit/hyperactivity disorder (ADHD) symptoms impact RT-ISV in individuals with ASD remains elusive. We assessed 97 high-functioning youths with co-occurring ASD and ADHD (ASD+ADHD), 124 high-functioning youths with ASD only, 98 youths with ADHD only, and 249 typically developing youths, 8–18 years of age, using the Conners Continuous Performance Test (CCPT). We compared the conventional CCPT parameters (omission errors, commission errors, mean RT and RT standard error (RTSE) as well as the ex-Gaussian parameters of RT (mu, sigma, and tau) across the four groups. We also conducted regression analyses to assess the relationships between RT indices and symptoms of ADHD and ASD in the ASD group (i.e., the ASD+ADHD and ASD-only groups). The ASD+ADHD and ADHD-only groups had higher RT-ISV than the other two groups. RT-ISV, specifically

RTSE and tau, was significantly associated with ADHD symptoms rather than autistic traits in the ASD group. Regression models also revealed that sex partly accounted for RT-ISV variance in the ASD group. A post hoc analysis showed girls with ASD had higher tau and RTSE values than their male counterparts. Our results suggest that RT-ISV is primarily associated with co-occurring ADHD symptoms/diagnosis in children and adolescents with ASD. These results do not support the hypothesis of response variability as a transdiagnostic phenotype for ASD and ADHD and warrant further validation at a neural level

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Journal of Clinical Medicine. 2019;8.

DIFFERENCES IN HYPERACTIVITY AND INATTENTION BETWEEN ADOLESCENTS PARTICIPATING AND NON-PARTICIPATING IN A NATIONAL POLISH AFTER-SCHOOL ATHLETICS PROGRAM.

Glabska D, Guzek D, Mellova B, et al.

Among the hyperactivity and inattention components, being predictors of the Attention Deficit Hyperactivity Disorder (ADHD) phenotype, there are restlessness, fidgeting, distractibility, lack of reflectiveness and lack of attention components. So far, it was observed that they may be associated with an excessive body mass in children. The aim of the study was to analyze differences of the hyperactivity and inattention between adolescents participating and non-participating in a national Polish after-school athletics program (12-13 years) in a case-control sample. The #goathletics study was conducted among a group of 1014 adolescents-507 representatives for the nationwide physical activity program "Athletics for All" and 507 pair-matched non-participating ones. Assessment of the hyperactivity and inattention was based on a Strengths and Difficulties Questionnaire-Hyperactivity-Inattention subscale (SDQ-HI). It was observed, that in spite of the fact, that the general frequency of hyperactivity and inattention did not differ between groups, the frequency of specific components differed. Especially in the case of girls, for adolescents participating in a national Polish after-school athletics program, the positive attention component was more often observed (39.7%) than for adolescents non-participating (30.0%). It may be concluded, that hyperactivity and inattention components may be less common in the case of active adolescents, than in the case of others

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Journal of Clinical Medicine. 2019;8.

DIETARY PROFILES, NUTRITIONAL BIOCHEMISTRY STATUS, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: PATH ANALYSIS FOR A CASE-CONTROL STUDY.

Wang L-J, Yu Y-H, Fu M-L, et al.

This study aims to investigate dietary and nutritional biochemistry profiles of attention-deficit/hyperactivity disorder (ADHD) and to explore their potential relationship by path analysis. We enrolled 216 children with ADHD and 216 age-, height-and gender-matched controls from 31 elementary schools in Taiwan. Dietary intake of the participants was assessed using a food frequency questionnaire (FFQ). Fasting blood samples were collected to determine the serum levels of multiple nutritional markers. Moreover, we employed a structural equation model (SEM) to link diet, nutritional markers and ADHD. Compared to healthy control, ADHD children had significantly lower serum levels of vitamin B12, folate, vitamin B6, ferritin concentration, and monounsaturated fatty acids (MUFA), but higher levels of serum saturated fatty acids (SFA), n-6/n-3 fatty acid ratio, and inorganic phosphorous concentration. Children with ADHD had more intake of nutrient-poor foods such as high sugar and high fat foods, and had less intake of vegetable, fruit, protein-rich foods than their counterpart. SEM analysis showed that the poor nutritional biochemistry profiles linked the association between unhealthy dietary patterns and ADHD. In conclusion, an unhealthy dietary pattern may be a predecessor of the poor nutritional biochemistry status, and managing diet and nutrition conditions should be considered to improve ADHD symptoms in children

J Exp Child Psychol. 2019 Jun;182:86-101.

DIFFICULTIES OF CHILDREN WITH SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PROCESSING TEMPORAL INFORMATION CONCERNING EVERYDAY LIFE EVENTS.

Mioni G, Capodieci A, Biffi V, et al.

It has been hypothesized that children with attention-deficit/hyperactivity disorder (ADHD) present difficulties in processing time durations. However, so far evidence on this difficulty and its related mechanisms has been unclear and collected only with rating scales or laboratory experimental tasks. The current study examined whether this difficulty can be seen in children carrying out everyday actions (e.g., telephone calls, cooking activities) and to what extent it is influenced by working memory (WM) abilities. In total, 182 children aged 7 to 10 years were included in the study: 91 children with ADHD symptoms and 91 typically developing (TD) children matched for gender and other characteristics. We administered sequence reordering, time reproduction, and duration comparison tasks, and as stimuli we used six movies lasting 10 to 60 s showing three women completing six different actions. We also collected measures of verbal and visuospatial WM tests (digit span and Corsi task). Children with ADHD symptoms tended to underestimate the long durations and were less accurate than TD children in remembering the exact order of events and in comparing the duration of two different events. These difficulties appeared to be related to WM abilities

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J Pediatr Psychol. 2019 Jun;44:517-26.

TECHNOLOGY USE AND SLEEP IN ADOLESCENTS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER. Bourchtein E, Langberg JM, Cusick CN, et al.

Objectives: This study used a multi-informant approach to examine differences in types and rates of technology used by adolescents with and without attention-deficit/hyperactivity disorder (ADHD), associations between technology use and sleep/daytime sleepiness, and whether technology use was differentially related to sleep/daytime sleepiness in adolescents with and without ADHD.

Methods: Eighth graders with (n = 162) and without (n = 140) ADHD were recruited. Adolescents completed questionnaires assessing time spent using technology, sleep-wake problems, school-night time in bed, and daytime sleepiness. Parents and teachers reported on adolescents' technology use and daytime sleepiness, respectively.

Results: Adolescents with ADHD had significantly greater total technology, television/movie viewing, video game, and phone/video chatting use than adolescents without ADHD. Adolescents with ADHD engaged in twice as much daily video game use compared to those without ADHD (61 vs. 31 min). Controlling for medication use, ADHD status, pubertal development, sex, and internalizing symptoms, greater parent- and adolescent-reported technology use was associated with more sleep-wake problems and less time in bed. ADHD status did not moderate the relations between technology use and these sleep parameters. In contrast, ADHD status moderated the association between parent-reported technology use and teacher-reported daytime sleepiness, such that this association was significant only for adolescents with ADHD.

Conclusions: Technology use, although more prevalent in adolescents with ADHD, is linked with more sleep problems and reduced school-night sleep duration regardless of ADHD status. Technology use is associated with teacher-rated daytime sleepiness only in adolescents with ADHD. Clinicians should consider technology usage when assessing and treating sleep problems

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J Pediatr Psychol. 2019 Jun;44:576-88.

POSITIVE ILLUSORY BIAS STILL ILLUSORY? INVESTIGATING DISCREPANT SELF-PERCEPTIONS IN GIRLS WITH ADHD.

Tu JW, Owens EB, Hinshaw SP.

Objective: To examine whether girls with attention deficit/hyperactivity disorder (ADHD) demonstrate positive illusory self-perceptions during adolescence and young adulthood.

Methods: We tested, across a 5-year longitudinal span, whether self-perceptions versus external-source ratings were more strongly predictive of young adulthood impairment and depressive symptoms. Participants

included an ethnically diverse sample of 140 girls with ADHD and 88 comparison girls, aged 11–18 years (M = 14.2) at adolescent and 19–24 years (M = 19.6) at young adult assessment.

Results: Although girls with ADHD rated themselves more positively than indicated by external ratings, their self-reports still did not differ significantly from external ratings in both scholastic competence and social adjustment domains. Comparison girls, on the other hand, rated themselves significantly less positively than indicated by external ratings in social adjustment. Positive discrepancy scores in adolescence did not significantly predict depressive symptoms in young adulthood and vice versa. Crucially, measures of actual competence in adolescence were more strongly associated with young adulthood impairments than were inaccurate self-perceptions for girls with ADHD.

Conclusions: Our findings continue to challenge the existence of a positive illusory bias among girls with ADHD, including any association of such bias with key indicators of impairment

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J Psychiatr Res. 2019;115:158-64.

ALTERED MICRORNA 5692B AND MICRORNA LET-7D EXPRESSION LEVELS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Aydin SU, Kabukcu BB, Cetin GO, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder. Its etiology is not clearly understood yet, but neurobiological, genetic and environmental factors are shown to play a role. The relationship between ADHD and miRNAs has been studied quite recently, and few studies have been conducted up to now. In this study, peripheral blood expression levels of miR-5692b, miR-let-7d, miR-124-3p, miR-4447 and miR-107 of 30 children and adolescents with combined type ADHD were compared to 30 healthy controls to understand the roles of these miRNAs in the ADHD etiopathogenesis. Compared to controls, levels of miR-5692b (p = 0.006) were found higher and levels of miR-let-7d (p = 0.017) were found lower in the ADHD group. There was no significant difference in terms of miR-124-3p, miR-4447, and miR-107 levels between the groups. In conclusion, our findings support other studies suggesting the importance of miRNAs in the pathogenesis of ADHD. Regarding the regulatory role of miRNAs in gene regulation, their contribution to etiopathogenesis and heterogeneity of ADHD should be investigated further

J Psychiatr Res. 2019;116:138-46.

THE RELATIONSHIP BETWEEN ALPHA ASYMMETRY AND ADHD DEPENDS ON NEGATIVE AFFECT LEVEL AND PARENTING PRACTICES.

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Alperin BR, Smith CJ, Gustafsson HC, et al.

Atypical frontal alpha asymmetry is associated with the approach/withdrawal and affective processes implicated in many psychiatric disorders. Rightward alpha asymmetry, associated with high approach, is a putative endophenotype for attention deficit/hyperactivity disorder (ADHD). However, findings are inconsistent, likely because of a failure to consider emotional heterogeneity within the ADHD population. In addition, how this putative risk marker interacts with environmental factors known to increase symptom severity, such as parenting practices, has not been examined. The current study examined patterns of alpha asymmetry in a large sample of adolescents with and without ADHD, including the moderating role of negative affect and inconsistent discipline. Resting-state EEG was recorded from 169 well-characterized adolescents (nADHD = 79). Semi-structured clinical interviews and well-validated rating scales were used to create composites for negative affect and inconsistent discipline. The relationship between alpha asymmetry and ADHD diagnosis was moderated by negative affect. Right asymmetry was present only for those with ADHD and low levels of negative affect. In addition, greater right alpha asymmetry predicted severity of ADHD symptoms for those with the disorder, but only in the context of inconsistent parenting practices.

Results confirm right alpha asymmetry is a possible endophenotype in ADHD but highlight the need to consider emotional heterogeneity and how biological risk interacts with child environment in order to fully characterize its relationship to disorder liability and severity

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Journal of the National Cancer Institute. 2019;111:201-09.

BRAIN ACTIVITY ASSOCIATED WITH ATTENTION DEFICITS FOLLOWING CHEMOTHERAPY FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.

Fellah S, Cheung YT, Scoggins MA, et al.

Background: The impact of contemporary chemotherapy treatment for childhood acute lymphoblastic leukemia on central nervous system activity is not fully appreciated.

Methods: Neurocognitive testing and functional magnetic resonance imaging (fMRI) were obtained in 165 survivors five or more years postdiagnosis (average age = 14.4 years, 7.7 years from diagnosis, 51.5% males). Chemotherapy exposure was measured as serum concentration of methotrexate following high-dose intravenous injection. Neurocognitive testing included measures of attention and executive function. fMRI was obtained during completion of two tasks, the continuous performance task (CPT) and the attention network task (ANT). Image analysis was performed using Statistical Parametric Mapping software, with contrasts targeting sustained attention, alerting, orienting, and conflict. All statistical tests were two-sided.

Results: Compared with population norms, survivors demonstrated impairment on number-letter switching (P < .001, a measure of cognitive flexibility), which was associated with treatment intensity (P = .048). Task performance during fMRI was associated with neurocognitive dysfunction across multiple tasks. Regional brain activation was lower in survivors diagnosed at younger ages for the CPT (bilateral parietal and temporal lobes) and the ANT (left parietal and right hippocampus). With higher serum methotrexate exposure, CPT activation decreased in the right temporal and bilateral frontal and parietal lobes, but ANT alerting activation increased in the ventral frontal, insula, caudate, and anterior cingulate.

Conclusions: Brain activation during attention and executive function tasks was associated with serum methotrexate exposure and age at diagnosis. These findings provide evidence for compromised and compensatory changes in regional brain function that may help clarify the neural substrates of cognitive deficits in acute lymphoblastic leukemia survivors

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Learn Instr. 2019 Jun;61:138-47.

DO STUDENTS LEARN BETTER WHEN SEATED CLOSE TO THE TEACHER? A VIRTUAL CLASSROOM STUDY CONSIDERING INDIVIDUAL LEVELS OF INATTENTION AND HYPERACTIVITY-IMPULSIVITY.

Blume F, Göllner R, Moeller K, et al.

This study investigated whether students in grades 5 and 6 learned better when seated proximally to the teacher during a virtual classroom math lesson, taking individual levels of inattention and hyperactivity-impulsivity (i.e., ADHD symptoms) into account. In general, students learned better in the proximal seat location compared to a distant one. Additionally, more intense symptom levels impaired learning more. When considering individual levels of ADHD symptoms, students' learning outcomes did not specifically benefit from a proximal seat location. Consequently, the present study did not support the general assumption that a proximal seat location fosters academic achievement in students experiencing individual levels of inattention and hyperactivity-impulsivity

Medicina (Argentina). 2019;79:51-56.

DIFFERENCES IN EARLY VISUAL CEREBRAL PROCESSING IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIV-ITY DISORDERS WITH PREDOMINANCE OF NO ATTENTION.

Ortiz AT, Turrero A.

To evaluate attentional processes to visual stimuli that do not require motor response, a study with evoked potentials was carried out on 17 children with attention deficit disorder predominantly inattentive (ADDH-I) and 15 controls between the ages of 7 and 11 years. The latency and localization of sources of the early visual evoked potentials P100 and N100 were analyzed during the performance of a visual oddball task (20% horizontal and 80% vertical lines) where the vertical lines did not require motor response. The results indicate that ADDH-I group process visual information that does not require motor response with a greater increase in brain activity and through the ventral temporal pathway, while the control group does so by means of the dorsal parietal stream. This neurobiological process of visual information processing by ventral temporal pathway of ADDH-I group could be due to alterations in emotional processes that directly influence visual recognition or as consequence of deficit in the control of attentional processes by the dorsal parietal pathway

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Medicina (Argentina). 2019;79:68-71.

TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CLINICAL PRACTICE. A RETROSPECTIVE STUDY. Lopez-Lopez A, et al.

Attention deficit hyperactivity disorder (ADHD) is a complex and heterogeneous neurode-velopmental disorder, of a chronic nature, of multifactorial etiology, mainly due to genetic and environmental factors. We conducted a retrospective analytical study of the therapeutic management of children diagnosed with ADHD. A sample of 82 children diagnosed with ADHD (74.4% children and 25.6% girls) was studied. 96.3% of the cases presented some associated disorder. Pharmacological treatment was the treatment of choice (90.2%). 46.0% received immediate release methylphenidate, 51.4% sustained release methylphenidate and atomoxetine was only prescribed in 2.7% of patients. 20.3% of the sample abandoned pharmacological treatment at some point. Pharmacological treatment was the most frequent option in our sample, and methylphenidate immediate release the drug of choice for treatment initiation. The alternatives to stimulants are used in very low percentage of the patient. No significant differences were found between the type of treatment regarding the subtype of ADHD or gender, but we found significant difference in relation with the age of onset of treatment

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Medicine (Baltimore). 2019 Jun;98:e15957.

A META-ANALYTIC INVESTIGATION OF THE IMPACT OF MINDFULNESS-BASED INTERVENTIONS ON ADHD SYMPTOMS. Xue J, Zhang Y.

BACKGROUND: Mindfulness-based interventions (MBIs) have been reported to be efficacious in treating attention deficit hyperactivity disorder (ADHD). However, the value of the control effect of MBIs on ADHD core symptoms remains controversial. To clarify the literature on the control effect of MBIs on the symptoms of ADHD and guide future researches, an effect-size analysis was conducted.

METHODS: A systematic search in PubMed, Embase, Web of Science, Medline, Cochrane Library, China National Knowledge Infrastructure, and Wangfang Data databases was performed up to January 11, 2019. The overall effect size of MBIs on ADHD core symptoms (ie, inattention and hyperactivity/impulsivity) was recorded by the metric of Hedges' g with 95% confidence interval, Z-value, and P-value.

RESULTS: Eleven eligible studies featuring 682 participants were included in the meta-analysis. The overall results indicated that MBIs had large effects on inattention (Hedges' g = -0.825) and hyperactivity/impulsivity (Hedges' g = -0.676) relative to the control group. Results from subgroup analyses between self- and observer rating on ADHD symptoms revealed that the effect of MBIs both remained in a large range and self-rated ADHD core symptom had a greater impact on heterogeneity across the studies. Meta-regression found that the overall effect might be moderated by participant age group and control condition.

CONCLUSION: The present meta-analysis suggested that MBIs had large effects in reducing ADHD core symptoms in comparison with the control group. Future researches are needed to assess follow-up effects of MBIs on ADHD core symptoms and explore the correlation between the individual level of mindfulness and reduction of ADHD symptoms

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Neuropsychiatr Dis Treat. 2019;15:763-71.

SLEEP PROBLEMS IN CHILDREN WITH AUTISM SPECTRUM DISORDER: CLINICAL CORRELATES AND THE IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Gunes S, Ekinci O, Feyzioglu A, et al.

Purpose: High prevalence of sleep problems has been reported in children with autism spectrum disorder (ASD). However, there is limited literature about the types and clinical correlates of sleep problems. This study aims to compare sleep disturbances between children with ASD and healthy children and investigate the relationship between sleep difficulties and clinical symptoms of ASD.

Materials and methods: The sample consisted of 112 children in ASD patient group and 112 healthy controls, with an age range of 2-18 years. The ChildrenΓÇÖs Sleep Habits Questionnaire (CSHQ) was used for sleep problems; Turgay DSM-IV Disruptive Behavior Disorders Rating Scale parent form (T-DSM-IV-S) was used to assess hyperactivity/impulsivity and inattentiveness; Childhood Autism Rating Scale (CARS), Autism Behavior Checklist, and Aberrant Behavior Checklist were used to evaluate the severity of autistic symptoms and behavioral problems.

Results: Total score, bedtime resistance, and sleep anxiety subscores of CSHQ were significantly higher in children with ASD than the control group. Among ASD children, intellectual capacity was not found to be associated with CSHQ scores. Bedtime resistance and night waking subscores of CSHQ were found to be positively correlated with CARS total score. Inattentiveness subscore of Parent T-DSM-IV-S was significantly higher in children with moderate-to-severe sleep problems.

Conclusion: Sleep difficulties in ASD patients may occur independently of intellectual disability. Bedtime resistance and night waking appear to be linked with ASD symptoms. Inattentiveness in ASD children may be associated with moderate-to-severe sleep problems

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Neuropsychiatr Dis Treat. 2019;15:1193-209.

SUPPLEMENTATION WITH HIGH-CONTENT DOCOSAHEXAENOIC ACID TRIGLYCERIDE IN ATTENTIONDEFICIT HYPERACTIVITY DISORDER: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL.

Rodriguez C, Garcia T, Areces D, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is a complex disorder in terms of etiology, clinical presentation, and treatment outcome. Pharmacological and psychological interventions are recommended as primary treatments in ADHD; however, other nonpharmacological intervention such as a dietary supplementation with omega-3 polyunsaturated fatty acids (¤ë-3 PUFAs) has emerged as an attractive option. Purpose: The objective of the present study was to assess whether dietary supplementation with highly concentrated ¤ë-3 docosahexaenoic acid (DHA) triglyceride may improve symptoms in ADHD.

Method: A 6-month prospective double-blind placebo-controlled randomized clinical trial was designed in 66 patients with ADHD, aged between 6 and 18 years. Participants in the experimental group received a combination of ¤ë-3 fatty acids (DHA 1,000 mg, eicosapentaenoic acid 90 mg, and docosapentaenoic acid 150 mg). Instruments included d2-test, AULA Nesplora, EDAH scales, and abbreviated Conner's Rating Scale.

Results: In the cognitive test, between-group differences were not found, but within-group differences were of a greater magnitude in the DHA group. Between-group differences in favor of the DHA arm were observed in behavioral measures, which were already detected after 3 months of treatment. Results were not changed when adjusted by ADHD medication.

Conclusions: This study provides further evidence of the beneficial effect of supplementation with ¤ë-3 DHA in the management of ADHD

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Neurosci Lett. 2019 Jun;703:191-97.

EEG CORRELATES OF MATH ANXIETY DURING ARITHMETIC PROBLEM SOLVING: IMPLICATION FOR ATTENTION DEFICITS.

Liu J, Li J, Peng W, et al.

Anxiety about math can lead to long-term negative consequences related to academic achievement and professional success. However, it remains unclear how elevated math-anxiety modulates brain activity while solving arithmetic problems. In the current study, we recorded electrophysiological responses throughout arithmetic problem solving, both at the period of anticipating an upcoming arithmetic problem and solving an arithmetic problem. Results showed that, after controlling for mathematical performance, people with higher math anxiety tended to show stronger beta band oscillation and P300 amplitude while expecting the arithmetic problems, as well as stronger gamma band activity while solving the arithmetic problems. These results suggest that individuals highly anxious about math might use more attentional resources during the course of anticipating the upcoming arithmetic problems, and showed greater attentional bias toward arithmetic problems during solving arithmetic problems

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Nicotine Tob Res. 2019;21:638-47.

CIGARETTE SMOKING PROGRESSION AMONG YOUNG ADULTS DIAGNOSED WITH ADHD IN CHILDHOOD: A 16-YEAR LONGITUDINAL STUDY OF CHILDREN WITH AND WITHOUT ADHD.

Mitchell JT, Howard AL, Belendiuk KA, et al.

Introduction: Children with attention-deficit/hyperactivity disorder (ADHD) are at increased risk for smoking cigarettes, but there is little longitudinal research on the array of smoking characteristics known to be prognostic of long-term smoking outcomes into adulthood. These variables were studied into early adulthood in a multisite sample diagnosed with ADHD combined type at ages 7-9.9 and followed prospectively alongside an age- and sex-matched local normative comparison group (LNCG).

Methods: Cigarette smoking quantity, quit attempts, dependence, and other characteristics were assessed in the longitudinal Multimodal Treatment Study of Children with ADHD (MTA) eight times to a mean age of 24.9 years: ADHD n = 469: LNCG n = 240.

Results: In adulthood, the ADHD group had higher rates of daily cigarette smoking, one or more quit attempts, shorter time to first cigarette of the day, and more severe withdrawal than the LNCG. The ADHD group did not appear to have better smoking cessation rates despite a higher proportion quitting at least once. Smoking quantity and nicotine dependence did not differ between groups. The ADHD group reported younger daily smoking onset and faster progression from smoking initiation to daily smoking across assessments. Finally, ADHD symptom severity in later adolescence and adulthood was associated with higher risk for daily smoking across assessments in the ADHD sample.

Conclusions: This study shows that ADHD-related smoking risk begins at a young age, progresses rapidly, and becomes resistant to cessation attempts by adulthood. Prevention efforts should acknowledge the speed of uptake; treatments should target the higher relapse risk in this vulnerable population. Implications: Although childhood ADHD predicts later smoking, longitudinal studies of this population have yet to fully characterize smoking behaviors into adulthood that are known to be prognostic of long-term smoking outcome. The current study demonstrates earlier and faster progression to daily smoking among those with a childhood ADHD diagnosis, as well as greater risk for failed quit attempts. Prevention efforts should address speed of smoking uptake, while treatments are needed that address smoking relapse risk. The current study also demonstrates ADHD symptom severity over development increases daily smoking risk, implicating the need for continuous ADHD symptom management

Nord J Psychiatry. 2019;73:302-07.

ALTERED SERUM LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND GLIAL-DERIVED NEUROTROPHIC FACTOR BUT NOT FIBROBLAST GROWTH FACTOR-2 IN TREATMENT-NAIVE CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Yurteri N, ahin, Tufan AE.

Background and aim: Recent evidence suggests that growth factors might be involved in the pathophysiology of attention deficit hyperactivity disorder (ADHD). The aim of this study was to determine whether serum levels of brain-derived neurotrophic factor (BDNF), glial-derived neurotrophic factor (GDNF), neurotrophin-3 (NT-3), nerve growth factor (NGF), fibroblast growth factor-2 (FGF-2) and vascular endothelial growth factor (VEGF) were altered in children with ADHD.

Methods: Serum levels of BDNF, GDNF, NT-3, NGF, VEGF and FGF-2 were analyzed in 49 treatment-naive children with ADHD and age, gender matched 36 healthy controls using enzyme-linked immunosorbent assay. ADHD symptoms were scored by Du Paul ADHD Rating Scale and Strengths and Difficulties Questionnaire.

Results: We found that serum VEGF levels were significantly lower (p < 0.001) and GDNF levels were significantly higher in ADHD group compared to control group (p = 0.003). However, we found no correlations between ADHD symptoms and serum VEGF or GDNF levels. Furthermore, we observed no significant alterations in serum BDNF, NT-3, NGF, FGF-2 levels in children with ADHD.

Conclusion: To our knowledge, the present study is the first to examine serum VEGF and FGF-2 levels in children with ADHD. Our results indicate that VEGF and GDNF might be involved in the etiology of ADHD. Further studies are required to determine the role of growth factors in the etiology and consequently in the treatment of ADHD

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Noropsikiyatr Ars. 2019;56:27-31.

EFFECTS OF METHYLPHENIDATE ON REACTION TIME IN CHILDREN WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER.

Given A, Altinkaynak M, Dolu N, et al.

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is associated with a broad range of neuropsychological impairments that are attenuated with methylphenidate (MPH) treatment. The aim of this study was to determine how MPH effects attentional functioning in terms of reaction time (RT) in ADHD.

Methods: Eighteen pre-medicated ADHD children (7 to 12 years old) and eighteen gender matched normal controls (7 to 12 years old) were included in the study. Participants performed an auditory attention task and the RT of participants to each target response was calculated automatically. The same test was repeated 3 months after OROS-MPH administration for ADHD group. RT, RT standard deviation (RTSD), and response errors (omission and commission errors) were compared between control and pre-MPH ADHD groups, and between Pre-MPH and post-MPH ADHD groups.

Results: Relative to control subjects, significantly longer RTs, higher RTSD and more errors of omission were observed in unmedicated ADHD children during auditory attention task. Analyses revealed significant effects of medication across all measures except commission errors. After treatment RTs were faster, RTSD values were lower, and errors of omission were attenuated compared to pre-medication condition in ADHD group. There were no significant differences in terms of commission errors between groups.

Conclusion: In this study it was observed that MPH reduced RTs to stimuli, attenuated omission errors during the task in ADHD group and after 3 months of treatment ADHD children showed similar patterns in RT as compared to controls. Results suggest that when treating ADHD, it might help clinicians to evaluate objective and non-invasive cognitive outcomes such as RT, RTSD and response errors to evaluate the effects of treatment

PLoS ONE. 2019;14.

EFFECTS OF METHYLPHENIDATE ON THE ERP AMPLITUDE IN YOUTH WITH ADHD: A DOUBLE-BLIND PLACEBO-CONTROLLED CROSS-OVER EEG STUDY.

Rubinson M, Horowitz I, Naim-Feil J, et al.

Methylphenidate (MPH) is a first line drug for attention-deficit/hyperactivity disorder (ADHD), yet the neuronal mechanisms underlying the condition and the treatment are still not fully understood. Previous EEG studies on the effect of MPH in ADHD found changes in evoked response potential (ERP) components that were inconsistent between studies. These inconsistencies highlight the need for a well-designed study which includes multiple baseline sessions and controls for possible fatigue, learning effects and between-days variability. To this end, we employ a double-blind placebo-controlled cross-over study and explore the effect of MPH on the ERP response of subjects with ADHD during a Go/No-Go cognitive task. Our ERP analysis revealed significant differences in ADHD subjects between the placebo and MPH conditions in the frontal-parietal region at 250ms-400ms post stimulus (P3). Additionally, a decrease in the late 650ms-800ms ERP component (LC) is observed in frontal electrodes of ADHD subjects compared to controls. The standard deviation of response time of ADHD subjects was significantly smaller in the MPH condition compared to placebo and correlated with the increased P3 ERP response in the frontoparietal electrodes. We suggest that mental fatigue plays a role in the decrease of the P3 response in the placebo condition compared to preplacebo, a phenomenon that is significant in ADHD subjects but not in controls, and which is interestingly rectified by MPH

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PLoS ONE. 2019;14.

THE VALIDITY OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ) FOR CHILDREN WITH ADHD SYMPTOMS.

Hall CL, Guo B, Valentine AZ, et al.

Background The Strengths and Difficulties Questionnaire (SDQ) is widely used to assess child and adolescent mental health problems. However, the factor structure of the SDQ is subject to debate and there is limited evidence investigating measurement equivalence invariance (ME/I) between treatment groups, informants, and across time.

Method A randomised controlled trial (RCT) recruited 250 participants (6–17 years) who had been referred for an attention deficit hyperactivity disorder (ADHD) assessment. Participants and their clinician either received or did not receive a QbTest report (computer task measuring attention, impulsivity and activity). Parents and teachers completed the SDQ at baseline and 6-months later. This study aimed to understand the factor structure of the SDQ in a clinic referred ADHD sample, and validate the scale as a screening/diagnostic aide and as a measure of treatment outcome both in clinical and research settings. Exploratory Structural Equation Modelling (ESEM) was performed to examine the factor structure, and ME/I was assessed between treatment groups, informants, and time points. The criterion validity of the SDQ predictive algorithm for ADHD was compared with clinician and research diagnoses using logistic regression and tests of diagnostic accuracy.

Results A 5-factor structure provided the best fit with strong factorial invariance between treatment groups and across time points, but not across informants (parent and teacher ratings). SDQ ratings of probable hyperactivity disorder were good predictors of clinical (OR = 10.20, 95% CI 2.18-48.71,p = 0.003) and research diagnoses of ADHD (OR = 6.82, 95%CI 1.95-23.84, p = 0.003), and research diagnoses of Hyperkinetic disorder (OR = 4.02, 95%CI 1.13-14.25,p = 0.031). Further examination of the SDQ hyperactivity probable rating showed good specificity (84.5%-74.5%) but poor sensitivity (45.0-42.5%) for ADHD.

Conclusion The findings indicate the SDQ is a valid outcome measure for use in RCTs and clinical settings. However, care should be taken when using the SDQ predictive algorithm to screen for ADHD in clinically referred samples

PLoS ONE. 2019;14.

A RANDOMIZED CONTROLLED TRIAL OF A BRAIN-COMPUTER INTERFACE BASED ATTENTION TRAINING PROGRAM FOR ADHD.

Lim CG, Poh XWW, Fung SSD, et al.

Objective The use of brain-computer interface in neurofeedback therapy for attention deficit hyperactivity disorder (ADHD) is a relatively new approach. We conducted a randomized controlled trial (RCT) to determine whether an 8-week brain computer interface (BCI)-based attention training program improved inattentive symptoms in children with ADHD compared to a waitlist-control group, and the effects of a subsequent 12-week lower-intensity training.

Study design We randomized 172 children aged 6ΓÇô12 attending an outpatient child psychiatry clinic diagnosed with inattentive or combined subtypes of ADHD and not receiving concurrent pharma-cotherapy or behavioral intervention to either the intervention or waitlist-control group. Intervention involved 3 sessions of BCI-based training for 8 weeks, followed by 3 training sessions per month over the subsequent 12 weeks. The waitlist-control group received similar 20-week intervention after a wait-time of 8 weeks.

Results The participants Γ ÇÖ mean age was 8.6 years (SD = 1.51), with 147 males (85.5%) and 25 females (14.5%). Modified intention to treat analyzes conducted on 163 participants with at least one follow-up rating showed that at 8 weeks, clinician-rated inattentive symptoms on the ADHD-Rating Scale (ADHD-RS) was reduced by 3.5 (SD 3.97) in the intervention group compared to 1.9 (SD 4.42) in the waitlist-control group (between-group difference of 1.6; 95% CI 0.3 to 2.9 p = 0.0177). At the end of the full 20-week treatment, the mean reduction (pre-post BCI) of the pooled group was 3.2 (95% CI 2.4 to 4.1).

Conclusion The results suggest that the BCI-based attention training program can improve ADHD symptoms after a minimum of 24 sessions and maintenance training may sustain this improvement. This intervention may be an option for treating milder cases or as an adjunctive treatment

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Prof Psychol Res Pr. 2019 Jun.

WHEN MEASURES DIVERGE: THE INTERSECTION OF PSYCHOMETRIC INSTRUMENTS AND CLINICAL JUDGMENT IN MULTIMODAL ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ASSESSMENT.

Bottini S, Polizzi CP, Vizgaitis A, et al.

Adults are increasingly seeking evaluation for attention-deficit/hyperactivity disorder (ADHD). Current guidelines emphasize a multimodal assessment of ADHD in adults, but do not address how practitioners should integrate findings from multiple measures. The present study examines associations among self-report, behavioral, and neuropsychological measures used during multimodal assessment in an outpatient ADHD assessment group. Archival data of 45 adults seeking assessment were analyzed. Findings indicate measures exhibited weak or no relation to one another, suggesting measures commonly used in ADHD assessment likely assess different underlying constructs. Implications and recommendations for clinicians diagnosing adult ADHD are discussed. The importance of other sources of diagnostic information (e.g., clinical interview, behavioral observations) and consultation among colleagues are also discussed

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Psychiatry and Clinical Psychopharmacology. 2019.

PROCESSING SPEED MAY IMPROVE EARLIER THAN RESPONSE INHIBITION/ INTERFERENS IN CHILDREN WITH ADHD-COMBINED TYPE RECEIVING METHYLPHENIDATE: A SINGLE-CENTER STUDY.

Cetin FH, et al.

OBJECTIVES: The aim of this study was to determine the order of improvement in response inhibition, interference capacity, and processing speed in the Stroop test after starting methylphenidate treatment in children with ADHD.

METHODS: This study included a total of 52 children aged 7-16 years who were diagnosed with combined-type ADHD for the first time and who began to use methylphenidate treatment. The Stroop test was applied to each subject at least 3 times (before treatment and at the first and second months of treatment) in the follow-up visits.

RESULTS: The participants completed the fifth section of the Stroop test at a median duration of 42.09 sec (quartiles: 35.58-54.0 sec) before treatment, while the median duration was 34.49 sec (quartiles: 27.43-34.48 sec) at the first month of treatment and 32.18 sec (quartiles: 26.97-32.18 sec) at the second month of treatment. The task completion duration showed a statistically significant improvement from the first month of treatment (p < 0.001). When the participants were compared in terms of the number of errors and corrections they made in the fifth section of the Stroop test, there was no significant difference between pretreatment measurements and post-treatment first month measurements (p > 0.05). The number of errors and corrections were statistically significantly lower in the second month of treatment compared to pretreatment and 1st mont of the treatment (p < 0.05).

CONCLUSIONS: This study demonstrated that processing speed, response inhibition, and interference capacity assessed by the Stroop test improved with methylphenidate treatment in children with ADHD. This study is the first study to show that these improvements occur in a certain order over time

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Psychiatry Res. 2019;278:188-93.

SHORTER REM LATENCY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Diaz-Romaín A, Buela-Casal G.

The discrepancies in prior research about the actual sleep problems underlying attention-deficit/hyperactivity disorder (ADHD) demand more studies of children with this disorder. This study aimed to compare the subjective and objective sleep characteristics of 20 children with ADHD (DSM-IV criteria) and 20 typically developing children (aged 7-11 years). We assessed the children using sleep questionnaires and polysomnography recordings and analysed differences between the two groups using two-tailed Mann-Whitney U exact tests and Rosenthal's r as effect size measure. We also assessed associations between sleep measures and psychopathology using Spearman's correlation coefficients. No significant difference was found between the groups in almost any objective sleep variable, except for shorter REM latency in the ADHD group. Children with ADHD also showed significantly higher levels of daytime sleepiness and greater general sleep problems than control children, as reported by their parents, after discarding the primary sleep problems commonly associated with ADHD. Significant correlations were found between psychopathology and sleep measures. Our findings might support the link between narcolepsy-like sleep phenotype and ADHD. However, longitudinal research combining objective and subjective assessments should further explore the involvement of other variables, such as ADHD subtypes, medication, and comorbid symptoms in this relationship

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Rev Psiguiatr Clin. 2019;46:40-43.

ASSOCIATIONS OF PARENTAL BONDING AND ADOLESCENT INTERNET ADDICTION SYMPTOMS WITH DEPRESSION AND ANXIETY IN PARENTS OF ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Wong C-K. Chen Y-M. Yen C-F.

Objectives: The aim of the present study was to evaluate the associations of parental bonding and adolescents ΓÇÖ Internet addiction symptoms with depression and anxiety in parents of adolescents with attention deficit/hyperactivity disorder (ADHD).

Methods: Parental depression and anxiety symptoms, parental bonding, and adolescents ΓÇÖ Internet addiction symptoms were assessed in 46 parent-child dyads using the Center for Epidemiological Studies Depression Scale, State-Trait Anxiety Inventory, Parental Bonding Instrument (PBI), and Chen Internet Addiction Scale, respectively. Forward stepwise multiple regression analysis was used to examine the associations of parental bonding and adolescents Internet addiction symptoms with parental depression and anxiety.

Results: Low care/affection on the PBI was significantly associated with parental depression, and overprotection on the PBI and adolescents Internet addiction were significantly associated with parental anxiety.

Discussion: Parental bonding and adolescents Γ ÇÖ Internet addiction are related to depression and anxiety in parents of adolescents with ADHD

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S Afr J Psychiatry, 2019:25.

FINE MOTOR DEFICITS AND ATTENTION DEFICIT HYPERDISORDER IN PRIMARY SCHOOL CHILDREN.

Mokobane M, Pillay BJ, Meyer A.

Background: Many children with attention deficit hyperactivity disorder (ADHD) displamotor deficiencies during their daily routine, which may have impact on their developmentacourse. Children with ADHD who experience motor deficiencies often display deficits in taskrequiring movements, such as handwriting.

Aim: This study investigated deficiencies in fine motor skills in primary school children with ADHD. The study further sought to establish whether ADHD subtypes differ in deficiencies fine motor performance, recorded for both the dominant and non-dominant hands.

Methods: The Disruptive Behavior Disorders Rating Scale, completed by educators and parents, was used to screen for ADHD symptoms. Researchers confirmed the diagnosis of ADHD. Motor functioning was assessed using the Grooved Pegboard and Maze Coordination. The children diagnosed with ADHD were matched for age and gender with controls without ADHD. The sample consisted of an ADHD group (160) and control group (160) of primary school children from the Moletjie area.

Results: Children with ADHD (predominantly inattentive subtype) and ADHD (combined subtype) performed significantly more poorly than the control group on the Grooved Pegboard (p < 0.05) with both the dominant and non-dominant hand. No significant difference between the hyperactivity and impulsiveness subtype and the controls were found. There was no difference on the Maze Coordination Task (p > 0.05) between the ADHD subtypes and the controls.

Conclusion: Difficulties in fine motor skills are prevalent in children with ADHD, particularly in the ADHD-PI and ADHD-C. Problems are encountered in distal, complex, speeded tasks. The effect may lead to poor handwriting and academic performance

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SSM - Population Health. 2019;8.

ADHD REMISSION, INCLUSIVE SPECIAL EDUCATION, AND SOCIOECONOMIC DISPARITIES.

Kim M, King MD, Jennings J.

To understand how institutional environments and socioeconomic backgrounds may influence health outcomes, we examined the relationship among special education environments, socioeconomic status (SES), and likelihood of ADHD remission in children. While the majority of children experience remission by adulthood, the likelihood of remission varies across different SES levels and education environments. We find that for low SES children the likelihood of remission is higher in states that have more inclusive special education regimes. In contrast, for more advantaged children, the odds of remission do not depend on the level of special education inclusivity. Our findings suggest that providing more inclusive education can reduce disparities in behavioral disorders and are particularly important for less advantaged children. In doing so, this study contributes to the fundamental cause and health inequality literature by adding to a growing body of work showing how institutional environments can affect socioeconomic gradients in health treatment and outcomes

Value Health. 2019;22:S233.

PMH44 ASSESSMENT OF ADHERENCE TO ADHD TREATMENT GUIDELINES AND IMPACT ON HEALTH RESOURCE UTILIZATION.

Nayak DV, Nayak R.

Objectives: The 2011 American Academy of Pediatrics (AAP) guidelines recommend the use of evidence-based psychotherapy as a first-line of treatment in ADHD and as a preferred alternative to stimulant

medications, particularly in preschool children. This study assesses compliance with ADHD treatment guidelines and the extent of psychotherapy use and stimulant medication prescribing in preschoolers vs. older children (elementary school & adolescents).

Methods: Retrospective data, obtained from the Medical Expenditure Panel Survey (MEPS, 2011-2015), was utilized to obtain ADHD sample which was divided into three age groups: preschoolers, elementary schoolers, and adolescents. A chi-square analysis was performed to compare the use of ADHD stimulants and psychotherapy in the three age groups. Differences in the utilization of office-based visits, outpatient visits and ER visits among the three age groups were analyzed using a one-way ANOVA to assess the impact of chosen therapy.

Results: Out of 135,487 preschool children with ADHD, 78.3% used stimulant medications only, whereas only 13.4% used psychotherapy alone, and 8.4% used a combination therapy. Compared to children in elementary school and adolescents, preschoolers had higher number of office-based visits (10.41 vs 9.90 & 7.68; p<0.0001), outpatient visits (3.41 vs 0.27 & 0.28; p<0.0001) and ER visits (0.43 vs 0.19 & 0.19; p<0.0001). ANOVA revealed significant group differences overall; preschoolers had more ER visits and the mean difference (MD) was statistically significant in comparison to elementary schoolers (MD=0.238, p<0.0001), and to adolescents (MD=0.239, p<0.0001).

Conclusions: Adherence to AAP treatment guidelines for stimulant prescribing and behavioral therapy in preschoolers is less than optimal. Overprescribing of stimulant drugs is associated with increased medical care utilization, particularly in preschoolers and younger children. Routine prescribing of ADHD stimulants in preschoolers must be done in accordance with the treatment guidelines to avoid risky consequences and to decrease cost of care

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Value Health. 2019;22:S235.

PMH52 ARE PHYSICIANS COMPLYING WITH AAP-2011 TREATMENT GUIDELINES FOR ADHD? A COMPARATIVE ANALYSIS OF SPECIALIST VS. NONSPECIALIST PRESCRIBING AND USE OF PSYCHOTHERAPY IN CHILDREN.

Nayak D, Nayak R.

Objectives: Over-prescribing of stimulant medications in ADHD is common and most prescribing today is done by non-specialists compared to specialists. The 2011 American Academy of Pediatrics (AAP) guidelines recommend evidence-based psychotherapy as an alternative to stimulant medications, particularly in preschool-aged children. The study seeks to examine differences in ADHD treatment patterns in young children with respect to provider types (specialists vs. non-specialists) and assess the role of socio-demographics and other factors as predictors of stimulant drug use and use of psychotherapy.

Methods: A retrospective, cross-sectional research data, obtained from the Medical Expenditure Panel Survey (MEPS, 2011-2015), was utilized to obtain ADHD sample divided into three age groups: preschoolers, elementary schoolers, and adolescents. Variations in specialist vs. non-specialist prescribing of stimulant medications was assessed using a chi-square analysis. Two logistic regression analyses were also performed to examine the effect of socio-demographics and other factors on stimulant prescribing and use of psychotherapy by provider type.

Results: In general, a higher proportion of preschoolers received CNS stimulants alone (78.3%) as compared to those receiving psychotherapy alone (13.4%) or combination of the two (8.4%). Preschoolers who received non-specialist services received more stimulant prescriptions compared to those receiving specialist services (24.6% vs 21.6%; p<0.0001). Logistic regression analysis results showed that elementary school kids were 5 times more likely (OR=5.012, 95%Cl=4.976-5.048, p<0.0001), and adolescents were 3.69 times more likely (OR=3.69, 95%Cl=3.663-3.717, p<0.0001) to use stimulants compared to preschoolers. Significant predictor effects of socio-demographics, insurance status and provider type on both stimulant use and the use of psychotherapy were also observed.

Conclusions: Non-specialists engage in more ADHD stimulant prescribing and are less likely to recommend psychotherapy than specialists. Specialists provide more guideline-consistent care in general. Non-specialists should be encouraged to provide guideline-consistent care, particularly in young children, to avoid treatment complications and preventable drug-related problems

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Value Health, 2019;22;S235.

PMH53 COLLECTIVE MONITORING OF ADHD SYMPTOMS AND BEHAVIORS VIA MOBILE APPLICATION (AKL-X01): AN EVALUATION OF CAREGIVER-REPORTED USABILITY, VALUE, AND ENGAGEMENT.

Abraham J, Johns J, Hibbert S, et al.

Objectives: Clinical guidelines for the management of children/adolescents with attention-deficit hyperactivity disorder (ADHD) recommend that caregivers and teachers contribute to the assessment of behaviors and symptoms and resulting treatment decisions. Caregivers of children/adolescents with ADHD lack a way to easily and consistently monitor their child's progress at home or at school. Having the ability to track symptoms and behaviors in an accessible and user-friendly digital platform could help caregivers gain valuable insights into the child's functioning and treatment progress and enable meaningful conversations with the child, child's teacher and HCPs. Methods: AKL-X01 is a caregiver mobile application in development for use by caregivers of children/adolescents with ADHD to collectively track behavior and ADHD symptoms. An alpha build of AKL-X01 was based on user research with caregivers and teachers. The alpha AKL-X01 application was released for beta testing from May-Sept 2018, enabling caregivers to select and track behaviors and ADHD symptoms, view visualizations of tracked behaviors over time, and invite and give consent to teachers to track via a complementary web app. It also sent reminders to parents to track. Results: Beta testing of AKL-X01 was conducted with 125 caregivers of children/adolescents with ADHD (7 to 17 years of age). Data from online survey respondents (n=55/125), semi-structured interviews (n=14/125) and user tracking (all 125 caregivers) explored three key objectives: Usability: Assessing usability and comprehension of app Value: Understanding whether AKL-X01 delivered value in real-world implementation; in particular, to facilitate meaningful conversations with the child, HCPs and teachers Engagement; Test whether habit formation occurred with a minimum viable product. Conclusions: Data from the beta test of AKL-X01 showed positive caregiver feedback, regular tracking in over 25% of users through the end of testing and promising results for enabling meaningful conversations with children and their HCPs

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REVIEW



Prescription prevalence of psychotropic drugs in children and adolescents: an analysis of international data

Daniele Piovani 1 • Antonio Clavenna 1 • Maurizio Bonati 1

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Abstract

Purpose We conducted a review and meta-analysis to establish the international pooled prevalence of psychotropic drugs in children and adolescents, and comment on recent trends.

Methods Medline, Embase, and PsycINFO were searched for studies with annual prevalence estimates of attention deficit hyperactivity disorder (ADHD) medications, antidepressants, antipsychotics, sedative/hypnotics and anxiolytics in outpatient children and adolescents. Data were extracted regarding the representativeness, sampling frame, and the quality of reporting. **Results** A total of 59 studies reporting prevalence data for 23 countries were collected. Most studies were conducted in Europe (42) and were at high or moderate risk of bias (35).

The global random-effect pooled prevalence was 15.3% (95% confidence interval [CI], 7.6-25.7%) for ADHD medications, 6.4% (95%CI 4.3-8.7) for antidepressants, and 5.5% (95%CI 3.6-7.8) for antipsychotics. Heterogeneity was extremely high ($I^2 > 99\%$). Large increases were found in the prevalence of ADHD medications in most countries, particularly up until 2010. The antidepressants' trend was U-shaped in most countries with the lowest prevalence in 2007–2009 and rise more recently. Large to weak increases in the prevalence of antipsychotics were seen until 2011, and contrasting data were found more recently. Data on anxiolytics and sedative/hypnotics were limited.

Conclusions The study provides global estimates of paediatric psychotropic drug prevalence and its trends. Systematic monitoring is lacking in most countries, and very heterogeneous reporting is common across studies.

Keywords Child · Adolescent · Prevalence · Psychotropic drugs · Prescriptions · Outpatients

Introduction

In the last few decades, psychotropic drugs have become a staple in paediatric mental disorder treatment. However, epidemiological studies show that the prevalence of prescription of these drugs varies widely in different areas of the world [1, 2]. The prevalence of mental disorders cannot explain alone up to tenfold or more differences in the prevalence of prescription (e.g. antipsychotics or ADHD medications in North

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America compared with most European countries) [1, 3]. This evidence has prompted various reactions from both the academic world and lay people. First, there is concern that children may currently be over-treated in some parts of the world, and second, that the prevalence of psychotropic drugs may be increasing [4]. On the other hand, in some European countries, psychotropic medications are prescribed so rarely that it seems probable that not all children who could benefit receive them [5]. Given the considerable debate surrounding psychopharmacological treatments in paediatrics, several drug utilization studies have been done in the last two decades. Monitoring the prevalence of prescriptions at the population level is a powerful tool for measuring the effectiveness of policies, interventions, and trends. There are, however, some challenges in evaluating and comparing prevalence studies conducted in different countries. For example, there are many differences in the structure of healthcare systems, drug approval, policy, regulation, and access to mental health services [4, 5]. Since licensing of psychotropic drugs in children and



adolescents differs widely in the world, so does their off-label use [6, 7]. Moreover, so far the effects of sampling have not been considered sufficiently when comparing prevalence data across countries [1]. The majority of studies are based on surveys or local samples from a circumscribed area with often unknown representativeness. All these factors are important if the aim is to compare prevalence across countries.

The aim of the current study was to answer two research questions: (1) What is the overall prevalence estimate of prescriptions of ADHD medications, antidepressants, antipsychotics, sedative/hypnotics, and anxiolytics in children and adolescents? (2) Have prevalence estimates changed recently?

To answer these questions, we made a systematic review and meta-analysis of pharmacoepidemiological studies on prescription databases on the prevalence of psychotropic drugs in children and adolescents. We also assessed the risk of bias associated with the different sampling frames, the national representativeness, and the quality of reporting. Studies published after 2007 were analysed so as to update and expand previous reviews [2, 8].

Methods

Data sources and searches

We systematically searched Medline, Embase and PsycINFO databases from 1 January 2007 to 31 March 2018, to retrieve studies reporting of prevalence data on paediatric psychotropic drugs (antidepressants, antipsychotics, ADHD medications, anxiolytics, and hypnotics/sedatives) since 2005.

Search terms included "drug utilization", pharmacoepidemiology, "drug prescription(s)", "prescription prevalence", "prescribing prevalence" and "annual prevalence" as relevant Mesh and Emtree terms and in titles and abstracts, and prescription(s), prescribing and "medication use" in titles. The search was combined with psychotropic(s), psychopharmacologic, antidepressant(s), antidepressive(s), antipsychotic(s), sedative(s), hypnotic(s), benzodiazepine(s), serotonin reuptake inhibitors, SSRI, ADHD, psychostimulant(s), stimulant(s), attention-deficit/hyperactivity, and attention-deficit hyperactivity, in titles and as relevant Mesh and Emtree terms. The search was further combined with children, childhood, adolescence, adolescent(s), paediatric(s), paediatric, and infant(s) in titles and abstracts, and as relevant Mesh and Emtree terms.

We excluded studies conducted in hospitals; those on nonmedical drug use, addiction, or abuse; those on pregnancy or pregnant women; and those on suicide and self-harm, case reports, editorials, commentaries, lecture, and congresses. The complete Medline search can be found in Supplemental table 1. No language or age restrictions were imposed.

Study selection

The titles and abstracts of identified articles were screened to exclude irrelevant studies. Two reviewers, DP and AC, abstracted the data independently. The full text of the selected articles was retrieved and read. The bibliographies of the articles and reviews were scanned. Studies were eligible for inclusion if they:

- Were original studies conducted on prescription databases (surveys were excluded for homogeneity)
- Reported the annual prevalence for antidepressants, antipsychotics, ADHD medications, anxiolytics and/or sedative/hypnotics, or one or more of their subclasses (e.g. only SSRIs, or only atypical antipsychotics)
- Were conducted on children and adolescents not older than 19 years, or, if conducted on the overall population, included prevalence data stratified by age for the paediatric population (studies exclusively on pre-schoolers were excluded because the use of psychotropic drugs in this population is negligible)
- Reported the number of prevalent cases and the denominator, or it was possible to calculate them with acceptable accuracy

Data extraction

The following information was collected from each study: first author's last name; country/countries; year of publication; sample size for the overall study and by age strata; annual prevalence for the most recent year available; prevalent cases; drug class/classes included. When available, prevalence data was evaluated by sex. In case of incomplete data (e.g. number of prevalent cases or sample size was missing), the first or last author was contacted in order to have access to the raw data.

Psychotropic drugs were defined according to the World Health Organization categories and comprised the following subgroups of the Anatomic Therapeutic Chemical (ATC) classification system: antipsychotics (N05A), antidepressants (N06A), centrally acting sympathomimetics (ADHD medications, N06BA), anxiolytics (N05B), and sedative/hypnotics (N05C). Prevalence data regarding other subclasses of psychotropic drugs were reported in some studies (e.g. herbal remedies for depression, other pharmacological treatments for ADHD, benzodiazepines, z-hypnotics, etc.). These data were collected but not included in the meta-analyses.

Risk of bias

Risk of bias was assessed using a modified tool developed by Hoy et al. for assessing this variable in prevalence studies [9]. Since we included only prevalence studies conducted on



prescription databases, the items 4 to 8 (non-response-bias, data collected directly from subjects, case definition, reliability and validity of measurement, same mode of data collection for all subjects) were not relevant for this meta-analysis. Concerning item 9 (appropriate length of the shortest prevalence period reported), only studies with at least 1 year of observation and reporting annual prevalence were included. Overall, the risk of bias assessment included items regarding the representativeness of the sample, sampling frame, random selection or census, and reporting of appropriate numerator and denominator.

A study was considered to have a high overall risk of bias if < 3 criteria were met, moderate risk of bias if 3 criteria were met, and low risk of bias if 4 criteria were met. In case of multinational studies including data from different databases, the lowest score was attributed to the study and each prevalence data was evaluated for national representativeness. Disagreements among reviewers were discussed, and agreement was reached by consensus.

Meta-analysis

Each class of psychotropic drug was investigated separately. The outcome considered was the annual prescription prevalence for the most recent year available.

In the first phase were considered only studies reporting data for the overall paediatric population. In order to compare homogeneous studies, only those reporting prevalence for an age interval starting from 0 to 3 years old to a maximum of 17 to 19 years were initially considered. For ADHD medications, studies including data for amphetamines and derivatives were considered separately. For antidepressants and antipsychotics, studies with a maximum age of 17 years were considered separately from those with a maximum of 19 years because, in late adolescence, the prevalence rises considerably, and the two age intervals may be not comparable.

We considered only the most representative and/or recent study from each country, for each drug class. Only one study for each country (for each drug class) was analysed. In case of uncertainty, the study with the lowest score in risk of bias assessment was considered. Studies reporting the trends of psychotropic drugs in each single country were also qualitatively reported.

Other meta-analyses were done on the following subgroups: adolescents, school-age children, and children and adolescents excluding pre-schoolers (5–7 to 17 years old) in the group of studies reporting the prevalence of ADHD medications.

The Freeman-Tukey transformation (arcsine square root transformation) was used to calculate the weighted summary proportion under the random effects model [10, 11]. MedCalc Statistical Software version 18.2.1 (MedCalc Software byba, Ostend, Belgium; http://www.medcalc.org; 2018) was used for the meta-analyses.

Results

Figure 1 reports the search and selection of the 59 relevant studies [12–69]:

- 8 studies included data on more than one psychotropic drug class, and 5 of these included data on all the psychotropic classes of interest (ADHD medications, antidepressants, antipsychotics, sedative/hypnotics, and anxiolytics) [12, 19, 22, 32, 34].
- 18 included data for ADHD medications only [13–18, 20, 21, 23–27, 29–31, 33, 35].
- 15 included data for antidepressants only [14–50, 52].
- 13 included data for antipsychotics only [3, 53–64].
- 5 included data for anxiolytics and/or sedative/hypnotics only [65–69].

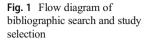
The characteristics of the included studies are provided in Supplemental table 2. Six of the 59 articles were multinational studies [3, 13, 18, 35, 37, 58], and 53 gave data on a single country. The prevalence data for at least one class was reported for 23 countries. Europe was the most represented area (42 studies), followed by North America; fewer studies were retrieved from Asia and Oceania. One Colombian study represented South America, and no studies were retrieved from Africa. The most represented countries were Germany (12 studies), Denmark, Norway, UK, and USA (8), The Netherlands (7), Canada (5), Finland, and Iceland (4).

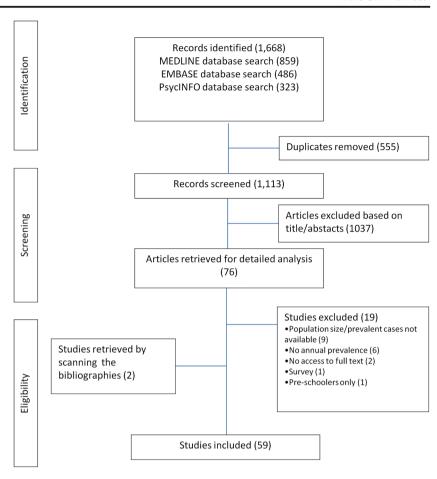
Ten studies were conducted on the general population but included paediatric prevalence data. Eleven studies included data starting from 5 or 6 years of age, mostly on ADHD medications [13, 20, 21, 24, 27, 29, 33, 35, 39, 45, 48]. Of the 15 studies containing prevalence data stratified by age groups, very different intervals were reported. Two were done only in adolescents [43, 51], and two others only in school-age children [23, 25]. Ten studies did not report prevalence data by sex, and 11 reported prevalence data stratified by age, but not for the entire study population, or only reported partial data (Table 1 and Supplemental table 2).

Figure 2 reports the studies included in this review by drug class and year of publication. The number of studies retrieved increased in recent years: most studies (34/59) were published in the last 3 years.

Twenty-four studies (41%) were at low risk of bias, 17 were at moderate risk (29%), and 18 were at high risk (30%). Most studies were conducted on a nationally representative sample (question one, 38/59; 64%). Four of six multinational studies were considered at high risk of bias according to the predetermined criteria. The risk of bias scores are illustrated in supplemental figure 1.







Overall paediatric population

Table 1 lists the 33 studies reporting data for the overall paediatric population (from age 0–3 up until 17–19 years) by drug class. We found 18 studies for antipsychotics, 16 for antidepressants, 12 for ADHD medications (in addition to 8 studies from 5–7 to 17 years of age), and 5 for anxiolytics and/or sedative/hypnotics. The global pooled prevalence by class considering only the most recent studies by country (22 studies) is summarised in Table 2. Heterogeneity was extremely wide in all the meta-analyses ($I^2 > 99\%$).

ADHD medications

Among the 12 studies on ADHD medications, USA and Germany were the most represented countries (3 studies), followed by Denmark (2 studies). The study-specific prevalence ranged from 0.19% in Italy [28] to 53% in USA [16]. Considering the most recent data for each country (7 studies, 11 countries), the random-effect pooled prevalence was 15.31% (95%CI, 7.59–25.66). There were no studies at high risk of bias in this meta-analysis. Prevalence by sex was available only in 4 studies (8 countries) and was on average much higher in males (19.74%, 95%CI, 6.52

to 39.9) than females (6.40‰, 95%CI, 2.00–13.25). The random-effect pooled prevalence was 7.2‰ (95%CI, 1.48–17.17‰) in 5 countries where amphetamine and derivatives were not approved, and 24.01‰ (95%CI 13.45–37.53) in 7 countries where they were approved (Fig. 3).

Eight studies (11 countries) excluding the pre-school age (5–7 to 15–17 years old) were collected [13, 20, 21, 24, 27, 29, 33, 35]. Similarly to previous studies, the pooled prevalence considering only countries in which amphetamine and derivatives were approved (31.67‰; 95%CI 21.44–43.82) was higher than in countries where they were not (11.16‰; 95%CI 5.19–19.36).

A total of 11/12 studies reported prevalence trends, but only 5 of these (7 countries) gave prevalence trends until 2012 or more recently. Bachmann and colleagues showed a larger increase in prevalence in The Netherlands, Germany, UK, and Denmark compared with a moderate rise in USA [13]. Other studies showed the greatest rises in prevalence before 2009–2010, and moderate increases in the last few years until 2014–2015 in USA, Canada, and Norway [16, 17, 26]. Studies investigating the entire paediatric population with the exclusion of pre-schoolers showed similar data. Furu and colleagues showed a large, steady rise in prevalence from 2008 to 2012 in Iceland, Finland, and Sweden, whereas in Norway the increase was moderate, and in Denmark prevalence levelled off from 2010 [18].



Table 1 Studies reporting prevalence data for the overall paediatric population (from age 0 to 3 up to 17 to 19 years) ordered by author name. Only data for the most recent year are shown

Author and year of publication	Country and period	Age (years)	Sample size (No.)	Prevalence (%o)	Trend in prevalence † (%)	M/F ratio
ADHD medications						
Abbas 2016 [12]	Germany 2004–2012 [‡]	≤17	4,996,705	19.4	+ 54%	_
Bachmann 2017 [13]	USA 2006–2012 commercial [‡]	≤19	105,188	36.8	+10%	2.63
	Germany 2005–2012 [‡]	_ ≤19	1,414,623	21.7	+ 62%	3.60
	UK 2005–2012 [‡]	_ ≤19	827,906	5.42	+ 54%	5.00
	The Netherlands 2005–2012 [‡]	_ ≤19	131,954	39	+ 111%	3.04
	Denmark 2005–2012	_ ≤19	1,203,817	15	+ 305%	2.69
Burcu 2016 [16]	USA 2010–2014 [‡]	≤19	1,213,012	53	+ 15%	2.2
Castle 2007 [17]	USA 2000–2005 commercial [‡]	≤19	574,600	44	-	2.35
Hartz 2016 [19]	Norway 2004–2014 [‡]	≤17	1,125,161	14.8	+ 33%	2.45
Kovess 2015 [22]	France 2010	≤17 ≤17	128,298	2.26	-	4.44
Morkem 2017 [26]	Canada 2005–2015 [‡]	≤17 ≤17	143,644	23.3	_	2.7
Piovani 2016 [28]	Italy 2006–2011	≤17 ≤17	5,019,564	0.19	+ 90%	5.46
2 3	•		, ,	22.1		3.5
Schubert 2010 [30]	Germany 2000–2007	≤ 18 1–17	~63,000 ~9,190,000	8.3		4.1
Song 2016 [31]	South Korea 2007–2011					
Steinhausen 2014 [32]	Denmark 1996–2010	≤17	105,903	7.29	+ 189%	2.99
Zoega 2009 [34]	Iceland 2003–2007 [‡]	≤17	79,469	28.4	+ 13%	0
Antidepressants						
Abbas 2016 [12]	Germany 2004–2012	≤17	4,996,705	2.2	+ 5%	_
Bachmann 2016 [37]	USA 2006–2012	≤19	105,188	15.8	+ 25%	0.92
	UK 2005–2012	≤19	827,906	10.5	+ 54%	0.43
	The Netherlands 2005–2012	≤19	131,954	6	+ 18%	0.63
	Denmark 2005–2012	≤19	1,203,817	10	+ 60%	0.46
Chien 2012 [38]	Taiwan 1997-2005	_ ≤17	229,454	4.7	_	1.19
Clavenna 2011 [40]	Italy 2004–2008	_ ≤17	~76,000	0.68	_	0
Dorks 2013 [41]	Germany 2006	≤ 17	2,599,685	1.66	_	0.8
Foulon 2010 [42]	Finland 2002–2005	= 17 ≤ 19	~1,230,000	5.93	_	0.54
Hartz 2016 [19]	Norway 2004–2014	<u>-</u> 17 ≤ 17	1,125,161	5.9	+ 181%	0.2
Hoffman 2014 [44]	Germany 2004–2012	≤17 ≤19	1,414,623	4.8	+ 50%	0.56
Kovess 2015 [22]	France 2010	≤17 ≤17	128,298	2.92	-	0.76
		≤17 ≤19	248,645	15.4		- -
Meng 2013 [46]	Canada 1986–2007		· · · · · · · · · · · · · · · · · · ·		100/	
Piovani 2016 [28]	Italy 2006–2011	≤17	5,019,564	1.02	- 19%	0.80
Sarginson 2017 [49]	UK 2000–2015	3–17	~600,000	4.9	-	-
Schröder 2017 [50]	Germany 2004–2011	≤17	2,090,135	2.1	+ 29%	0.64
Steinhausen 2014 [32]	Denmark 1996–2010	≤17	105,903	2.67	+ 24%	0.53
Volkers 2007 [52]	The Netherlands 2005	≤17	62,969	2	_	0.51
Zoega 2009 [34]	Iceland 2003–2007	≤17	79,469	23.4	-9%	0
Antipsychotics						
Abbas 2016 [12]	Germany 2004–2012	≤17	4,996,705	3.1	+ 29%	_
Alessi-Severini 2012 [53]	Canada 1999-2008	≤18	\sim 270,000	7.9	_	2.3
Bachmann 2014 [54]	Germany 2005–2012	≤19	1,414,623	3.2	_	2.32
Clavenna 2011 [40]	Italy 2004–2008	≤ 17	~76,000	0.3	_	0
Edelsohn 2017 [55]	USA 2008–2013 Medicaid	_ ≤17	286,996	30.5	-38%	2.03
Hálfdánarson 2017 [3]	Australia 2014	_ ≤ 19	~400,000	3.8	_	1.96
1141144114115011 2017 [5]	Colombia 2014	≤19	~ 270,000	1.3	_	3.33
	Denmark 2014	≤19	~1,200,000	4	_	1.22
	Finland 2014	≤19	~1,000,000	8		1.04
	France 2014	≤19	~ 100,000	3.8		2.41
	Germany 2014	≤19 ≤19	~ 1,500,000	3.4	_	1.83
	•				_	
	Iceland 2014	≤19 ≤10	~80,000	13.1	_	1.81
	Japan 2014	≤19	~ 580,000	3.2	_	1.46
	Lithuania 2014	≤19	~530,000	0.5	_	1.25
	The Netherlands 2014	≤19	~150,000	8.9	_	2.67
	N. Zealand 2014	≤19	~800,000	5	_	1.0
	Norway 2014	≤19	\sim 1,200,000	2.7	-	1.04
	Spain 2014	≤19	~ 220,000	6.6	-	2.33
	Sweden 2014	≤19	\sim 1,750,000	2.5	_	1.33
	Taiwan 2013	_ ≤19	~ 180,000	30.8	_	0.90
	USA public 2010	≤ 19	~ 6,000,000	20.5	_	2.01
	USA private 2010	≤ 19	~ 1,800,000	7.3	_	1.52
Hartz 2016 [19]	Norway 2004–14	≤17	1,125,161	1.9	+ 27%	1.38
Hsu 2013 [56]	Taiwan 1997–05	≤17 ≤17	229,454	23.9	-	1.06
1104 2013 [30]						0
Kalverdiik 2008 [57]	The Netherlands 1007 05	< u	11961			
Kalverdijk 2008 [57] Kalverdijk 2017 [58]	The Netherlands 1997–05 USA 2012	≤ 19 ≤ 19	119,612 105,188	6.8 7.9		1.95



Table 1 (continued)

Author and year of publication	Country and period	Age (years)	Sample size (No.)	Prevalence (%o)	Trend in prevalence † (%)	M/F ratio
	UK 2012	≤19	827,906	1.4	_	1.88
	The Netherlands 2012	≤19	131,954	10.3	_	2.87
	Denmark 2012	≤19	1,203,817	4.8	_	1.38
Kovess 2015 [22]	France 2010	≤17	128,298	2.8	_	2.27
Piovani 2016 [28]	Italy 2006-2011	≤17	5,019,564	0.7	+ 15%	2.34
Rani 2008 [61]	UK 1992–2005	≤18	789,467	0.77	_	1.48
Ronsley 2013 [62]	Canada 1996-2011	≤18	909,105	6.37	_	~1.9
Schröder 2017 [63]	Germany 2004–2011	≤17	2,090,135	2.6	_	2.43
Schubert 2009 [64]	Germany 2000–2006	≤19	56,169	2.8	_	_
Steinhausen 2014 [32]	Denmark 1996–2010	≤17	105,903	2.05	+ 45%	1.69
Zoega 2009 [34]	Iceland 2003-2007	≤17	79,469	10.6	+ 19%	0
Anxiolytics, sedative/hypnotics						
Abbas 2016 [12]	Germany 2004–2012	≤17	4,996,705	A 3.3	- 13%	_
				H 3.2	-30%	_
Hartz 2016 [19]	Norway 2004–2014	≤17	1,125,161	A 3.9	- 19%	1.02
				H 9.8	+ 128%	1.26
Kovess 2015 [22]	France 2010	≤17	128,298	A + H 20.1	_	0.79
Steinhausen 2014 [32]	Denmark 1996-2010	≤17	105,903	A 0.33	-35%	1.29
Zoega 2009 [34]	Iceland 2003-2007	≤17	79,469	A 1.82	+21%	0
_				H 2.59	+ 225%	0

[†] Percentage difference in annual prevalence between 2005 (or oldest prevalence data available after 2005), and the most recent data available.

Studies stratified by age

Seven studies (11 countries) reported the prevalence of ADHD medications in school-age children, but with very different age intervals (from 5–9 to 6–12 years old), ranging from 0.29‰ in Italy [28] to 50.8‰ in USA [13]. The pooled prevalence tended to be higher in countries where amphetamines were approved (21.71‰; 95%CI, 12.64–33.16), compared with those where they were not (8.49‰; 95%CI, 1.28 to 21.96).

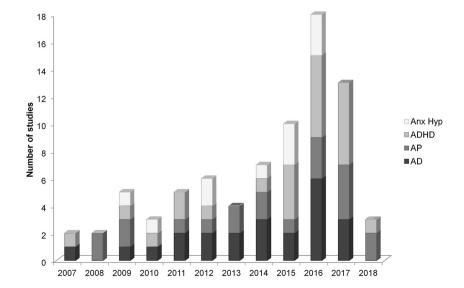
Five studies (9 countries) reported the prevalence of ADHD medications in adolescents, ranging from 0.3‰ in Italy [28] to 88‰ in USA [13]. No meta-analysis was done because most studies differed widely in the age intervals.

Fig. 2 Studies reporting paediatric psychotropic drug prevalence by drug class and year of publication (studies investigating more than one drug class are counted more times). For 2018, only the first trimester was considered. Anx Hyp, anxiolytics-hypnotics; ADHD, medicine for attention deficit hyperactivity disorder; AP, antipsychotics; AD, antidepressants

Antidepressants

Overall paediatric population

Of the 16 studies on antidepressants, Germany was the most represented country (4 studies), followed by Denmark, Italy, The Netherlands, and UK (2 studies). Thirteen studies were included in the meta-analyses: 9 studies (9 countries) considered children and adolescents until 17 years of age, and 4 studies (7 countries) until 19 years. The overall random-effect pooled prevalence, irrespective of age intervals, was 6.35% (95%CI, 4.34–8.73‰). The pooled prevalence was similar (5.95 ‰; 95%CI, 3.83–8.53) when excluding studies





^{*}Amphetamines are included. A anxiolytics, H hypnotics and sedatives. A + H anxiolytics and hypnotics/sedatives. \circ , analysed but not reported for the overall population

Table 2 Summary of the global paediatric pooled prevalence by class of psychotropic drug considering the most recent and representative study available for each country; 95% confidence intervals are in brackets

Class of psychotropic drug	Global pooled prevalence (‰)	Global pooled prevalence excluding high risk of bias studies [†] (%e)
ADHD medications	15.3 (7.6–25.7)	15.3 (7.6–25.7)
Antidepressants	6.4 (4.3–8.7)	6.0 (3.8–8.5)
Antipsychotics	5.3 (3.5–7.4)	3.7 (2.4–5.4)

[†] In case of multinational studies classified as "high risk of bias" as a whole, only nationally representative data were considered

at high risk of bias and considering only nationally representative data from the multinational study [19]. Prevalence by sex was available only in 5 studies (9)

countries) and was on average higher in females (7.69%, 95%CI 3.61–13.29%) than males (4.51%, 95%CI 2.56–7.00%).

Fig. 3 Meta-analysis of the most recent studies on the prevalence of ADHD medications in children and adolescents (A) in countries/ studies in which amphetamines and derivatives were not approved/not included, and (B) in countries/studies in which amphetamines and derivatives were approved and included. Note: in Germany, dexamphetamine was approved in 2011 and two studies were analysed. The first (2007) was included in the first metaanalysis (A), and the second (2012) was included in the second meta-analysis (B)

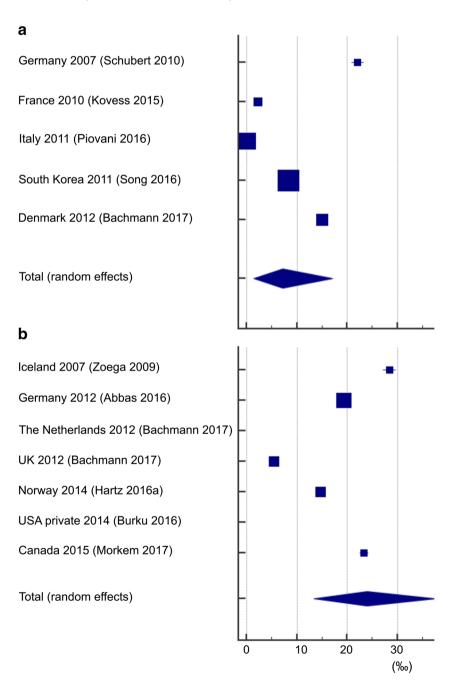
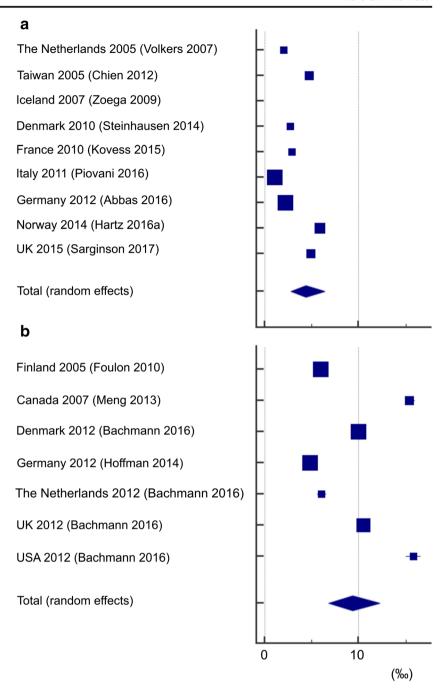




Fig. 4 Meta-analysis of the studies on the prevalence of antidepressants in children and adolescents considering the most recent study by country (A) up to age 17, and (B) up to age 19



Among studies reporting the prevalence until 17 years of age, the random-effect pooled prevalence was 4.42% (95%CI, 2.81–6.39%), whereas it was 9.33% (95%CI, 6.79–12.26%) considering studies reporting the prevalence until 19 years of age (Fig. 4). Only 4 studies (4 countries) reported prevalence data on sub-classes of antidepressants in the whole paediatric population. The pooled prevalence of SSRIs was non-significantly higher (3.22%, 95%CI, 0.85–7.11%) than that of tricyclic antidepressants (2.58%, 95%CI, 0.561–6.05), but data were scarce and dated.

A total of 11/14 studies reported annual prevalence trends, while 5 (7 countries) reported them up until 2012 or more

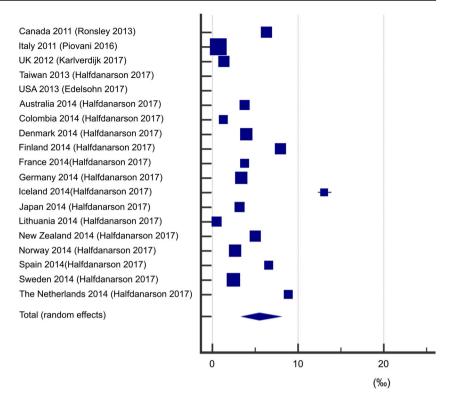
recently. A multinational study reported an increasing trend in USA, UK, Germany, Denmark, and the Netherlands [37], while other studies reported a U-shaped trend in Germany [12], Norway [19], and UK [49], with prevalence decreasing in 2006–2008 and rapidly rising afterwards. The prevalence of SSRI increased moderately in Germany [12] and Ireland [47], and more rapidly in Denmark [48].

Studies stratified by age

Six studies (10 countries) reported the prevalence of antidepressants in school-age children. The random-effect pooled



Fig. 5 Meta-analysis of the studies on the prevalence of antipsychotics in children and adolescents considering the most recent study by country



prevalence was 1.38‰ (95%CI, 0.84–2.06), and the prevalence ranged from 0.3‰ in UK to 8.8‰ in USA [37]. Although eight studies (10 countries) reported the prevalence in adolescents, only five reported homogeneous data as regards age. One study (5 countries) reported data on 10–14-year-old children (pooled-prevalence 7.22‰; 95%CI, 3.82–11.67) and 15–19-year-olds (29.29‰; 95%CI 19.13–41.53) [37]. Four other studies reported data for adolescents 11–12 to 17 years old (4.87 ‰; 95%CI, 2.47–8.07), ranging from 2.66 ‰ in Italy [28] to 7.4‰ in Taiwan [38].

Antipsychotics

Overall paediatric population

Of the 18 studies on antipsychotics, Germany was the most represented country (5 studies), followed by The Netherlands and Denmark (3 studies). Four studies (19 countries) were included in the meta-analysis. The random-effect pooled prevalence was 5.49‰ (95%CI, 3.60–7.77‰), ranging from 0.5‰ in Lithuania to 30.8‰ in Taiwan (Fig. 5) [3]. The pooled prevalence was lower (3.84‰; 95%CI, 2.35–5.69) when excluding high risk of bias studies and considering only nationally representative data from the multinational study [3]. A sensitivity analysis did not show any difference in the pooled prevalence when stratifying the studies by age (up to 17–18 years compared with those reporting prevalence data up to 19 years of age). Prevalence was on average higher in males

(7.19‰, 95%CI 4.61–10.35) than females (4.36‰, 95%CI 2.59–6.59).

A total of 13/16 studies reported prevalence trends for antipsychotics, but only four reported them until 2012 or more recently. Two were German and showed a slight to moderate increase [12, 54]. A Norwegian study showed an increase in prevalence up until 2011 followed by a plateau, or slightly decreasing trend [19]. There was a steep decreasing trend until 2013 in USA [55]. A large increase in prevalence was seen for atypical antipsychotics in the last decade in German studies [12, 64], South Korea [60], and Canada [63], only partly counterbalanced by drops in typical antipsychotics.

Studies stratified by age

Of the five studies reporting prevalence in school-age children, three used comparable age intervals. Prevalence ranged from 0.49 % in Italy [28] to 21.7 % in Taiwan [56]. Prevalence in adolescents ranged from 1.58 to 29.2% in the same studies and countries.

Anxiolytics and sedative/hypnotics

The five studies reporting data on anxiolytics and sedative/hypnotics were European. The prevalence of sedative/hypnotics ranged from 2.59% in Iceland [34] to 9.8% in Norway [19], and that of anxiolytics from 0.33% in Denmark [32] to 3.9% In Norway [19].



Four of the five studies reported prevalence trends, but only two gave them until 2012 or more recently. The sedative/hypnotics prevalence was decreasing in Germany [12], and increasing in Norway [19], while anxiolytics prevalence showed a slight decrease in both countries. Data for adolescents and school-age children were very scarce, and not comparable.

Discussion

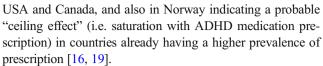
We conducted the first meta-analysis on the global pooled prevalence of psychotropic drugs in children and adolescents. The prevalence of prescription varied widely across countries. Most studies were published in the last 3 years, attesting to the growing interest in monitoring the prescription of these drugs in paediatrics. Compared with previous reviews on the topic, this analysis confirms that Europe and North America continue to be the most represented areas, though currently most studies are European [2, 8]. The reporting methodology differed widely across studies and was not improved significantly over time. Prevalence data was often reported using noncomparable age intervals, especially for school-age children or adolescents. Only small numbers of studies investigated sub-classes of psychotropic drugs, and most of them reported old data. Not all the studies gave information by sex, even though this is recognised as one of the most important variables for improving the homogeneity of reporting in pharmacoepidemiologic studies [70]. This is particularly important for specific psychotropic drug classes, those with close prevalence in males and females.

Most studies were at moderate to high risk of bias, and a significant proportion reported non-nationally representative data. Systematic monitoring is still lacking in most countries, and throughout Africa. All these factors limited the comparison of prevalence across studies, and their synthesis.

ADHD medications

ADHD medications were confirmed as the most prescribed class of psychotropic drugs globally (about 1.5%). Some exceptions were found in Europe, notably in France, and in Italy [22, 28, 71]. The global prevalence of ADHD is estimated at 5.3–7.2% [72, 73]. However, three out of four ADHD studies in our sample were European and there is agreement that, in Europe, the disease prevalence is about 5% [72, 73]. This means that, based on the most recent prescription data, about one out of three or four diagnosed patients would be pharmacologically treated globally, ranging from about one treated out 100 diagnosed children in Italy to about one out of two in Germany.

Large increases were found in the prevalence of ADHD medications up until at least 2010 in most countries. This was generally followed by a reduction of the increase in



Prevalence was higher in countries where amphetamine and derivatives were approved, than in countries where they were not. It is hard to understand the real reason. First, the difference may be due to the fact that amphetamines are approved in countries with a broader attitude to the use of psychotropic drugs over the whole lifespan [74], or second, the approval of amphetamines may itself be a driver of higher prevalence. In USA, the stimulant's potential for abuse as a cognitive enhancer is recognised both in ADHD patients, who are willing to exaggerate symptoms in order to get more drug, and in students with or without prescription [75]. A nationwide survey showed that one out of five young adults declared they used or had used stimulants to boost academic or work performance (New Survey). These problems have been known for more than a decade in North America, are very hard to tackle, and are among the most important reasons for enforcing systematic monitoring.

Antidepressants

The global pooled-prevalence of antidepressants was about 0.6%, with the highest in Iceland (2%) and North America (1.5%), and the lowest in Italy (about 0.1%). SSRIs accounted for the majority of antidepressants prescribed globally, and the few studies investigating their trends observed increases. In 2004, the US Food and Drug Administration (FDA) issued a safety warning about the twofold higher risk of suicidal behaviour in adolescents receiving antidepressants, particularly SSRIs [76]. Data suggest that, in most countries, the trend for antidepressants was increasing or U-shaped, with prevalence rising again after 2008–2010, and in some cases stabilizing at slightly lower values than those at the beginning of the 2000s.

A significant effect of age was found. In a sub-analysis, we stratified the studies reporting the prevalence up to 17 years of age, and those reporting prevalence up to 19, finding the prevalence was almost double higher among the latter. Antidepressants are among the psychotropic drugs with the largest increase in prevalence in late adolescence (even exponential) [28, 48].

As a methodological note, for antidepressants, only studies reporting the same age intervals should be considered, particularly for one-on-one comparisons.

Antipsychotics

The global prevalence estimate of antipsychotics was about 0.5%, with the highest in Taiwan and the USA (about 3%), and the lowest in Lithuania and Italy (<0.1%). The few studies investigating antipsychotics by class showed that the ratio of atypical to typical antipsychotics increased considerably in the study period, confirming that atypical drugs were the prevalent



treatment. Antipsychotics have drawn particular attention for their side-effects, large proportion of off-label use, and lack of long-term studies [77]. In recent years, in some countries such as USA and The Netherlands, the reduction of antipsychotic prescribing in youth has become a priority [78, 79].

Anxiolytics and sedative/hypnotics

The results for anxiolytics and sedative/hypnotics were severely limited by the lack of data, as few studies were comparable. The greatest variability was for sedative-hypnotics, though only few European studies were analysed. Some were excluded because of heterogeneity in the definition of an "anxiolytic", a "sedative/hypnotic", or a benzodiazepine drug. Furthermore, few studies reported data for comparable age intervals. These drugs have addiction potential, and their medical or non-medical use in adolescents has been associated with a two- to threefold higher risk of substance use disorders in adulthood. For these reasons, the lack of monitoring in most countries is worrying.

Strengths and weaknesses

The study has some strengths. It gives the first estimates of the global prevalence of psychotropic drugs in paediatrics. The analyses were conducted by grouping the studies by comparable age intervals, and the global pooled-prevalence was calculated considering the most recent and representative data available for each country. The risk of bias was evaluated with particular attention to national representativeness. The pooled prevalence was also computed by excluding high risk of bias studies, showing that sometimes the global estimates did not change (i.e. antidepressants), while in others the difference was meaningful (i.e. antipsychotics). Only big data from prescription databases were included in an attempt to improve methodological homogeneity, and to provide meaningful estimates. This last point can also be seen as a limitation of the study, because surveys were excluded.

Another limitation is the imbalance of the data collected, as already stated, which over-represents Europe compared with other areas of the world. Also, the prevalence data retrieved from systems with partially reimbursable drugs and private insurances may vary considerably in relation to the share of reimbursement and type of insurance. Further limitation is that we did not include data from most child and adolescent mental health services, because, in those studies, it is very difficult to obtain annual prevalence data.

Despite the precautions taken to include the most homogeneous and comparable studies, there were cases in which the differences among countries reached a hundredfold, indicating extreme heterogeneity. The review also showed that there are specific areas in the world where psychotropic drugs are prescribed to children much more commonly (e.g. USA,

Canada, Iceland, Taiwan), independently from the class of drug considered. There are also large differences within the same continent: for example in the Mediterranean areas of Europe, psychotropic drugs are prescribed much less frequently than in most Nordic countries.

In part, differences between countries may be related to drug regulation (e.g. prescription versus over the counter drugs). The fact that melatonin is a prescription drug in Norway may explain the highest prevalence of sedative/hypnotics reported in this country [19]. St John's wort can be reimbursed in Germany if prescribed by a physician, and this can have influenced the estimated prevalence of antidepressant prescription.

As other authors have pointed out, most of the differences across countries can be ascribed to heterogeneity in the diagnostic processes, policies, regulations, access to mental health services, guidelines, cultural perceptions, the role of non-pharmacologic alternatives, and the uncertainty of indications (i.e. difficulty in placing cut-offs for the prescription of a drug) [4, 5, 80]. Besides these factors, there are also differences in the prevalence of mental disorders, particularly across contexts with different levels of socio-economic well-being [81, 82]. The sum of all these circumstances in some countries facilitates over-diagnose, over-prescription, or even addiction, while allowing under-diagnosis and/or the preference for alternative treatments elsewhere.

As a final remark, as we noted, off-label prescription of psychotropic drugs is particularly common in paediatrics. However, since regulations for approval have grey areas in many parts of the world, what should be encouraged is evidence-based and rational use of psychotropic drugs, independently from licensing [83].

Conclusions

We have provided global estimates of the paediatric prevalence of ADHD medications, antipsychotics, antidepressants, anxiolytics and sedative/hypnotics. The role of psychopharmacological treatments in youth is debated in many countries. There are still unresolved questions such as long-term safety issues, addressing not rational use, the potential for abuse and the growing scarcity of resources that may hinder or delay access to healthcare services. Different countries suffer more from some issues than others, and the balance of these circumstances ultimately affects the prevalence of the drugs. Although monitoring prevalence at the population level is the most powerful tool for measuring the effectiveness of policies and interventions, systematic monitoring is still lacking in most countries. Even though more studies have been published in recent years, and this is welcome, the quality of reporting needs to be improved.



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Authors' individual contributions All the authors contributed equally to the design of the study. DP and AC reviewed the studies. DP wrote the first draft of the manuscript. AC contributed to writing the manuscript. MB supervised the study. All authors contributed to and have approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest

References

- Steinhausen HC (2015) Recent international trends in psychotropic medication prescriptions for children and adolescents. Eur Child Adolesc Psychiatry 24(6):635–640. https://doi.org/10.1007/ s00787-014-0631-y
- Clavenna A, Bonati M (2009) Drug prescriptions to outpatient children: a review of the literature. Eur J Clin Pharmacol 65(8):749

 755. https://doi.org/10.1007/s00228-009-0679-7
- Hálfdánarson Ó, Zoëga H, Aagaard L, Bernardo M, Brandt L, Fusté AC, Furu K, Garuoliené K, Hoffmann F, Huybrechts KF, Kalverdijk LJ, Kawakami K, Kieler H, Kinoshita T, Litchfield M, López SC, Machado-Alba JE, Machado-Duque ME, Mahesri M, Nishtala PS, Pearson SA, Reutfors J, Saastamoinen LK, Sato I, Schuiling-Veninga CCM, Shyu YC, Skurtveit S, Verdoux H, Wang LJ, Yahni CZ, Bachmann CJ (2017) International trends in antipsychotic use: a study in 16 countries, 2005-2014. Eur Neuropsychopharmacol 27(10):1064–1076. https://doi.org/10.1016/j.euroneuro.2017.07.001
- Rapoport JL (2013) Pediatric psychopharmacology: too much or too little? World Psychiatry 12(2):118–123. https://doi.org/10. 1002/wps.20028
- Taylor E (2013) Pediatric psychopharmacology: too much and too little. World Psychiatry 12(2):124–125. https://doi.org/10.1002/ wps.20030
- Sharma AN, Arango C, Coghill D, Gringras P, Nutt DJ, Pratt P, Young AH, Hollis C (2016) BAP position statement: off-label prescribing of psychotropic medication to children and adolescents. J Psychopharmacol 30(5):416–421. https://doi.org/10.1177/ 0269881116636107
- Persico AM, Arango C, Buitelaar JK, Correll CU, Glennon JC, Hoekstra PJ, Moreno C, Vitiello B, Vorstman J, Zuddas A, European Child and Adolescent Clinical Psychopharmacology Network (2015) Unmet needs in paediatric psychopharmacology: present scenario and future perspectives. Eur Neuropsychopharmacol 25(10):1513–1531. https://doi.org/10.1016/j.euroneuro.2015.06.009
- Bonati M, Clavenna A (2005) The epidemiology of psychotropic drug use in children and adolescents. Int Rev Psychiatry 17(3):181– 188. https://doi.org/10.1080/09540260500093768
- Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, Baker P, Smith E, Buchbinder R (2012) Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol 65(9):934–939. https://doi.org/10. 1016/j.jclinepi.2011.11.014
- DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7(3):177–188
- Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T (2013) Metaanalysis of prevalence. J Epidemiol Community Health 67(11): 974–978. https://doi.org/10.1136/jech-2013-203104

- Abbas S, Ihle P, Adler JB, Engel S, Günster C, Linder R, Lehmkuhl G, Schübert I (2016) Psychopharmacological prescriptions in children and adolescents in Germany. Dtsch Arztebl Int 113(22–23): 396–403. https://doi.org/10.3238/arztebl.2016.0396
- Bachmann CJ, Wijlaars LP, Kalverdijk LJ, Burcu M, Glaeske G, Schuiling-Veninga CCM, Hoffmann F, Aagaard L, Zito JM (2017) Trends in ADHD medication use in children and adolescents in five western countries, 2005-2012. Eur Neuropsychopharmacol 27(5): 484–493. https://doi.org/10.1016/j.euroneuro.2017.03.002
- Beau-Lejdstrom R, Douglas I, Evans SJ, Smeeth L (2016) Latest trends in ADHD drug prescribing patterns in children in the UK: prevalence, incidence and persistence. BMJ Open 6(6):e010508. https://doi.org/10.1136/bmjopen-2015-010508
- Boland F, Galvin R, Reulbach U, Motterlini N, Kelly D, Bennett K, Fahey T (2015) Psychostimulant prescribing trends in a paediatric population in Ireland: a national cohort study. BMC Pediatr 15:118. https://doi.org/10.1186/s12887-015-0435-3
- Burcu M, Zito JM, Metcalfe L, Underwood H, Safer DJ (2016) Trends in stimulant medication use in commercially insured youths and adults, 2010-2014. JAMA Psychiatry 73(9):992–993. https:// doi.org/10.1001/jamapsychiatry.2016.1182
- Castle L, Aubert RE, Verbrugge RR, Khalid M, Epstein RS (2007) Trends in medication treatment for ADHD. J Atten Disord 10(4): 335–342. https://doi.org/10.1177/1087054707299597
- Furu K, Karlstad Ø, Zoega H, Martikainen JE, Bahmanyar S, Kieler H, Pottegård A (2017) Utilization of stimulants and atomoxetine for attention-deficit/hyperactivity disorder among 5.4 million children using population-based longitudinal data. Basic Clin Pharmacol Toxicol 120(4):373–379. https://doi.org/10.1111/bcpt.12724
- Hartz I, Skurtveit S, Steffenak AK, Karlstad Ø, Handal M (2016) Psychotropic drug use among 0-17 year olds during 2004-2014: a nationwide prescription database study. BMC Psychiatry 16(12): 12. https://doi.org/10.1186/s12888-016-0716-x
- Hodgkins P, Sasané R, Meijer WM (2011) Pharmacologic treatment of attention-deficit/hyperactivity disorder in children: incidence, prevalence, and treatment patterns in the Netherlands. Clin Ther 33(2):188–203. https://doi.org/10.1016/j.clinthera.2011.03.001
- Hoshen MB, Benis A, Keyes KM, Zoëga H (2016) Stimulant use for ADHD and relative age in class among children in Israel. Pharmacoepidemiol Drug Saf 25(6):652–660. https://doi.org/10. 1002/pds.3962
- Kovess V, Choppin S, Gao F, Pivette M, Husky M, Leray E (2015) Psychotropic medication use in French children and adolescents. J Child Adolesc Psychopharmacol 25(2):168–175. https://doi.org/10. 1089/cap.2014.0058
- Librero J, Izquierdo-María R, García-Gil M, Peiró S (2015) Children's relative age in class and medication for attention-deficit/hyperactivity disorder. A population-based study in a health department in Spain. Med Clin (Barc) 145(11):471–476. https://doi.org/10.1016/j.medcli. 2015.02.022
- Lillemoen PK, Kjosavik SR, Hunskår S, Ruths S (2012) Prescriptions for ADHD medication, 2004-08. Tidsskr Nor Laegeforen 132(16):1856–1860. https://doi.org/10.4045/tidsskr. 11.1270
- Man KKC, Ip P, Hsia Y, Chan EW, Chui CSL, Lam MPS, Wong WHS, Chow CB, Yung A, Wong ICK (2017) ADHD drug prescribing trend is increasing among children and adolescents in Hong Kong. J Atten Disord 21(14):1161–1168. https://doi.org/10.1177/ 1087054714536047
- Morkem R, Patten S, Queenan J, Barber D (2017) Recent trends in the prescribing of ADHD medications in Canadian primary care. J Atten Disord:1087054717720719. https://doi.org/10.1177/ 1087054717720719
- Nyarko KA, Grosse SD, Danielson ML, Holbrook JR, Visser SN, Shapira SK (2017) Treated prevalence of attention-deficit/hyperactivity disorder increased from 2009 to 2015 among school-aged



- children and adolescents in the United States. J Child Adolesc Psychopharmacol 27(8):731–734. https://doi.org/10.1089/cap. 2016.0196
- Piovani D, Clavenna A, Cartabia M, Bonati M (2016) Psychotropic medicine prescriptions in Italian youths: a multiregional study. Eur Child Adolesc Psychiatry 25(3):235–245. https://doi.org/10.1007/ s00787-015-0726-0
- Prosser B, Lambert MC, Reid R (2015) Psychostimulant prescription for ADHD in new South Wales: a longitudinal perspective. J Atten Disord 19(4):284–292. https://doi.org/10.1177/1087054714553053
- Schubert I, Köster I, Lehmkuhl G (2010) The changing prevalence of attention-deficit/hyperactivity disorder and methylphenidate prescriptions: a study of data from a random sample of insurees of the AOK Health Insurance Company in the German state of Hesse, 2000-2007. Dtsch Arztebl Int 107(36):615–621. https://doi.org/10. 3238/arztebl.2010.0615
- Song I, Shin JY (2016) Prescribing patterns for attention deficit hyperactivity disorder medications among children and adolescents in Korea, 2007-2011. Epidemiol Health 38:e2016045. https://doi. org/10.4178/epih.e2016045
- Steinhausen HC, Bisgaard C (2014) Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark. Acta Psychiatr Scand 129(3):221–231. https://doi.org/10.1111/acps.12155
- Stuhec M, Locatelli I (2017) Age-related pharmacotherapy of attention deficit hyperactivity disorder in Slovenia in children and adolescents: a population-based study. Eur Psychiatry 42:129

 133. https://doi.org/10.1016/j.eurpsy.2017.01.002
- Zoëga H, Baldursson G, Hrafnkelsson B, Almarsdóttir AB, Valdimarsdóttir U, Halldórsson M (2009) Psychotropic drug use among Icelandic children: a nationwide population-based study. J Child Adolesc Psychopharmacol 19(6):757–764. https://doi.org/ 10.1089/cap.2009.0003
- Zoëga H, Furu K, Halldórsson M, Thomsen PH, Sourander A, Martikainen JE (2011) Use of ADHD drugs in the Nordic countries: a population-based comparison study. Acta Psychiatr Scand 123(5): 360–367. https://doi.org/10.1111/j.1600-0447.2010.01607.x
- Autti-Rämö I, Sourander A, Seppänen J, Martikainen JE (2011)
 Use of antidepressants among 0-26 year olds in Finland during 1997-2007. Eur J Psychiat 25(3):164–172. https://doi.org/10. 4321/S0213-61632011000300006
- Bachmann CJ, Aagaard L, Burcu M, Glaeske G, Kalverdijk LJ, Petersen I, Schuiling-Veninga CC, Wijlaars L, Zito JM, Hoffmann F (2016) Trends and patterns of antidepressant use in children and adolescents from five western countries, 2005-2012. Eur Neuropsychopharmacol 26(3):411–419. https://doi.org/10.1016/j. euroneuro.2016.02.001
- Chien IC, Hsu YC, Tan HK, Lin CH, Cheng SW, Chou YJ, Chou P (2013) Trends, correlates, and disease patterns of antidepressant use among children and adolescents in Taiwan. J Child Neurol 28(6): 706–712. https://doi.org/10.1177/0883073812450319
- Chon MW, Lee J, Chung S, Kim Y, Kim HW (2017) Prescription pattern of antidepressants for children and adolescents in Korea based on nationwide data. J Korean Med Sci 32(10):1694–1701. https://doi.org/10.3346/jkms.2017.32.10.1694
- Clavenna A, Andretta M, Pilati P, Dusi M, Gangemi M, Gattoni MB, Lombardo G, Zoccante L, Mezzalira L, Bonati M (2011) Antidepressant and antipsychotic use in an Italian pediatric population. BMC Pediatr 11(40). https://doi.org/10.1186/1471-2431-11-40
- Dörks M, Langner I, Dittmann U, Timmer A, Garbe E (2013) Antidepressant drug use and off-label prescribing in children and adolescents in Germany: results from a large population-based cohort study. Eur Child Adolesc Psychiatry 22(8):511–518. https:// doi.org/10.1007/s00787-013-0395-9

- Foulon V, Svala A, Koskinen H, Chen TF, Saastamoinen LK, Bell JS (2010) Impact of regulatory safety warnings on the use of anti-depressants among children and adolescents in Finland. J Child Adolesc Psychopharmacol 20(2):145–150. https://doi.org/10.1089/cap.2009.0040
- Hartz I, Skurtveit S, Hjellvik V, Furu K, Nesvåg R, Handal M (2016) Antidepressant drug use among adolescents during 2004-2013: a population-based register linkage study. Acta Psychiatr Scand 134(5):420–429. https://doi.org/10.1111/acps.12633
- Hoffmann F, Glaeske G, Bachmann CJ (2014) Trends in antidepressant prescriptions for children and adolescents in Germany from 2005 to 2012. Pharmacoepidemiol Drug Saf 23(12):1268– 1272. https://doi.org/10.1002/pds.3649
- 45. John A, Marchant AL, Fone DL, McGregor JI, Dennis MS, Tan JO, Lloyd K (2016) Recent trends in primary-care antidepressant prescribing to children and young people: an e-cohort study. Psychol Med 46(16):3315-3327. https://doi.org/10.1017/S0033291716002099
- Meng X, D'Arcy C, Tempier R (2014) Long-term trend in pediatric antidepressant use, 1983-2007: a population-based study. Can J Psychiatr 59(2):89–97. https://doi.org/10.1177/070674371405900204
- O'Sullivan K, Boland F, Reulbach U, Motterlini N, Kelly D, Bennett K, Fahey T (2015) Antidepressant prescribing in Irish children: secular trends and international comparison in the context of a safety warning. BMC Pediatr 15:119. https://doi.org/10.1186/ s12887-015-0436-2
- Pottegård A, Zoëga H, Hallas J, Damkier P (2014) Use of SSRIs among Danish children: a nationwide study. Eur Child Adolesc Psychiatry 23(12):1211–1218. https://doi.org/10.1007/s00787-014-0523-1
- Sarginson J, Webb RT, Stocks SJ, Esmail A, Garg S, Ashcroft DM (2017) Temporal trends in antidepressant prescribing to children in UK primary care, 2000-2015. J Affect Disord 210:312–318. https:// doi.org/10.1016/j.jad.2016.12.047
- Schröder C, Dörks M, Kollhorst B, Blenk T, Dittmann RW, Garbe E, Riedel O (2017) Extent and risks of antidepressant off-label use in children and adolescents in Germany between 2004 and 2011. Pharmacoepidemiol Drug Saf 26(11):1395–1402. https://doi.org/10.1002/pds.4289
- Steffenak AK, Wilde-Larsson B, Nordström G, Skurtveit S, Hartz I (2012) Increase in psychotropic drug use between 2006 and 2010 among adolescents in Norway: a nationwide prescription database study. Clin Epidemiol 4:225–231. https://doi.org/10.2147/CLEP. \$31624
- Volkers AC, Heerdink ER, van Dijk L (2007) Antidepressant use and off-label prescribing in children and adolescents in Dutch general practice (2001-2005). Pharmacoepidemiol Drug Saf 16(9): 1054–1062
- Alessi-Severini S, Biscontri RG, Collins DM, Sareen J, Enns MW (2012) Ten years of antipsychotic prescribing to children: a Canadian population-based study. Can J Psychiatr 57(1):52–58. https://doi.org/10.1177/070674371205700109
- Bachmann CJ, Lempp T, Glaeske G, Hoffmann F (2014) Antipsychotic prescription in children and adolescents: an analysis of data from a German statutory health insurance company from 2005 to 2012. Dtsch Arzteb Int 111(3):25–34. https://doi.org/10. 3238/arztebl.2014.0025
- Edelsohn GA, Karpov I, Parthasarathy M, Hutchison SL, Castelnovo K, Ghuman J, Schuster JM (2017) Trends in antipsychotic prescribing in Medicaid-eligible youth. J Am Acad Child Adolesc Psychiatry 56(1):59–66. https://doi.org/10.1016/j.jaac. 2016.10.005
- Hsu YC, Chien IC, Tan HK, Lin CH, Cheng SW, Chou YJ, Chou P (2013) Trends, correlates, and disease patterns of antipsychotic use among children and adolescents in Taiwan. Soc Psychiatry



- Psychiatr Epidemiol 48(12):1889–1896. https://doi.org/10.1007/s00127-013-0702-2
- Kalverdijk LJ, Tobi H, van den Berg PB, Buiskool J, Wagenaar L, Minderaa RB, de Jong-van den Berg LT (2008) Use of antipsychotic drugs among Dutch youths between 1997 and 2005. Psychiatr Serv 59(5):554–560. https://doi.org/10.1176/ps.2008.59.5.554
- Kalverdijk LJ, Bachmann CJ, Aagaard L, Burcu M, Glaeske G, Hoffmann F, Petersen I, Schuiling-Veninga CCM, Wijlaars LP, Zito JM (2017) A multi-national comparison of antipsychotic drug use in children and adolescents, 2005-2012. Child Adolesc Psychiatry Ment Health 11(55):55. https://doi.org/10.1186/ s13034-017-0192-1
- Lee H, Song DH, Han E, Kang HY (2018) Nationwide epidemiologic study of atypical antipsychotic use among pediatric population with mental illness in Korea. J Child Adolesc Psychopharmacol 28(3):205–215. https://doi.org/10.1089/cap. 2017.0111
- Montastruc F, Bénard-Laribière A, Noize P, Pambrun E, Diaz-Bazin F, Tournier M, Bégaud B, Pariente A (2018) Antipsychotics use: 2006-2013 trends in prevalence and incidence and characterization of users. Eur J Clin Pharmacol 74(5):619–626. https://doi.org/10.1007/s00228-017-2406-0
- Rani F, Murray ML, Byrne PJ, Wong IC (2008) Epidemiologic features of antipsychotic prescribing to children and adolescents in primary care in the United Kingdom. Pediatrics 121(5):1002– 1009. https://doi.org/10.1542/peds.2007-2008
- Ronsley R, Scott D, Warburton WP, Hamdi RD, Louie DC, Davidson J, Panagiotopoulos C (2013) A population-based study of antipsychotic prescription trends in children and adolescents in British Columbia, from 1996 to 2011. Can J Psychiatr 58(6):361– 369. https://doi.org/10.1177/070674371305800608
- Schröder C, Dörks M, Kollhorst B, Blenk T, Dittmann RW, Garbe E, Riedel O (2017) Extent and risks of antipsychotic off-label use in children and adolescents in Germany between 2004 and 2011. J Child Adolesc Psychopharmacol 27(9):806–813. https://doi.org/10.1089/cap.2016.0202
- Schubert I, Lehmkuhl G (2009) Increased antipsychotic prescribing to youths in Germany. Psychiatr Serv 60(2):269. https://doi.org/10. 1176/appi.ps.60.2.269
- Bénard-Laribière A, Noize P, Pambrun E, Bazin F, Verdoux H, Tournier M, Bégaud B, Pariente A (2016) Comorbidities and concurrent medications increasing the risk of adverse drug reactions: prevalence in French benzodiazepine users. Eur J Clin Pharmacol 72(7):869–876. https://doi.org/10.1007/s00228-016-2044-y
- Cunningham CM, Hanley GE, Morgan S (2010) Patterns in the use of benzodiazepines in British Columbia: examining the impact of increasing research and guideline cautions against long-term use. Health Policy 97(2–3):122–129. https://doi.org/10.1016/j. healthpol.2010.03.008
- Hartz I, Furu K, Bratlid T, Handal M, Skurtveit S (2012) Hypnotic drug use among 0-17 year olds during 2004-2011: a nationwide prescription database study. Scand J Public Health 40(8):704-711. https://doi.org/10.1177/1403494812464446
- John A, Marchant AL, McGregor JI, Tan JO, Hutchings HA, Kovess V, Choppin S, Macleod J, Dennis MS, Lloyd K (2015) Recent trends in the incidence of anxiety and prescription of anxiolytics and hypnotics in children and young people: an e-cohort study. J Affect Disord 183:134–141. https://doi.org/10.1016/j.jad. 2015.05.002
- O'Sullivan K, Reulbach U, Boland F, Motterlini N, Kelly D, Bennett K, Fahey T (2015) Benzodiazepine prescribing in children under 15 years of age receiving free medical care on the General Medical Services scheme in Ireland. BMJ Open 5(6):e007070. https://doi.org/10.1136/bmjopen-2014-007070

- Sequi M, Campi R, Clavenna A, Bonati M (2013) Methods in pharmacoepidemiology: a review of statistical analyses and data reporting in pediatric drug utilization studies. Eur J Clin Pharmacol 69(3):599–604. https://doi.org/10.1007/s00228-012-1354-y
- Reale L, Bartoli B, Cartabia M, Zanetti M, Costantino MA, Canevini MP, Termine C, Bonati M, Lombardy ADHD Group (2017) Comorbidity prevalence and treatment outcome in children and adolescents with ADHD. Eur Child Adolesc Psychiatry 26(12): 1443–1457. https://doi.org/10.1007/s00787-017-1005-z
- Thomas R, Sanders S, Doust J, Beller E, Glasziou P (2015) Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics 135(4):e994–e1001. https:// doi.org/10.1542/peds.2014-3482
- Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA (2007) The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry 164(6):942–948. https://doi.org/10.1176/ajp.2007.164.6.942
- Jorm AF, Patten SB, Brugha TS, Mojtabai R (2017) Has increased provision of treatment reduced the prevalence of common mental disorders? Review of the evidence from four countries. World Psychiatry 16(1):90–99. https://doi.org/10.1002/wps.20388
- Arria AM, DuPont RL (2010) Nonmedical prescription stimulant use among college students: why we need to do something and what we need to do. J Addict Dis 29(4):417–426. https://doi.org/ 10.1080/10550887.2010.509273
- Hammad TA, Laughren T, Racoosin J (2006) Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry 63(3):332–339. https://doi.org/10.1001/archpsyc.63.3.332
- Lee ES, Vidal C, Findling RL (2018) A focused review on the treatment of pediatric patients with atypical antipsychotics. J Child Adolesc Psychopharmacol 28(9):582–605. https://doi.org/ 10.1089/cap.2018.0037
- Olfson M, King M, Schoenbaum M (2015) Treatment of young people with antipsychotic medications in the United States. JAMA Psychiatry 72(9):867–874. https://doi.org/10.1001/ jamapsychiatry.2015.0500
- Hilverdink P, Daamen W, Vink C (2015) Children and youth support and care in the Netherlands. Neth Youth Inst (www.nji.nl/english); Rapport (8). http://www.youthpolicy.nl/en/Download-NJi/Publicatie-NJi/Children-and-youth-support-and-care-in-The-Netherlands.pdf
- Vitiello B (2008) An international perspective on pediatric psychopharmacology. Int Rev Psychiatry 20(2):121–126. https://doi.org/ 10.1080/09540260801887710
- Kaplan GA, Shema SJ, Leite CM (2008) Socioeconomic determinants of psychological well-being: the role of income, income change, and income sources during the course of 29 years. Ann Epidemiol 18(7):531–537. https://doi.org/10.1016/j.annepidem. 2008.03.006
- World Health Organization and Calouste Gulbenkian Foundation (2014) Social determinants of mental health. World Health Organization, Geneva
- Bonati M, Jacqz-Aigrain E, Choonara I (2017) Licensed medicines, off-label use or evidence-based. which is most important? Arch Dis Child 102:53–54. https://doi.org/10.1136/archdischild-2016-311527

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Difficulties of children with symptoms of attention-deficit/hyperactivity disorder in processing temporal information concerning everyday life events



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ABSTRACT

It has been hypothesized that children with attention-deficit/hyper activity disorder (ADHD) present difficulties in processing time durations. However, so far evidence on this difficulty and its related mechanisms has been unclear and collected only with rating scales or laboratory experimental tasks. The current study examined whether this difficulty can be seen in children carrying out everyday actions (e.g., telephone calls, cooking activities) and to what extent it is influenced by working memory (WM) abilities. In total, 182 children aged 7 to 10 years were included in the study: 91 children with ADHD symptoms and 91 typically developing (TD) children matched for gender and other characteristics. We administered sequence reordering, time reproduction, and duration comparison tasks, and as stimuli we used six movies lasting 10 to 60 s showing three women completing six different actions. We also collected measures of verbal and visuospatial WM tests (digit span and Corsi task). Children with ADHD symptoms tended to underestimate the long durations and were less accurate than TD children in remembering the exact order of events and in comparing the duration of two different events. These difficulties appeared to be related to WM abilities.

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent, important, and debilitating neurodevelopmental disorder with substantial long-term health and economic consequences that go beyond the recognized poor cognitive, social, behavioral, and academic characteristics (Barkley, 2014). Adequate temporal abilities are required to successfully adapt to the temporal constraints of the environment (e.g., not too fast or too slow response times, crossing a busy street, social interactions) (Grondin, 2010). Current ADHD theory and empirical works suggest that individuals with ADHD have deficits in time processing that may contribute to poor cognitive and behavioral outcomes (Noreika, Falter, & Rubia, 2013; Toplak, Dockstader, & Tannock, 2006). Temporal processing skills may play an important role in the deficits observed in ADHD. Impulsivity can be defined as a temporally inadequate and premature behavioral style where responses are made early, inaccurately, and without consideration of future consequences. Deficits in time estimation or an altered sense of time could indeed underlie several problems of impulsiveness such as problems with waiting behavior, delaying responses, and delaying gratification.

One of the most influential models of time processing, scalar expectancy theory (SET; Gibbon, Church, & Meck, 1984), posits that timing behavior is based on the output of an internal clock; temporal processing depends on the number of pulses (temporal information) emitted by a pacemaker and stored in an accumulator. It has been suggested that internal time runs faster for children with ADHD than for typically developing (TD) children (Barkley, Koplowitz, Anderson, & McMurray, 1997; Rubia, Schuri, Cramon, & Poeppel, 1997). These results can be linked to a series of factors (e.g., motivation-modulated delay aversion; Sonuga-Barke, Taylor, Sembi, & Smith, 1992), suggesting that children with ADHD are impulsive in reacting to long durations but not to very short durations (Barkley, 2001). However, temporal dysfunction in children with ADHD has also been linked to poor attentional and working memory (WM) abilities. Attentional factors have long been argued as important in both healthy adults' and children's time perception (Zakay, 1992), and subjective time is in fact viewed as a direct function of the amount of attention allocated to processing the passage of time (Grondin, 2010; Zakay & Block, 1995, 1996). According to attentional gate model (Zakay & Block, 1995, 1996), an attentional gate controls the flow of temporal information from the pacemaker to the accumulator; when attention is fully dedicated to timing, the gate is open wide, leading to more pulses into the accumulator and resulting in longer perceived durations and more accurate temporal judgments (Zakay & Block, 1995, 1996). Conversely, when attention is not fully allocated to processing time, less temporal information is stored in the accumulator and the temporal interval is judged to be shorter than the actual duration, thereby producing temporal underestimation (Zakay & Block, 1995, 1996). All this suggests that children with attention problems, such as those with ADHD, should show greater impairment in time processing than TD children, especially in underestimating long durations (Noreika et al., 2013; Toplak et al., 2006; Zakay, 1992). In fact, given the limited storage capacity of their attentional system and also their high level of inattention, children with ADHD might allocate less attention to processing temporal information, which would result in temporal underestimation (Noreika et al., 2013; Toplak et al., 2006).

Previous studies have indeed found temporal difficulties in children with ADHD in a number of tasks (i.e., duration discrimination, finger tapping, and duration reproduction tasks; Mioni, Santon, Stablum, & Cornoldi, 2016; Noreika et al., 2013; Toplak et al., 2006). In particular, time reproduction tasks have been widely used in children with ADHD (Barkley et al., 1997; Noreika et al., 2013; Toplak et al., 2006) because they can be easily understood (Droit-Volet, 2010) and are appropriate when relatively long temporal intervals are used (Mioni, 2018; Mioni, Stablum, McClintock, & Grondin, 2014). In these tasks, participants are required to reproduce the duration of the stimulus that has previously been presented (standard duration). First participants experience the standard duration, and then they are required to delimit a time period of the same length. Temporal performance in a time reproduction task primarily depends on attention and working memory, which are necessary to elaborate and subsequently retrieve and reproduce the specific duration (Mioni et al., 2014, 2016; Mioni, 2018). The

results revealed lower accuracy (generally greater temporal underestimation with longer intervals) and higher temporal variability in children with ADHD compared with controls (Noreika et al., 2013).

Although some studies have reported temporal impairment in children with ADHD (e.g., Noreika et al., 2013; Toplak et al., 2006), other studies have shown that this deficit might not be general (Noreika et al., 2013; Smith, Taylor, Warner-Rogers, Newman, & Rubia, 2002) and argued that such a deficit might depend on the nature of the task (Meaux & Chelonis, 2003) and on the type of required response (Bauermeister et al., 2005). Furthermore, empirical support for the hypothesized temporal deficits in children with ADHD has been based on studies conducted in laboratory settings that used traditional timing tasks (Noreika et al., 2013; Toplak et al., 2006). Rigorous constraints were placed on the behavior of the children with ADHD, thereby possibly either exaggerating or, conversely, masking the true magnitude of these temporal dysfunctions.

Although laboratory paradigms are essential to test and develop theoretical understanding, they generally lack ecological validity (Rapport, Chung, Shore, Denney, & Isaacs, 2000). Surprisingly, temporal abilities have hardly ever been studied in experimental conditions similar to everyday life situations. This point is crucial not only because these situations may better predict children's actual behavior in real life but also because they are less abstract than typical temporal tasks and include content that can be more meaningful and motivating for children. Indeed, it has been argued that motivational factors may also contribute to failures in temporal tasks in children with ADHD (Carlson, Mann, & Alexander, 2000; McInerney & Kerns, 2003; Van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005).

In the current study, we decided to test the temporal abilities of children with ADHD and TD children in a series of different temporal tasks while using everyday activities of different durations. We also manipulated the method of the reproduction task and asked the children to either imagine the action, wait for the same amount of time it had been presented and then press a key (imagine condition), or mimic the action for the same amount time it had been presented and then press a key (mimic condition). In this way, we were able to examine whether the request for a motor response could reduce any possible difficulty in time processing. It is well known that individuals tend to activate mirror processes that represent the actions they observe and lead them to imitate those actions (Iacoboni, 2009; Rizzolatti, Fabbri-Destro, & Cattaneo, 2008). It has also been observed that replicating an action for the same length of time could be more meaningful for children and could also support their attention.

Interestingly, we also introduced two other temporal tasks to assess two important aspects of time processing and everyday life experience: *sequential organization* of events and *temporal comparison*. The ability of children to remember the correct order of appearance of events (sequential organization task) may be preserved even if information on their respective durations is lost. One example could be getting dressed to go to school. Children do not need to know the exact time they take to put socks on (in seconds), but they need to know the sequence of events (i.e., socks before shoes). Similarly, examining the ability to discriminate between different durations allows one to investigate whether some general representation of temporal information is preserved in children with ADHD despite a possible impairment at their internal clock level. If temporal misperception in ADHD is caused only by variation in the internal clock, no errors should be found in a time duration comparisons task because all durations should be affected in the same way.

As we mentioned above, processing and long-term maintenance of time information seem supported by a temporary memory system able to maintain and process information. It has indeed been suggested that the success of children with ADHD in reproduction tasks might be related to WM measures (Marx et al., 2010). However, evidence is still scarce, and to our knowledge it has never been investigated whether WM modality (verbal vs. visuospatial) may be more greatly involved and whether this involvement may concern correct recall of the order of events and ability to compare different durations. There is evidence suggesting that space and time share common mechanisms (Walsh, 2003), and therefore it could be argued that visuospatial WM is more related to time processing than verbal WM. Nevertheless, also the opposite prediction could be made, especially in the case of the sequential organization task, due to the fact that verbal WM implies a stronger constraint on the maintenance of the serial order (Baddeley, 1996). We collected measures of both verbal (digit span; Wechsler, 2003) and spatial (Corsi task; Mammarella, Toso, Pazzaglia, & Cornoldi, 2008) WM abilities.

In sum, the current study aimed to investigate temporal abilities in children with ADHD and TD children by proposing more naturalistic stimuli (video representing everyday activities of durations ranging between 10 and 60 s) and using three different tasks: duration reproduction, sequential ordering of events, and duration comparisons.

In general, we predicted temporal impairment in children with ADHD compared with controls. More specifically, for the reproduction task, we predicted an effect of duration—as standard durations increased, children with ADHD would show lower accuracy and greater under-reproduction than controls due to attentional and WM dysfunctions (Mioni et al., 2014, 2016; Mioni, 2018). We also examined whether temporal misperception could depend not only on inefficient encoding but also on the characteristics of the required response. We anticipated that this error could be reduced if children were involved in the mimic response condition because we believed that the motor–mimic response could enhance imitative meaningful representations and favor temporal performance.

Concerning the other two tasks, in the absence of clear previous evidence, we predicted a general temporal impairment in children with ADHD that would also affect the sequential organization and temporal comparison tasks. However, on the basis of the hypothesis that time reproduction is more demanding and that it specifically taps temporal abilities, we hypothesized that children with ADHD might find no difficulty or less difficulty in these two tasks.

Method

Participants

In total, 182 primary school children were included in the study (Table 1): 91 children with symptoms of ADHD and 91 TD children. Among children with ADHD, 3 were excluded because they were absent from school at the time of testing. The groups were matched for gender, grade, age, family environment, and average estimated intelligence based on the information offered by the teachers and parents. The following rating scales were used: SDAI (Scala per i Disturbi di Attenzione|Iperattività per Insegnanti [ADHD scale for teachers]; Capodieci, 2017; Marzocchi, Re, & Cornoldi, 2010) and two items from SDAG (Scala per i Disturbi di Attenzione/Iperattività per Genitori [ADHD scale for parents]; Marzocchi et al., 2010). Within each group, participants were randomly divided into two subgroups depending on the condition used to perform the time reproduction task: imagine (children with ADHD = 47, TD children = 42) or mimic (children with ADHD = 44, TD children = 49) condition (see "Materials and general procedure" section). No differences were observed between subgroups. Because explicit diagnoses of ADHD are infrequently made in Italy, children with ADHD were identified by the authors based on a screening process that included interviews and required a score of 14 or higher (the diagnostic cutoff given in the manual) on one or both subscales of the SDAI (Marzocchi et al., 2010). Also required was the presence of either inattentive symptoms or hyperactive/impulsive symptoms (or both) in the home context, and this was based on the written reports provided by the parents, who filled in two items of the scale and provided a brief interview. Children with symptoms of

Table 1Means (and standard deviations) for the characteristics of the two groups and results of the group comparisons with the Student's *t* test and Cohen's *d*.

	Range	Children with ADHD M (SD)	TD children M (SD)	t	р	d
Age (years)	7.5-10	8.75 (1.25)	8.81 (1.33)	0.35	.724	0.04
SDAI inattention	0-27	14.81 (6.11)	3.58 (2.92)	15.83	.001	2.34
SDAI hyperactivity	0-27	10.83 (6.47)	1.78 (2.28)	12.59	.001	1.86
SDAG inattention	0-3	1.55 (1.11)	1.21 (0.90)	2.27	.024	0.33
SDAG hyperactivity	0-3	1.04 (1.07)	0.54 (0.64)	3.86	.001	0.57

Note. ADHD, attention-deficit/hyperactivity disorder; TD, typically developing; SDAI, ADHD scale for teachers (Marzocchi et al., 2010); SDAG, ADHD scale for parents (Marzocchi et al., 2010).

ADHD were mostly inattentive (n = 50), whereas the remaining ones were either of the hyperactive (n = 20) or combined (n = 21) presentation.

Exclusion criteria were dyslexia, dyscalculia, other comorbid diagnoses (e.g., conduct disorder), and poor comprehension of the instructions. To control for WM ability, we administered the digit span subtest from the Wechsler Intelligence Scale for Children–Fourth Edition (WISC-IV; Wechsler, 2003) and the Corsi task from BVS (*Batteria per la valutazione visiva e spaziale* [Battery for Visuospatial Assessment]; Mammarella et al., 2008), both including the forward and backward versions of the test. Thus, we acquired measures of verbal and visuospatial WM resulting from the combination of the scores obtained in the two versions.

Procedure

All participants were tested in a quiet room of their primary school in Bari or Padova, Italy, during an individual meeting with the experimenter that lasted approximately 40 min. The temporal sequence and time reproduction task were presented on a 14-inch computer monitor, with participants seated at a distance of approximately 60 cm from the monitor. Children agreed to participate in the study and were informed that their participation was voluntary and that they could end it at any time. The study was conducted in accordance with the ethical guidelines of the Department of General Psychology, University of Padova, and received ethical and institutional approval by the school board. Moreover, all the children's parents gave their written consent.

Materials and general procedure

SDAI and SDAG

These scales are widely used in Italy and have been validated for the Italian population, with high inter-judge and test–retest reliabilities (r > .80 in both cases), discriminatory power, and concurrent validity obtained by correlating the scales with other scales (r > .95; Marzocchi et al., 2010).

The SDA (*Scale per i Disturbi di Attenzione/iperattività* [ADHD scale]) has a version for parents (SDAG) and one for teachers (SDAI). These scales reflect exactly the 18 symptoms listed in the Diagnostic and Statistical Manual of Mental Disorders–Fifth Edition (DSM-5; American Psychiatric Association, 2013) for diagnosing ADHD and include two subscales, one for inattention (nine items) and one for hyperactivity/impulsivity (nine items). Teachers and parents are asked to closely monitor a child's behavior for about 2 weeks and report the frequency of the types of symptomatic behavior described in each item. Scores for the items of the SDAI and SDAG scales range from 0 (*problem behavior never recorded*) to 3 (*problem behavior very often recorded*).

The SDAI scale also includes questions regarding the family environment and estimated intelligence together with the specific items about inattentive and hyperactive/impulsive symptoms. In the current study, the teachers were invited to fill in the whole scale, whereas in the case of the parents, due to the difficulty of involving all the parents in such a complex effort, only two items of the corresponding scale (SDAG) were administered, one about the presence of inattentive behaviors and the other about the presence of hyperactive/impulsive behaviors. The parents were also administered an informal interview aiming to confirm the presence in the home context of the ADHD symptoms emerging in the school context. Previous studies with a similar population of parents (Capodieci, Lachina, & Cornoldi, 2018; Capodieci, Rivetti, & Cornoldi, 2016; Re, Capodieci, & Cornoldi, 2015) had found that many parents did not return the questionnaire if they needed to fill it in by themselves, thereby causing loss of important information, whereas they agreed to answer simple questions and fill in only two items during the interview with the experimenter. On the same occasion, parents signed the informed consent and received detailed information about the task and the experimental procedure.

Timing task: Video production

The temporal stimuli were six actions presented in short videos showing three actresses performing six everyday activities in a kitchen. The actions were presented in the same constant order: a phone call, reading, cleaning the cooker, sweeping the floor, cooking, and playing cards. In each video,

the activities were presented for durations of 10 to 60 s, balancing the durations of the different actions. To maintain the videos in approximately the same structure and overall duration (210 s), the order of the actions remained the same but the order of duration was balanced (Fig. 1A), with each action starting when the previous one was almost over. Participants were individually tested in a quiet room at their school and were instructed to watch the video, presented on a computer screen, because they would be subsequently interviewed about the film and tested on the duration of the actions. A practice trial was run in order to ensure that children had understood the nature of a reproduction task; the experimenter scribbled on a sheet of paper for 35 s, and children needed to reproduce the action for the same length of time. The overall video duration was kept relatively short in order not to lower child motivation and attention. An observer located in front of the children to check that they were looking directly at the screen and were not distracted by other information found that all children followed the video with attention and appeared motivated to the task. Immediately after the end of the video presentation, six cards representing the same actions were randomly placed on the table, and children needed to perform the sequential organization task. If children made any errors in the sequence, the correct sequence was shown to them to test the duration of the different actions following the order in which they had been presented. At the end of the time reproduction task, children were administered the time comparison task.

Sequential organization task

For the sequential organization task, which immediately followed the presentation of the video, we created six cards representing the six actions shown in the videos and presented them to the children in random order. They were asked to sequentially reorder the cards according to the sequence seen in the video. One point was attributed to each card–action set in the correct order (maximum score = 6 points). The definition of the correct order was based on the procedure adopted in a previous work (Lanfranchi, Cornoldi, & Vianello, 2004), according to which an item is considered correctly ordered if it precedes an item that has been presented successively.

Time reproduction task

The time reproduction task required participants to reproduce the duration of the actions presented earlier. During the reproduction phase, in one condition (half of the participants) the children were asked to imagine doing the action, wait for the same interval of time, and then press a key (imagine condition); in the second condition, the children were asked to mimic the action presented for the same time as the action observed in the video and then press a key (mimic condition) (Fig. 1B). Both absolute and relative errors were computed for each action.

Temporal comparison task

Using the same cards previously used in the sequential organization task, pairs of actions were presented and the children were asked to judge which of the two actions had lasted longer in the video they had seen. Eight pairs of actions were presented, with temporal intervals between actions lasting 40 s (10-50 and 60-20 s), 30 s (50-20 and 10-40 s), 20 s (30-10 and 40-20 s), and 10 s (30-40 and 60-50 s). One comparison was used to explain the task to the children (60-10 s). For the scoring, 1 point was attributed to each correct comparison (maximum score = 8 points).

Results

Time reproduction task

Performance in the time reproduction task was analyzed in terms of absolute and relative errors (Glicksohn & Hadad, 2012; Mioni, 2018). The absolute error was calculated by putting in absolute value (i.e., without reference to the direction of the error) the difference between time reproduction (Rd) and target duration (Td) divided by the target duration [absolute error = |Rd - Td|/Td]. A greater absolute error indicated poorer performance given that the time reproduced was further from the target duration. The relative error was obtained by dividing each participant's time performance by the

Activity	Video 1	Video 2	Video 3	Video 4	Video 5	Video 6
Phone call	40	50	20	60	30	10
Reading	50	30	10	40	60	20
Cleaning the cooking	30	10	40	20	50	60
Sweeps the floor	20	60	30	10	40	50
Cooking	60	20	50	30	10	40
Play cards	10	40	60	50	20	30

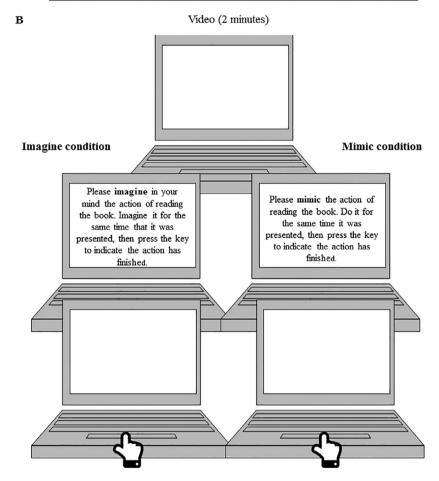


Fig. 1. Description of the time reproduction task used. (A) Description of videos with activities and durations. (B) Graphical representation of the experimental procedure used during the time reproduction task in the imagine and mimic conditions. Participants first watched the full video and then read the instruction to reproduce the duration of each action depending on the experimental condition (imagine or mimic). Participants were instructed to press a key to conclude the reproduction.

time duration of the interval presented for that trial [relative error = Rd/Td]. This also provided an index of the direction of errors, with coefficients above and below 1.0 being indicative of over-reproduction and under-reproduction, respectively. Separate repeated-measures analyses of variance

(ANOVAs) on absolute and relative errors were computed with group (ADHD vs. TD) and condition (imagine vs. mimic) as between-participants factors and action duration (10, 20, 30, 40, 50, or 60 s) as the within-participant factor. All significant analyses were followed by post hoc analyses performed with Bonferroni correction to reduce the Type I error rate, and the effect size was estimated as partial eta squared (η_p^2) .

Analyses of absolute error revealed significant effects of group, F(1, 178) = 110.83, p < .001, $\eta^2 = .38$, and action duration, F(5, 890) = 4.43, p < .001, $\eta_p^2 = .02$. Children with ADHD were less accurate than TD children (children with ADHD: M = .56; TD children: M = .31), and long durations produced greater errors (Figs. 2 and 3A). Group interacted with action duration, F(5, 890) = 2.94, p = .012, $\eta_p^2 = .02$, indicating that children with ADHD were less accurate than TD children as action duration increased (all ps < .001, $\eta_p^2 \ge .07$), but children with ADHD and TD children equally reproduced 10-s action duration

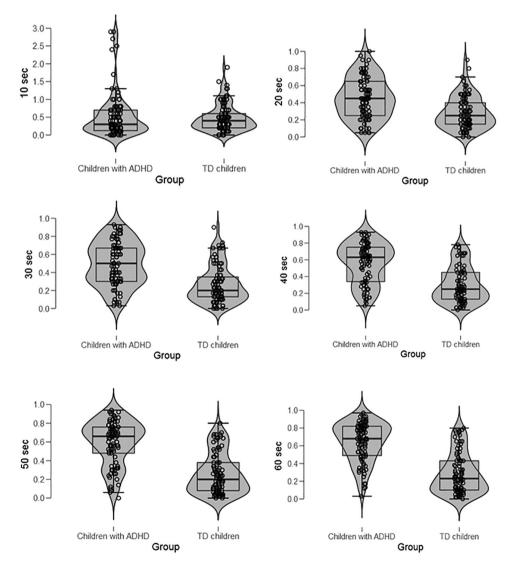
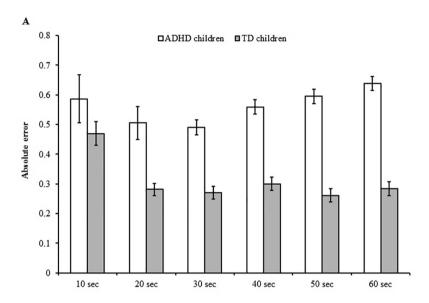


Fig. 2. Mean proportional absolute error for children with ADHD and TD children as a function of time durations. Each dot represents a participant.

 $(p = .201, \eta_p^2 = .01)$. Children with ADHD were less accurate in reproducing 50- and 60-s durations than in reproducing 30-s ones, whereas no differences between durations were observed among TD children (Figs. 2 and 3A). No main effect of condition or other significant interactions were observed (all $ps \ge .053, \eta_p^2 \ge .01$).

Analyses of relative error revealed significant effects of group, F(1, 178) = 25.63, p < .001, $\eta^2 = .13$, and action duration, F(5, 890) = 90.49, p < .001, $\eta_p^2 = .34$. Children with ADHD under-reproduced more than TD children with ADHD: M = .56; TD children: M = .31), and in general all children under-reproduced action duration as durations increased. Moreover, group interacted with action



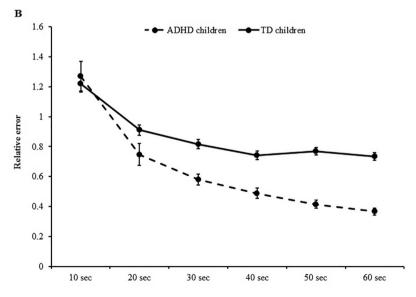


Fig. 3. Mean proportional absolute errors (A) and mean relative errors (B) for children with ADHD and TD children as a function of time durations.

duration, F(5, 890) = 7.85, p < .001, $\eta_p^2 = .04$, children with ADHD under-reproduced more than TD children as action duration increased (all $ps \le .042$, $\eta_p^2 \ge .02$), but children with ADHD and TD children equally reproduced 10-s action durations (p = .669, $\eta_p^2 = .01$) (Fig. 3B). No main effect of condition or other significant interactions were observed (all $ps \ge .189$, $\eta_p^2 \ge .01$).

Sequential organization task and temporal comparison task

Analyses showed that children with ADHD were less accurate than TD children in both sequential organization and temporal comparison tasks (Table 2). All children did relatively well in the sequential organization task—at least in accordance with the liberal criterion we had adopted—showing that, in general, they were able to remember the order of the actions presented. However, the mean number of errors was three times higher ($\bar{x} = 1.54$) among children with ADHD than among TD children ($\bar{x} = .51$), and the group difference was highly significant with a large effect size (d = 1.29).

Because the data from the temporal comparison task consisted of a series of dichotomous responses (correct/incorrect) repeated by the participants, logistic mixed-effects models were used (Baayen, Davidson, & Bates, 2008); this approach has been shown to be appropriate for forcedchoice repeated responses (Jaeger, 2008). Distance (as a within-participant factor: 40, 30, 20, or 10) and group (as a between-participants factor: control vs. ADHD) were entered into the model as fixed effects, Participants were entered as random effects. The significance of the effects was tested using likelihood ratio tests for nested models (Pinheiro & Bates, 2000), Odds ratios (ORs) were used as measures of effect size. The analysis was conducted using the "lme4" package (Bates, Mächler, Bolker, & Walker, 2015) of the R software. A significant main effect of distance emerged, $\chi^2(3) = 107.46$, p < .001; the analysis of the model coefficients showed that the performance at a distance of 40 was significantly superior to the performance at both a distance of 20 (OR = 0.60, p = .004) and a distance of 10 (OR = 0.25, p < .001) but was not significantly superior to the performance at a distance of 30 (OR = 1.20, p = .34); furthermore, the performance at a distance of 20 was significantly superior to the performance at a distance of 10 (OR = 0.41, p < .001). A significant main effect of group also emerged, $\chi^2(1) = 76.94$, p < .001 (Fig. 4); the analysis of the model coefficients showed that the performance of the control group was significantly better than the performance of the ADHD group (OR = 0.32, p < .001). The interaction between distance and group, however, was not significant, $\chi^2(3) = 2.21$, p = .53.

WM performance and correlation analyses

Children with ADHD obtained significantly lower scores in the WM measures than TD children (Table 2). Table 3 presents the correlations between the overall performances in the three time processing tasks (for the case of the time reproduction task, the mean absolute error was considered) and the performances in the verbal and visuospatial WM tasks (combined score for the forward and backward versions).

In general, a higher level of WM performance corresponded to better time processing. As can be seen in Table 3, the three time processing tasks significantly correlated with the two WM tasks. In

Table 2Means (and standard deviations) for the score on WM measures and results of the group comparisons with the Student's *t* test and Cohen's *d*.

	Children with ADHD <i>M</i> (<i>SD</i>)	TD children M (SD)	t	р	d
Digit span forward	4.96 (1.05)	5.30 (1.00)	2.23	.027	0.33
Digit span backward	2.96 (0.96)	3.30 (0.78)	2.62	.010	0.39
Verbal WM (mean score)	7.91 (1.59)	8.59 (1.32)	3.14	.002	
Corsi task forward	4.26 (0.96)	4.59 (0.94)	2.33	.021	0.31
Corsi task backward	3.40 (1.04)	3.66 (0.99)	1.75	.082	0.26
Visuospatial WM (mean score)	7.66 (1.66)	8.25 (1.64)	2.43	.016	

Note. WM, working memory; ADHD, attention-deficit/hyperactivity disorder; TD, typically developing.

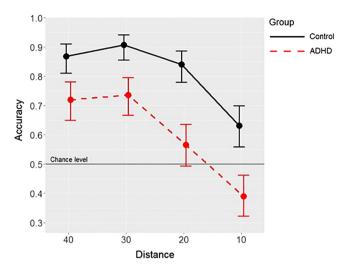


Fig. 4. Estimated accuracy in the time comparison task as a function of the distance between the two compared times. Error bars represent 95% confidence intervals.

particular, verbal WM correlated negatively with mean absolute error (r = -.26) and positively with sequential organization task (r = .26) and temporal organization task (r = .30), and visuospatial WM correlated negatively with mean absolute error (r = -.30) and positively with sequential organization task (r = .27) and temporal organization task (r = .20). These correlations were similar in the two groups when considered separately.

However, WM performance did not explain the group differences in time processing. For example, the group differences in time reproduction remained when we controlled for WM (included as covariate). Analyses of absolute error revealed significant effects of group, F(1, 176) = 94.08, p < .001, $\eta_p^2 = .35$, and visuospatial WM, F(1, 176) = 8.30, p = .004, $\eta_p^2 = .04$. The Group × Action Duration interaction, F(5, 880) = 1.20, p = .076, $\eta_p^2 = .08$, was no longer significant. Confirming our previous results, analyses of relative error revealed significant effects of group, F(1, 176) = 18.41, p < .001, $\eta_p^2 = .09$, and action duration, F(5, 880) = 3.05, p = .010, $\eta_p^2 = .02$, and a significant Group × Action Duration interaction, F(5, 880) = 7.43, p < .001, $\eta_p^2 = .04$].

Discussion

There is increasing evidence that children with ADHD have weaknesses in time processing (Barkley et al., 1997; Noreika et al., 2013; Toplak et al., 2006), which have been hypothesized as possibly crucially related to some typical characteristics of these children such as attentional processes, inhibition capacity, and WM. However, it has also been reported that for some time processing tasks and conditions children with ADHD may be just as competent as TD children (Smith et al., 2002). Furthermore, despite the fact that clinical reports and questionnaire-based observations typically concern these children's behaviors in meaningful everyday contexts, available experimental evidence has mainly considered reproduction of abstract durations in laboratory-based tasks (Mioni et al., 2016; Talbot & Kerns, 2014). These kinds of tasks do not offer experimental evidence concerning difficulty in the time processing of events, in the specific pattern of these difficulties and in possibly underlying cognitive mechanisms.

A first important result of the current study has been to confirm that children with ADHD are less correct than TD children in processing time information, also with reference to meaningful actions. This was found in three tasks/events—temporal sequencing, duration reproduction, and duration comparison—that have different characteristics and implications, thereby showing that the difficulty is rather general and not limited to a specific task. The main task that required reproducing durations

Table 3 Pearson's correlation analyses for children with ADHD, TD children, and the total sample between temporal tasks (time reproduction, sequential organization, and temporal comparison) and WM measures (verbal and visuospatial).

	ADHD children n = 91		TD children n	TD children n = 91			All sample n = 182		
	Time reproduction task	Sequential organization task	Temporal comparison task	Time reproduction task	Sequential organization task	Temporal comparison task	Time reproduction task	Sequential organization task	Temporal comparison task
Verbal WM Visuospatial WM	126 280**	.178 [*] .216 [*]	.223* .108	217° 221°	.148 .205	.203 [*] .126	265** 305**	.260** .267**	.304** .197**

Note. ADHD, attention-deficit/hyperactivity disorder; TD, typically developing; WM, working memory.

^{*} p < .05 * p < .001

offered further information. First, the difficulty observed in children with ADHD was quite general and was not affected by the type of required response, either imagine or mimic. The fact that the children were not helped by repeating the observed action could be due to the fact that the two-response condition did not change representations in the children's minds, in line with the hypothesis that the activity of imagining an action involves the same processes as performing that action (Decety, 1996; Jeannerod & Frak, 1999). In any case, the general difficulty that children with ADHD had with the task shows that they also have difficulty with meaningful and potentially motivating actions. Second, the error of children with ADHD mainly concerned the underestimation of relatively long durations (in the current study, especially 40 and 50 s), whereas this effect was not found for shorter durations and was even reversed for the shortest duration (10 s). This tendency to underestimate long durations is in line with, and extends, previous evidence (Mullins, Bellgrove, Gill, & Robertson, 2005) and could be due to different factors, for example, these children's lack of self-control that produces loss of attention for prolonged activities and reduction of response times. The effect could be also associated (as hypothesized by Antrop et al., 2006) with the typical delay aversion presented by children with ADHD, in association with the underestimation of the duration of events and overestimation of the duration of delays, and the consequent anticipation of the response. However, it should be underlined that difficulty in representing durations was also observed when the memory for exact durations was not required and the children were only asked to compare durations. This also excludes that difficulty in duration reproduction is simply due to a more rapid mental clock that shortens relatively long durations because, in that case, all durations should have maintained the same patterns of differences, making the time comparison task easier.

In sum, the time processing deficit of children with ADHD proved to be very general given that it concerned not only memory for actual durations but also memory for the relative length of the durations and also particularly different temporal information, that is, the memory of the order in which different actions were carried out. This last result appears to be important because it extends the evidence concerning the time processing difficulties of children with ADHD and may offer an explanation for some difficulties these children have in understanding meaningful sequences of events as happens, for example, in story comprehension (Lorch, Milich, Astrin, & Berthiaume, 2006).

The most trivial explanation of these results could be that the children with ADHD participating in the experiment did not pay attention to the video, but this does not seem to be the case given that all the children showed interested in it, were (in the case of the mimic group) able to repeat the actions, and said that they had liked the task and had paid attention to the video.

Therefore, the failure in all three time processing tasks seems to be due to a general difficulty these children have in processing temporal information. Results showed that WM supports time processing given that significant correlations were found between WM tasks and all the time processing tasks. The WM weaknesses that children with ADHD have been shown to have (Martinussen & Tannock, 2006) could be a factor in explaining their time processing deficits. In particular, it cannot be excluded that WM abilities, which in children with ADHD also involve poor serial recall (Kasper, Alderson, & Hudec, 2012), may have had a specific role in the loss of serial information.

However, it should be noted that, due to time constraints decided by the schools where the study was carried out, we were able to collect only a limited number of potentially relevant measures; concerning WM, we could not administer time-demanding highly controlled WM tasks. We collected only two measures that, according to some models of WM, represent mainly passive or modestly active WM components (e.g., Cornoldi, Giofrè, Calgaro, & Stupiggia, 2013, Cornoldi & Vecchi, 2003) that, in children with ADHD, are less crucially impaired than more active components. In fact, also in the current study, neither the difference in WM measures nor the correlation with time processing tasks was particularly high (Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001). In this respect, it should also be noted that, despite a slight difference (i.e., the nonsignificant interaction in the case of absolute error), the difficulty of children with ADHD in time processing persisted even after controlling for WM.

The current study has some limitations that need to be considered in future research. For example, if the schools had given permission to test the children on other measures and to collect other information, it might have been possible to examine the role of other aspects potentially involved in time processing such as attention, active WM, and inhibition. Future research should examine this issue and replicate the study with larger clinical samples of children with explicit diagnoses of ADHD

and other disorders (e.g., children with learning disabilities and borderline intellectual functioning). In Italy, ADHD is generally diagnosed with caution and typically only in very severe cases in children who usually have several comorbidities. In addition, the use of ADHD scales for teachers and parents tends to emphasize the presence of attentional problems, with the consequence that children of the inattentive type can be overrepresented. Future research should use more specific and complete questionnaires and diagnostic tools in order to put together a well-diagnosed ADHD group and investigate differences between children with different ADHD symptoms (predominantly inattentive, predominantly impulsive/hyperactive, and combined) and possibly associated profiles such as sluggish cognitive tempo symptoms. It should also be noted that, in the absence of a diagnosis, we preferred not to consider separately the performance of children with different manifestations (inattentive, impulsive/hyperactive, and combined). However, preliminary analyses suggest that the pattern of performance did not substantially vary depending on ADHD manifestation. For example, the analysis of the data from the sequential organization task using the ADHD presentation as another between-participants factor did not find any significant effect related to ADHD manifestations (p = .76).

Future research should also check for boundary conditions related to the experimental research. For example, we considered only actions carried out in the home, they were performed only by female actresses in the videos, and we balanced the durations of the actions but not the action order: these aspects should be considered in future research studies in order to examine their roles.

Albeit with the above limitations, the current study has important educational and clinical implications. In school and life contexts, it is fundamental to consider the time processing difficulties of children with ADHD given that all academic disciplines require understanding and managing the concept of time and that meeting deadlines is one of the main requests in everyday life and at school. For this reason, in a clinical context with children with ADHD, it would be important to work on time processing, managing time, and planning to help them perform better in time-based school and extraschool activities.

Conclusion

Our study supports the hypothesis that children with s ADHD have a general time processing deficit compared with TD children and also sheds light on the important role of WM. Some studies have shown that this deficit might not be general (Smith et al., 2002) and could depend on the nature of the task (Meaux & Chelonis, 2003) or on the type of required response (Bauermeister et al., 2005). Furthermore, empirical support for the hypothesis of temporal deficits in children with ADHD has been based on studies conducted in laboratory settings using traditional timing tasks (Noreika et al., 2013; Toplak et al., 2006). In our study, instead we considered experimental situations close to the ones children with ADHD may meet in everyday life, and we found time processing difficulties in all the tasks proposed (sequential organization, temporal comparison, and time reproduction). Cognitive and behavioral functioning of children with ADHD, including temporal-related problems, is more relevant and manifest in the course of everyday activities in complex environments (Rapport et al., 2000) than in laboratory settings. Using an experimental task proposing everyday life situations is, we believe, a strength of our study, not only because we think that these situations may better predict children's actual behavior in real life but also because they are less abstract than typical duration tasks and include event content that can be more meaningful and motivating for the children.

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References

- American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.
- Antrop, I., Stock, P., Verté, S., Wiersema, J. R., Baeyens, D., & Roeyers, H. (2006). ADHD and delay aversion: The influence of non-temporal stimulation on choice for delayed rewards. *Journal of Child Psychology and Psychiatry*, 47, 1152–1158.
- Baayen, R. H., Davidson, D. J., & Bates, D. M. (2008). Mixed-effects modeling with crossed random effects for subjects and items. *Journal of Memory and Language*, 59, 390–412.
- Baddeley, A. (1996). Exploring the central executive. Quarterly Journal of Experimental Psychology, 49, 5–28.
- Barkley, R. A. (2001). The executive functions and self-regulation: An evolutionary neuropsychological perspective. Neuropsychology Review, 11, 1–29.
- Barkley, R. A. (2014). Attention-deficit hyperactivity disorder: A handbook for diagnosis and treatment (4th ed.). New York: Guilford. Barkley, R. A., Edwards, G., Laneri, M., Fletcher, K., & Metevia, L. (2001). Executive functioning, temporal discounting, and sense of time in adolescents with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). Journal of Abnormal Child Psychology, 29, 541–556.
- Barkley, R. A., Koplowitz, S., Anderson, T., & McMurray, M. B. (1997). Sense of time in children with ADHD: Effects of duration, distraction, and stimulant medication. *Journal of the International Neuropsychological Society*, 3, 359–369.
- Bates, D., Mächler, M., Bolker, B. M., & Walker, S. C. (2015). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software* 67, 1–48.
- Bauermeister, J. J., Barkley, R. A., Martínez, J. V., Cumba, E., Ramírez, R. R., Reina, G., ... Salas, C. C. (2005). Time estimation and performance on reproduction tasks in subtypes of children with attention deficit hyperactivity disorder. *Journal of Clinical Child & Adolescent Psychology*, 34, 151–162.
- Capodieci, A. (2017). L'uso delle scale di valutazione per l'identificazione dei casi con ADHD: Il confronto tra la rilevazione in base a punteggi di gravità, cut-off e numero di sintomi [The use of rating scales for the identification of ADHD: A comparison between criteria of intensity, cut-offs, and number of symptoms]. *Psicologia Clinica e dello Sviluppo*, 21, 277–290.
- Capodieci, A., Lachina, S., & Cornoldi, C. (2018). Handwriting difficulties in children with attention deficit hyperactivity disorder (ADHD). Research in Developmental Disabilities, 74, 41–49.
- Capodieci, A., Rivetti, T., & Cornoldi, C. (2016). A cooperative learning classroom intervention for increasing peers' acceptance of children with ADHD. *Journal of Attentional Disorder*, *4*, 41–49.
- Carlson, C. L., Mann, M., & Alexander, D. K. (2000). Effects of reward and response cost on the performance and motivation of children with ADHD. *Cognitive Therapy and Research*, 24, 87–98.
- Cornoldi, C., Giofrè, D., Calgaro, G., & Stupiggia, C. (2013). Attentional WM is not necessarily specifically related with fluid intelligence: The case of smart children with ADHD symptoms. *Psychological Research Psychologische Forschung*, 77, 508–515.
- Cornoldi, C., & Vecchi, T. (2003). Visuo-spatial working memory and individual differences. Hove, UK: Psychology Press. Decety, J. (1996). Do imagined and executed actions share the same neural substrate? Cognitive Brain Research, 3(2), 87–93.
- Droit-Volet, S. (2010). Stop using time reproduction tasks in a comparative perspective without further analyses of the role of the motor response: The example of children. *European lournal of Cognitive Psychology*, 22, 130–148.
- Gibbon, J., Church, R. M., & Meck, W. (1984). Scalar timing in memory. In J. Gibbon & L. Allan (Eds.). *Timing and time perception* (Vol. 423, pp. 52–77). New York: New York Academy of Sciences.
- Glicksohn, J., & Hadad, Y. (2012). Sex differences in time production revisited. Journal of Individual Differences, 33, 35-42.
- Grondin, S. (2010). Timing and time perception: A review of recent behavioral and neuroscience findings and theoretical directions. *Attention, Perception, & Psychophysics*, 72, 561–582.
- lacoboni, M. (2009). Imitation, empathy, and mirror neurons. Annual Review of Psychology, 60, 653-670.
- Jaeger, T. F. (2008). Categorical data analysis: Away from ANOVAs (transformation or not) and towards logit mixed models. *Journal of Memory and Language*, 59, 434–446.
- Jeannerod, M., & Frak, V. (1999). Mental imaging of motor activity in humans. Current Opinion in Neurobiology, 9, 735–739.
- Kasper, L. J., Alderson, R. M., & Hudec, K. L. (2012). Moderators of working memory deficits in children with attention-deficit/ hyperactivity disorder (ADHD): A meta-analytic review. Clinical Psychology Review, 32(7), 605–617. https://doi.org/10.1016/ j.cpr.2012.07.001.
- Lanfranchi, S., Cornoldi, C., & Vianello, R. (2004). Verbal and visuospatial working memory deficits in children with Down syndrome. *American Journal of Mental Retardation*, 109, 456–466.
- Lorch, E. P., Milich, R., Astrin, C. C., & Berthiaume, K. S. (2006). Cognitive engagement and story comprehension in typically developing children and children with ADHD from preschool through elementary school. *Developmental Psychology*, 42, 1206–1219.
- Mammarella, I. C., Toso, C., Pazzaglia, F., & Cornoldi, C. (2008). BVS–Corsi: Batteria per la valutazione della memoria visiva e spaziale (con CD–ROM) [Battery for evaluating visual and spatial memory (with CD–ROM)]. Trento, Italy: Erickson.
- Martinussen, R., & Tannock, R. (2006). Working memory impairments in children with attention-deficit hyperactivity disorder with and without comorbid language learning disorders. *Journal of Clinical and Experimental Neuropsychology*, 28, 1073–1094.
- Marx, I., Hübner, T., Herpertz, S. C., Berger, C., Reuter, E., Kircher, T., ... Konrad, K. (2010). Cross-sectional evaluation of cognitive functioning in children, adolescents and young adults with ADHD. *Journal of Neural Transmission*, 117, 403–419.
- Marzocchi, G. M., Re, A. M., & Cornoldi, C. (2010). BIA: Batteria Italiana per l'ADHD [Italian Battery for ADHD]. Trento, Italy: Centro Studi Erickson.
- McInerney, R. J., & Kerns, K. A. (2003). Time reproduction in children with ADHD: Motivation matters. *Child Neuropsychology*, 9, 91–108.
- Meaux, J. B., & Chelonis, J. J. (2003). Time perception differences in children with and without ADHD. *Journal of Pediatric Health Care*, 17(2), 64–71.
- Mioni, G. (2018). Methodological issues in the study of prospective timing. In A. Vatakis, F. Balcı, M. Di Luca, & Á. Correa (Eds.), Timing and time perception: Procedures, measures, and applications (pp. 79–97). Leiden, Netherlands: Brill Academic.

- Mioni, G., Santon, S., Stablum, F., & Cornoldi, C. (2016). Time-based prospective memory difficulties in children with ADHD and the role of time perception and working memory. *Child Neuropsychology*, 23, 588–608.
- Mioni, G., Stablum, F., McClintock, S. M., & Grondin, S. (2014). Different methods for reproducing time, different results. Attention, Perception, & Psychophysics, 76, 675–681.
- Mullins, C., Bellgrove, M. A., Gill, M., & Robertson, I. H. (2005). Variability in time reproduction: Difference in ADHD combined and inattentive subtypes. *Journal of the American Academy of Child & Adolescent Psychiatry*, 44, 169–176.
- Noreika, V., Falter, C. M., & Rubia, K. (2013). Timing deficits in attention-deficit/hyperactivity disorder (ADHD): Evidence from neurocognitive and neuroimaging studies. *Neuropsychologia*, *51*, 235–266.
- Pinheiro, J. C., & Bates, D. M. (2000). Mixed-effects models in S and S-PLUS (Statistics and Computing series). New York: Springer-Verlag.
- Rapport, M. D., Chung, K. M., Shore, G., Denney, C. B., & Isaacs, P. (2000). Upgrading the science and technology of assessment and diagnosis: Laboratory and clinic-based assessment of children with ADHD. *Journal of Clinical Child Psychology*, 29, 555–568.
- Re, A. M., Capodieci, A., & Cornoldi, C. (2015). Effect of training focused on executive functions (attention, inhibition, and working memory) in preschoolers exhibiting ADHD symptoms. Frontiers in Psychology, 6. https://doi.org/10.3389/fpsyg.2015.01161.
- Rizzolatti, G., Fabbri-Destro, M., & Cattaneo, L. (2008). Mirror neurons and their clinical relevance. *Nature Reviews Neurology*, 5, 24–34
- Rubia, K., Schuri, U. V., Cramon, I., & Poeppel, E. (1997). Time estimation as a neuronal network property: A lesion study. *NeuroReport*, 8, 1273–1276.
- Smith, A., Taylor, E., Warner-Rogers, J., Newman, S., & Rubia, K. (2002). Evidence for a pure time perception deficit in children with ADHD. *Journal of Child Psychology and Psychiatry*, 43, 529–542.
- Sonuga-Barke, E. J. S., Taylor, E., Sembi, S., & Smith, J. (1992). Hyperactivity and delay aversion: The effect of delay on choice. *Journal of Child Psychology and Psychiatry*, 33, 387–398.
- Talbot, K.-D. S., & Kerns, K. A. (2014). Event- and time-triggered remembering: The impact of attention deficit hyperactivity disorder on prospective memory performance in children. *Journal of Experimental Child Psychology*, 127, 126–143.
- Toplak, M. E., Dockstader, C., & Tannock, R. (2006). Temporal information processing in ADHD: Findings to date and new methods. *Journal of Neuroscience Methods*, 151, 15–29.
- Van Meel, C. S., Oosterlaan, J., Heslenfeld, D. J., & Sergeant, J. A. (2005). Motivational effects on motor timing in attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, 44, 451–460.
- Walsh, V. (2003). A theory of magnitude: Common cortical metrics of time, space and quantity. *Trends in Cognitive Sciences*, 7, 483–488.
- Wechsler, D. (2003). Wechsler Intelligence Scale for Children-fourth edition (WISC-IV). Milano, Italy: Pearson.
- Zakay, D. (1992). The role of attention in children's time perception. Journal of Experimental Child Psychology, 54, 355-371.
- Zakay, D., & Block, R. A. (1995). An attentional gate model of prospective time estimation. In M. Richelle, V. D. Keyser, G. D. Ydeualle, & A. Vandierendonck (Eds.), Time and the dynamic control of behavior (pp. 167–178). Liege, Belgium: University of Liege Press
- Zakay, D., & Block, R. A. (1996). The role of attention in time estimation processes. Advances in Psychology, 115, 143-164.

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The need for paediatric registries to assess long-term brain effects of psychotropic medications: The case of bipolar disorder

The proposal by Vieta et al. (2018) of organizing a consensus conference on the need for pediatric registries to assess long-term brain effects of psychotropic medicines must be supported. "The why", "the what", "the who", and "the how" of the consensus (as well of these registries) should be clarified, however, so that outcomes can be achievable and effective (de Groot et al., 2017).

The particularity of the developing brain and the still limited knowledge on the therapeutic effects and safety of psychotropic drugs in children and adolescents justify "the why". Patient registries ("the what") already exist in Europe for many diseases and drugs and have been increasingly important in supporting the lifetime evaluation of the benefit-risk ratio of authorized medicines by the regulators, as acknowledged, and sometimes required, by the European Medicines Agency (Boury et al., 2017). There are a few examples of patient registries also in the child and adolescent psychiatry area, e.g. for methylphenidate (Murray et al., 2013) and ADHD (Bonati et al., 2018). It is discriminating, however, to choose between product and disorder registries, and obviously not just for the data to be collected. In psychiatry (also concerning childhood and adolescence) the use of drugs is always one of the interventions, not always the first and not always alone, and often in complex conditions. It would therefore be more valuable to support disorder/care registries that accurately reflect the entire population of patients receiving different treatments, with and without drugs, in order to also compare the safety and effectiveness in users of other or similar treatments. Priorities, and criteria, should be defined for setting up patient registries for psychiatric disorders in children and adolescents with pharmacological or non-pharmacological treatment indications.

Researchers, clinicians, patient associations, regulators, and stakeholders must be involved ("the who") to maximize the efficacy and results of registries. Additional essential characteristics of a health related registry are its independence and transparency in the organization, coordination, management, and evaluation of collected data. All this affects "the how" of setting up and maintaining a registry. At the regional and national levels the Ministry of Health (Bonati et al., 2018) and patient associations, as well as

European Commission, can support registries also with funds, although, unfortunately, for limited periods that do not cover the duration of the target disorder. Moreover, the available budget should be adequate enough to not affect appropriate sample size, number of variables, and quality of data of registries. "The how", therefore, is once again the core of a challenging and praiseworthy initiative to be addressed during, and after, a consensus conference.

References

Bonati, M., Reale, L., Zanetti, M., Cartabia, M., Fortinguerra, F., Capovilla, G., Chiappedi, M., Costantino, A., Effedri, P., Luoni, C., Martinelli, O., Molteni, M., Ottolini, A., Saccani, M.Lombardy ADHD Group, 2018. A regional ADHDcenter-based network project for the diagnosis and treatment of children and adolescents with ADHD. J. Atten. Disord. 22, 1173-1184.

Bouvy, J.C., Blake, K., Slattery, J., De Bruin, M.L., Arlett, P., Kurz, X., 2017. Registries in European post-marketing surveil-lance: a retrospective analysis of centrally approved products, 2005-2013. Pharmacoepidemiol. Drug Saf. 26, 1442-1450.

De Groot, S., van der Linden, N., Franken, M.G., Blommestein, H.M., Leeneman, B., van Rooijen, E., van der Hoeven, J.J.M., Wouters, M.W., Westgeest, H.M., Uyl-de Groot, C.A., 2017. Balancing the optimal and the feasible: a practical guide for setting up patient registries for the collection of real-world data for health care decision making based on Dutch experiences. Value Health 20, 627-636.

Murray, M.L., Insuk, S., Banaschewski, T., Neubert, A.C., Mc-Carthy, S., Coghill, D., Dittmann, R.W., Konrad, K., Panei, P., Rosenthal, E., Sonuga-Barke, E.J., Wong, I.C.K., 2013. An inventory of European data sources for the long-term safety evaluation of methylphenidate. Eur. Child. Adolesc. Psychiatry 22, 605-618.

Vieta, E., Arango, C., Rush, A.J., 2018. The need for paediatric registries to assess long-term brain effects of psychotropic medications: the case of bipolar disorder. Eur. Neuropsychopharmacol. 28, 1181-1184.

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I diritti sono per tutti i tipi di mente

L'autismo è la manifestazione delle complesse alterazioni di alcune funzioni del sistema nervoso centrale la cui causa è ancora sconosciuta. Si stima che oggi in Italia l'autismo interessi I bambino ogni 77, in un rapporto di 4 a I tra maschi e femmine. Non esiste una cura efficace e appropriata ma lo sviluppo di bambini con autismo può beneficiare di interventi comportamentali ed educativi specialistici, adeguati, precoci, duraturi, multidisciplinari e basati sulle evidenze scientifiche. Le differenze nell'utilizzo dei farmaci tra paese e paese. Posto rimedio a una iniquità italiana.

La definizione e condivisione di procedure diagnostiche appropriate e una maggior sensibilizzazione degli operatori sanitari e degli insegnanti ed educatori sono i fattori che hanno contribuito a stimare che oggi in Italia l'autismo interessa 1 bambino ogni 77, in un rapporto di 4 a 1 tra maschi e femmine.

Vuol dire che dei nati nel 2018 circa 6000 manifesteranno prima del compimento dei 3 anni una qualche forma, dalla più grave alla più lieve, di quei disturbi del neurosviluppo che compaiono in modo sfumato da farli definire "disturbi dello spettro dell'autismo" (ASD).

Vuol dire anche che oggi in Italia ci sono circa 100.000 bambini e adolescenti che per forme e gravità diverse vivono nello spettro (marcate difficoltà nell'interazione sociale e nella comunicazione; comportamenti, attività e interessi ripetitivi e stereotipati) e con loro altrettante famiglie.

L'autismo è la manifestazione delle complesse alterazioni di alcune funzioni del sistema nervoso centrale, la cui causa è ancora sconosciuta. Alcuni fattori possono contribuire insieme al manifestarsi dei sintomi in soggetti predisposti (per esempio cause ereditarie o ambientali) sebbene le modalità siano ancora sconosciute e rimangano potenziali. Comunque, l'autismo non è imputabile ai genitori, all'esposizione a metalli pesanti e neppure alle vaccinazioni dell'infanzia.

Terapie

Non esiste a tutt'oggi una cura efficace e appropriata, tuttavia lo sviluppo di bambini con autismo può beneficiare di interventi comportamentali ed educativi specialistici, adeguati, precoci e duraturi. Gli interventi devono essere multidisciplinari e basati sulle evidenze scientifiche. Alcuni bambini con autismo possono anche trarre beneficio dal trattamento farmacologico. Al contrario trattamenti nutrizionali (per esempio dieta priva di glutine o latticini) o terapie chelanti non sono suffragate da evidenze scientifiche.

Purtroppo l'organizzazione dei servizi per i disturbi neuropsichiatrici dell'età evolutiva e le risposte ai bisogni di cura di pazienti e famiglie si caratterizzano per l'ampia disuguaglianza territoriale, sia regionale che locale. Interventi efficaci sul percorso diagnostico, terapeutico, di non

esclusione sociale sono stati individuati da numerosi progetti che attendono ancora di essere messi a sistema.

Al momento non vi è alcuna terapia farmacologica specifica per i deficit sociocomunicativi dell'ASD. Gli psicofarmaci sono utilizzati per trattare i sintomi concomitanti di iperattività, irritabilità e aggressività, spesso in associazione con approcci comportamentali ed educativi. Circa un bambino su tre con ASD in UK è in terapia con almeno un farmaco, negli USA due ogni tre, mentre in Italia molto meno; approcci culturali diversi e attitudini terapeutiche differenti condizionano la prescrizione dei farmaci nelle diverse nazioni. Così, per esempio, le prescrizioni di antibiotici in Italia ai bambini e agli adolescenti sono almeno il triplo che in Inghilterra, ma quelle degli psicofarmaci solo un terzo di quelle inglesi a parità di indicazione.

A contribuire alle differenze di utilizzo dei farmaci tra le nazioni bisogna inoltre contemplare i criteri, le ragioni e le normative di registrazione e di distribuzione dei farmaci nei singoli Paesi.

Succede quindi che un farmaco possa essere venduto in una nazione e non in un'altra confinante. Oppure che in una nazione sia registrato e distribuito per una indicazione, mentre in una nazione confinante registrato e distribuito anche per altre indicazioni o per età differenti.

Diritto alla salute

I farmaci antipsicotici atipici (risperidone e aripiprazolo) sono risultati efficaci nel ridurre i comportamenti problematici e ripetitivi nei bambini con autismo, eppure la loro licenza d'uso negli USA e in Europa è differente, sebbene le ditte produttrici siano le stesse.

Negli USA i due farmaci possono essere prescritti anche per l'irritabilità associata a ASD, mentre in Europa questa indicazione non è contemplata, sebbene le linee guida internazionali e numerosi studi clinici ne documentino l'efficacia (seppur parziale).

Le decisioni spettano alle ditte produttrici secondo il loro interesse, ma anche alle Agenzie Regolatorie nazionali nell'interesse dei pazienti di disporre dei farmaci più appropriati in termini di efficacia e sicurezza.

A tutt'oggi la prescrizione di questi due farmaci per l'ASD in Italia erano cosiddette off-label (fuori dalle indicazioni) con la conseguenza che i pazienti (le famiglie) dovevano pagarseli (anche alcune centinaia di €/anno).

Per far fronte a questa iniqua situazione l'Istituto si è attivato presso l'Agenzia Italiana del Farmaco (Aifa) presentando una richiesta formale supportata da ampia documentazione scientifica affinché anche in Italia, come negli USA, il farmaco fosse prescrivibile anche per i disturbi associati all'ASD e fosse rimborsabile dal SSN. Al termine dell'iter valutativo la richiesta è stata accettata così che i pazienti potranno beneficiarne in Italia come negli USA: un diritto alla salute sinora negato è stato evaso.



DIALOGHI DI GESTALT

L'esperienza dialettica nelle relazioni d'aiuto Ciclo di incontri CSTG 2018/2019



ADHD Seminario interattivo sul Disturbo da Deficit di Attenzione e Iperattività

Conduce la dott.ssa Elena Vlacos
Psicoterapeuta del Centro di Riferimento Regionale Mondino di Pavia

DATA 18 luglio

DALLE 19.00 ALLE 21

Via Cadamosto 6 – Milano (MM Porta Venezia)

Una serata dedicata alla discussione sul Disturbo da Deficit di Attenzione e Iperattività, per comprendere insieme cosa significa la dicitura ADHD, e le varie caratteristiche sintomatologiche; per capire cosa si può fare con un bambino con ADHD a casa, in famiglia, e a scuola con l'insegnante e i compagni.

L'ADHD non si ferma solo ad iperattività e disattenzione ma spesso si manifesta con un corollario di altri problemi, come i disturbi dell'apprendimento (DSA), del comportamento e della condotta, tic, disturbo d'ansia e rabbia.

Un incontro per parlare insieme di come affrontare e gestire i problemi di crescita e in età adulta per chi ha l'ADHD, per non incorrere in rischi più gravi come i <u>disturbi da dipendenza da sostanze o dipendenze comportamentali</u> (gioco d'azzardo, binge eating, dipendenza sessuale, dipendenza affettiva, ecc.).

Discuteremo insieme anche sui vari tipi di trattamento, da quello farmacologico a quello individuale e di gruppo (psicoterapia, parent training, teacher training, mindfulness).



A chi è rivolto il seminario?

AI GENITORI che desiderano comprendere maggiormente il problema del figlio già diagnosticato, o hanno il sospetto che il proprio figlio possa avere l'ADHD, e per capire quando richiedere la legge 104.

AGLI INSEGNANTI che vogliono approfondire la loro conoscenza sul disturbo per poterlo gestire meglio in classe e con i genitori dell'alunno; e per essere informati sui procedimenti da attuare (PDP, PEI, BES, sostegno scolastico, assistente ad personam a scuola e a casa)

AGLI OPERATORI agli educatori, psicologi, medici, logopedisti, TNPEE e altre figure che si occupano dei bambini con problemi comportamentali, e vogliono sapere di più sull'iperattività, la disattenzione, e i disturbi del comportamento.

AI PAZIENTI ADHD dai 12 anni agli adulti, che desiderano essere partecipi alle cure e ai trattamenti dedicati a loro.

ELENA VLACOS

E' psicoterapeuta, neuropsicologa per l'ADHD, formatrice e autrice di diversi articoli su studi condotti sulla meditazione mindfulness e l'ADHD. Già co-fondatrice e presidente dell'Associazione no profit AMPRA e fondatrice del Centro Clinico Italiano per l'ADHD di Milano.

Lavora come psicoterapeuta presso i propri studi privati a Pavia, Binasco e Milano e presso le sedi dell'IRCCS Mondino di Pavia e Milano.

Riferimenti utili: www.elenavlacos.it, www.ampra.it/ADHD, www.mhcenter.it

Tutti gli incontri sono gratuiti e gli eventuali attestati di partecipazione verranno dati in loco, previa richiesta in segreteria.

Per informazioni e prenotazione scrivere a segreteria@cstg.it

Il CSTG è co-fondatore della Federazione Italiana di Scuole e Istituti di Gestalt (FISIG), membro della Associazione Europea di Gestalt Terapia (AETG), Federazione Italiana delle Associazioni di Psicoterapia-FIAP e della European Association for Psychotherapy (EAP).

I DISTURBI DEL COMPORTAMENTO IN ETÀ EVOLUTIVA: MODELLI DI INTERVENTO



Bergamo, 21 novembre 2019 - Centro Congressi Giovanni XXIII

9.00 Introduzione ai lavori **Gian Marco Marzocchi** - Università di Milano Bicocca

9.15 Il contributo dell'Acceptance and Commitment Therapy all'intervento comportamentale con i genitori di bambini con disturbo del comportamento

Anna Prevedini - IESCUM e ACT-Italia

10.00 I disturbi di comportamento in classe: esperienze di teacher training **Fabio Celi** - *Centro Studi Versilia e Università di Pisa*

10.45 - 11.15 Pausa

11.15 Seminario con discussione casi: Coping Power Program e protocolli Mindfulness: l'esperienza di "Al di là delle Nuvole"

Pietro Muratori & Lisa Polidori - IRCCS Stella Maris di Calambrone, Pisa

12.45 - 14.15 Pranzo

- 14.15 L'intervento sul disturbo da disregolazione dell'umore dirompente **Mario Di Pietro** Istituto di Terapia Cognitiva e Comportamentale, Padova
- 15.00 L'integrazione tra la psicoterapia e la farmacoterapia nei disturbi comportamentali in età evolutiva

Francesco Rovetto - Università Pavia & Sigmund Freud University Milano

15.45 Seminario con discussione casi: Disattiviamo il pilota automatico.
Un programma di intervento per bambini e adolescenti finalizzato a promuovere comportamenti consapevoli orientati ai valori personali

Laura Vanzin & Valentina Mauri - IRCCS Medea di Bosisio Parini

17.30 Conclusione e compilazione del questionario ECM



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Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza (Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)

Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia (in attuazione della D.G. sanità n. 3798 del 08/05/2014, n. 778 del 05/02/2015, n. 5954 del 05/12/2016, N. 1077 del 02/02/2017 N. 1938 del 15/02/2019) Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" "Percorsi diagnostico-terapeutici per l'ADHD".

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