NEWSLETTER

INDICE:

BIBLIOGRAFIA ADHD SETTEMBRE 2021

Acta Obstetricia et Gynecologica Scandinavica. 2021.

MATERNAL POLYCYSTIC OVARY SYNDROME AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN OFFSPRING AT 3 YEARS OF AGE: ODENSE CHILD COHORT.

Dalgaard CM, Andersen MS, Jensen RC, et al.

Introduction: Previous data suggested a link between maternal polycystic ovary syndrome (PCOS) and offspring attention deficit hyperactivity disorder (ADHD), which could be mediated by higher prenatal androgen exposure.

Material and methods: The study was part of the prospective Odense Child Cohort and included 1776 pregnant women, 165 (9%) with PCOS and 1607 (91%) controls. ADHD symptoms at 3 years of age were defined using the parent-reported questionnaire Child Behavior Checklist/1.5-5 (scores >90th centile of Danish national standard). Maternal blood samples were collected in the third trimester measuring total testosterone by mass spectrometry, sex hormone-binding globulin, and calculated free testosterone. Offspring anogenital distance was measured at 3 months of age. Regression models were performed with presence of ADHD symptoms as the dependent variable and adjusted for maternal age, body mass index, parity, smoking status, educational level, and parental psychiatric diagnoses.

Results: ADHD symptoms were present in 105/937 (11%) boys and 72/839 (9%) girls. In boys, maternal PCOS was positively associated with ADHD symptoms (unadjusted odds ratio [OR] 1.91, 95% CI 1.07-3.43, p = 0.03, adjusted OR 2.20, 95% CI 1.20-4.02, p = 0.01), whereas maternal PCOS was not associated with ADHD symptoms in girls. Maternal total testosterone, free testosterone, and offspring anogenital distance were not associated with higher risk of ADHD symptoms in the offspring.

Conclusions: Higher risk of ADHD in boys born of mothers with PCOS were not associated with maternal third-trimester testosterone levels or offspring anogenital distance

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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.

Acta Psychiatr Scand. 2021.

MALE TO FEMALE RATIOS IN AUTISM SPECTRUM DISORDERS BY AGE, INTELLECTUAL DISABILITY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Posserud MB, Skretting Solberg B, Engeland A, et al.

Objective: To examine the gender distribution in ASD in adults compared with children and the impact of comorbid intellectual disability (ID) and attention-deficit/hyperactivity disorder (ADHD) on the male to female ratio (MFR).

Methods: We estimated the MFR and the male prevalence ratio (PR) for ASD in adults and children using the Medical Birth Registry of Norway, including all individuals born during 1967-2011. We examined variation with age, comorbid ID and ADHD as defined by diagnoses in the Norwegian Patient Registry during 2008-2015 and/or a dispensed prescription for ADHD medication.

Results: The sample included 1,701,206 adults and 804,146 children, including 8,995 (0.5%) adults and 8,056 (1.0%) children with ASD, 53,822 (3.2%) adults and 26,967 (3.4%) children with ADHD and 9,178 (0.5%) adults and 5,038 (0.6%) children with ID. The MFR for ASD was 3.67 in children and 2.57 in adults, corresponding to a male PR in ASD of 1.54 (95% CI 1.53-1.56) and 1.41 (1.39-1.24), respectively. Comorbid ID decreased the MFR and the male PR in both adults and children, whereas comorbid ADHD significantly increased the male PR in children. The MFR and the population prevalence of ASD, ADHD and ID decreased from children to younger adults and yet further to older adults.

Conclusion: We found a lower MFR and male PR in adults than in children. Findings suggest the strong male predominance seen in childhood/clinical studies of ASD diminishes in adult samples, possibly reflecting the influence of non-aetiological factors such as later diagnosis in females, diagnostic biases and diagnostic trends

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Acta Psychol (Amst). 2021 Sep;219:103386.

COGNITIVE AND PERSONALITY DIFFERENCES BETWEEN ADOLESCENTS WITH AND WITHOUT ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Herrera-Gutiarrez E, Gamez-Amor J, et al.

Background: The relationships between cognitive and personality profile in teenagers with and without ADHD were assessed.

Method: Two groups of teenagers, one with ADHD (N = 135; mean age = 13.93) and another group without ADHD (N = 199, mean age = 14.29) were evaluated using the K-BIT and 16PF-APQ tests.

Results: In cognitive variables, the results revealed that the ADHD group returned higher scores in the Matrices subtest and the IQ test. In personality variables, the group with ADHD exhibited higher scores in Tough-Mindedness and lower scores in Self-Control than the group without the disorder. The canonical correlation analysis applied to each group revealed a differing pattern of interrelationships between the cognitive-personality variables in the two groups. In adolescents with ADHD, we observed that higher scores in cognitive variables were associated with a more extroverted personality and less self-control, while in adolescents without ADHD, higher scores in cognitive variables were associated with less tough-mindedness and lower levels of self-control.

Conclusions: The cognitive and personality variables of adolescents with and without ADHD differ. These results will be useful for establishing a cognitive and personality profile for this section of the population. The educational implications of the study are under discussion

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Alcohol Clin Exp Res. 2021.

MATERNAL AND OFFSPRING GENETIC RISK SCORE ANALYSES OF FETAL ALCOHOL EXPOSURE AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER RISK IN OFFSPRING.

Haan E, Sallis HM, Ystrom E, et al.

Background: Studies investigating the effects of prenatal alcohol exposure on childhood attention-deficit hyperactivity disorder (ADHD) symptoms using conventional observational designs have reported inconsistent findings, which may be affected by unmeasured confounding and maternal and fetal ability to metabolize alcohol. We used genetic variants from the alcohol metabolizing genes, alcohol dehydrogenase

(ADH) and aldehyde dehydrogenase (ALDH), as proxies for fetal alcohol exposure to investigate their association with risk of offspring ADHD symptoms around age 7-8 years.
Methods: We used data from 3 longitudinal pregnancy cohorts: Avon Longitudinal Study of Parents and Children (ALSPAC), Generation R study (GenR), and the Norwegian Mother, Father and Child Cohort study (MoBa). Genetic risk scores (GRS) for alcohol use and metabolism using 36 single nucleotide polymorphisms (SNPs) from ADH and ALDH genes were calculated for mothers (NALSPAC = 8196; NMOBA = 13,614), fathers (NMOBA = 13,935), and offspring (NALSPAC =8,237; NMOBA =14,112; NGENR =2,661). Associations between maternal GRS and offspring risk of ADHD symptoms were tested in the full sample to avoid collider bias. Offspring GRS analyses were stratified by maternal drinking status.
Results: The pooled estimate in maternal GRS analyses adjusted for offspring GRS in ALSPAC and MoBa was OR = 0.99, 95%CI 0.97-1.02. The pooled estimate in offspring GRS analyses stratified by maternal drinking status across all the cohorts was as follows: ORDRINKING = 0.98, 95% CI 0.94-1.02; ORNO DRINKING = 0.99, 95% CI 0.97-1.02. These findings remained similar after accounting for maternal genotype data in ALSPAC and maternal and paternal genotype data in MoBa.
Conclusions: We did not find evidence for a causal effect of fetal alcohol exposure on risk of ADHD symptoms in offspring. The results may be affected by limited power to detect small effects and outcome assessment

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Am J Psychiatry. 2021 Sep;178:854-64.
GENETIC, CLINICAL, AND SOCIODEMOGRAPHIC FACTORS ASSOCIATED WITH STIMULANT TREATMENT OUTCOMES IN ADHD.
Brikell I, Wimberley T, AlbiÃ±ana C, et al.
OBJECTIVE: Stimulant medications are effective for treating attention deficit hyperactivity disorder (ADHD), yet discontinuation and switch to nonstimulant ADHD medications are common. This study aimed to identify genetic, clinical, and sociodemographic factors influencing stimulant treatment initiation, discontinuation, and switch to nonstimulants in individuals with ADHD.
METHODS: The authors obtained genetic and national register data for 9,133 individuals with ADHD from the Danish iPSYCH2012 sample and defined stimulant treatment initiation, discontinuation, and switch from prescriptions. For each stimulant treatment outcome, they examined associations with polygenic risk scores (PRSs) for psychiatric disorders and clinical and sociodemographic factors using survival analyses, and conducted genome-wide association studies (GWASs) and estimated single-nucleotide polymorphism heritability (h(2)(SNP)).
RESULTS: Eighty-one percent of the sample initiated stimulant treatment. Within 2 years, 45% discontinued stimulants and 15% switched to nonstimulants. Bipolar disorder PRS (hazard ratio=1.05, 95% CI=1.02, 1.09) and schizophrenia PRS (hazard ratio=1.07, 95% CI=1.03, 1.11) were associated with discontinuation. Depression, bipolar disorder, and schizophrenia PRSs were marginally but not significantly associated with switch (hazard ratio range, 1.05-1.07). No associations were observed for ADHD and autism PRSs. Individuals diagnosed with ADHD at age 13 or older had higher rates of stimulant initiation, discontinuation, and switch (hazard ratio range, 1.27-2.01). Psychiatric comorbidities generally reduced rates of initiation (hazard ratio range, 0.84-0.88) and increased rates of discontinuation (hazard ratio range, 1.19-1.45) and switch (hazard ratio range, 1.40-2.08). h(2)(SNP) estimates were not significantly different from zero. No GWAS hits were identified for stimulant initiation or discontinuation. A locus on chromosome 16q23.3 reached genome-wide significance for switch.
CONCLUSIONS: The study findings suggest that individuals with ADHD with higher polygenic liability for mood and/or psychotic disorders, delayed ADHD diagnosis, and psychiatric comorbidities have a higher risk for stimulant treatment discontinuation and switch to nonstimulants. Despite the study's limited sample size, one putative GWAS hit for switch was identified, illustrating the potential of utilizing genomics linked to prescription databases to advance ADHD pharmacogenomics

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Am J Med Genet Part A. 2021.

CROSS-SECTIONAL AND LONGITUDINAL FINDINGS IN PATIENTS WITH PROXIMAL 22Q11.2 DUPLICATION: A RETROSPECTIVE CHART STUDY.

Verbesselt J, Zink I, Breckpot J, et al.

Duplications on Chromosome 22q11.2 (22q11.2 dup) are associated with a wide spectrum of physical and neurodevelopmental features. In this chart review, physical, developmental, and behavioral features of 28 patients with 22q11.2 dup (median age-á=-á17.11 years) are reported, and phenotypes of de novo and inherited duplications are compared. Common medical anomalies include nutritional problems (57%), failure to thrive (33%), transient hearing impairment (52%), and congenital heart defects (33%). Developmental, speech-language, and motor delay are common in infancy, while attention (64%), learning (60%), and motor problems (52%) are typically reported at primary school age. Attention-deficit/hyperactivity disorders are diagnosed in 44%. Median full-scale intelligence quotient is in the borderline range (IQ 76), with one-fifth of patients having mild intellectual disability. Longitudinal data in 11 patients, with the first assessment at a median age of 5.2 years and the second assessment at a median age of 8.8 years, indicate that almost two-third of patients have a relative stable cognitive trajectory, whereas one-third show a growing into deficit profile. In patients with de novo duplications, there is a trend of more failure to thrive, while more patients with inherited duplications follow special education

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Annals of Indian Academy of Neurology. 2017;20:S30.

COGNITIVE FUNCTIONS IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS (ALS).

Narula KB, Panda A, Sinha U.

Introduction: ALS, though, primarily is degenerative disorder of motor neurons; there are reports of cognitive dysfunction in these patients. Frontotemporal dementia and ALS is reported to overlap clinically and genetically.

Objective: To study 1.The incidence of cognitive impairment in patients with ALS, 2.Which cognitive functions are more impaired, 3. Whether there is any relationship of cognitive impairment to the site of onset (bulbar or limbs onset). Material and

Methods: Twentythree consecutive patients of amyotrophic lateral sclerosis, attending to neurology department at Institute of Human Behavior& Allied Sciences (IHBAS), Delhi were recruited after taking written informed consent. Patients with a diagnosis of dementia and other neurologic conditions affecting cognition were excluded. Multiple areas of cognition were assessed using the Mini Mental State Examination (MMSE), Digitsymbol Substitution Test (DSS), Digit Vigilance Test (DVT), Triads Test, NI Back Test, Token test, Wisconsin Card Sorting Test (WCST), Ray Auditory Verbal Learning Test (RAVL), and Complex Figure Test (CFT). In patients with at least two abnormal tests of the neuropsychological battery a cognitive impairment was diagnosed.

Results: Out of 23 patients, 16 were males and 7 females, in age range 32-78yrs (Mean age 9.96-+10.67), 16 with limb onset and 7 with bulbar onset. 73% of patient demonstrated impairment on cognitive testing (ICT). Those with ICT and unimpaired cognitive tests had similar clinical features but differed in cognitive performances. Those with cognitive impairment manifested a relatively selective deficit in attention, executive function, memory, visuo-constructive ability and psychomotor speed. Bulbar onset group demonstrated higher cognitive impairment than limb onset group.

Conclusion: Diversity of cognitive impairment was seen in ALS patients. The various domains affected were attention, executive function, memory, visuo-constructive ability and psychomotor speed in that order

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Arch Dis Child. 2021 Sep;106:842-48.

GESTATIONAL AGE AT BIRTH AND CHILD SPECIAL EDUCATIONAL NEEDS: A UK REPRESENTATIVE BIRTH COHORT *STUDY.*

Alterman N, Johnson S, Carson C, et al.

OBJECTIVE: To examine the association between gestational age at birth across the entire gestational age spectrum and special educational needs (SENs) in UK children at 11 years of age.

METHODS: The Millennium Cohort Study is a nationally representative longitudinal sample of children born in the UK during 2000-2002. Information about the child's birth, health and sociodemographic factors was collected when children were 9 months old. Information about presence and reasons for SEN was collected from parents at age 11. Adjusted relative risks (aRRs) were estimated using modified Poisson regression, accounting for confounders.
RESULTS: The sample included 12 081 children with data at both time points. The overall prevalence of SEN was 11.2%, and it was inversely associated with gestational age. Among children born <32 weeks of gestation, the prevalence of SEN was 27.4%, three times higher than among those born at 40 weeks (aRR=2.89; 95% CI 2.02 to 4.13). Children born early term (37-38 weeks) were also at increased risk for SEN (aRR=1.33; 95% CI 1.11 to 1.59); this was the same when the analysis was restricted to births after labour with spontaneous onset. Birth before full term was more strongly associated with having a formal statement of SEN or SEN for multiple reasons.
CONCLUSION: Children born at earlier gestational ages are more likely to experience SEN, have more complex SEN and require support in multiple facets of learning. This association was observed even among children born early-term and when labour began spontaneously

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Assessment. 2021 Sep;28:1570-82.

CONFIRMATORY FACTOR ANALYSIS AND EXPLORATORY STRUCTURAL EQUATION MODELING OF THE STRUCTURE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN ADULTS.

Gomez R, Stavropoulos V.

This study examined the structure of attention-deficit/hyperactivity disorder (ADHD) symptoms in an adult community sample using first-order confirmatory factor analysis, exploratory structural equation modeling (ESEM), and bifactor confirmatory factor analysis and ESEM models, with two group factors (inattention [IA] and hyperactivity/impulsivity [HY/IM]) and two different three group factors (IA, hyperactivity [HY], and impulsivity [IM]; and IA, motoric HY/IM, and verbal HY/IM). A total of 738 adults (males = 374 and females = 364) between 17 and 72 years of age completed the Adult ADHD Self-Report Scale. The results provided most support for the ESEM model with group factors for IA, motoric HY/IM, and verbal HY/IM. The factors in this model were reasonably well defined, had good internal consistency omega reliabilities, and had support for their external validities, thereby making it a suitable model for ratings of the ADHD symptoms presented in the Adult ADHD Self-Report Scale. The theoretical and clinical implications of the findings are discussed

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Autism Res. 2021 Sep;14:1996-2001.

GASTROINTESTINAL SYMPTOMS AND SENSORY ABNORMALITIES ASSOCIATED WITH BEHAVIORAL PROBLEMS IN CHILDREN WITH NEURODEVELOPMENTAL DISORDERS.

Kurokawa S, Nomura K, Miyaho K, et al.

Behavioral problems directly affect the quality of life of caregivers and children with autism spectrum disorder (ASD) and/or attention-deficit/hyperactivity disorder (ADHD), and is known to be associated with clinical factors such as gastrointestinal (GI) symptoms, sensory abnormalities, intellectual abilities, and use of medication. However, previous studies have not considered these relationships comprehensively. We conducted a cross-sectional study of 6-12-year-old children with diagnoses of ASD and/or ADHD at two hospitals in Japan. Scores for the aberrant behavior checklist (ABC), autism-spectrum quotient (AQ), and Conners 3, as well as information on daily sleep and exercise, GI symptoms, and Short Sensory Profile, were collected. Each factor was subjected to a correlation analysis to investigate its effect on ABC scores. A stepwise multiple linear regression analysis for the factors with $p<0.05$ was performed. Data were obtained from 60 patients with a mean age of 8.3 years; 21 had ASD alone, 18 had ADHD alone, and 21 had ASD+ADHD. The correlation analyses identified six factors associated with ABC severity: (a) methylphenidate use, (b) Conners hyperactivity score, (c) Conners inattention score, (d) AQ score, (e) SSP score, and (f) GI symptom score. The multiple regression showed that "GI symptoms" and "sensory abnormalities" were independently associated with ABC severity. Although further studies are needed to show a causal relationship, appropriate assessment of GI symptoms and sensory abnormalities may help

alleviate some problematic behaviors and improve the quality of life of children with neurodevelopmental disorders and their families.
LAY SUMMARY: Behavioral problems in children with neurodevelopmental disorders are known to be associated with many factors. This study aimed to comprehensively investigate the known factors. We have discovered that "gastrointestinal symptoms" and "sensory abnormalities" were independently associated with Behavioral problems. Our results suggest that it is important for clinicians and caregivers to pay more attention to children's GI symptoms and sensory abnormalities that may not present as obvious symptoms or complaints

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Autism Res. 2021.
MATERNAL PRENATAL SELENIUM LEVELS AND CHILD RISK OF NEURODEVELOPMENTAL DISORDERS: A PROSPECTIVE BIRTH COHORT STUDY.
Lee ASE, Ji Y, Raghavan R, et al.
Selenium (Se) is an essential trace element involved in various biological processes, including neurodevelopment. Available literature indicates that both Se deficiency and excess may be detrimental to health. It is also known that Se can cross the placenta from maternal to fetal circulation. To date, the role of maternal Se status in child long-term neurodevelopment is largely unexplored. This study investigated the temporal and dose response associations between maternal Se status and child risk of neurodevelopmental disorders including autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). It consisted of 1550 mother infant dyads from the Boston Birth Cohort. Maternal red blood cell (RBC) Se levels were measured in samples collected within 72 h of delivery (biomarker of third trimester Se status). Pediatric neurodevelopmental diagnoses were obtained from electronic medical records. Data analyses showed that maternal RBC Se levels were positively associated with child risk of developing ASD, with an adjusted odds ratio of 1.49 for ASD (95% CI: 1.09, 2.02) per IQR increase in Se. There was also a positive association between maternal Se and ADHD (OR: 1.29; 95% CI: 1.04, 1.56, per IQR increase in Se). These associations remained robust even after adjusting for pertinent covariables; and there was no significant interaction between Se and these covariables. Our findings suggest that prenatal exposure to high maternal Se levels may adversely affect child neurodevelopment. Our findings warrant further investigation; if confirmed, optimizing maternal prenatal Se levels may be necessary to maximize its health benefits while preventing undue risk

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Behav Ther. 2021.
BUILDING A THEORETICAL MODEL FOR SUPPORTING TEENS AUTONOMY DAILY (STAND): A NETWORK ANALYSIS OF FAMILY-PERCEIVED CHANGES.
Sibley MH, Johansson M, Monroy JM, et al.
Little is known about processes through which behavior therapy (BT) for adolescent ADHD improves outcomes. The purpose of this study was to build a theoretical model for the processes through which a BT for adolescent ADHD (Supporting Teens Autonomy Daily; STAND) impacts functioning. Seventy-eight audio recordings from a standard therapeutic task in the final STAND session were analyzed as parents and adolescents (ages 11ΓÇô16) reflected upon what changed during STAND and why. Qualitative coding sorted parent and teen statements into orthogonal categories of perceived changes. Network analysis examined inter-relations between categories. Results indicated twenty-one categories of perceived change areas. Parent use of behavioral strategies, adolescent motivation, and adolescent organization skills were central nodes in the network of perceived changes, with strong relations to academic and parent-teen relationship outcomes. A model is proposed in which skills training in STAND increases parent behavioral strategy use and teen organization skills, while Motivational Interviewing (MI) in STAND increase parent behavioral strategy use and initial adolescent motivation. In turn, parent behavioral strategy use is proposed to further reinforce teen motivation through contingency management, thereby increasing teen application of organization skills to daily life. As a result of improved teen motivation and organization skills, the model proposes that ADHD symptoms, academic problems, and parent-teen conflict abate. We discuss secondary mechanisms and outcomes in this model, the possibility of person-specific processes, implications for

community-based adaptation of STAND, and plans to validate this conceptual model using sophisticated mediational models

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Behav Change. 2021.

THE EFFECT OF PARENTING PROGRAMME ON THE SYMPTOMS AND THE FAMILY FUNCTIONING OF CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER WHO HAVE RESIDUAL SYMPTOMS DESPITE MEDICAL TREATMENT.

Turan B, Esin IS, Dursun OB.

This study aims to determine the effects of the Parents Plus Children's Programme (PPCP) on children's symptoms of attention deficit and hyperactivity disorder (ADHD) and on family functionality and parenting stress. The children in the study were aged 6-11 years, and they had been diagnosed with ADHD and had residual symptoms despite effective dosage and timing of their medication. Forty-six couples, who with their children met the eligibility criteria, were enrolled and randomly allocated to the PPCP or the control group. The intervention involved a 9-week, 2 h a week, parenting group exercise. Those in the PPCP group improved significantly more over time on Conners' Parent Rating Scale-Revised, Family Assessment Device, and Parent Stress Index than those in the control condition. The trial is the first clinical study involving the parents of children with ADHD that addresses residual symptoms and functional impairments that remain despite the administration of the maximum effective dose of pharmacological treatment

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Biol Psychol. 2021;165.

CAN NEUROPHYSIOLOGICAL MARKERS OF ANTICIPATION AND ATTENTION PREDICT ADHD SEVERITY AND NEUROFEEDBACK OUTCOMES?

Aggensteiner PM, Albrecht B, Strehl U, et al.

Neurophysiological measures of preparation and attention are often atypical in ADHD. Still, replicated findings that these measures predict which patients improve after Neurofeedback (NF), reveal neurophysiological specificity, and reflect ADHD-severity are limited. Methods: We analyzed children's preparatory (CNV) and attentional (Cue-P3) brain activity and behavioral performance during a cued Continuous Performance Task (CPT) before and after slow cortical potential (SCP)-NF or semi-active control treatment (electromyogram biofeedback). Mixed-effects models were performed with 103 participants at baseline and 77 were assessed for pre-post comparisons focusing on clinical outcome prediction, specific neurophysiological effects of NF, and associations with ADHD-severity. Results: Attentional and preparatory brain activity and performance were non-specifically reduced after treatment. Preparatory activity in the SCP-NF group increased with clinical improvement. Several performance and brain activity measures predicted non-specific treatment outcome. Conclusion: Specific neurophysiological effects after SCP-NF were limited to increased neural preparation associated with improvement on ADHD-subscales, but several performance and neurophysiological measures of attention predicted treatment outcome and reflected symptom severity in ADHD. The results may help to optimize treatment

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BMC Med. 2021;19.

ELEVATED RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN JAPANESE CHILDREN WITH HIGHER GENETIC SUSCEPTIBILITY TO ADHD WITH A BIRTH WEIGHT UNDER 2000 G.

Rahman MS, Takahashi N, Iwabuchi T, et al.

Background: Both genetic and pre- and perinatal factors, including birth weight, have been implicated in the onset of attention deficit hyperactivity disorder (ADHD) traits among children. This study aimed to elucidate to what extent the genetic risk of ADHD moderates the association between birth weight and ADHD traits among Japanese children.

Methods: We conducted a longitudinal birth cohort study (Hamamatsu Birth Cohort for Mother and Children Study) to investigate the association of genetic risk for ADHD and low birth weight with ADHD traits among Japanese children. Out of 1258 children, we included 796 who completed follow-ups at 8 to 9 years of age.

Birth weight was categorized as <2000 g, 2000ΓÇô2499 g, and ΓëÑ2500 g. Polygenic risk score for ADHD was generated using the summary data of a large-scale genome-wide association study. The Rating Scale IV (ADHD-RS) assessed ADHD traits (inattention and hyperactivity/impulsivity) based on parental reports. Following previous studies, sex, birth order of the child, gestational age at birth, motherΓÇÖs age at delivery, educational attainment, pre-pregnancy body mass index, pre-pregnancy or during pregnancy smoking status, alcohol consumption during pregnancy, father's age, education, and annual family income were considered as covariates. Multivariable negative binomial regression was applied to evaluate the association between birth weight and ADHD traits, while adjusting for potential covariates. The interaction term between birth weight categories and binary polygenic risk was added to the model. Results: Birth weight of 2000-2499 g was not associated with ADHD traits. Birth weight under 2000 g was significantly associated with both inattention and hyperactivity. When accounting for higher and lower genetic risk for ADHD, only those with higher genetic risk and birth weight < 2000 g were associated with inattention (rate ratio [RR] 1.56, 95% CI 1.07-2.27) and hyperactivity (RR 1.87, 95% CI 1.14-3.06). Conclusions: Birth weight under 2000 g, together with the genetic risk of ADHD, contributes to higher levels of ADHD traits among Japanese children aged 8 to 9 years. The suggested association between low birth weight and ADHD is confined to children with a genetic susceptibility to ADHD, indicating the relevance of genetic-environmental interactions in the etiology

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Brain Imaging Behav. 2021.

QUANTITATIVE SYNTHETIC MRI REVEALS GREY MATTER ABNORMALITIES IN CHILDREN WITH DRUG-NA+»VE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Su S, Chen Y, Dai Y, et al.

To investigate the quantitative profiles of brain grey matter (GM) in pediatric drug-na+»ve ADHD patients using synthetic magnetic resonance imaging (SyMRI). A total of 37 drug-na+»ve pediatric ADHD and 27 age- and gender-matched healthy controls (HC) were enrolled in this study. Each subject underwent both SyMRI and conventional 3D T1-FSPGR scans. Quantitative parameters, T1 and T2 maps, were extracted from the SyMRI data. Between-group quantitative maps were compared using a general linear model analysis. Pearson correlation analysis was conducted to assess the association between significantly altered MR indices and clinical measurements in ADHD. Compared with the HC group, altered T1 and T2 relaxometry times in the ADHD group were mainly distributed in GM regions of the cerebellum, attention and execution control network, default mode network, and limbic areas. Moreover, the T1 value of the right cerebellum 8 was negatively correlated with the attention concentration level in ADHD (R = 0.140, P = 0.0225). With regards to T2 map, the associations were observed between the attention level of ADHD patients and left fusiform gyrus (R = 0.251, P = 0.0016), and right cerebellum crus2 (R = 0.142, P = 0.0214). Altered T1, T2 values found in specific regions of GM, including cerebellum, attention and execution control network, default mode network, and limbic areas, may reveal widespread micromorphology changes, i.e., brain iron deficiency, low myelin content, and enlarged vascular interstitial space in ADHD patients. Thus, T1, T2 values might be promising imaging markers for future ADHD studies

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Brain Imaging Behav. 2021.

TARGETING WORKING MEMORY TO MODIFY EMOTIONAL REACTIVITY IN ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY.

Kaiser A, Reneman L, Lucassen PJ, et al.

Understanding the neural mechanisms of emotional reactivity in Attention-Deficit/Hyperactivity Disorder (ADHD) may help develop more effective treatments that target emotion dysregulation. In adult ADHD, emotion regulation problems cover a range of dimensions, including emotional reactivity (ER). One important process that could underlie an impaired ER in ADHD might be impaired working memory (WM) processing. We recently demonstrated that taxing WM prior to the exposure of emotionally salient stimuli reduced physiological and subjective reactivity to such cues in heavy drinkers, suggesting lasting effects of WM activation on ER. Here, we investigated neural mechanisms that could underlie the interaction between WM and ER in adult ADHD participants. We included 30 male ADHD participants and 30 matched controls. Participants performed a novel functional magnetic resonance imaging paradigm in which active WM-blocks

were alternated with passive blocks of negative and neutral images. We demonstrated group-independent significant main effects of negative emotional images on amygdala activation, and WM-load on paracingulate gyrus and dorsolateral prefrontal cortex activation. Contrary to earlier reports in adolescent ADHD, no impairments were found in neural correlates of WM or ER. Moreover, taxing WM did not alter the neural correlates of ER in either ADHD or control participants. While we did find effects on the amygdala, paCG, and dlPFC activation, we did not find interactions between WM and ER, possibly due to the relatively unimpaired ADHD population and a well-matched control group. Whether targeting WM might be effective in participants with ADHD with severe ER impairments remains to be investigated

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Brain Sciences. 2021;11.

ADGRL3, FGF1 AND DRD4: LINKAGE AND ASSOCIATION WITH WORKING MEMORY AND PERCEPTUAL ORGANIZATION CANDIDATE ENDOPHENOTYPES IN ADHD.

Cervantes-Henriquez ML, Acosta-L+¦pez JE, Ahmad M, et al.

Attention deficit hyperactivity disorder (ADHD) is a highly heritable neurobehavioral disorder that affects children worldwide, with detrimental long-term consequences in affected individuals. ADHD-affected patients display visualΓÇômotor and visuospatial abilities and skills that depart from those exhibited by non-affected individuals and struggle with perceptual organization, which might partially explain impulsive responses. Endophenotypes (quantifiable or dimensional constructs that are closely related to the root cause of the disease) might provide a more powerful and objective framework for dissecting the underlying neurobiology of ADHD than that of categories offered by the syndromic classification. In here, we explore the potential presence of the linkage and association of single-nucleotide polymorphisms (SNPs), harbored in genes implicated in the etiology of ADHD (ADGRL3, DRD4, and FGF1), with cognitive endophenotypes related to working memory and perceptual organization in 113 nuclear families. These families were ascertained from a geographical area of the Caribbean coast, in the north of Colombia, where the community is characterized by its ethnic diversity and differential gene pool. We found a significant association and linkage of markers ADGRL3-rs1565902, DRD4-rs916457 and FGF1-rs2282794 to neuropsychological tasks outlining working memory and perceptual organization such as performance in the digits forward and backward, arithmetic, similarities, the completion of figures and the assembly of objects. Our results provide strong support to understand ADHD as a combination of working memory and perceptual organization deficits and highlight the importance of the genetic background shaping the neurobiology, clinical complexity, and physiopathology of ADHD. Further, this study supplements new information regarding an ethnically diverse community with a vast African American contribution, where ADHD studies are scarce

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Brain Sciences. 2021;11.

CHANGES IN SLEEP PATTERNS AND DISORDERS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDERS AND AUTISM SPECTRUM DISORDERS DURING THE COVID-19 LOCKDOWN.

Bruni O, Breda M, Ferri R, et al.

Background. The COVID-19 lockdown determined important changes in the sleep of a large percentage of the world population. We assessed the modifications of reported sleep patterns and disturbances in Italian children and adolescents with autism spectrum disorders (ASD) or attention deficit hyperactivity disorders (ADHD), compared to control children, before and during the COVID-19 lockdown in Italy.

Methods. Parents of 100 ASD, 236 ADHD patients, and 340 healthy children filled out an anonymous online survey and a modified version of the Sleep Disturbance Scale for Children (SDSC), advertised via social media, to evaluate sleep patterns and disturbances of their children before and during the lockdown.

Results. Before the lockdown, bedtime and risetime were not different between the three groups. During the lockdown, ADHD children tended to have a later bedtime and risetime than ASD and controls, while ASD children tended to maintain similar bedtime and risetime. Overall, during the lockdown, a reduced sleep duration significantly differentiated clinical groups from controls. Anxiety at bedtime, difficulties in falling asleep, and daytime sleepiness increased in all groups during the lockdown. Hypnic jerks, rhythmic movement disorders, night awakenings, restless sleep, sleepwalking, and daytime sleepiness increased in ASD and ADHD patients, in particular.

Conclusions. This is the first study comparing sleep habits and disorders in ASD and ADHD during the lockdown showing specific differences consistent with the core characteristics of two neurodevelopmental disorders

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Br J Anaesth. 2021.

MODERATORS OF THE ASSOCIATION BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EXPOSURE TO ANAESTHESIA AND SURGERY IN CHILDREN.

Shi Y, Dykhoff HJ, Guevara LRH, et al.

Background: Children's exposure to anaesthesia has been associated with risk of developing attention-deficit/hyperactivity disorder (ADHD). The goal of this study was to determine if selected patient characteristics moderate the association between exposure to anaesthesia and ADHD.

Methods: In a cohort of children born in between 2006 and 2012, exposure to anaesthesia before the age of 5 yr was categorised into unexposed, singly, or multiply exposed. Weighted proportional hazard regression was performed to evaluate the hazard ratios (HRs) of ADHD diagnosis related to anaesthesia exposure. Interaction analyses were performed to evaluate potential moderators.

Results: Among 185 002 children in the cohort, 9179 were diagnosed with ADHD. Compared with unexposed children, a single exposure to anaesthesia was associated with a HR of 1.39, (95% confidence interval [CI], 1.32-1.47) for ADHD. Multiple exposures were associated with a HR of 1.75 (95% CI, 1.62-1.87). In the analyses evaluating moderators of the association between exposure and ADHD, only the interaction for race was statistically significant (P=0.006); exposure increased the incidence of ADHD to a greater extent in non-White compared with White children. Among children with a single exposure, the age at exposure did not affect the relationship between exposure and incidence of ADHD (P=0.78).

Conclusions: Exposure of young children to anaesthesia and surgery is associated with an increased incidence of ADHD, with more exposures associated with greater risk. Compared with White children, non-White children are at greater risk for reasons that are unknown but need to be further explored

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Cardiol Young. 2021;31:969-72.

TREATMENT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN WITH CHD.

Pierick AR, Lynn M, McCracken CM, et al.

Introduction: The prevalence of attention deficit/hyperactivity disorder in the general population is common and is now diagnosed in 4%-12% of children. Children with CHD have been shown to be at increased risk for attention deficit/hyperactivity disorder. Case reports have led to concern regarding the use of attention deficit/hyperactivity disorder medications in children with underlying CHD. We hypothesised that medical therapy for patients with CHD and attention deficit/hyperactivity disorder is safe.

Methods: A single-centre, retrospective chart review was performed evaluating for adverse events in patients aged 4-21 years with CHD who received attention deficit/hyperactivity disorder therapy over a 5-year span. Inclusion criteria were a diagnosis of CHD and concomitant medical therapy with amphetamines, methylphenidate, or atomoxetine. Patients with trivial or spontaneously resolved CHD were excluded from analysis.

Results: In 831 patients with CHD who received stimulants with a mean age of 12.9 years, there was only one adverse cardiovascular event identified. Using sensitivity analysis, our median follow-up time was 686 days and a prevalence rate of 0.21% of adverse events. This episode consisted of increased frequency of supraventricular tachycardia in a patient who had this condition prior to initiation of medical therapy; the condition improved with discontinuation of attention deficit/hyperactivity disorder therapy.

Conclusion: The incidence of significant adverse cardiovascular events in our population was similar to the prevalence of supraventricular tachycardia in the general population. Our single-centre experience demonstrated no increased risk in adverse events related to medical therapy for children with attention deficit/hyperactivity disorder and underlying CHD. Further population-based studies are indicated to validate these findings

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Child Adolesc Psychiatry Ment Health. 2021;15.

WISC-IV PERFORMANCE OF CHILDREN WITH CHRONIC TIC DISORDER, OBSESSIVE-COMPULSIVE DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS FROM A GERMAN CLINICAL STUDY.

Wanderer S, Roessner V, Strobel A, et al.

Background: Chronic Tic Disorder (CTD), Obsessive-Compulsive Disorder (OCD) and Attention-Deficit/Hyperactivity Disorder (ADHD) are complex neuropsychiatric disorders that frequently co-occur. The aim of this study was to examine WISC-IV performance of a clinical cohort of children with CTD, OCD and/or ADHD.

Methods: N = 185 children aged 6 to 17-áyears from Germany with CTD, OCD and/or ADHD were examined with the WISC-IV that comprises four index scores (VCI: Verbal Comprehension Index, PRI: Perceptual Reasoning Index, WMI: Working Memory Index, PSI: Processing Speed Index) and a Full Scale Intelligence Quotient (FSIQ). WISC-IV profiles of children with CTD-only, OCD-only, ADHD-only, CTD+ADHD, CTD+OCD and CTD+OCD+ADHD were compared with the WISC-IV norm (N = 1650, M = 100 and SD = 15) and among each other.

Results: Unpaired t-tests revealed that children with ADHD-only showed significant lower PSI scores, whereas children with CTD-only and OCD-only had significant higher VCI scores as compared to the German WISC-IV norm. One-way ANOVA revealed that children with ADHD-only showed significant lower WMI scores as compared to children with CTD+OCD.

Conclusions: We were able to confirm previous evidence on WISC-IV profiles in ADHD in a German clinical sample and contribute new findings on cognitive performance in children with (non-)comorbid CTD and OCD that have to be seen in light of the studyΓÇÖs limitations

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Child Neuropsychol. 2021.

RELATIONSHIP BETWEEN SLUGGISH COGNITIVE TEMPO, IQ AND ACADEMIC ACHIEVEMENT TEST SCORES, AND ACADEMIC IMPAIRMENT IN AUTISM, ADHD, AND ELEMENTARY SCHOOL SAMPLES.

Mayes SD, Kallus R, Bangert LR, et al.

Sluggish cognitive tempo (SCT) is of renewed interest. The relationship between SCT, IQ and achievement scores, and academic impairment ratings was investigated in 218 students with autism and 676 with ADHD (6-16 years) and 549 elementary school students (IQ 80). Mothers rated their children on the Pediatric Behavior Scale. Children in the autism/ADHD sample were also rated by teachers. Correlations between SCT and IQ and achievement scores (Verbal Comprehension, Perceptual Reasoning, Working Memory, Processing Speed, reading, math, and written expression) were all negative and were nonsignificant in the total autism/ADHD and elementary school samples, except for small correlations with Processing Speed and a timed math test. In contrast, mother and teacher SCT ratings were significantly related to mother and teacher academic and cognitive impairment ratings. SCT was not a significant predictor of achievement scores or academic impairment ratings in regression analysis. The strongest predictor of achievement test scores was IQ, and the strongest predictors of academic impairment were mother and teacher cognitive impairment ratings. Teacher inattention ratings predicted teacher academic impairment ratings in autism/ADHD and mother inattention ratings predicted mother academic impairment ratings in elementary school children. Therefore, inattention was more predictive of academic functioning than was SCT. Research shows a weak link between SCT and processing speed (contrary to what is implied by the term sluggish cognitive tempo), and other neuropsychological test scores are not consistently associated with SCT. It remains to be determined if neuropsychological tests can be developed to measure and further our understanding of SCT

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Child Neuropsychol. 2021.

IS THERE A RELATION BETWEEN VISUAL MOTOR INTEGRATION AND ACADEMIC ACHIEVEMENT IN SCHOOL-AGED CHILDREN WITH AND WITHOUT ADHD?

Carames CN, Irwin LN, Kofler MJ.

Objective: Visual motor integration (VMI) and its subcomponents are positively associated with academic achievement in early elementary school-age children, However, our understanding of this association in older

elementary school-aged children, and specifically children with ADHD, is limited. The current study included older school-aged children with and without ADHD and examined the relation between VMI subcomponents and three core academic achievement domains.
Method: A well-characterized, clinically evaluated sample of 39 children ages 8-13 years (M=10.07, SD=1.56; 14 girls); 67.5%White/non-Hispanic) were assessed for ADHD symptoms and administered tests assessing their VMI and core academic skills.
Results: Children with ADHD exhibited significantly lower VMI skills (d=1.16, p =.004), but did not differ significantly from their non-ADHD peers in terms of visual perception or motor coordination skills (both p>.18). Further, backward-entry step-wise regression analyses indicated that children's visual perception skills (b=.38; p=.001), motor coordination skills (b=.25; p=.028), and IQ (b=.60; p < .001) predicted their reading skills. Children's VMI skills (b=.28; p=.007), visual perception skills (b=.21; p=.034), motor coordination skills (b=.21; p=.049), IQ (b=.60; p<.001), and sex (b=.33; p<.001) predicted their math skills. Children's motor coordination skills (b=.50; p=.003) and ADHD symptoms (b=-.44; p=.01) predicted their written language skills.
Conclusions: Results indicate that children with ADHD exhibit more difficulties with VMI skills than their peers, and that these difficulties are related to the integration of visual perception and motor coordination skills. In addition, these results provide further evidence for the significant influence that VMI skills have on school-aged children's academic achievement

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Child Neuropsychol. 2021.

PSYCHOMETRIC PROPERTIES OF THE BEHAVIOR RATING INVENTORY OF EXECUTIVE FUNCTION, SECOND EDITION (BRIEF2) IN A SAMPLE OF CHILDREN WITH ADHD IN IRAN.

Parhoon K, Moradi A, Alizadeh H, et al.

This study investigated the psychometric properties of a Persian translation of the Behavior Rating Inventory of Executive Function(BRIEF2) in 253 children with ADHD in Iran (137 boys, 116 girls)ages 8 to 12-áyears old (M =10.04; SD=1.42). The parents of the children completed the Persian BRIEF2 and the Childhood Executive Functioning Inventory (CHEXI). The findings indicated that the Persian version of BRIEF2 had good reliability (internal and test-retest) and satisfactory to good validity (convergent and construct). With respect to its construct validity, confirmatory factor analysis revealed that a three-factor solution was the best model fit for the nine subscales of the BRIEF2, which supports the valid interpretation of the three BRIEF2 indexes in the Persian BRIEF2. These findings support the clinical relevance of the Persian BRIEF in Iranian children with ADHD, as well as the multidimensional nature of executive functions

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Child Neuropsychol. 2021.

THE ASSOCIATION BETWEEN HYPERACTIVE BEHAVIOUR AND COGNITIVE INHIBITION IMPAIRMENTS IN YOUNG CHILDREN.

Burley DT, Anning KL, Van Goozen SHM.

Hyperactivity is one of the core features of attention-deficit hyperactivity disorder (ADHD), and yet there is evidence that hyperactive behavior in children with ADHD is not ubiquitous and could be a compensatory response to high cognitive demands. No research has yet objectively measured hyperactive behavior in young children who are demonstrating early signs of ADHD or examined the role of emotional state on hyperactivity levels.The current study measured motor activity using actigraphy during baseline, cognitive inhibition (Flanker task), and emotion arousing (Impossibly Perfect Circles task) conditions in 95 children aged 4-7 years old with developmental difficulties, including emerging symptoms of ADHD. We examined the relationship between objectively recorded activity, parent-rated hyperactivity problems, using the Strengths and Difficulties Questionnaire (SDQ), and cognitive inhibition task performance.Parent ratings of hyperactivity (but not inattention) symptoms were positively related to recorded hyperactivity, and this relationship was specific to activity measured during the cognitive inhibition task. Impaired cognitive inhibition performance was related to increased measured movement and this association was strongest in children who were rated as having the highest levels of hyperactive behavior.These findings confirm theoretically predicted associations between objectively recorded hyperactivity and impaired executive functioning and

support the notion that hyperactivity in children emerges in response to high cognitive demands. The results encourage further investigation into the role of hyperactivity as a transdiagnostic dimension that can explain variation within and between different types of diagnostic classifications

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Child Care Health Dev. 2021 Sep;47:667-74.

QUALITY OF LIFE IMPROVEMENT IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER REDUCES FAMILY'S STRAIN: A STRUCTURAL EQUATION MODEL APPROACH.

Rocco I, Bonati M, Corso B, et al.

Objectives: The objective of the study is to analyse how the quality of life of children diagnosed with attention-deficit/hyperactivity disorder (ADHD) impacts the relationship between disease severity and family burden.
Method: The data collected by a longitudinal, observational study involving 1478 children with ADHD residing in 10 European countries (aged 6 to 18 years) were analysed to evaluate the relationships between ADHD severity, the children's quality of life and family burden.
Results: The disorder's severity directly and indirectly affected the children's health-related quality of life (HRQoL) and family burden. The degree of family burden was modulated by the children's HRQoL.
Conclusions: One of the primary causes of the stress experienced by parents of children with ADHD is their perception of the child's reduced HRQoL and not the symptom severity itself. Efforts to minimize symptom severity cannot alone reduce family burden

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Child Youth Serv Rev. 2021 Sep;128.

TREATING ATTENTION PROBLEMS IN CHILDREN EXPOSED TO INTIMATE PARTNER VIOLENCE: EVALUATING THE PRESCHOOL KIDS' CLUB.

Clark HM, Galano MM, Grogan-Kaylor AC, et al.

Childhood exposure to intimate partner violence (IPV) increases risk for symptoms of inattention and hyperactivity, and yet no known evaluations of interventions for IPV-exposed children have demonstrated effectiveness in treating their attention problems. This study examined the utility of the Preschool Kids' Club (PKC), a treatment program tailored to the needs of preschool-aged children whose mothers had experienced IPV, in reducing children's attention problems during this critical developmental period. Participants (N = 120) were preschool-aged children who, with their mothers, participated in an eight-year randomized controlled trial (RCT) of the PKC. Longitudinal multi-level modeling was used to evaluate the main effect of intervention participation on children's attention problems, as well as moderating effects of IPV exposure and maternal depression. Although there was no main effect of intervention participation, children's outcomes were moderated by IPV exposure. Specifically, among children exposed to high levels of IPV, symptoms of inattention and hyperactivity were significantly lower for intervention participants than children in the control group one year post-intervention. These improvements were not sustained in the eight-year follow-up. Results provide support for the use of trauma-specific interventions for children exhibiting attention problems following exposure to high levels of IPV. However, more comprehensive and long-term treatment may be necessary to promote enduring change

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Clin Pediatr (Phila). 2021 Oct;60:452-58.

INTEGRATION AND IMPACT OF TELEMEDICINE IN UNDERSERVED PEDIATRIC PRIMARY CARE.

Walters J, Johnson T, DeBlasio D, et al.

Telemedicine, more novel in provision of pediatric care, rapidly expanded due to the recent coronavirus disease 2019 pandemic. This study aimed to determine the feasibility of telemedicine for acute and chronic care provision in an underserved pediatric primary care center. Items assessed included patient demographic data, chief complaint, and alternative care locations if telemedicine was not available. In our setting, 62% of telemedicine visits were for acute concerns and 38% for chronic concerns. Of acute telemedicine visits, 16.5% of families would have sought care in the Emergency Department/Urgent Care, and 11.3% would have opted for no care had telemedicine not been offered. The most common chronic issues addressed were attention deficit hyperactivity disorder (80.3%) and asthma (16.9%). Racial disparities existed among our

telemedicine visits with Black patients utilizing telemedicine services less frequently than non-Black patients. Telemedicine is feasible for pediatric acute and chronic care, but systems must be designed to mitigate widening racial disparities

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Clin Case Stud. 2021;20:351-67.

PROLONGED EXPOSURE THERAPY: A CASE OF COMORBID PTSD, ADHD, AND GAD.

DiBacco TA, Gaynor ST.

This case study displays the successful application of Prolonged Exposure (PE) for a client with diagnoses of Posttraumatic Stress Disorder (PTSD), Attention Deficit Hyperactivity Disorder (ADHD), and Generalized Anxiety Disorder (GAD). To our knowledge ADHD has not been examined as a predictor or moderator of PE outcomes. As such, practitioners have precious little information about how to proceed in such cases, which highlights the importance of careful individual assessment and case conceptualization. There is also a dearth of information on the effects of combining PE (a research-supported psychological intervention for PTSD) with psychostimulant medication (a research-supported pharmacological intervention for ADHD). The present case study illustrates a positive synergy between psychostimulant treatment and PE. The unique adjustments made to deliver services (including in the face of COVID-19) are described as well as what this case suggests about the effects of psychostimulant use on PTSD symptoms and the new learning that occurs during PE

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Clinical Nutrition ESPEN. 2021;44:342-47.

FOOD INTAKE AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN: A CASE_CONTROL STUDY.

Jamshidnia A, Tavallaei M, Hosseinzadeh M.

Background: The purpose of present study was to determine and compare food intake in children with attention deficit hyperactivity disorder (ADHD) and healthy children.

Materials and methods: In this case-control study, 110 hyperactive children who had referred to Khatam Al-Anbia Clinic and Imam Hussein Psychological Center in Yazd were selected. In addition, for each case, two healthy controls homogenized in terms of age and sexes were enrolled from primary schools in Yazd, from the same urban region of the cases. After completing the general information questionnaires, height and weight were measured. The food intake of individuals was evaluated through a validated food frequency questionnaire comprising 186 items. As for quantitative and categorical variables, the independent t-test and chi-square test were used respectively, and the values were reported as mean and standard deviation. Independent T-test was used to compare food intake between the two groups.

Results: No significant difference was identified between body mass index and energy intake of the two groups. Hyperactive children proved to have a higher rate of physical activity than non-hyperactive children ($p = 0.001$). Vitamin B12 and riboflavin consumption in hyperactive children proved to be significantly lower than that of the healthy group ($p = 0.02$). Intake of refine grain in the case group was significantly higher compared to the control group ($p = 0.02$). Healthy children consumed fruits and vegetable ($p = 0.02$), low fat milk ($p = 0.003$) and egg ($p = 0.01$) more than children with ADHD.

Conclusion: The present study revealed that hyperactive children consume less fruit and vegetables, low-fat milk and eggs as well as food sources containing B vitamins while consuming higher levels of refined grains. Future studies such as cohort and interventional types are needed to confirm these results

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Clin Pharmacol Drug Dev. 2021;10:68-69.

PHARMACOKINETICS REVIEW OF METHYLPHENIDATE PRODUCTS IN PRESCHOOLERS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Desai JM, Zhuang L.

Statement of Purpose, Innovation or Hypothesis: In 2018, around 9.8 percent of US children had been diagnosed with attention deficit hyperactivity disorder (ADHD). The median age of onset of ADHD is four years and sometimes severe ADHD symptoms are diagnosed at the age of three years. Methylphenidate (MPH) is a first-line medication for ADHD patients with a variety of dosage forms and durations of effect. Up

to date, MPH is not yet approved in preschoolers (four to five years) with ADHD. A systematic review of pharmacokinetics (PK) of MPH in preschoolers with ADHD was conducted to identify the challenges and opportunities. Description of Methods and Materials: We did a thorough search of publicly-available information such as drugs@FDA and PubMed databases focusing on pharmacokinetics (PK) of MPH in preschoolers with ADHD using keywords of 'preschoolers', 'ADHD' and 'PK study'. Data and Results: The FDA has approved 14 MPH products, among which one product is only approved to be used in children aged 6 to 12 years, four MPH products are approved to be used in children aged 6 to 12 years and adolescents (13 to 17 years), and all other MPH products are approved in children aged 6 to 12 years, adolescents and adults. PK studies have been conducted in preschoolers for a few MPH products. The pharmacokinetic profiles of MPH appear to be comparable across age groups after adjustment for bodyweight. The dose-normalized exposures (Cmax and AUC) in preschoolers were expected to be 2-to 3-fold higher than those observed in children aged 6 to 12 years and adolescents. Population PK models across age groups have been successfully established for several MPH products. Due to the enrollment difficulty and ethical issues, quantitative approaches may be useful to characterize PK of MPH in preschoolers with limited PK information (e.g., small sample size and sparse PK samples). Moreover, MPH is known to display a strong exposure-response relationship and FDA guidance indicates that efficacy extrapolation may be a reasonable approach for preschoolers with ADHD. Therefore, quantitative models may serve as a critical role to provide dose recommendations in preschoolers with ADHD. Interpretation, Conclusion or Significance: It is challenging to extensively evaluate efficacy and safety of MPH products in preschoolers. The PK of MPH in preschoolers can be considered as key evidence to facilitate dose selection and for use in the safety study. There is an opportunity to apply quantitative models to overcome the practical issues and support efficient drug development for MPH products in preschoolers with ADHD

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Dent Clin North Am. 2021 Oct;65:753-73.

SEDATION AND ANESTHESIA FOR THE ADOLESCENT DENTAL PATIENT.

Cooke M, Tanbonliong T.

This article focuses on sedation/anesthesia of adolescent patients in the dental setting. Preoperative evaluation, treatment planning, monitoring, and management are critical components to successful sedation. The authors discuss commonly administered agents and techniques to adolescents, including nitrous oxide/oxygen analgesia. The levels and spectrum of sedation and anesthesia are reviewed. Common comorbidities are also presented as they relate to sedation of the adolescent dental patient

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Developmental Medicine & Child Neurology. 2021 Sep;63:1107-13.

CHILDHOOD NEURODEVELOPMENTAL DISORDERS AND MATERNAL HYPERTENSIVE DISORDER OF PREGNANCY.

Chen KR, Yu T, Kang L, et al.

Aim: To examine the association of maternal chronic hypertension and pregnancy-induced hypertension (PIH)/preeclampsia with childhood neurodevelopmental disorders (NDDs) in a large-scale population-based cohort.

Method: We conducted a linked Taiwan National Health Insurance Research Database cohort study of children born between 2004 and 2008 (n=877 233). Diagnoses of autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), developmental delay, intellectual disability, cerebral palsy (CP), and epilepsy/infantile spasms were identified from birth to the end of 2015. Cox proportional hazards models were fitted with adjustment for potential confounders to estimate the effect of maternal hypertensive disorder of pregnancy on childhood outcomes.

Results: Compared with the offspring of unexposed mothers, offspring of mothers with chronic hypertension or PIH/preeclampsia exhibited increased risk of developing a wide spectrum of NDDs. Chronic hypertension was associated with increased risks of ADHD (hazard ratio 1.22, 95% confidence interval [CI] 1.13–1. 31), developmental delay (1.29, 1.21–1.38), intellectual disability (1.67, 1.43–1.95), CP (1.45, 1.14–1.85), and epilepsy/infantile spasms (1.31, 1.10–1.56) in the offspring, whereas PIH/preeclampsia was associated with increased risks of ASD (1.27, 1.12–1.43), ADHD (1.23, 1.17–1.29), developmental delay (1.29, 1.24–1.35), intellectual disability (1.53, 1.37–1.71), CP (1.44, 1.22–1.70), and epilepsy/infantile spasms (1.36, 1.22–1.52)

in the offspring after adjustment for potential confounders. The co-occurrence of maternal diabetes, preterm deliveries, or fetal growth restriction further increased the risk.
Interpretation: Chronic hypertension or PIH/preeclampsia seems to be sufficient to increase the risk of childhood NDDs

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Dev Med Child Neurol. 2021.
INTERFERENCE WITH PRENATAL, PERINATAL, AND NEONATAL BRAIN DEVELOPMENT IS ASSOCIATED WITH A HIGH RISK FOR AUTISM AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Kraegeloh-Mann I.

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Dev Psychol. 2021 Aug;57:1359-71.
GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO CO-OCCURRING ADHD AND EMOTIONAL PROBLEMS IN SCHOOL-AGED CHILDREN.
Gustavson K, Torvik FA, Eilertsen EM, et al.
Children with attention deficit hyperactivity disorder (ADHD) often experience co-occurring emotional problems. ADHD with this comorbidity is associated with poorer outcomes than ADHD without comorbidity. Better understanding of the etiology of comorbidity could improve prevention of negative outcomes for children with ADHD. The sample consisted of 567 twin pairs, 3,632 sibling pairs, and 2,340 cousin pairs from the Norwegian Mother, Father and Child Cohort Study. Mothers rated offspring symptoms of ADHD, anxiety, and depression at 8 years of age. Biometric modeling was performed to examine genetic and environmental contributions to co-occurring symptoms of ADHD and emotional problems in the children. We fitted four variable (inattention, hyperactivity/impulsivity, anxiety, and depression) covariance matrices of additive genetic, common environmental, twin- and individual-specific environmental effects. Genetic, shared environmental, and individual-specific environmental factors contributed to the correlation between ADHD and depression. The pattern was similar for both inattention and hyperactivity/impulsivity. Familial risk factors (genetic and shared environment), but not individual-specific environmental factors contributed to the positive correlations between each of the two ADHD subdomains and anxiety. The genetic contributions to ADHD-depression comorbidity only partly overlapped with genetic contributions to ADHD-anxiety comorbidity. Our findings indicate that shared risk factors for ADHD and comorbid depression were familial as well as individual-specific, while shared risk factors for ADHD and comorbid anxiety were primarily familial

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Diabetes. 2021;70.
PREVALENCE OF MENTAL, BEHAVIORAL, AND DEVELOPMENTAL DISORDERS AMONG YOUTH WITH DIABETES, UNITED STATES (2016-2019).
Barrett CE, Bullard KM, Park J, et al.
Diabetes (DM) is among the most common chronic diseases diagnosed in youth in the United States. In adults, a bi-directional relationship has been demonstrated between DM and mental, behavioral, and developmental disorders (MBDD). Such comorbidities may significantly impact the quality of life of patients with DM and disease management. However, little is known about the association of DM and MBDD in youth. To examine the magnitude of overlap between these chronic conditions, we calculated prevalence estimates using the 2016-2019 National Survey of Children's Health, an annual, cross-sectional survey of non-institutionalized US children aged 0-17 years (N = 131,774). Parents were asked if their child was ever diagnosed with DM or with any of the following MBDDs: attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder, learning disability, intellectual disability, developmental delay, anxiety, depression, behavioral or conduct problems, Tourette syndrome, or speech disorder. We present crude prevalence estimates and predictive margins adjusted for age, sex, and race/ethnicity, both weighted to be representative of the US youth population. Among US youth, prevalence estimates were 0.45% (95%CI: 0.36-0.55) for DM and 22.7% (22.2-23.2) for any MBDD. Crude prevalence of any MBDD varied by DM status (DM: 43.7% [34.5-53.4]; no DM: 22.6% [22.1-23.1]). Compared with youth without DM, those with DM had a higher adjusted prevalence of any MBDD (prevalence ratio: 1.55 [1.20-2.00]) and individual MBDDs (p <.05),

except for ADHD, Tourette syndrome and speech disorder. These results suggest a significant health burden with more than 2 out of 5 youth with DM having any MBDD. Future work examining potential causal pathways could be beneficial. Understanding associated factors may ultimately lead to future preventative strategies for MBDD and DM in youth

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Endokrynologia Polska. 2018;69:241-45.

INTELLECTUAL PERFORMANCE OF CHILDREN OF MOTHERS WITH AN UNTREATED THYROID DISORDER IN THE FIRST TRIMESTER OF PREGNANCY.

Komendov I, et al.

Introduction: The focus of the present study was the importance of the mother's thyroid function for foetal development in the first trimester, when the baby is totally dependent on the mother for thyroid hormones.

Materials and methods: The study consisted of testing the intellectual performance of children with both euthyroid and thyroid-dysfunction mothers. The experimental group comprised 60 children of mothers with an untreated thyroid disorder in the first trimester of pregnancy (TSH 3.5 mlU/L [standard 0.15-3.5] and/or TPO-Ab 20 lU/L [standard < 20]). The control group contained 132 children whose mothers showed no symptoms of a thyroid disorder either before or during pregnancy/postpartum. Both groups of children were administered the Wechsler Intelligence Scale for Children - Third Edition (WISC-III), whereby the intellectual performance of the experimental-group children was compared with that of the control-group children. The comparison included the percentage of children with IQ Γëñ 85 and SLD and/or ADD risks. Our research is a follow-up to a blanket thyroid screening of 1649 pregnant women conducted during 2004-2006 in the region around Havl+¡ckuv Brod.

Results: The research found no significant difference between the two groups of children with respect to their intellectual abilities, either regarding their overall IQ (p = 0.67), verbal IQ (p = 0.81), performance IQ (p = 0.41), or the individual scores (VCI: P = 0.85; POI: P = 0.54, FDI: P = 0.57; PSI: P = 0.13), nor did the experimental group show a significantly higher occurrence of children with IQ 85 than the control group (p = 0.66). However, the experimental group did exhibit a statistically significant increase in the percentage of children with a suspected SLD or clinically significant attention issues (p = 0.05).

Conclusion: Untreated thyroid disorders in the first trimester of pregnancy can increase the risk of the child developing attention or learning issues

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Environ Res. 2021 Sep;200:111345.

NEURODEVELOPMENTAL IMPACT OF THE OFFSPRING BY THYROID HORMONE SYSTEM-DISRUPTING ENVIRONMENTAL CHEMICALS DURING PREGNANCY.

Salazar P, Villaseca P, Cisternas P, et al.

Everyday use chemicals have been demonstrated to be endocrine disruptors. Since normal thyroid function during pregnancy is transcendental for the neurodevelopment of the offspring, knowledge of endocrine disrupting chemicals (EDC) is of main importance. The aim of our study is to recognize and describe EDC actions in pregnant women and focus on neurodevelopmental processes that can lead to neurotransmitter imbalance and cognitive impairment, and the possible clinical outcomes in the newborn and child. We searched PubMed databases for animal studies and clinical trials evaluating chemicals recognized as thyroid disruptors -perchlorate, phthalates, bisphenol A-, as well as chemicals with potential thyroid disruption activity -parabens, pesticides and persistent organic pollutants, on thyroid hormones (THs) levels and their bioavailability during pregnancy, and the outcome in newborns, infants and children. We also exhibit evidence from worldwide cohort studies to this regard. The publications reviewed show: 1) known endocrine disruptors have an association with hormonal thyroid levels, where an effect of increase or decrease in TH concentrations has been reported depending on the chemical exposed 2) associations between TH, EDCs and neurocognitive disorders have been addressed, such as ADHD, though no conclusive impact on potential related disorders as autism has been established, 3) perchlorate has demonstrated effects on thyroid levels on iodine uptake. In conclusion, detrimental risks and long-term consequences after in-utero

exposure to EDCs are being reported in several cohort studies and further research must be conducted to establish a well-known cause-effect association

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Epidemiology. 2021 Sep;32:664-71.

FETAL GROWTH TRAJECTORIES AMONG SMALL FOR GESTATIONAL AGE BABIES AND CHILD NEURODEVELOPMENT.

Ferguson KK, Sammallahti S, Rosen E, et al.

BACKGROUND: Being born small for gestational age (SGA, <10th percentile) is a risk factor for worse neurodevelopmental outcomes. However, this group is a heterogeneous mix of healthy and growth-restricted babies, and not all will experience poor outcomes. We sought to determine whether fetal growth trajectories can distinguish who will have the worst neurodevelopmental outcomes in childhood among babies born SGA.
METHODS: The present analysis was conducted in Generation R, a population-based cohort in Rotterdam, the Netherlands (N = 5,487). Using group-based trajectory modeling, we identified fetal growth trajectories for weight among babies born SGA. These were based on standard deviation scores of ultrasound measures from mid-pregnancy and late pregnancy in combination with birth weight. We compared child nonverbal intelligence quotient (IQ) and attention deficit hyperactivity disorder (ADHD) symptoms at age 6 between SGA babies within each growth trajectory to babies born non-SGA.
RESULTS: Among SGA individuals (n = 656), we identified three distinct fetal growth trajectories for weight. Children who were consistently small from mid-pregnancy (n = 64) had the lowest IQ (7 points lower compared to non-SGA babies, 95% confidence interval [CI] = -11.0, -3.5) and slightly more ADHD symptoms. Children from the trajectory that started larger but were smaller at birth showed no differences in outcomes compared to children born non-SGA.
CONCLUSIONS: Among SGA children, those who were smaller beginning in mid-pregnancy exhibited the worst neurodevelopmental outcomes at age 6. Fetal growth trajectories may help identify SGA babies who go on to have poor neurodevelopmental outcomes

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Eur Child Adolesc Psychiatry. 2021.

EXAMINING THE INFLUENCE OF IRRITABILITY AND ADHD ON DOMAINS OF PARENTING STRESS.

Flynn MM, Rosen PJ, Reese JS, et al.

Parents of children with ADHD typically report higher levels of parenting stress than parents of typically developing children. Children with ADHD display developmentally inappropriate levels of hyperactivity, impulsivity, and inattention. Some children with ADHD are also prone to particularly high levels of tonic irritability that may explain some of the impairments typically found in ADHD. The present study sought to determine the unique impact of ADHD and tonic irritability on child-related parenting stress domains (e.g., difficult child, parentΓÇôchild dysfunctional interactions). 145 mothers of children with and without ADHD aged 7ΓÇô12-áyears participated in the current study. Mothers completed self-report measures of parenting stress as well as a diagnostic structured interview. Ecological momentary assessment (EMA) was used to assess tonic irritability in an ecological environment. Indirect effects models were specified using PROCESS Model 4. For the parent child dysfunctional interaction domain, the data were best fit by a model specifying a significant total effect of ADHD that was fully accounted for by an indirect effect through irritability. For the difficult child domain, model testing indicated a significant total effect of ADHD that was partially accounted for by an indirect effect through irritability. The current study adds support to the growing body of literature acknowledging the role of tonic irritability in children with ADHD. Furthermore, the results provide novel insight in the complex relation of irritability, child ADHD, and domains of parenting stress

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Frontiers in Pediatrics. 2021;9.

FEEDING AND EATING DISORDER AND RISK OF SUBSEQUENT NEURODEVELOPMENTAL DISORDERS: A POPULATION-BASED COHORT STUDY.

Shan H, Li F, Zhang J, et al.

Background: There are limited data concerning the long-term mental health of children with feeding and eating disorder (FED). We aimed to investigate whether children with FED are at greater risks of developing

emotional/behavioral disorders with onset usually during childhood, attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and intellectual disability (ID).
Methods: We conducted a population-based cohort study, including all singleton births in Denmark from January 1, 1995, to December 31, 2015. For each child diagnosed with FED, 10 age- and sex-matched controls who did not meet the criteria for FED were randomly selected from the general population. Associations were estimated with Cox regression modes adjusting for other perinatal and maternal factors, and sibling analyses were performed for controlling potential confounding by shared familial (genetic or environmental) factors.
Results: Of the 1,256,989 individuals in the cohort, there were 1967 (53.4% girls) children diagnosed with FED. Children with FED had higher risks for clinically diagnosed emotional/behavioral disorders with onset usually in childhood (hazard ratio [HR], 2.78; 95% CI, 2.34ΓÇô3.31), ADHD (HR, 1.74; 95% CI, 1.33-2.26), ASD (HR, 3.05; 95% CI, 2.36-3.94), and ID (HR, 6.38; 95% CI, 4.48-9.11), compared with matched controls. Girls with FED are at greater risks for emotional/behavioral disorders and ID, but not ADHD and ASD. Alike, in sibling analysis, increased rates are also observed for other neurodevelopmental disorders, but not for ADHD.
Conclusion: Children with FED are associated with substantially increased risks of emotional/behavioral disorders, ADHD, ASD, and ID. This study highlights the importance of carefully monitoring neurodevelopmental disorders in children with FED

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Frontiers in Pediatrics. 2021;9.
PRENATAL IGE AS A RISK FACTOR FOR THE DEVELOPMENT OF CHILDHOOD NEURODEVELOPMENTAL DISORDERS.
Straughen JK, Sitarik AR, Johnson CC, et al.
Background: Few studies have examined if maternal allergic disease is associated with an offspring's neurodevelopment. We hypothesized that Th-2 biased maternal immune function assessed as total serum immunoglobulin (Ig) E is associated with attention deficit hyperactivity disorder (ADHD).
Methods: Data are from the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (WHEALS), a racially and socioeconomically diverse birth cohort in metropolitan Detroit, Michigan. Maternal total IgE was measured prenatally and at 1-month postpartum. Child total IgE was assessed at birth, 6 months, and 2 years of age. ADHD diagnosis was based on the parental report at the 10ΓÇô12-year study visits or medical chart abstraction. Total IgE was log2 transformed. Poisson regression models with robust error variance were used to calculate the risk ratios (RR). Inverse probability weighting was used to correct for potential bias due to a loss to follow-up and non-response.
Results: Of the 636 maternal-child pairs in the analysis, 513 children were neurotypical and 123 had ADHD. Maternal prenatal total IgE was significantly associated with ADHD even after adjustment for potential confounders (RR = 1.08, 95% CI 1.03ΓÇô1.13). Maternal and child IgE measures were positively and significantly correlated, but child total IgE was not associated with ADHD at any time point.
Conclusions: Maternal prenatal IgE may influence neurodevelopment, but additional studies are needed to confirm and expand these findings

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Front Psychiatry. 2021;12.
THE VIRTUAL CITY PARADIGMTM FOR TESTING VISUO-SPATIAL MEMORY, EXECUTIVE FUNCTIONS AND COGNITIVE STRATEGIES IN CHILDREN WITH ADHD: A FEASIBILITY STUDY.
Del Lucchese B, Belmonti V, Brovedani P, et al.
Navigation is a complex process, requiring target localization, route planning or retrieval, and physical displacement. Executive functions (EFs) such as working memory, inhibition and planning are fundamental for succeeding in this complex activity and are often impaired in Attention Deficit and Hyperactivity Disorder (ADHD). Our aim was to analyze the feasibility of a new ecological navigation task, the Virtual City paradigm (VC) to test visuo-spatial memory and EFs in children with ADHD. Visuo-spatial short and working memory, inhibition and planning skills were tested with standardized tasks. The VC, a new paradigm developed by our group, used the Virtual CarpetTM technology, consisting of a virtual town with houses, streets and crossroads projected on the ground. It includes a motion capture system, tracking body movement in 3D in

real time. In one condition, children were required to walk through the city and reach a sequence of houses. In the other, before walking, they had to plan the shortest path to reach the houses, inhibiting the prepotent response to start walking. The results show a good feasibility of the paradigm (feasibility checklist and ad hoc questionnaire), being ecological and motivating. VC measures of span positively correlated with visuo-spatial short and working memory measures, suggesting that VC heavily relies on efficient spatial memory. Individual subject analyses suggested that children with ADHD may approach this task differently from typically developing children. Larger samples of ADHD and healthy children may further explore the specific role of EFs and memory, potentially opening new avenues for intervention

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Hum Brain Mapp. 2021 Sep;42:4362-71.

ATYPICAL SULCAL PATTERN IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Li X, Wang W, Wang P, et al.

Neurodevelopmental disorders, such as attention-deficit/hyperactivity disorder (ADHD), are often accompanied by disrupted cortical folding. We applied a quantitative sulcal pattern analysis technique using graph structures to study the atypical cortical folding at the lobar level in ADHD brains in this study. A total of 183 ADHD patients and 167 typical developmental controls matched according to age and gender were enrolled. We first constructed sulcal graphs at the brain lobar level and then investigated their similarity to the typical sulcal patterns. The within-group variability and interhemispheric similarity in sulcal patterns were also compared between the ADHD and TDC groups. The results showed that, compared with controls, the left frontal, right parietal, and temporal lobes displayed altered similarities to the typical sulcal patterns in patients with ADHD. Moreover, the sulcal patterns in ADHD seem to be more heterogeneous than those in controls. The results also identified the disruption of the typical asymmetric sulcal patterns in the frontal lobe between the ADHD and control groups. Taken together, our results revealed the atypical sulcal pattern in boys with ADHD and provide new insights into the neuroanatomical mechanisms of ADHD

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Ideggyogyaszati Szemle. 2021;74:227-33.

PERSONALISED EPILEPSY TREATMENT.

Anna A.

Epilepsy is one of the most common chronic neurological disease in childhood. Patients with epilepsy - even with socalled benign epilepsy - need medication for years. During this time, children go through a very big change, not only gaining weight and height, but also changing hormonal and metabolic processes. Maturation processes in different brain areas also take place at different rates depending on age. All of these should be considered when preparing a therapeutic plan. In everyday practice after the diagnosis of epilepsy, the applied drug is most often selected based on the shape and type of seizure. However, a number of other factors need to be considered when designing a therapeutic strategy: 1. efficacy (form of epilepsy, type of seizure), 2. age, gender, 3. pharmacological properties of the drug, 4. adverse drug reaction profile, 5. lifestyle (community), figure (skinny, corpulent, obese), 6. other comorbidities (nutrition, behavioral and learning problems, circulatory disorders, kidney or liver disease), 7. expected interactions with other drugs already used, 8. genetics, 9. other aspects (drug registration and prescription rules). The purpose of this article is to help to decide which antiepileptic drugs are expected to have the least side effects in a particular child with different comorbidities and which medications should be avoided if possible

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Indian Journal of Forensic Medicine and Toxicology. 2021;15:1939-49.

ENHANCEMENT OF COPING PATTERNS AMONG PARENTS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Moawad NAA, Mourad GM, Ata F.

Background: Families of children with ADHD encounter greater difficulties such as family conflict, negative parent-child relationship, higher rates of parent stress and ineffective coping.

The aimof study: was to enhancement of coping patterns among parents of children with ADHD.

Study design: a quasi-experimental design was utilized to conduct this study.

Setting: This study was conducted at Pediatric Out-Patient Clinic atEl-Abbassia hospital for psychiatric and mental health.
Method: convenient sample of 50 parents were chosen for conducting this study.
Data collection tools: (1) Socio demographic and clinical characteristics data for children and their parents. (2) Parental stress scale. (3) Ways of coping Questionnaire.
Results: the present study revealed that there were highly statistically significant differences between pre- and post-program of parental stress regarding level of stress, there were highly statistically significant improvement between post-program compared to pre ΓÇôprogram regarding coping patterns of the parents have children with ADHD.
Conclusion: parents of children with ADHD had high level of stress, which decreased after implementation of the educational program with a highly statistical significant difference. In addition to the current study revealed that after the intervention there were improvements in coping patterns of parents.
Recommendations: Continuous education programs and counseling are important to improve parents adjustment toward care of their ADHD children

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Int J Environ Res Public Health. 2021 Sep;18.
POOR MENTAL HEALTH IN CAREGIVERS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ITS RELATIONSHIPS WITH CAREGIVERS' DIFFICULTIES IN MANAGING THE CHILDREN'S BEHAVIORS AND WORSENED PSYCHOLOGICAL SYMPTOMS DURING THE COVID-19 PANDEMIC.
Tseng HW, Tsai CS, Chen YM, et al.
The coronavirus disease 2019 (COVID-19) pandemic has thrown out a challenge to caregivers of children with attention-deficit/hyperactivity disorder (ADHD). The present study examined the factors related to the poor general mental health state of the caregivers of children with ADHD during the COVID-19 pandemic, including (1) difficulties of caregivers in asking their child to adopt protective behaviors against COVID-19, (2) difficulties of caregivers in managing the child's daily performance, and (3) worsened psychological symptoms in children. In total, 161 caregivers completed an online questionnaire to provide data regarding their general mental health state and difficulties in asking their child with ADHD to adopt protective behaviors against COVID-19 and in managing the child's after-school learning, sleep routine, and internet use, as well as worsened psychological symptoms. The results of multivariate logistic regression analysis demonstrated that caregivers' difficulties in managing ADHD children's self-protective behaviors and after-school learning and the children's worsened emotional symptoms were significantly associated with poor caregiver general mental health state. An intervention that enhances the mental health of caregivers of children with ADHD during the COVID-19 pandemic by addressing their difficulties in managing the children's behaviors and psychological problems is warranted

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Int J Environ Res Public Health. 2021;18.
RELATIONSHIP BETWEEN BULLYING VICTIMIZATION AND QUALITY OF LIFE IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN TAIWAN: MEDIATION OF THE EFFECTS OF EMOTIONAL PROBLEMS AND ADHD AND OPPOSITIONAL DEFIANT SYMPTOMS.
Lin CW, Lee KH, Hsiao RC, et al.
This cross-sectional study investigated the mediating effects of emotional problems including depression, anxiety, attention-deficit/hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD) symptoms on the association between bullying victimization and quality of life (QoL) among adolescents with ADHD in Taiwan. A total of 171 adolescents diagnosed as having ADHD participated in this study. Adolescents completed the School Bullying Experience Question-naire, the Taiwanese Quality of Life Questionnaire for Adolescents, the Taiwanese version of the Children's Depression Inventory and the Multidimensional Anxiety Scale for Children. Caregivers completed the Chinese version of the Swanson, Nolan, and Pelham Version IV Scale. Structural equation modeling (SEM) was used to examine the relationships among the variables. The results of SEM revealed that bullying victimization indirectly correlated with QoL through the mediation of emotional problems in adolescents with ADHD, whereas ADHD and ODD symptoms did not mediate the association between bullying victimization and QoL. Bullying victimization should be actively prevented and

intervened on to ensure better QoL in adolescents with ADHD. Moreover, emotional problems should be alleviated among adolescents with ADHD with bullying victimization experience to maintain their QoL

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Int J Environ Res Public Health. 2021;18.

TRENDS OF MENTAL DISORDERS AND TREATMENT CONTINUITY PREDICTORS OF NEW PATIENTS IN THE PAEDIATRIC PSYCHIATRY CLINIC OF A UNIVERSITY HOSPITAL.

Lee AR, Bahn GH.

This study analysed trends of first-time patients visiting the paediatric psychiatry clinic in a university hospital. The medical records from 2009 to 2016 of first-time patients visiting the Kyung Hee University Hospital were reviewed, focusing on children in grades 1ΓÇô12. We analysed the clinical diagnosis rate of mental disorders per 100,000 in the general population by gender and grade, and the characteristics of patients who sought outpatient care more than three times. The study included 1467 participants, of which 931 were males (63.5%). The number of male patients per 100,000 population significantly decreased from 4.14 in 2009 to 2.03 in 2016. While hyperkinetic disorders had the highest prevalence in males, neurotic disorders were most frequent in females. The rate of disruptive behaviour disorders in males and mental retardation in females decreased significantly during the data collecting period. The factors affecting treatment continuity were being female, 7th-12th graders, and diagnosis of depressive, hyperkinetic, and tic disorders. Physicians should consider the new paediatric patients gender, grade, and expected diagnosis from their first visit to improve treatment compliance

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Int J Environ Res Public Health. 2021;18.

EMPATHY QUOTIENT AND SYSTEMIZING QUOTIENT IN ELEMENTARY SCHOOL CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A COMPARATIVE STUDY.

Lasmono A, Ismail RI, Kaligis F, et al.

This study compares the Empathy Quotient (EQ) and Systemizing Quotient (SQ) scores of elementary school children with and without ADHD. The study also examined their brain types and, because sex plays a big role in empathy and systemizing ability, compared the results of the boys and girls. This cross-sectional study involved 122 participants, including 61 parents of children with ADHD and 61 parents of children without ADHD. The EQ, SQ and brain types were obtained using the Empathy and Systemizing Quotient in children (EQ-/SQ-C), validated in the Indonesian language. Data was analyzed using the SPSS program version 20 for Windows, with a p-value < 0.05 for statistical significance. There was a significant difference in EQ between children with and without ADHD, the score being lower in children with ADHD. There was also a significant difference in SQ among girls with and without ADHD, but not in boys. The brain types in both groups were not significantly different. The results indicate that children with ADHD have a lower ability to empathize compared to children without ADHD. Systemizing abilities were significantly lower in girls with ADHD than in girls without. Therefore, an intervention program focusing on improving empathy and systemizing ability needs to be developed in the community

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Int J Environ Res Public Health. 2021;18.

INCIDENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) DIAGNOSES IN NAVARRE (SPAIN) FROM 2003 TO 2019.

Leache L, Arrizibita O, Guti+®rrezΓÇÉvalencia M, et al.

(1) Background: Attention deficit hyperactivity disorder (ADHD) constitutes one of the leading mental health and behavioral disorders in childhood and adolescence. The main objective of this study was to analyze the time trend in the incidence of ADHD diagnoses in Navarre (Spain) from 2003 to 2019 in children and adolescents from 5 to 19 years old. Additionally, the seasonal trends of ADHD incidence and ADHD prevalence were determined.

(2) Methods: A population-based observational retrospective study, which included people born between 1991 and 2011 and who attended compulsory education between 2007 and 2017 in Navarre (Spain), was carried out with data from both the Education and Health Department databases.

(3) Results: The incidence rate increased from 4.18 cases per 1000 person years in 2003 to 7.43 cases per 1000 person years in 2009, before decreasing progressively to 2.1 cases per 1000 person years in 2019. A peak incidence rate at 7-8 years of age was observed, which is consistent across the study period and for both genders. Males were more than twice as likely to be diagnosed with ADHD than females, with similar time trends in both. A seasonal pattern in ADHD diagnosis was found, with peaks in February-March and the lowest rates in the summer months. Inattentive cases were much more frequent than hyperactive cases, whereas combined cases remained low across the study period.
(4) Conclusions: In this age-period-cohort analysis, a clear period and age effect was observed. We found a decreasing trend in the ADHD incidence rate since 2015. Further research is needed to confirm whether a change of trend is occurring globally

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Int J Psychophysiol. 2021;168:S75.

ELECTROPHYSIOLOGICAL (EEG, ERP, ERO) ALTERATIONS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Karaka S.

To provide a summary of the consistent or the available neuroelectric findings on children with attention deficit hyperactivity disorder (ADHD). Neuroelectricity was in the form of event-related potentials (ERPs), electroencephalogram (EEG) and event-related oscillations (EROs). Findings were evaluated within a framework of early and late attentional selectivity that included different types of attention. ADHD findings were compared to those on typically developing children (TDC). ADHD is characterized by amplitude variations in ERP components and a predominance of slow oscillation in EEG. The small number of studies on the EROs found amplitude variations that were attributed to diverse cognitive processes. ADHD research should be focused to the oscillatory components that make up the ERP waveform. The cognitive interpretations of the neuroelectric findings should be based on scientifically accepted cognitive schemas or frameworks

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Int J Psychophysiol. 2021;168:S57.

DESIGNING AND EVALUATING A SCALE-DRIVEN WEARABLE DIAGNOSTIC ASSESSMENT SYSTEM FOR CHILDREN WITH NEURODEVELOPMENTAL DISORDERS.

Chen Y.

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder among school-age children. Children with ADHD show inappropriate inattention, impulsivity, or hyperactivity compared to their peers. Among the existing diagnostic methods, the evaluation and diagnosis method based on scales is the most widely used. Currently, several scales are available for ADHD evaluation, among which the DSM-5 is the most authoritative and general diagnostic standard accepted worldwide. However, the scale only uses descriptive language and lacks quantitative standards. The score mainly depends on the subjective experience and judgment of doctors. It is easy to be interfered by people, and the reference value for clinical diagnosis is not high. We designed and developeda scale-driven wearable diagnostic assessment system named WeDA, a prototype system that integrates interactive screen, interactive objects, and wearable sensors. We used WeDA as a technical probe to evaluate how such a system can play a role in practice to help realize the auxiliary diagnosis of ADHD. Specifically, we have verified through experiments that such a system can achieve a comprehensive coverage of all ADHD related symptoms in DSM-5, and can also achieve high-precision ADHD recognition. We used WeDA in an experimental style to test the feasibility of our approach. In a bid to answer our question about the diagnosis effect, we explicitly aimed to assess the current diagnostic accuracy of ADHD diagnoses and the coverage of the DSM-5. Based on the results of all participants, we saw that every single task could achieve an 88%Γ¨ê+98% F-score, which indicates that the designed ten tasks are productive for ADHD diagnosis. And the accuracy of the subjective bias of -¦1 indicates that the prediction accuracy of all symptoms can be as high as 82%. Our work is built on the clinical literature, our comprehensive analysis of ADHD symptoms, the involvement of six classical cognitive paradigms and four interaction modes, and the wearable sensors based motion perception, an experiment with an effective functional prototype and interviews from doctors, parents and children that show the potential utility of such a system. We have demonstrated that many physical movement features extracted

from motion sensors have significant differences in ADHD and TD groups, and based on these features, we can identify ADHD with high accuracy. We also proved that the system could cover eighteen symptoms in DSM-5 with high accuracy

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Int J Psychophysiol. 2021;168:S74-S75.

SYMPOSIUM TITLE: ELECTROPHYSIOLOGICAL ALTERATIONS IN NEUROPSYCHIATRIC DISORDERS: HIGHLIGHTS.

Basar-Ero-lu C.

Studies on brain's electrophysiological activity goes back to 1928, 1939 and 1942 for electroencephalography (EEG), event-related potentials (ERPs) and event-related oscillations, respectively. The findings and formulations on the early basic research, and the normative data that they provided paved the way to research on neuropsychiatric disorders. The presentation on attention deficit hyperactivity disorder (ADHD) is an overview of the EEG, ERPs and EROs patterns that differentiate the attentional processing of children with ADHD from typically developing ones. The most consistent findings are the slow oscillations in EEG, and the amplitude variations in ERP. The presentation on ParkinsonΓÇÖs disease (PD) shows reduced power and phase-locking in delta and theta bands in response to cognitive and emotional load (via facial expressions), respectively. Impairment is observed over the parietal and occipital and frontal regions for cognitive and emotional tasks, respectively. The presentation on aging, mild cognitive impairment (MCI), PD and AlzheimerΓÇÖs disease (AD) shows that the continuum is characterized by decreased delta; MCI, with decreased theta and beta; AD, by increased gamma activity. The presentation on schizophrenia shows that disturbances pertain to not only the gamma band but also to the slower oscillations. According to the whole brain theory, schizophrenia is a disturbance of the simultaneously occurring oscillatory activity. This disturbance negatively affects the interaction between brain regions, and ultimately impairs integrative brain functioning. The electrophysiology of neuropsychiatric disorders should be studied from the whole brain theory perspective, employing multidisciplinary and multitechnological approaches for a comprehensive understanding of the area

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Int J Psychophysiol. 2021;168:S83.

NEUROFEEDBACK FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: EVIDENCE BASE AND RESULTS OF A LARGE RCT.

deBeus R.

Published trials have problems with selection & inadequate size of sample, suboptimal treatment protocols, lack of blinding, lack of convincing placebo sham of equal duration & intensity, poor sample retention, failure to record safety data, failure to measure learning curve, and suboptimal statistical approaches. Significant effects were found on ADHD symptoms rated by most proximal (least blinded) assessors but not with probably blinded ratings, or in trials with active/sham controls. Preliminary outcomes are described from the new NIMH-funded 2-site RCT, which randomized 142 children age 7-10 with combined or inattentive ADHD 3:2 to 38 sessions of neurofeedback or a refined sham that allowed therapists to be blind. The primary outcome is parent- and teacher-rated inattentive symptoms. Analysis is by mixed-effects models. The meta-analysis is re-presented with the new data incorporated. Of 329 screens who met categorical and dimensional criteria for ADHD, 79% had theta-beta ratios (TBRs) > 4.5 by the ADHD Suite, suggesting suitability of TBR-downtraining. Treatment fidelity was 98% as rated by the NF trainers, 84% as rated by an independent monitor. Correct post-treatment guesses of treatment assignment were 32% by children, 39% by therapists, and 34% by parents. Correct guesses of the sham treatment were 7%, 24% and 25%, respectively. Adverse events occurred proportionately in both treatment groups, and none were serious. Both treatments resulted in large (d>1.0) improvements from baseline to end of treatment, but they were not significantly different from each other. By Clinical Global Impression-Improvement rating, 60% of the NF group and 54% of the control group were responders (CGI-I of 1 or 2). An update of the meta-analysis including the new data showed a small (d=0.2) but significant benefit compared to control groups on teacher rating of symptoms. Follow-up at 13 months suggests further improvement for neurofeedback compared to a stable level for the sham control. In this largest, most rigorous NF RCT for ADHD to date, designed to address flaws of previous studies, the benefits reported for TBR NF appear to be largely nonspecific, not

specifically due to the NF itself, but to other favorable aspects of the total treatment package. There appear to be minor safety issues. Updated meta-analysis shows a small but significant advantage of NF over control groups by the most probably blinded rater (teacher). There may be a delayed specific benefit from NF after treatment end

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Int J Psychophysiol. 2021;168:S82.

SYMPOSIUM TITLE: EEG AND NFT: COVID-19 BRAIN ASSESSMENT TOOL (QEEG) AND NEUROFEEDBACK TRAINING AS A TREATMENT TOOL FOR ADHD & TRAUMA.

Rogel A.

This symposium is divided into three parts. The first focuses on quantitative EEG (qEEG) as an assessment tool to identify brain activities and regions that were affected by COVID-19 and correlate them with neuroinflammatory effects. Preliminary cases studies with patients post COVID-19 exposure as well as non-exposed neurotypical cases experiencing the neuroinflammatory effects of the COVID vaccination will be presented and reviewed. The next two presentations focuses on the use of EEG as a treatment tool for Neurofeedback training (NFT). One presentation shows that the NFT ΓÇ£packageΓÇØ significantly reduced over time symptoms in children with ADHD in a large-scale double-blind sham-controlled study. The second shows that NFT significantly reduced PTSD symptoms as well as improving executive functioning condition on children and adults with developmental trauma. In addition, NFT improved behavioral symptoms of the children with developmental trauma

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Int J Psychophysiol. 2021;168:S180.

RESEARCH ON CLASSIFICATION OF BRAIN FUNCTION NETWORK FEATURES OF CHILDREN WITH ADHD BASED ON MULTI-FEATURE HUB EVALUATION METHOD.

Zhiwei S, Zhihao Z, Zhongyi J, et al.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most typical neurological disorders affecting young children. Hub identification in brain function network analysis is an effective tool for ADHD auxiliary diagnose.

Methods: This study quoted a multiple-feature method to recognize hubs in the brain network that combine several different single-feature methods, including degree centrality, betweenness centrality, and closeness centrality. The quoted multi-feature fusion centrality indicator can assure both global characteristics and local characteristics during the identification of brain nodes. On this basis, an ADHD classification method based on node attribute features is constructed. This classification method can find out the attributes of nodes in the network as features to classify ADHD children and normal children.

Results: The experimental result shows that the hubs identified by the multi-feature fusion centrality method have a significant impact on the global efficiency of the network. Compared with the three single-feature centrality indicators, the multi-feature fusion centrality indicator can more effectively capture different brain regions in ADHD children and normal children. Meanwhile, the centrality values of different brain regions calculated by the four centrality methods are recognized as features, and SVM (the support vector machine) is used for classification. The classification accuracy based on the multi-feature fusion centrality method reaches 89.8%, and the accuracy is improved by more than 10% compared with the single-feature centrality method.

Conclusions: For clinical studies of children with ADHD based on fMRI data, experimental results demonstrate the multi-feature fusion center method quoted in this paper can recognize more different brain regions between ADHD children and normal children, such as the left anterior cingulate and paracingulate gyri, right median cingulate and paracingulate gyri, left superior occipital gyrus. This study shows the potential of using new graph theory analysis strategies to describe the changes of brain networks in children ADHD disorders. On the other hand, effective classification recognition rate can be used as a theoretical basis for the auxiliary diagnosis of ADHD children. With further validation, this may have clinical significance in diagnosis and adjuvant therapy of ADHD disorders

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Investigative Ophthalmology and Visual Science. 2021;62.

SHORT TERM VISUAL RELATED OCULAR SIDE EFFECTS DURING TREATMENT WITH D-MPH FOR ADHD.

Fainberg G, Leitner Y, Zur D, et al.

Purpose: To evaluate the short-term effect of dexmethylphenidate (D-MPH) on visual acuity, pupil size, anterior chamber depth (ACD), and accommodation-convergence reflex in children treated with D-MPH XR for attention-deficit/hyperactivity disorder (ADHD).

Methods: Prospective cohort study including 15 patients aged 8-16 (11.58-¦2.39) treated with D-MPH for ADHD. Patients were questioned for subjective complains such as blurred vision and photosensitivity. Ophthalmic evaluation was performed twice; prior to and 1.5 hours following D-MPH administration. The exam included evaluation of best corrected visual acuity at distance and near, accommodation range, convergence range, 3-D vision test and anterior chamber optical coherence tomography (OCT).

Results: A significant association between pupil diameter and D-MPH treatment dose was demonstrated (p=0.001). Additionally, a positive correlation between complains about blurred vision and D-MPH daily dosage was found. There were no significant changes in visual acuity, convergence range, stereo vision, accommodation range, or anterior chamber measures.

Conclusions: Our findings provide further support to the effect of stimulants on pupil diameter, as well as on subjective complains about blurred vision in a dose dependent manner. Additionally, future research is required to further investigate a potential role for pupil diameter as a marker of response to D-MPH

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Iranian Journal of Otorhinolaryngology. 2020;32:359-64.

DOES ADENOTONSILLECTOMY ALTER SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN?

Fallah R, Arabi Mianroodi A, Eslami M, et al.

Introduction: Attention deficit hyperactivity disorder (ADHD) has the highest prevalence among psychiatric disorders in children. The present study investigated the effect of adenotonsillectomy on the symptoms of ADHD in a 6-month follow-up.

Materials and Methods: This cross-sectional study was performed on 100 patients referred for respiratory problems during sleep due to adenotonsillar hypertrophy (ATH). The patients parents were asked to complete the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition checklist as a standard benchmark for ADHD before, 2 weeks, and 6 months after the surgery. The data were analyzed by SPSS software (version 20) through paired t-tests and McNemar's test.

Results: The age averages of male and female children were 7.15 and 8.4 years, respectively. The frequency of ADHD in the studied population was 30%, which is much higher than the prevalence of this disorder in the normal population. In the second week after the surgery, the mean score of ADHD decreased from 4.97-¦2.97 (attention deficit [AD]) and 6.77-¦1.61 (hyperactivity disorder [HD]) before the surgery to 3.86-¦2.25 (AD) and 4.28-¦2.02 (HD) 2 weeks after the surgery (P=0.001). After a 6-month followup, these figures further decreased (AD=2.34-¦2.32; HD=1.97-¦2.44; P<0.001).

Conclusion: Adenotonsillectomy had a significant effect on the improvement of ADHD symptoms. There is a necessity for checking patients with ADHD for ATH, especially in case of sleep disorders, sleep apnea, snoring, or mouth breathing

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Iran J Psychiatr Behav Sci. 2021;15.

A RANDOMIZED CONTROLLED TRIAL OF GROUP REALITY THERAPY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OPPOSITIONAL DEFIANT DISORDER IN ADOLESCENTS.

Nayeri MF, Soltanifar A, Moharreri F, et al.

Background: The non-pharmacological interventions for behavioral problems of adolescents diagnosed with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) are of great interest to researchers.

Objectives: This study aimed to examine the efficacy of group reality therapy in behavioral symptoms in ADHD and ODD.

Methods: Forty patients diagnosed with ADHD and ODD between 12 and 18 years were randomly assigned to two groups. The patients in the intervention group were participated in group reality therapy for five 120-

minute sessions, once a week. The patients in the control group were enrolled in five unstructured sessions without intervention. Conners Parent Short Form questionnaire, Strengths and Difficulties Questionnaire (SDQ), and depression, anxiety, and stress scale (DASS-21) were performed at baseline, the sixth week, and the tenth week for follow-up.
Results: Conners test showed a statistically significant difference in the intervention group in hyperactivity (P = 0.005), conduct (P < 0.001), and total score (P < 0.001) in the sixth week, as well as in conduct (P = 0.001), and total score (P = 0.008) in the tenth week. SDQ test analyzed based on partial Eta squared test, indicated the effect size in the intervention group was 81% and in the control group was 27%. Moreover, the DASS test in the intervention group showed improvement in depression, anxiety, and stress scores (P < 0.001).
Conclusions: Group reality therapy is effective in the improvement of disruptive behaviors and emotional symptoms in ADHD and ODD

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J Autism Dev Disord. 2021 Oct;51:3759-65.
SEX DIFFERENCES IN CO-OCCURRING CONDITIONS AMONG AUTISTIC CHILDREN AND YOUTH IN FLORIDA: A RETROSPECTIVE COHORT STUDY (2012-2019).
Angell AM, Deavenport-Saman A, Yin L, et al.
Autistic children have a high prevalence of co-occurring mental health, developmental/behavioral, and medical conditions, but research on sex/gender differences has been mixed. We used Florida healthcare claims data to characterize sex differences (female/male) in co-occurring conditions among autistic children ages 1-21 (N=83,500). After adjusting for age, race, ethnicity, urbanicity, and insurance, autistic girls had significantly higher odds of anxiety disorders, mood disorders, intellectual disability, developmental disorders, epilepsy, metabolic disorders, gastrointestinal disorders, and sleep disorders compared to autistic boys. Autistic girls had significantly lower odds of ADHD. The findings contribute to the growing body of research on the unique healthcare needs of autistic girls

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JAMA Network Open. 2021;4.
ASSOCIATION OF TIMING AND DURATION OF PRENATAL ANALGESIC OPIOID EXPOSURE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN.
Tronnes JN, Lupattelli A, Handal M, et al.
Importance: Prior studies have reported that the use of illicit opioids during pregnancy is associated with increased risk of attention-deficit/hyperactivity disorder (ADHD) in offspring; however, evidence regarding the association of analgesic opioids is limited.
Objective: To examine the association of timing and duration of prenatal analgesic opioid exposure with ADHD in children.
Design, Setting, and Participants: This cohort study uses data from the Norwegian Mother, Father and Child Cohort study (1999-2008), a nationwide birth cohort study linked to national health registries, with a mean (SD) follow-up of 10.8 (2.2) years. A total of 73784 live-born singleton children born to 62013 mothers who reported a pain-related condition before and/or during pregnancy were included, with 2 comparator groups: (1) mothers who did not use any opioids and (2) mothers who used opioids before pregnancy only. Data were analyzed from June to December 2020.
Exposures: Maternal self-report of analgesic opioid use during pregnancy, by timing (early and middle and/or late) and duration (5 weeks vs 4 weeks).
Main Outcomes and Measures: Diagnosis of ADHD or filled prescription for ADHD medication in children and symptoms of ADHD at child age 5 years, measured by Conners' Parent Rating Scale-Revised. Inverse probability of treatment weights were used to control for measured confounding. Cox regression was used to estimate hazard ratios (HRs) and 95% CIs.
Results: The analyses of ADHD diagnosis and ADHD symptoms included 73480 children (35996 [49.0%] girls; mean [SD] maternal age, 30.0 [4.6] years) and 31270 children (15377 [49.2%] girls; mean [SD] maternal age, 30.5 [4.4] years), respectively. Overall, 1726 children in the ADHD diagnosis sample (2.3%) and 667 children in the ADHD symptom sample (2.1%) were exposed to an analgesic opioid at least once during

gestation. No associations between timing of prenatal analgesic opioid exposure and ADHD diagnosis or symptoms was found. Exposure for 5 or more weeks was associated with an increased risk of ADHD diagnosis (HR, 1.60, 95% CI, 1.04-2.47) compared with exposure for 4 weeks or less; however, there was no such association for the risk of ADHD symptoms.
Conclusions and Relevance: In this cohort study, a slightly elevated risk of ADHD diagnosis after prenatal analgesic opioid exposure for 5 or more weeks was found compared with exposure for 4 weeks or less. This result may be driven by longer duration of use; however, the role of residual or unmeasured confounding cannot be excluded. This finding needs to be replicated in other studies

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J Affective Disord. 2021;295:1072-78.
DIAGNOSTIC PROGRESSION TO BIPOLAR DISORDER IN 17,285 ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A LONGITUDINAL FOLLOW-UP STUDY.
Chu CS, Tsai SJ, Hsu JW, et al.
Objective: We investigated the diagnostic progression to bipolar disorder (BD) among adolescents and young adults with attention-deficit/hyperactivity disorder (ADHD).
Methods: Using the Taiwan National Health Insurance Research Database, we enrolled adolescents and young adults aged 10ΓÇô29 years with ADHD between January 1, 2001, and December 31, 2010, who were followed up until December 31, 2011, to determine progression to BD. Cox regression analysis was used to examine candidate risk and protective factors.
Results: At the 11-year follow-up, the progression rate from ADHD to BD was 5.12%. Of the participants who progressed, 62.16% (322/518) progressed within the first 3 years. Risk factors for progression were as follows: older age (hazard ratio [HR], 1.058; 95% confidence interval [CI], 1.033-1.084), comorbidity with autistic spectrum disorder (HR, 1.839; 95% CI, 1.415-2.391), disruptive behavior disorder (HR, 1.434; 95% CI, 1.132-1.816), intelligence disability (HR, 1.744; 95% CI, 1.399-2.176), depressive disorder (HR, 1.978; 95% CI, 1.577-2.482), alcohol use disorder (HR, 1.705; 95% CI, 1.057-2.751), cluster A (HR, 2.508; 95% CI, 1.167-5.391) or B (HR, 2.718; 95% CI, 1.974-3.741) personality disorder, and a family history of BD (HR, 2.618; 95% CI, 1.823-3.758) Identified protective factors were male sex (HR, 0.771; 95% CI, 0.630ΓÇô0.943) and cluster C personality disorder (HR, 0.278; 95% CI, 0.086-0.898).
Conclusion: The study demonstrated the specific risk and protective factors for BD progression among adolescents and young adults with ADHD. It is important for clinician and mental health care providers to recognize identified factors to focus on early detection and prompt intervention

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J Child Adolesc Psychopharmacol. 2021;31:430-38.
THE OCCURRENCE OF OVERWEIGHT AND OBESITY IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ACCORDING TO THREE DIFFERENT DIAGNOSTIC CRITERIA FOR OBESITY.
Racicka-Pawlukiewicz E, Han-ç T, Ku-ç K, et al.
Objective: This study aimed to assess the prevalence of overweight and obesity in the group of children and adolescents with attention-deficit/hyperactivity disorder (ADHD) according to three different diagnostic criteria for obesity. The effect of ADHD treatment on the risk of obesity was controlled. Materials and
Methods: The study group consisted of 58 subjects aged from 8 to 17 years with ADHD. Control group consisted of 62 healthy age- and sex-matched children and adolescents. Overweight and obesity were assessed according to International Obesity Task-Force (IOTF), World Health Organization (WHO) and European Childhood Obesity Group (ECOG) criteria.
Results: There was a significantly higher incidence of obesity in ADHD group according to WHO (ADHD vs. Control: 17.2% vs. 3.2%, p = 0.01) and IOTF criteria (ADHD vs. Control: 10.3% vs. 1.6%, p = 0.04), but no significant difference according to ECOG criteria. There was significantly higher occurrence of overweight (20.7% vs. 12.8%, p < 0.001), obesity (10.3% vs. 3.5%, p < 0.001), and overweight and obesity (31.0% vs. 16.3%, p < 0.001) in the ADHD group compared to the Polish population. The analysis did not show a statistically significant relationship between the amount of taken psychostimulant and the occurrence of overweight and obesity.

Conclusions: The prevalence of overweight and obesity in the group of ADHD children and adolescents varies depending on the choice of diagnostic criteria. At the same time, it is significantly more frequent than in the general population. We suggest that future studies should give a clear rationale for the selection of cutoff points to minimize errors that could confound data analysis and interpretation

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J Child Fam Stud. 2021 Sep;30:2315-27.

EXAMINING TEMPORAL COGNITION IN PRESCHOOLERS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: INSIGHTS FROM PARENT–CHILD INTERACTIONS.

Tobia V, Landis T, Graziano P.

Increasing evidence supports the existence of time-related impairments in school-aged children and adults with Attention-Deficit/Hyperactivity Disorder (ADHD), but this deficit has not yet been investigated in preschoolers with ADHD. The aim of the current study was to determine the extent to which time-related impairments can be identified within the context of parent–child interactions in preschoolers with ADHD. Participants for this study included 29 children with ADHD and 34 typically developing (TD) children (63.5% male; Mage = 4.77, SD = 0.65; 82.5% Hispanic/Latinx), and their parents. A ten-minute play session was video-recorded for each parent-child dyad. The verbal interactions were transcribed and coded for words/expressions related to the categories of time (e.g., 'later', 'tomorrow'), as well as mathematics (e.g., 'two more', 'some'), and space (e.g., 'here/there', 'behind'). The proportion of tokens (total number of terms) and types (different terms) of each category was calculated in relation to the total verbal production for each individual (i.e., parents and children separately), and differences between groups were analyzed. Results indicated that compared to TD children, children with ADHD showed a poorer vocabulary of time-related words (d = 0.63), whereas similar rates between groups were found for the math- and space-related words. Correlation analyses revealed significant associations between the types of time-related words used by children, and problems with attention and executive functioning. These results offer some evidence for not only the presence of time-related deficits in preschoolers with ADHD, but also the association between time-related deficits and impairments in cognitive functioning

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J Child Fam Stud. 2021 Sep;30:2204-14.

A PROSPECTIVE STUDY OF MATERNAL EXPOSURE TO SMOKING DURING PREGNANCY AND BEHAVIORAL DEVELOPMENT IN THE CHILD.

Roigé-Castellví J, Murphy MM, Voltas N, et al.

Prenatal smoke exposure (PSE) is a risk factor for adverse outcomes in the offspring, including those affecting psychological development. However, it is uncertain whether these associations are the direct result of PSE or other confounding factors. The aim of this study was to examine the possible relationship between PSE and behavioral development in children at 7.5 years of age, considering several prenatal, neonatal and postnatal covariates. A cohort of 266 mother-child pairs was followed from the first trimester of pregnancy until the children reached 7.5 years of age. PSE was assessed using a questionnaire from prenatal clinical records and corroborated by plasma cotinine determinations in the first and second trimesters and in the cord. Mother-child pairs were classified into one of four groups: unexposed, exposed to passive smoking, first trimester active smoking only and active smoking throughout pregnancy. Child behavior was assessed using the Child Behavior Checklist for ages 6–18 and the Childhood Autism Spectrum Test. In multiple linear regression models, smoking during pregnancy was associated with higher scores in affective problems (ß = 0.298; p = 0.004). No significant associations were found between smoking during pregnancy and externalizing problems. Findings indicate that PSE is negatively associated with behavioral development in childhood

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J Child Neurol. 2021 Aug;36:768-75.

SUBCONCUSSIVE HEAD IMPACTS AND NEUROCOGNITIVE FUNCTION OVER 3 SEASONS OF YOUTH FOOTBALL.

Rose SC, Yeates KO, Nguyen JT, et al.

Objective: To determine the association between repetitive subconcussive head impacts and neurobehavioral outcomes in youth tackle football players.

Methods: Using helmet-based sensors, we measured head impacts for 3 consecutive seasons of play in 29 male players age 9-11. Cumulative impact g's were calculated. Players completed a battery of outcome measures before and after each season, including neuropsychological testing, vestibular-ocular sensitivity, and self- and parent-reported measures of symptoms and attention-deficit hyperactivity disorder (ADHD).

Results: Average cumulative impact over 3 seasons was 13 900g. High-intensity hits predicted worse change for self-reported social adjustment (P = .001). Cumulative impact did not predict change in any of the outcome measures. History of ADHD, anxiety, and depression predicted worse change for self-reported symptoms and social adjustment, independent of head impacts. When players were stratified into 3 groups based on cumulative impact across all 3 seasons, differences in outcome measures existed prior to the start of the first season. These differences did not further increase over the course of the 3 seasons.

Conclusion: Over 3 consecutive seasons of youth tackle football, we found no association between cumulative head impacts and neurobehavioral outcomes. Larger sample sizes and longer follow-up times would further assist in characterizing this relationship

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J Child Psychol Psychiatry. 2021 Aug;62:1010-18.

SEX DIFFERENCES IN PARENT–OFFSPRING RECURRENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Solberg BS, Hegvik TA, Halmøy A, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a highly heritable neurodevelopmental disorder sharing genetic risk factors with other common psychiatric disorders. However, intergenerational recurrence patterns of ADHD from parents to sons and daughters are not known. We aimed to examine the risk of ADHD in offspring of parents with ADHD and parents with other psychiatric disorders by parental and offspring sex, using parents without the specific disorders as comparison.

Methods: In a generation study linking data from several population-based registries, all Norwegians born 1967–2011 (n = 2,486,088; Medical Birth Registry of Norway) and their parents were followed to 2015. To estimate intergenerational recurrence risk, we calculated prevalence differences (PD) and the relative risk (RR) of ADHD in offspring by parental ADHD, bipolar disorder (BD), schizophrenia spectrum disorder (SCZ), major depression (MDD), all by parental and offspring sex.

Results: The absolute prevalence of ADHD in offspring of parents with ADHD was very high, especially in sons of two affected parents (41.5% and 25.1% in sons and daughters, respectively), and far higher than in offspring of parents with BD, SCZ or MDD. Intergenerational recurrence risks were higher for maternal than paternal ADHD (RRmaternal 8.4, 95% confidence interval (CI) 8.2–8.6 vs. RRpaternal 6.2, 6.0–6.4) and this was also true on the absolute scale (PDmaternal 21.1% (20.5–21.7) vs. PDpaternal 14.8% (14.3–15.4)). RRs were higher in daughters, while PDs higher in sons. Parental SCZ, BD and MDD were associated with an approximately doubled risk of offspring ADHD compared to parents without the respective disorders, and estimates did not differ significantly between daughters and sons.

Conclusions: The intergenerational recurrence risks of ADHD were high and higher from mothers with ADHD than fathers with ADHD. Other parental psychiatric disorders also conferred increased risk of offspring ADHD, but far lower, indicating a sex- and diagnosis-specific intergenerational recurrence risk in parents with ADHD

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J Child Psychol Psychiatry. 2021 Aug;62:971-78.

ADHD AND RISK FOR SUBSEQUENT ADVERSE CHILDHOOD EXPERIENCES: UNDERSTANDING THE CYCLE OF ADVERSITY.

Lugo-Candelas C, Corbeil T, Wall M, et al.

Background: Children with adverse childhood experiences (ACEs) are more likely to develop Attention-Deficit/Hyperactivity Disorder (ADHD). The reverse relationship – ADHD predicting subsequent ACEs – is

vastly understudied, although it may be of great relevance to underserved populations highly exposed to ACEs.
Methods: Participants were 5- to 15-year-olds (48% females) with (9.9%) and without ADHD (DSM-IV criteria except age of onset) in a longitudinal population-based study of Puerto Rican youth. In each wave (3 yearly assessments, W1-3), ten ACEs (covering parental loss and maladjustment and child maltreatment) were examined, plus exposure to violence. Logistic regression models examined ADHD (including subtypes) and subsequent risk for ACEs. Also considered were interactions by age, sex, number of W1 ACEs, and recruitment site.
Results: Children with W1 ADHD were more likely to experience subsequent adversity (OR: 1.63; 95% CI: 1.12–2.37) accounting for child age, sex, public assistance, maternal education, site, disruptive behavior disorders, and W1 ACEs. Inattentive (OR: 2.00; 95% CI: 1.09–3.66), but not hyperactive/impulsive or combined ADHD, predicted future ACEs.
Conclusions: ADHD predicts subsequent risk for ACEs, and the inattentive presentation may confer the most risk. Inattentive presentations could pose a bigger risk given differences in symptom persistence, latency to access to treatment, and treatment duration. The present study suggests a pathway for the perpetuation of adversity, where bidirectional relationships between ADHD and ACEs may ensnare children in developmental pathways predictive of poor outcomes. Understanding the mechanism underlying this association can help the development of interventions that interrupt the cycle of adversity exposure and improve the lives of children with ADHD

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J Child Psychol Psychiatry. 2021 Sep;62:1110-19.

IMPACT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMORBIDITY ON LONGITUDINAL COURSE IN INTERNET GAMING DISORDER: A 3-YEAR CLINICAL COHORT STUDY.

Lee J, Bae S, Kim BN, et al.

Background: Although attention-deficit/hyperactivity disorder (ADHD) symptoms were identified as a key risk factor for Internet gaming disorder (IGD), the effect of ADHD comorbidity on longitudinal course of IGD in the clinical population remains to be further examined. This study aimed to investigate whether ADHD comorbidity in IGD patients affects the recovery, recurrence rates, and trajectories of IGD symptoms, and examine the relationship between the changes in IGD and ADHD symptoms.
Methods: The study included 128 IGD patients without any psychiatric comorbidities (pure-IGD group) and 127 IGD patients with comorbid ADHD (ADHD-IGD group) aged 11 to 42 years. IGD and ADHD were diagnosed according to DSM-5 criteria at enrollment. Participants were offered 8-week treatment with additional care provided as needed and followed up over a 3-year period. IGD diagnosis was reassessed annually and used as a dichotomous outcome. The severity of IGD and ADHD symptoms was measured using the Young Internet Addiction Scale and the Korean ADHD rating scale, respectively, at baseline and each annual follow-up.
Results: The recovery rates of IGD by Year 3 were 60% and 93% in ADHD-IGD and in pure-IGD groups, respectively. The ADHD-IGD group showed lower rates of recovery, higher odds of recurrence within 1 year, and higher severity of IGD symptoms over time than the pure-IGD group. Family environment was also associated with the trajectories of IGD symptoms. The changes in ADHD symptoms were significantly associated with the changes in IGD symptoms.
Conclusions: This study found that ADHD comorbidity in IGD patients was associated with poor clinical course of IGD and that the changes in ADHD symptoms were associated with the changes in IGD symptoms over time. Our findings suggest that evaluation and treatment of ADHD symptoms and family environment in IGD patients may be important in improving the prognosis of IGD

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J Child Psychol Psychiatry. 2021 Sep;62:1140-49.

CHARACTERIZING NEUROANATOMIC HETEROGENEITY IN PEOPLE WITH AND WITHOUT ADHD BASED ON SUBCORTICAL BRAIN VOLUMES.

Li T, Rooij D, Roth Mota N, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder. Neuroanatomic heterogeneity limits our understanding of ADHD's etiology. This study aimed to parse heterogeneity of ADHD and to determine whether patient subgroups could be discerned based on subcortical brain volumes.

Methods: Using the large ENIGMA-ADHD Working Group dataset, four subsamples of 993 boys with and without ADHD and to subsamples of 653 adult men, 400 girls, and 447 women were included in analyses. We applied exploratory factor analysis (EFA) to seven subcortical volumes in order to constrain the complexity of the input variables and ensure more stable clustering results. Factor scores derived from the EFA were used to build networks. A community detection (CD) algorithm clustered participants into subgroups based on the networks.

Results: Exploratory factor analysis revealed three factors (basal ganglia, limbic system, and thalamus) in boys and men with and without ADHD. Factor structures for girls and women differed from those in males. Given sample size considerations, we concentrated subsequent analyses on males. Male participants could be separated into four communities, of which one was absent in healthy men. Significant case–control differences of subcortical volumes were observed within communities in boys, often with stronger effect sizes compared to the entire sample. As in the entire sample, none were observed in men. Affected men in two of the communities presented comorbidities more frequently than those in other communities. There were no significant differences in ADHD symptom severity, IQ, and medication use between communities in either boys or men.

Conclusions: Our results indicate that neuroanatomic heterogeneity in subcortical volumes exists, irrespective of ADHD diagnosis. Effect sizes of case–control differences appear more pronounced at least in some of the subgroups

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J Child Psychol Psychiatry. 2021 Sep;62:1132-39.

PROSPECTIVE IMPACT OF COVID-19 ON MENTAL HEALTH FUNCTIONING IN ADOLESCENTS WITH AND WITHOUT ADHD: PROTECTIVE ROLE OF EMOTION REGULATION ABILITIES.

Breaux R, Dvorsky MR, Marsh NP, et al.

Background: The impact of chronic stressors like the COVID-19 pandemic is likely to be magnified in adolescents with pre-existing mental health risk, such as attention-deficit/hyperactivity disorder (ADHD). This study examined changes in and predictors of adolescent mental health from before to during the COVID-19 pandemic in the Southeastern and Midwestern United States.

Methods: Participants include 238 adolescents (132 males; ages 15–17; 118 with ADHD). Parents and adolescents provided ratings of mental health symptoms shortly before the COVID-19 pandemic and in spring and summer 2020.

Results: Adolescents on average experienced an increase in depression, anxiety, sluggish cognitive tempo, inattentive, and oppositional/defiant symptoms from pre-COVID-19 to spring 2020; however, with the exception of inattention, these symptoms decreased from spring to summer 2020. Adolescents with ADHD were more likely than adolescents without ADHD to experience an increase in inattentive, hyperactive/impulsive, and oppositional/defiant symptoms. Adolescents with poorer pre-COVID-19 emotion regulation abilities were at-risk for experiencing increases in all mental health symptoms relative to adolescents with better pre-COVID-19 emotion regulation abilities. Interactive risk based on ADHD status and pre-COVID-19 emotion regulation abilities was found for inattention and hyperactivity/impulsivity, such that adolescents with ADHD and poor pre-COVID-19 emotion regulation displayed the highest symptomatology across timepoints. Lower family income related to increases in inattention but higher family income related to increases in oppositional/defiant symptoms.

Conclusions: The early observed increases in adolescent mental health symptoms during the COVID-19 pandemic do not on average appear to be sustained following the lift of stay-at-home orders, though studies evaluating mental health across longer periods of time are needed. Emotion dysregulation and ADHD increase risk for sustained negative mental health functioning and highlight the need for interventions for

these populations during chronic stressors. Results and clinical implications should be considered within the context of our predominately White, middle class sample

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J Clin Psychopharmacol. 2021;41:605-06.
ATOMOXETINE-ASSOCIATED EYEBROW ALOPECIA IN A GIRL WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Zhang Y, Xu X, Zhang K.

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J Clin Sleep Med. 2021;17:1749-50.
CONTINUED CHALLENGES FOR PARENTS AND CLINICIANS IN MAINTAINING SLEEP HEALTH FOR CHILDREN WITH ADHD during the COVID-19 pandemic.
Malhotra S, Kancherla BS.

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J Clin Sleep Med. 2021;17:1759-65.
THE IMPACT OF LOCKDOWN ON SLEEP PATTERNS OF CHILDREN AND ADOLESCENTS WITH ADHD .
Bruni O, Giallonardo M, Sacco R, et al.
Study Objectives: The current study examined the impact of home confinement (lockdown) because of the COVID-19 pandemic on the sleep patterns of children and adolescents with attention-deficit hyperactivity disorder (ADHD).
Methods: Nine hundred ninety-two parents of children and adolescents with ADHD filled out an anonymous online survey through the ADHD family association website. The survey investigated the sleep patterns and disturbances (using a modified version of the Sleep Disturbance Scale for Children) and screen exposure time before and during lockdown.
Results: During lockdown, 59.3% of children and 69.4% of adolescents with ADHD reported a change of bedtime, with a significant increase in patients with ADHD who went to sleep at 11 PM or later. Sleep duration, in contrast, resulted in 2 opposing processes with more children and adolescents sleeping either less than 6 hours/night or 10-11 hours/night. Among children and adolescents, respectively, 19.9% and 22% slept less than they did before lockdown, whereas 21.4% and 27.4% slept for more hours. Bedtime delay and decreased sleep duration were associated with an increase in screen time exposure. Moreover, patients with ADHD reported an increase in sleep disturbances when compared to their previous condition, mainly including difficulties falling asleep, anxiety at bedtime, night awakenings, nightmares, and daytime sleepiness.
Conclusions: Lockdown impacted sleep-wake rhythms by strengthening the maladaptive sleep patterns reported in usual-life conditions in children and adolescents with ADHD

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J Educ Psychol. 2021 Sep.
BEHAVIORAL SELF-REGULATION AMONG CHILDREN WITH HYPERACTIVITY AND INATTENTION IN THE FIRST YEAR OF SCHOOL: A POPULATION-BASED LATENT PROFILE ANALYSIS AND LINKS WITH LATER ADHD DIAGNOSIS.
Granziera H, Collie RJ, Martin AJ, et al.
We used latent profile analysis to identify major behavioral self-regulation profiles among children who were assessed as developmentally vulnerable in terms of hyperactivity and inattention. We examined three domains of behavioral regulation: (a) cognitive–behavioral regulation by way of learning behaviors; (b) social-behavioral regulation by way of socially responsible behaviors; and (c) emotional-behavioral regulation by way of aggressive-disruptive behaviors. We employed data from the population of New South Wales (NSW) children who were in their first year of school (viz., kindergarten) and who had been assessed as developmentally vulnerable in terms of hyperactivity and inattention in the Australian Early Development Census in 2009 (Cohort 1; N = 10,223) and 2012 (Cohort 2; N = 9,360). In both cohorts, we identified six similar profiles: the well-regulated (12%), moderately-regulated (25%), aggressive-regulated (7%), mixed-unregulated (32%), nonaggressive-unregulated (10%), and aggressive-unregulated profiles (14%).

Sociodemographic characteristics were significantly associated with profile membership. For Cohort 1, we also found that the profiles differed in the extent to which children went on to receive a formal Attention Deficit/Hyperactivity Disorder (ADHD) diagnosis. Together, the findings have implications for early intervention for various behavioral self-regulation profiles among developmentally vulnerable children.
Educational Impact and Implications Statement—We examined behavioral self-regulation profiles among kindergarten children who were assessed as developmentally vulnerable in terms of hyperactivity and inattention. We examined three types of behavioral self-regulation: learning behaviors (e.g., staying on task), socially responsible behaviors (e.g., exhibiting respect for others), and aggressive-disruptive behaviors (e.g., hurting other children). To identify the profiles, we determined how students fared on the three behaviors and then grouped similar children into profiles according to patterns of similar behavior. Results revealed six profiles that were replicated across two cohorts of children. In addition, results yield understanding about profiles that were more (or less) likely to be associated with a subsequent diagnosis of ADHD up to 5 years later. The findings hold implications for efforts to promote behavioral self-regulation among children, along with the development of interventions that are targeted to the unique needs of each profile

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Journal of Intellectual Disabilities. 2021.

EFFECT OF THE USE OF AN IPAD ON THE ATTENTION SPAN OF A CHILD WITH SMITH MAGENIS SYNDROME: A SINGLE CASE STUDY.

Rikken-Evers MT, Smith KD, Sterkenburg PS.

Aims: To assess the effectiveness of iPad use on the attention span of a child with Smith Magenis Syndrome (n = 1), compared to attention span while working on the same tasks manually. Methods: An AB design with a baseline and an intervention phase was used. Three manual tasks were chosen for the baseline, which matched the participant's intellectual age by the Early Intervention
Method: a jigsaw puzzle (six pieces), a shape sorter, and matching pictures. These same tasks were performed on an iPad during the intervention phase. Six baseline and nine intervention phase films were included in the analysis. The 15 films were independently scored twice by two observers: once to observe the types of distractions that occurred (such as standing up from the chair, calling the teacher, or turning around on the chair), and a second time to measure the effective working time.
Results: iPad use led to a 45% decrease in the number of total distractions. The effective working time improved by 8% and showed a more consistent range compared to working on tasksbmanually. While task enjoyment was not directly measured, the observers and teachers agreed that working on the iPad appeared to be more enjoyable.
Conclusions: In this single case study the participant showed that in his case iPad use can be effective in decreasing his distractions and therefore can improve his attention span. Enjoyment was higher while working with the iPad than performing tasks manually. This technology could therefore create more learning engagement for the participant, which could positively impact his behavior. Further research into iPad implementation for children with intellectual disabilities, poor fine motor skills, and/or attention deficits is needed

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J Intellect Disabil Res. 2021;65:703-04.

WHAT WE NEED TO KNOW ABOUT CALLOUS-UNEMOTIONAL TRAITS AND YOUTHS FUNCTIONING?

Myriam S, Valarie B.

Background: Children and adolescents with conduct disorders (CD) are at increased risk of developing persistent antisocial behaviour in adulthood. Not all follow a negative trajectory, and research explains this heterogeneity by the severity of callous-non-emotional (CU) traits. The study answers a key research question: how do EC traits affect child and adolescent functioning?
Methods: A systematic literature review conducted through different databases (PubMed, Scopus and Web of Science) has analysed 52 studies published from 2015 to 2020. In order to analyse the effects of high CU traits on youths functioning, results were articulated around the five dimensions of the AAIDD model.
Results/Aims: Out of the 52 studies, 47 analysed links between CU traits and neurobiological or mental health, 20 family and school contexts, 8 focused on social adjustment, 10 on social interactions and 19

measured links with the cognitive functioning, especially executive functions. Outcomes show that CU traits are not specific to children with conduct disorders but may also be observed in children and adolescents with other disorders as ASDs or ADHD. This supports other authors' conclusion that early disruptive behaviours could have a neurodevelopmental basis.
Conclusions: Results indicate a need to investigate CU traits also with IDD children and adolescents. They also argue for early interventions in both physical health (e.g. nutrient supplementation, environmental enrichment) and family and school care (e.g. positive reinforcement of prosocial behaviours, emotion recognition, parental interventions).
From Science to Practice: Assessing the presence of UC traits in early childhood is necessary to prevent the emergence of co-morbid disorders by targeting multimodal interventions to positively influence the life trajectories of these young people

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J Intellect Disabil Res. 2021;65:808.

INCIDENCE OF MENTAL HEALTH DISORDERS AND BEHAVIOURAL COMPLICATIONS IN A LARGE COHORT OF TEENAGERS WITH 47, XXY (KLINEFELTER SYNDROME).

Song SQ, Samango-Sprouse C, Sadeghin T, et al.

Background: 47, XXY occurs in approximately 1:600 live male births and is believed to have an increased incidence of ADHD and anxiety disorders. This study reports on a large cohort of males with 47, XXY between 12 and 18 years and occurrence of diagnosed psychological disorders, psychiatric hospitalizations and legal/school difficulties. This study analyses the potential impact of timing of diagnosis and status of testosterone treatment.
Methods: Detailed, three-generation pedigree family histories were collected for 122 teenagers with 47, XXY between 12 and 18 years. Psychiatric diagnoses were made by outside licensed professionals. The cohort was separated into four groups depending on timing of diagnosis and testosterone treatment (Group A [n = 55]: prenatally diagnosed and untreated; Group B [n = 42]: prenatally diagnosed and treated; Group C [n = 14]: postnatally diagnosed and untreated; Group D [n = 11]: postnatally diagnosed and treated). One-way ANOVA and post hoc analyses using the Bonferroni procedure were used.
Results: Of 122 teenagers, 43.44% had no psychiatric history. 50.82% were diagnosed with ADHD, 31.97% with anxiety disorder, 7% with depression and 1.64% with autism spectrum or bipolar disorder. Four boys (3.28%) had history of psychiatric admissions. Two boys (1.64%) experienced legal trouble. In addition, three boys (2.46%) had a school suspension/expulsion. There was no difference between the four groups for occurrence of familial psychiatric history. One-way ANOVA identified differences within the incidence of any psychiatric disorder (P = 0.007). Post hoc analysis revealed a significant difference between Groups B and D, with Group B having less psychiatric diagnoses (P = 0.012).
Conclusion: This study identified an increased incidence of psychiatric disorders in postnatally diagnosed males with 47, XXY. This finding outlines the positive effect of early detection and intervention on mental health and behaviour in these males. Supplemental research is needed to investigate the risk of emergence of psychiatric disorders in this population

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J Intellect Disabil Res. 2021;65:811.

CROSS-SECTIONAL AND LONGITUDINAL CHARACTERISATION OF THE DEVELOPMENTAL PHENOTYPE IN 22Q11.2 DUPLICATION.

Verbesselt J, Zink I, Breckpot J, et al.

Background: 22q11.2 duplication is a recurrent copy number variant (CNV) associated with a wide spectrum of physical and neurodevelopmental features and a high rate of familial transmission. In this study, we aim to contribute to the developmental phenotype of this recurrent CNV.
Methods: We conducted a retrospective chart review and analysed the digital medical records of 28 patients with proximal 22q11.2 duplications, focusing on physical, developmental and behavioural features, including longitudinal data in a subgroup (n = 11). Additionally, the phenotypes of de novo (n = 8) and inherited (n = 13) 22q11.2 duplications were compared.

Results: Common physical anomalies include nutritional problems (57%), failure to thrive (33%), transient hearing impairment (52%) and congenital heart defects (33%). Developmental, speech-language and motor delay are common in infancy, whereas attention (64%), learning (60%) and motor problems (52%) are typically reported at primary school age. Attention-deficit/hyperactivity disorders are diagnosed in 44%. Average full-scale intelligence quotient is in the borderline range (FSIQ 79), with one-third of patients functioning in the borderline range (FSIQ 71-84) and one-fifth of patients having mild intellectual disability (FSIQ 55-70). Longitudinal IQ data (n = 11) indicate that almost two-thirds of patients have a relative stable cognitive trajectory, whereas one-third show a growing into deficit profile. In patients with de novo duplications, there is a trend of more failure to thrive, although more patients with inherited duplications attend special education.
Conclusion: The present study confirms a wide heterogeneous physical and neurodevelopmental phenotype in patients with proximal 22q11.2 duplications and provides for the first time longitudinal IQ data in a subgroup of patients. When children are diagnosed with 22q11.2 duplications prenatally or early in life, healthcare professionals should be aware of an increased risk of nutritional problems, heart defects and hearing problems and should initiate neurodevelopmental support early in life, given the high risk of developmental delay, learning and attention problems

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Journal of Neural Engineering. 2021;18.

RESTING STATE DYNAMIC FUNCTIONAL CONNECTIVITY IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Ahmadi M, Kazemi K, Kuc K, et al.

Attention deficit/hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity and impulsivity. In this study, we investigated group differences in dynamic functional connectivity (dFC) between 113 children with inattentive (46 ADHDI) and combined (67 ADHDC) ADHD and 76 typically developing (TD) children using resting-state functional MRI data. For dynamic connectivity analysis, the data were first decomposed into 100 independent components, among which 88 were classified into eight well-known resting-state networks (RSNs). Three discrete FC states were then identified using k-means clustering and used to estimate transition probabilities between states in both patient and control groups using a hidden Markov model. Our results showed state-dependent alterations in intra and inter-network connectivity in both ADHD subtypes in comparison with TD. Spending less time than healthy controls in state 1, both ADHDI and ADHDC were characterized with weaker intra-hemispheric connectivity with functional asymmetries. In this state, ADHDI further showed weaker inter-hemispheric connectivity. The patients spent more time in state 2, exhibiting characteristic abnormalities in corticosubcortical and corticocerebellar connectivity. In state 3, a less frequently state observed across the ADHD and TD children, ADHDC was differentiated from ADHDI by significant alterations in FC between bilateral temporal regions and other brain areas in comparison with TD. Across all three states, several strategic brain regions, mostly bilateral, exhibited significant alterations in both static functional connectivity (sFC) and dFC in the ADHD groups compared to TD, including inferior, middle and superior temporal gyri, middle frontal gyri, insula, anterior cingulum cortex, precuneus, calcarine, fusiform, superior motor area, and cerebellum. Our results show distributed abnormalities in sFC and dFC between different large-scale RSNs including cortical and subcortical regions in both ADHD subtypes compared to TD. Our findings show that the dynamic changes in brain FC can better explain the underlying pathophysiology of ADHD such as deficits in visual cognition, attention, memory and emotion processing, and cognitive and motor control

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Journal of Neurosurgery. 2021;135:73.

EFFECTS OF STIMULANT-BASED THERAPY ON THE INCIDENCE OF CONCUSSION AND THE RECOVERY OF NEUROCOGNITIVE DYSFUNCTION POST-INJURY AMONG YOUNG ATHLETES WITH ADHD .

Al M, Dreher N, Hannah T, et al.

Introduction: With an estimated 1.6-3.8 million annual injuries, concussions are the leading cause of injury among youth athletes in the United States. We sought to evaluate the effects of stimulant-use among youth

with ADHD on the incidence of concussion and the recovery of symptoms and neurocognitive dysfunction post-injury.
Methods: Immediate Post-concussion Assessment and Cognitive Testing (ImPACT) was administered to 7,453 adolescent athletes at the start of the season. Throughout the season concussions were diagnosed by physicians. ImPACT was readministered at two postdiagnostic follow-ups, the first a median of 2 days post-concussion (FU1) and the second a median of 7 days post-concussion (FU2). Subjects were divided into three categories: those with ADHD on stimulant-based therapy (ADHD+meds; n=167), those with ADHD not on stimulant-based therapy (ADHD-only; n=354), and those with no ADHD (non-ADHD; n=6932). Concussion incidence was calculated as the total number of diagnosed concussions per total number of patient-years. The recovery of neurocognitive dysfunction post-injury was calculated as standardized deviations from baseline to FU1 and then FU2 in the five ImPACT composite scores. Univariate results were confirmed with multivariate analysis.
Results: The ADHD+meds cohort had a reduced risk for concussions as compared to the ADHD-only (OR 0.51[0.37-0.71], p<0.0001) and non-ADHD groups (OR 0.50[0.37-0.67], p<0.0001). At FU1 ImPACT scores were elevated from baseline to a similar extent in the ADHD+meds cohort as compared to the other two groups. However, by FU2 deviations from baseline were lower among the ADHD+meds group as compared to the non-ADHD group in verbal memory (OR 0.46[0.28-0.76], p=0.002), visual memory (OR 0.27[0.10-0.66], p=0.005), and visual motor skills (OR 0.58[0.33-0.99], p=0.048). The deviation at FU2 was also lower among the ADHD+meds group as compared to the ADHD-meds group in visual memory (OR 0.56[0.33-0.96], p=0.04) and visual motor skills (OR 0.42[0.22-0.81], p=0.01).
Conclusion: Stimulant-use among ADHD youth is associated with 1) reduced risk for concussion and 2) reduced deviations from baseline in verbal memory, visual memory, and visual motor skills at seven days post-diagnosis, suggesting improved neurocognitive recovery on ImPACT

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J Pediatr Endocrinol Metab. 2021.

INVESTIGATION OF QUALITY OF LIFE IN OBESE ADOLESCENTS: THE EFFECT OF PSYCHIATRIC SYMPTOMS OF OBESE ADOLESCENT AND/OR MOTHER ON QUALITY OF LIFE.

Islk A, et al.

The present study assessed the obese adolescents' health-related quality of life (HRQoL) based on both adolescent-reported and maternal-reported questionnaires to clarify adolescent-related psychiatric factors, maternal psychiatric factors, and body mass index (BMI) percentile variables that independently affect the quality of life (QoL). A total of 190 adolescents (120 females and 70 males) were included in the study. The impact of clinical and psychiatric factors on the Pediatric Quality of Life Inventory-Child Version (PedsQL-C) scores was analyzed using hierarchical linear regression methods. The final models showed that only the Revised Child Anxiety and Depression Scale-Child Version major depressive disorder scores negatively predicted the physical, psychosocial, and total health scores of the PedsQL-C. The psychosocial scores of the PedsQL-P were negatively predicted by the Strengths and Difficulties Questionnaire emotional, and Conners' Parent Rating Scale-Revised-Short Form (CPRS-R-S) attention-deficit/hyperactivity disorder (ADHD) index scores. The PedsQL-P total scores were negatively predicted by the CPRS-R-S ADHD index scores. The findings of this study indicate that the adolescents' psychiatric symptoms and BMI percentile played a significant role in the PedsQL subscale functioning of obese adolescents compared to maternal psychiatric symptoms

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Journal of Pediatric Research. 2021;8:326-29.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND GLUTEN SENSITIVITY IN CHILDREN.

Karsal-lu CT, Hizal G, et al.

Aim: Dietary factors are considered one of the possible environmental risk factors for attention-deficit hyperactivity disorder (ADHD). The aim of this study was to demonstrate the relationship between ADHD and celiac disease (CD) and non-celiac gluten sensitivity (NCGS) in children.
Materials and Methods: In this prospective study, children with ADHD, aged 6-18 years, were asked about the presence of gastrointestinal symptoms and their relationship with gluten intake with a previously prepared

questionnaire form. Also, they were screened for CD [anti-tissue transglutaminase immunoglobulin (Ig) A and total IgA] and NCGS (anti-gliadin IgA/IgG antibodies).
Results: Of the 117 children (76% male), the mean age was 9.2-¦2.4 years. Ninety-six patients (82%) had no gastrointestinal complaints. There was no relationship between gluten intake and complaints in the patients who had constipation (12.8%), recurrent abdominal pain (2.5%), dyspeptic symptoms (1.7%), and irritable bowel syndrome (0.8%). None of the patients had anti-tissue transglutaminase IgA or IgG positivity. Only 1 (0.8%) patient had anti-gliadin IgA, and 6 (5.1%) patients had anti-gliadin IgG positivity. There was no relation between the presence of symptoms and anti-gliadin IgG positivity (p=0.08).
Conclusion: There was no increase in the frequency of CD and NCGS in children with ADHD

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Journal of School Psychology. 2021 Aug;87:18-27.
ORGANIZATION INTERVENTIONS AS A MEDIATOR OF CHANGE IN GRADES IN THE CHALLENGING HORIZONS PROGRAM.
Evans SW, Allan D, Xiang J, et al.
This study evaluated whether an organization intervention was a mediator of change for grade point average (GPA) in a randomized clinical trial of a school-based treatment program for adolescents with attention deficit hyperactivity disorder (ADHD). A demographically diverse sample of 148 participants (105 males) with a diagnosis of ADHD were recruited from nine middle schools. Comprehensive diagnostic evaluations were completed and participants were randomized into one of three conditions (two active treatment conditions, one control condition) for a randomized clinical trial that lasted an entire school year. The results of the trial are reported elsewhere (Evans et al., 2016; Schultz et al., 2017); in this study we evaluated four of the criteria for determining mediation as reported by Kazdin (2007) to determine whether response to the organization intervention in this school-based treatment program mediated the relationship between dosage and GPA beyond previous GPA. The results provided evidence that response to the organization intervention mediated the relationship between intervention dosage and change in GPA

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J Am Acad Child Adolesc Psychiatry. 2021 Sep;60:1147-56.
POLYGENIC RISK AND THE COURSE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER FROM CHILDHOOD TO YOUNG ADULTHOOD: FINDINGS FROM A NATIONALLY REPRESENTATIVE COHORT.
Agnew-Blais JC, Belsky DW, Caspi A, et al.
Objective: To understand whether genetic risk for attention-deficit/hyperactivity disorder (ADHD) is associated with the course of the disorder across childhood and into young adulthood.
Method: Participants were from the Environmental Risk (E-Risk) Longitudinal Twin Study, a population-based birth cohort of 2,232 twins. ADHD was assessed at ages 5, 7, 10, and 12 with mother- and teacher-reports and at age 18 with self-report. Polygenic risk scores (PRSs) were created using a genome-wide association study of ADHD case status. Associations with PRS were examined at multiple points in childhood and longitudinally from early childhood to adolescence. We investigated ADHD PRS and course to young adulthood, as reflected by ADHD remission, persistence, and late onset.
Results: Participants with higher ADHD PRSs had increased risk for meeting ADHD diagnostic criteria (odds ratios ranging from 1.17 at age 10 to 1.54 at age 12) and for elevated symptoms at ages 5, 7, 10, and 12. Higher PRS was longitudinally associated with more hyperactivity/impulsivity (incidence rate ratio = 1.18) and inattention (incidence rate ratio = 1.14) from age 5 to age 12. In young adulthood, participants with persistent ADHD exhibited the highest PRS (mean PRS = 0.37), followed by participants with remission (mean PRS = 0.21); both groups had higher PRS than controls (mean PRS = -0.03), but did not significantly differ from one another. Participants with late-onset ADHD did not show elevated PRS for ADHD, depression, alcohol dependence, or marijuana use disorder.
Conclusion: Genetic risk scores derived from case-control genome-wide association studies may have relevance not only for incidence of mental health disorders, but also for understanding the longitudinal course of mental health disorders

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J Am Acad Child Adolesc Psychiatry. 2021;60:1234-77.

SYSTEMATIC REVIEW: HOW THE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER POLYGENIC RISK SCORE ADDS TO OUR UNDERSTANDING OF ADHD AND ASSOCIATED TRAITS.

Ronald A, de Bode N, Polderman TJC.

Objective: To investigate, by systematically reviewing the literature, whether the attention-deficit/hyperactivity disorder (ADHD) polygenic risk score (PRS) associates with ADHD and related traits in independent clinical and population samples.

Method: PubMed, Embase and PsychoInfo were systematically searched, alongside study bibliographies. Quality assessments were conducted, and a best-evidence synthesis was applied. Studies were excluded when the predictor was not based on the latest ADHD genome-wide association study, when PRS was not based on genome-wide results, or when the study was a review. Initially, 197 studies were retrieved (February 22, 2020), and a second search (June 3, 2020) yielded a further 49 studies. From both searches, 57 studies were eligible, and 44 studies met inclusion criteria.

Results: Included studies were published in the last 3 years. Over 80% of the studies were rated excellent, based on a standardized quality assessment. Evidence of associations between ADHD PRS and the following categories was strong: ADHD, ADHD traits, brain structure, education, externalizing behaviors, neuropsychological constructs, physical health, and socioeconomic status. Evidence for associations with addiction, autism, and mental health were mixed and were, so far, inconclusive. Odds ratios for PRS associating with ADHD ranged from 1.22% to 1.76%; variance explained in dimensional assessments of ADHD traits was 0.7% to 3.3%.

Conclusion: A new wave of high-quality research using the ADHD PRS has emerged. Eventually, symptoms may be partly identified based on PRS, but the current ADHD PRS is useful for research purposes only. This review shows that the ADHD PRS is robust and reliable, associating not only with ADHD but many outcomes and challenges known to be linked to ADHD

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Journal of the Pediatric Infectious Diseases Society. 2021;10:S22.

ATTENTION DEFICIT HYPERACTIVE DISORDER AND OPPOSITIONAL DEFIANT DISORDER IN ADOLESCENTS LIVING WITH HIV/AIDS-A CROSS SECTIONAL STUDY.

Bhat KG, Nalwalla Z, Joseph N.

Introduction Perinatally HIV infected neonates are surviving into adulthood with an impact on mental and emotional health. Attention deficit hyperactive disorder (ADHD) and Oppositional Defiant disorder (ODD) are few of the common behavioral disorders, which have been found to have a higher prevalence amongst HIV infected children.

Objectives The objectives were to assess the proportion of ADHD and ODD in adolescents living with HIV/AIDS and to find its association with various factors.

Materials and Methods 88 adolescents aged 10-19 years living with HIV/AIDS were included in the study. The Swanson, Nolan Pelham (SNAP-IV) scale was administered to the caretakers and children were assessed for the proportion of ADHD/ODD. Association between those who scored positive with duration of treatment, CD4 counts, stage of disease and socio-demographic variables were done using statistical tests.

Results Our study included 88 participants, of whom 9 scored positive in the inattention subset resulting in a proportion of 10.2%. 5 participants had symptoms of hyperactivity/impulsivity resulting in a proportion of 5.6% and 1 had combined symptoms with a proportion of 1.1%. 13 scored positive in the opposition/defiant subset resulting in a proportion of 14.7%. No statistical significance was found between duration of treatment, CD4 count, stage of disease, socio-demographic variables and ADHD/ODD.

Conclusion The proportion of ADHD and ODD in this study was found to be comparable to the general population. A holistic approach to improve the long-term health of these youth is needed to ensure that our success in achieving survival of HIV-infected children from infancy is maintained into adulthood

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Learn Motiv. 2021 Aug;75.

COMPARISON OF EXECUTIVE FUNCTIONS IN DISRUPTIVE MOOD DYSREGULATION DISORDER AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Sharifi A, Shojaeian N, Mashhadi A, et al.

Objective: The aim of the current study was to compare the executive functioning of children with disruptive mood dysregulation disorder (DMDD) with matched groups of children diagnosed with ADHD and typically developing children (TD). Groups were matched in terms of age, gender, and IQ.

Methods: A total of 41 children aged 6–12 years old with DMDD (N = 11), ADHD (N = 15) and TD (N = 15) performed GO/NO-GO, N-Back, CPT tasks to assess executive functions of inhibition, working memory, and attention, respectively. Their parent completed BDEFS-CA.

Results: The analyses of variances indicated significant differences in all EF tasks between both groups of ADHD and DMDD and those of TD children. There were no significant differences between ADHD and DMDD children. In the Go/No-Go task, individuals with DMDD obtained greater scores in Commission error and Reaction times than ADHD and TD groups. In the N-back task, both DMDD and ADHD groups were similar, and they obtained less rate than typical individuals. While we found no significant differences in both ADHD and DMDD groups in the CPT task.

Conclusion: TD children outperformed all children diagnosed with DMDD and ADHD in all EF tasks

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Medical Journal of Malaysia. 2021;76:28.

ASSOCIATION BETWEEN ALLERGIC DISEASES AND ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD) SYMPTOMS IN CHILDREN AGES 6 - 12 YEARS OLD USING THE FILIPINO VERSION OF THE VANDERBILT ADHD PARENT RATING SCALE.

Madulara GM, Andaya AG.

Objective: The objective was to determine the association of allergic diseases and ADHD symptoms among children ages 6 - 12 years old based on parental report using the Filipino version of the Vanderbilt ADHD Parent Rating Scale.

Methods: Schoolaged children ages 6 to 12 years old with physician-diagnosed allergies (bronchial asthma, allergic rhinitis, atopic dermatitis) were randomly selected. Skin prick test (SPT) to aeroallergens was done. The parents completed the Filipino version of the Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS), a screening tool for ADHD.

Results: Among the 415 patients, 135 (32.5%) screened positive for ADHD symptoms. Upon assessment of the Vanderbilt parent rating subscale responses, 13.49% of the children were categorized as predominantly inattentive subtype, 6.02% as predominantly hyperactive/impulsive subtype, and 13.01% as combined inattention/hyperactivity. Three hundred and seventy-six (91%) children were diagnosed with asthma. Among these asthmatics, 119 (32%) had ADHD symptoms with the following subtypes - predominantly inattentive subtype (13.56%), predominantly hyperactive/ impulsive subtype (5.05%) and combined inattention/hyperactivity (13.03%). Combined inattention/hyperactivity subtype had a significant proportion of severe asthmatics, as compared to mild or moderate asthma (p value = 0.026). Furthermore, 389 (94%) children were diagnosed with allergic rhinitis. Among these patients, 130 (33%) had ADHD symptoms with the following subtypes - predominantly inattentive subtype (13.62%), predominantly hyperactive/ impulsive subtype (6.43%) and combined inattention/hyperactivity (13.37%). However, evidence is not sufficient to demonstrate a difference in ADHD subtypes with allergic rhinitis severity. Lastly, 206 (50%) children were diagnosed with atopic dermatitis. Among these patients, 71 (34%) had ADHD symptoms with the following subtypes - predominantly inattentive subtype (14.56%), predominantly hyperactive/ impulsive subtype (4.85%) and combined inattention/hyperactivity (15.05%). However, there is insufficient evidence to demonstrate a link between ADHD subtypes and atopic dermatitis severity.

Conclusion: Children with allergies, especially those with severe asthma are more likely to have ADHD symptoms

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Ned Tijdschr Geneeskd. 2021;165.
MEDICATIONS FOR PRESCHOOLERS WITH ADHD: STIMULANT OR A2-ADRENERGIC RECEPTOR AGONIST?
Van Herwaarden N.

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NeuroImage Clin. 2021;32.
SEX-SPECIFIC FRONTAL-STRIATAL CONNECTIVITY DIFFERENCES AMONG ADOLESCENTS WITH EXTERNALIZING DISORDERS.
Chai Y, Chimelis-Santiago JR, Bixler KA, et al.
Background: Sex-specific neurobiological underpinnings of impulsivity in youth with externalizing disorders have not been well studied. The only report of functional connectivity (FC) findings in this area demonstrated sex differences in fronto-subcortical connectivity in youth with attention-deficit/hyperactivity disorder (ADHD).
Methods: The current study used functional magnetic resonance imaging (fMRI) to examine sex differences in resting-state seed-based FC, self-rated impulsivity, and their interactions in 11-12-year-old boys (n = 43) and girls (n = 43) with externalizing disorders. Generalized linear models controlling for pubertal development were used. Seeds were chosen in the ventral striatum, medial prefrontal cortex, middle frontal gyrus and amygdala.
Results: Impulsivity scores were greater in boys than girls ($p < 0.05$). Boys showed greater positive connectivity within a ventromedial prefrontal-ventral striatal network. In addition, boys demonstrated weaker connectivity than girls within two medial-lateral prefrontal cortical networks. However, only boys showed greater medialΓÇôlateral prefrontal connectivity correlated with greater impulsivity.
Conclusions: The findings provide evidence supporting sex differences in both ventral striatal-ventromedial prefrontal and medialΓÇôlateral prefrontal functional networks in youth with externalizing disorders. These important networks are thought to be implicated in impulse control. Medial-lateral prefrontal connectivity may represent a male-specific biomarker of impulsivity

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Neurol Res Int. 2021;2021.
DEFICITS IN WORKING MEMORY AND THEORY OF MIND MAY UNDERLIE DIFFICULTIES IN SOCIAL PERCEPTION OF CHILDREN WITH ADHD.
Imanipour S, Sheikh M, Shayestefar M, et al.
Children with attention deficit hyperactivity disorder (ADHD) are prone to peer rejection and disliking due to difficulties in social perception and interaction. To address social perception impairments in ADHD, we examined children with ADHD in a noisy biological motion (BM) direction discrimination paradigm in association with sociocognitive factors including emotion regulation, theory of mind (TOM), and working memory compared to healthy controls. Our results showed that children with ADHD were poorer in discriminating BM direction in noisy environments ($F (1, 36) = 4.655$, $p=0.038$). Moreover, a significant correlation was found between working memory and TOM with BM discrimination in an ADHD group ($r = 0.442$, $p=0.01$, and $r = 0.403$, $p=0.05$, respectively). Our findings could suggest that social perception in noisy scenarios may be affected by memory and social cognitive abilities of children with ADHD

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Neuropsychology. 2021 Sep.
DEVELOPMENT OF EXECUTIVE FUNCTIONING FROM CHILDHOOD TO YOUNG ADULTHOOD IN AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A 10-YEAR LONGITUDINAL STUDY.
Fossum IN, Andersen PN, Øie MG, et al.
Objective: This 10-year longitudinal study investigated the developmental trajectories of executive functioning (EF) in individuals with autism spectrum disorder (ASD) or attention-deficit/hyperactivity disorder (ADHD), compared to typically developing (TD) individuals from childhood into young adulthood.
Method: There were 173 participants at baseline (T1; ASD = 38 (eight with co-occurring ADHD), ADHD = 85, TD = 50; Mage = 11.7 years, SD = 2.1), 168 at 2-year follow-up (T2) and 127 at 10-year follow-up (T3). Participants were assessed with three neuropsychological tests aimed at capturing central components of EF: working memory/Letter–Number Sequencing Test (LNS), inhibition/Color–Word Interference Test,

Condition 3 (CWIT3), and flexibility/Trail Making Test, Condition 4 (TMT4). Test results were analyzed using linear mixed models (LMM).
Results: At baseline, the TD participants outperformed the ASD and ADHD participants on all three tests. From T1 to T2, the ASD participants had less improvement than the ADHD and TD participants on the LNS test (p = .007 and .025, respectively), while having more improvement on the CWIT3 relative to the TD participants (p = .027). From T2 to T3, the ADHD participants had less improvement on the LNS test than the ASD and TD participants (p = .004 and .021, respectively).
Conclusions: The ASD and ADHD groups mainly displayed similar maturation on the neuropsychological measures, and displayed continuous impairment relative to the TD group. The need for support and facilitation of EF in school, workplace, and social arenas might continue into young adulthood among certain individuals with ASD and ADHD. (PsycInfo Database Record (c) 2021 APA, all rights reserved)
Key points:
Question: How does executive functioning (EF) develop from childhood into young adulthood in individuals with autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD) and typically developing (TD) individuals?
Findings: The ASD and ADHD groups mainly showed similar development for results on three neuropsychological tests aimed at capturing central components of EF, and continuous impairment relative to the TD group.
Importance: The clinical groups did not catch up with the performance of the TD group by young adulthood.
Next Steps: Future research could investigate whether adults with ASD and ADHD will display normalized EF relative to TD individuals when followed further into adulthood

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Neuropsychology. 2021 Sep.
EXECUTIVE FUNCTIONS AND WRITING SKILLS IN CHILDREN WITH AND WITHOUT ADHD.
Soto EF, Irwin LN, Chan ESM, et al.
Objective: Pediatric attention-deficit/hyperactivity disorder (ADHD) has been associated with impairments in executive functioning and academic writing skills. However, our understanding of the extent to which these children's writing difficulties are related to their underdeveloped executive functions—and whether this relation is attributable to specific executive functions—is limited.
Method: A clinically-evaluated and carefully-phenotyped sample of 91 children ages 8–13 (M = 10.60, SD = 1.25; 37 girls) were administered multiple, counterbalanced tests of the three core executive functions (working memory, inhibitory control, set shifting), assessed for ADHD symptoms via multiple-informant reports, and completed standardized, norm-referenced testing of three core writing skills (written expression, spelling, writing fluency).
Results: Bias-corrected, bootstrapped conditional effects modeling indicated that underdeveloped working memory exerted significant direct effects on all three writing skills, as well as indirect effects on written expression and spelling via the ADHD symptoms pathway (all 95% CIs exclude 0.0). In contrast, inhibitory control uniquely predicted spelling difficulties only, set shifting was not associated directly or indirectly with any assessed writing skill, and ADHD symptoms failed to uniquely predict writing skills after controlling for working memory. This pattern of results replicated across informants (parent vs. teacher ADHD symptom ratings), and was robust to control for age, sex, socioeconomic status (SES), majority/minority race/ethnicity status, intellectual functioning (IQ), decoding skills, language skills, and learning disability status.
Conclusion: These findings suggest multiple pathways to writing skill difficulties in children with ADHD, while suggesting that their overt behavioral symptoms may be less involved in their writing difficulties than their underlying neurocognitive vulnerabilities.
Key Points—
Question: Attention-deficit/hyperactivity disorder (ADHD) is associated with executive function deficits and difficulties with academic writing skills, but are these links attributable to specific executive functions?
Finding: Underdeveloped working memory abilities predicted written expression, spelling, and writing fluency, both directly and in most cases indirectly via working memory's role in regulating attentive behavior; inhibitory control predicted spelling only, whereas set shifting was not associated with any assessed academic writing skill.

Importance: The association between ADHD symptoms and writing skills appears to be attributable to the role of working memory in regulating behavior, such that ADHD symptoms no longer predicted most assessed writing skills when controlling for working memory, and indirect effects—when detected—accounted for only a small proportion of the relation between working memory and writing skills.
Next Steps: If replicated, these findings may help explain why evidence-based treatments that target overt ADHD symptoms have minimal impact on writing skills for children with ADHD

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Neurosci Biobehav Rev. 2021 Oct;129:117-32.

AUTISM SPECTRUM DISORDER: TRACE ELEMENTS IMBALANCES AND THE PATHOGENESIS AND SEVERITY OF AUTISTIC SYMPTOMS.

Baj J, Flieger W, Flieger M, et al.

The identification of biomarkers as diagnostic tools and predictors of response to treatment of neurological developmental disorders (NDD) such as schizophrenia (SZ), attention deficit hyperactivity disorder (ADHD), or autism spectrum disorder (ASD), still remains an important challenge for clinical medicine. Metallomic profiles of ASD patients cover, besides essential elements such as cobalt, chromium, copper, iron, manganese, molybdenum, zinc, selenium, also toxic metals burden of: aluminum, arsenic, mercury, lead, beryllium, nickel, cadmium. Performed studies indicate that children with ASD present a reduced ability of eliminating toxic metals, which leads to these metals' accumulation and aggravation of autistic symptoms. Extensive metallomic studies allow a better understanding of the importance of trace elements as environmental factors in the pathogenesis of ASD. Even though a mineral imbalance is a fact in ASD, we are still expecting relevant tests and the elaboration of reference levels of trace elements as potential biomarkers useful in diagnosis, prevention, and treatment of ASD

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Nutrients. 2021;13.

PERICONCEPTIONAL MATERNAL DIET CHARACTERIZED BY HIGH GLYCEMIC LOADING IS ASSOCIATED WITH OFFSPRING BEHAVIOR IN NEST.

Alick CL, Maguire RL, Murphy SK, et al.

Maternal periconceptional diets have known associations with proper offspring neurode-velopment. Mechanisms for such associations include improper energy/nutrient balances between mother and fetus, as well as altered offspring epigenetics during development due to maternal nutrient and inflammatory status. Using a comprehensive food frequency questionnaire and as-sessing offspring temperament with the Infant-Toddler Social and Emotional Assessment (n = 325, mean age = 13.9 months), we sought to test whether a maternal periconceptional diet characterized by high glycemic loading (MGL) would affect offspring temperament using adjusted ordinal re-gression. After limiting false discovery to 10%, offspring born to mothers in tertile 3 of glycemic loading (referent = tertile 1) were more likely to be in the next tertile of anxiety [OR (95% CI) = 4.51 (1.88-11.07)] and inhibition-related behaviors [OR (95% CI) = 3.42 (1.49-7.96)]. Male offspring were more likely to exhibit impulsive [OR (95% CI) = 5.55 (1.76-18.33)], anxiety [OR (95% CI) = 4.41 (1.33-15.30)], sleep dysregulation [OR (95% CI) = 4.14 (1.34 13.16)], empathy [6.68 (1.95-24.40)], and maladaptive behaviors [OR (95% CI) = 9.86 (2.81-37.18)], while females were more likely to exhibit increased anxiety-related behaviors [OR (95% CI) = 15.02 (3.14-84.27)]. These associations persisted when concurrently modeled with the maternal Mediterranean dietary pattern. In a subset (n = 142), we also found MGL associated with increased mean methylation of the imprint control region of SGCE/PEG10. In conclusion, these findings highlight the importance of maternal dietary patterns on offspring neurodevelopment, offering avenues for prevention options for mothers

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Nutr Rev. 2021;79:615-26.

BRAIN IRON CONCENTRATIONS IN THE PATHOPHYSIOLOGY OF CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.

Degremont A, Jain R, Philippou E, et al.

Context: Attention deficit/hyperactivity disorder (ADHD) is a neurological disorder associated with iron dysregulation in children. Although previous focus was on examining systemic iron status, brain iron content may be a more reliable biomarker of the disorder.
Objective: This systematic review examines whether children with ADHD have lower serum as well as brain iron concentrations, compared with healthy control subjects (HCS).
Data sources: A systematic literature search was conducted in Medline via PubMed, the Cochrane Library, Web of Science, Embase. and Ovid for papers published between 2000 and June 7, 2019.
Data extraction: Studies were included if the mean difference of iron concentration, measured as serum iron, serum ferritin, or brain iron, between children with ADHD and HCS was an outcome measure.
Data analysis: Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed. Risks of bias within and between studies were assessed using the quality assessment tools of the National Institutes of Health. Of 599 records screened, 20 case-control studies met the inclusion criteria. In 10 of 18 studies in which serum ferritin concentration was assessed, and 2 of 10 studies that assessed serum iron, a significant difference between children with ADHD and HCS was observed. Results of systemic iron levels were inconsistent. In 3 studies in which brain iron concentration was assessed, a statistically significant, lower thalamic iron concentration was found in children with ADHD than in HCS.
Conclusion: The evidence, though limited, reveals that brain iron rather than systemic iron levels may be more associated with the pathophysiology of ADHD in children. Larger, longitudinal, magnetic resonance imaging studies are needed to examine any correlations of iron deficiency in specific brain regions and symptoms of ADHD

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Pediatr Drugs. 2021.

EXECUTIVE FUNCTION OUTCOME OF TREATMENT WITH VILOXAZINE EXTENDED-RELEASE CAPSULES IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POST-HOC ANALYSIS OF FOUR RANDOMIZED CLINICAL TRIALS.

Faraone SV, Gomeni R, Hull JT, et al.

Aim: The aim of this study was to evaluate the effect of viloxazine extended-release capsules (viloxazine ER; Qelbree) on executive function deficits (EFDs) in pediatric subjects (6-17 years of age) with attention-deficit/hyperactivity disorder (ADHD).
Methods: Data from four phase III placebo-controlled trials of 100-600 mg/day viloxazine ER (6-8 weeks of treatment) were used to evaluate the change from baseline (CFB) in the Conners 3rd Edition Parent Short Form-Executive Function (C3PS-EF) content scale T-score. Subjects were defined as EFD responders if they had C3PS-EF T-score > 70 at baseline and < 65 at end of study. ADHD symptoms were assessed with ADHD Rating Scale 5th Edition (ADHD-RS-5). Subjects were defined as ADHD symptom responders if they had a 50% reduction in CFB ADHD-RS-5 Total score at Week 6. The number needed to treat (NNT) and Cohen's d effect sizes were estimated for EFD and ADHD symptoms.
Results: A total of 1154 subjects were included in the analysis. Statistically significant improvements in EFDs were observed with viloxazine ER versus placebo (p=0.0002). There were 52.5% of EFD or ADHD symptom responders in the viloxazine ER treatment group and 35.4% in the placebo group (p<0.0001). The NNT was 5.8. The Cohen's d effect size for EFD and ADHD symptoms was 0.31.
Conclusion: Consistent with the efficacy of viloxazine ER demonstrated in pivotal trials, viloxazine ER significantly reduced EFDs in subjects with ADHD. Moreover, a substantial proportion of subjects treated with viloxazine ER had large improvements in EFDs, ADHD symptoms, or both.
Clinical Trial Registration Numbers: NCT03247530, NCT03247517, NCT03247543, NCT03247556

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PLoS ONE. 2021;16.

REMOTE ASSESSMENT IN ADULTS WITH AUTISM OR ADHD: A SERVICE USER SATISFACTION SURVEY.

Adamou M, Jones SL, Fullen T, et al.

Advances in digital health have enabled clinicians to move away from a reliance on face to face consultation methods towards making use of modern video and web-based conferencing technology. In the context of the COVID-19 pandemic, remote telecommunication methods have become much more common place in mental health settings. The current study sought to investigate whether remote telecommunication methods are preferable to face to face consultations for adults referred to an Autism and ADHD Service during the COVID-19 pandemic. Also, whether there are any differences in preferred consultation methods between adults who were referred for an assessment of Autism as opposed to ADHD. 117 service users who undertook assessment by the ADHD and Autism Service at South West Yorkshire NHS Partnership Foundation Trust from April to September 2020 completed an adapted version of the Telehealth Usability Questionnaire (TUQ). Results demonstrated that service users found remote telecommunication to be useful, effective, reliable and satisfactory. Despite this, almost half of service users stated a general preference for face to face consultations. There was no difference in the choice of methods of contact between Autism and ADHD pathways. Remote telecommunication methods were found to be an acceptable medium of contact for adults who undertook an assessment of Autism and ADHD at an NHS Service during the COVID-19 pandemic

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Prax Kinderpsychol Kinderpsychiatr. 2021 Sep;70:520-40.

INPATIENT PSYCHODYNAMIC THERAPY FOR CHILDREN AND ADOLESCENTS WITH COMPLEX ADHD: RESULTS OF A NATURALISTIC CLINICAL TRIAL.

Cropp C, Kuchinke L, Streeck-Fischer A.

The Attention deficit/hyperactivity disorder (ADHD) is a common mental disorder in childhood and adolescence. However, it is a very heterogeneous disorder with subgroups of patients with mild symptoms and others with severe and complex impairments. Patients suffering from complex ADHD are usually characterized by multiple developmental disorders and impaired personality development. Due to the multimodal origin of the disorder, multimodal treatment approaches aimed at reducing the various deficits are usually indicated. The current study evaluated a multimodal inpatient psychodynamic treatment (PDT) for children and adolescents suffering from ADHD. 47 patients (age 9-17 years) were included in the study. Next to complex impairments (comorbid mental disorders, deficits regarding psychic structure, learning disorders and sensorimotor integration disorders), a high number of adverse childhood experiences (M = 11.71) was particularly remarkable in the sample. The PDT led to significant improvements regarding ADHD symptoms and general level of functioning. However, first symptom improvements were already evident at the end of the waiting period. For ten patients who participated in the follow-up assessment effects remained stable six months after treatment. Due to the high drop-out rate, however, the study results have to be regarded as preliminary

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Prax Kinderpsychol Kinderpsychiatr. 2021 Sep;70:499-519.

PSYCHOANALYTIC TREATMENTS WITHOUT MEDICATION AND BEHAVIORAL THERAPY TREATMENTS WITH AND WITHOUT MEDICATION IN CHILDREN WITH THE DIAGNOSIS OF ADHD AND/OR CONDUCT DISORDER.

Laezer KL, Tischer I, Gaertner B, et al.

The controlled, prospective intervention study without randomization with a non-inferiority study design investigates the effectiveness of psychoanalytic treatments without medication in comparison to behavioral therapy treatments with and without medication in children aged 6 to 11 years with a diagnosis of ADHD and/or conduct disorder. 73 children (58 boys and 15 girls) were included in the study. Diagnostics before treatment, at end of treatment and at follow-up after 38 months included a standardized clinical interview (DISYPS-KJ), questionnaires for parents, teachers and children (DISYPS-KJ, CBCL, TRF, CPRS, CTRS, ILK), intelligence test and behavioral observation of the child. Primary outcome criterion was disorder-specific symptom reduction at end of treatment and follow-up. Both treatment groups showed significant symptom reductions at end of treatment and at follow-up. There were no significant differences between treatment

groups. Parent and teacher ratings showed significant improvements in both groups at end of treatment and at follow-up on the ADHD index, oppositional behavior, and hyperactivity/impulsivity scales, as well as on the externalizing and internalizing behavior problems scales. Quality of life improved for children in both treatment groups

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Prev Med. 2021;153.

PARTICIPATION IN ORGANIZED SPORT AND DISRUPTIVE BEHAVIOR IN CHILDHOOD: A PROSPECTIVE, POPULATION-BASED STUDY.

Imbeault A, Pagani LS.

Child disruptive behavior refers to ongoing patterns of disorganized, uncooperative, and defiant behavior. Sport involvement promotes positive child development. However, few longitudinal studies have tested the association between organized sport participation and the behavioral components of disruptive behavior. First, we aim to examine the link between inattentive, hyperactive, aggressive, and oppositional behavior at age 4 years and trajectories of organized sport participation from ages 6 to 10 years. Then, we compare children, according to trajectory membership, on outcome differences on these same behaviors at age 12 years. Data are from the Quebec Longitudinal Study of Child Development (N = 1492). Child behavior was assessed by questionnaires completed by mothers at age 4 years and teachers at age 12 years. Preschool child inattention as perceived by mothers, significantly reduced the odds of middle childhood organized sport participation by 7% (95% CI = 1.00ΓÇô1.15). Low or inconsistent participation in organized sport was subsequently associated with increased inattention (d = 0.28) by the end of sixth grade. These findings are above and beyond individual and family characteristics and baseline behavior. No other associations were statistically significant. Inattentive children who participated less in organized sport showed a greater likelihood toward increases in attention deficit by the end of sixth grade. To improve engagement from these children, coaches and trainers should use strategies that support positive experiences such as developing a one-to-one alliance with the child, favoring social cooperation through team spirit, and focusing on the performance experience rather than the outcome of winning or losing

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2022;112.

ALTERED CORTICAL ACTIVATION ASSOCIATED WITH MIRROR OVERFLOW DRIVEN BY NON-DOMINANT HAND MOVEMENT IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Luo Y, Chen C, Adamek JH, et al.

Mirror overflow is involuntary movement that accompanies unilateral voluntary movement on the opposite side of the body, and is commonly seen in Attention-Deficit/Hyperactivity Disorder (ADHD). Children with ADHD show asymmetry in mirror overflow between dominant and non-dominant hand, yet there are competing mechanistic accounts of why this occurs. Using EEG during a sequential, unimanual finger-tapping task, we found that children with ADHD exhibited significantly more mirror overflow than typically developing (TD) controls, especially during the tapping of the non-dominant hand. Furthermore, source-level EEG oscillation analysis revealed that children with ADHD showed decreased alpha (8ΓÇô12 Hz) event-related desynchronization (ERD) compared with controls in both hemispheres, but only during tapping of the non-dominant hand. Moreover, only the ERD ipsilateral to the mirror overflow during non-dominant hand movement correlated with both magnitude of overflow movements and higher ADHD symptom severity (Conners ADHD Hyperactivity/Impulsiveness scale) in children with ADHD. TD controls did not show these relationships. Our findings suggest that EEG differences in finger-tapping in ADHD are related primarily to voluntary movement in the non-dominant hand. Our results are also consistent with the Ipsilateral Corticospinal Tract (CST) Hypothesis, which posits that the atypical persistence of mirror overflow in ADHD may originate in the sensorimotor areas ipsilateral to mirror overflow and be transmitted via non-decussating CST fibers

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Psychiatr Invest. 2021;18:763-69.

ABERRANT EFFECTIVE CONNECTIVITY OF THE VENTRAL PUTAMEIN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDE.

Lan Z, Sun Y, Zhao L, et al.

Objective The connectivity alterations in the putamen were found in revealing the neural correlates of attention-deficit/hyperactivity disorder (ADHD), but whether the effective connectivity of the putamen is atypical in ADHD remains unclear. Investigating this abnor-mality contributes to describing the neural circuit of ADHD at the level of macrostructural organization.

Methods Data were acquired from thirty-two boys with ADHD and fifty-two matched typically developing controls (TDC) from Peking University (Peking) dataset deposited at the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) platform. We examined the effective connectivity of the putamen using Granger causality analysis (GCA) and then determined whether these connections could differentiate ADHD from TDC.

Results Compared with TDC, the ADHD group showed decreased effective connectivity from the left ventral rostral putamen (VRto left calcarine (CAL), right medial part of the superior frontal gyrus, left orbital part of superior frontal gyrus and left middle occipigyrus (MOG). Increased effective connectivity from the left inferior occipital gyrus and right lingual gyrus to left VRP was also found ADHD. The result of the classification accuracy showed that 72.3% of participants were correctly classified using support vector mchine. Moreover, GCA values from the left VRP to left CAL and left MOG were significantly correlated with hyper/impulsive scores patients with ADHD.

Conclusion The findings may help extend our understanding of the ADHD-related neural loops

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Psychiatry Res. 2021;300.

RETROSPECTIVE ANALYSIS OF ADVERSE EVENTS ASSOCIATED WITH NON-STIMULANT ADHD MEDICATIONS REPORTED TO THE UNITED STATES FOOD AND DRUG ADMINISTRATION.

Pang L, Sareen R.

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders in children and although stimulant medications remain first line to treat the disorder, some families prefer nonstimulants. The goal is to analyze the adverse events (AE) associated with nonstimulant medications using post-marketing drug surveillance data. We aim to increase awareness and aide patient education. A retrospective study of adverse drug events with atomoxetine, clonidine, and guanfacine was performed using the Federal Drug Administration Adverse Event Reporting System (FAERS) Database. Results show that the most commonly reported AEs, as defined by FAERS, were ineffectiveness (9.91-14.15%) fatigue (8.93%), and somnolence (8.8-10.16%). Of those taking atomoxetine, suicidal and self-injurious ideation was reported to a similar degree amongst all age groups. Suicidal ideation was listed within the top 20 most reported AEs for all three medications. It is more likely that some patients will experience milder side effects. We suggest providing these data to patients to help overcome the stigma of starting medication, especially if they prefer nonstimulants. Serious AEs are still reported to a small degree, thus monitoring and consistent patient education remains important. We also recommend educating a wider demographic of patients about recognizing potential development of suicidal thoughts

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Psychiatry Res. 2021 Aug;302.

VARIATION IN LATENT SOCIAL PROFILES OF ADOLESCENT ADHD AND RELATED CLINICAL FEATURES.

Morris S, Ling M, Sheen J, et al.

Social impairment is a hallmark of Attention-deficit/hyperactivity disorder (ADHD), but the extent of variation in adolescent social strengths and weaknesses is unclear. We compared teacher-reported characteristics of social functioning in adolescents with a history of ADHD (N = 340), and without ADHD (N = 182) from the NIMH Collaborative Multisite Multimodal Treatment Study of Children with ADHD (MTA) at 72-month follow-up (13 – 15.9 years-old). Latent profile analysis of teacher-reported cooperation, assertion and self-control on the Social Skills Rating System (SSRS), was used to identify 'social profiles'. Their associations with clinical features were explored. Significant differences in social functioning were identified between

adolescents with a history of ADHD, and without ADHD (ES = 0.54 – 0.77). Four distinct social profiles were identified in adolescents with a history of ADHD: unskilled (N = 24, 7%), low average (N = 144, 42%), average (N = 141, 41%), and skilled (N = 31, 9%). Profiles with worse social functioning (low average, unskilled) displayed more symptoms of inattention, hyperactivity/impulsivity, oppositionality, depression, global impairment, and were less liked, more rejected and ignored by peers than average and skilled. Social profile membership was not associated with sex, anxiety symptoms, or remittance / persistence of ADHD. Social functioning in adolescents with a history of ADHD is variable, and associated with worse symptomology, global functioning, and peer relationships, irrespective of persistence or remittance of ADHD. Group level summaries of social difficulties in ADHD may be inadequate given nearly half of adolescents with a history of ADHD presented with average or skilled social profiles

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Psychiatry Res. 2021 Sep;303.

METHYLPHENIDATE AMELIORATES THE HOMEOSTATIC BALANCE BETWEEN LEVELS OF KYNURENINES IN ADHD CHILDREN.

Molina-Carballo A, Cubero-Millán I, Fernández-López L, et al.

The kynurenine pathway of tryptophan metabolism has been involved in ADHD. We quantified basal levels and daily fluctuations of tryptophan and several kynurenine metabolites, as well as their changes after treatment with methylphenidate (MPH). A total of 179 children were recruited, grouped into ADHD (n = 130) and healthy controls (CG,n = 49). Blood samples were drawn at 20:00 and 09:00 h and only in the ADHD group after 4.63±2.3 months of treatment. Nocturnal urine was collected between both draws. Factorial analysis (Stata12.0) was performed with Groups, Time, Hour of Day and Depressive Symptoms (DS) as factors. MPH significantly increased plasma Kynurenic acid (2.4 ± 1.03/2.78±1.3 ng/mL; baseline/post-treatment, morning; z = 1.96,p<0.05) and Xanthurenic acid (2.39±0.95/2.88±1.19 ng/mL; baseline/post, morning; z = 2.7,p<0.007) levels, both with higher values in the evening. In DS+ patients, MPH caused a pronounced decrease in evening Anthranilic acid [3.08±5.02/ 1.82±1.46 ng/mL, z = 2.68,p = 0.0074] until matching values to other subgroups. In urine, MPH decreased the excretion of both Nicotinamide and Quinolinic acids, but only in the DS- subgroup. The kynurenine pathway may participate in the highly clinical favorable response to MPH. The observed changes could be considered as protective (i.e. increased plasma kynurenic acid vs. decreased quinolinic acid excretion) based on the knowledge of its physiological homeostatic functions

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Psychol Rep. 2021 Oct;124:2063-91.

A PRELIMINARY EVALUATION OF THE UTILITY OF SLUGGISH COGNITIVE TEMPO SYMPTOMS IN PREDICTING BEHAVIORAL TREATMENT RESPONSE IN CHILDREN WITH BEHAVIORAL DIFFICULTIES.

Little K, Raiker J, Coxe S, et al.

Interest in symptoms of sluggish cognitive tempo (SCT) has led to a number of studies evaluating how these symptoms respond to treatment commonly utilized in youths with symptoms of ADHD. No study to date, however, has examined the extent to which symptoms of SCT predict behavioral treatment response in youths across multiple domains of functioning. The current preliminary investigation integrates a number of methodological (e.g., direct observations) and analytic (e.g., Poisson regression) refinements to evaluate the extent to which symptoms of SCT predict treatment responses across multiple domains including behavioral (e.g., interruptions, rule violations), social (e.g., social skills, negative verbalizations), and severe behavioral difficulties (e.g., intentional aggression) above and beyond other demographic characteristics (e.g., symptom severity, Full Scale Intelligence Quotient [FSIQ]). A relatively small sample of 37 children, aged six to 12 years (M=8.03, SD=1.83, 35 males: 2 females) attending an eight week multi-component intensive behavioral treatment program for youths with behavioral difficulties participated in the current study. Baseline parental perceptions of SCT were collected prior to the initiation of treatment. Results from this preliminary investigation revealed that pre-treatment SCT symptoms only predicted a less robust treatment response to time out which was associated also with parent's perceptions of underlying working memory problems. Results revealed also that pre-treatment SCT symptoms failed to predict paraprofessional counselor's and teacher's improvement ratings of both rule following and social skills following treatment. Notably, other

potential predictors (e.g., symptom severity, FSIQ) also largely failed to predict behavioral treatment response

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Psychol Med. 2021 Jul;51:1524-35.

AN INTEGRATED PROGRAM OF COMPUTER-PRESENTED AND PHYSICAL COGNITIVE TRAINING EXERCISES FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Wexler BE, Vitulano LA, Moore C, et al.

Background: This study integrated an experimental medicine approach and a randomized cross-over clinical trial design following CONSORT recommendations to evaluate a cognitive training (CT) intervention for attention deficit hyperactivity disorder (ADHD). The experimental medicine approach was adopted because of documented pathophysiological heterogeneity within the diagnosis of ADHD. The cross-over design was adopted to provide the intervention for all participants and make maximum use of data.

Methods: Children (n = 93, mean age 7.3 +/- 1.1 years) with or sub-threshold for ADHD were randomly assigned to CT exercises over 15 weeks, before or after 15 weeks of treatment-as-usual (TAU). Fifteen dropped out of the CT/TAU group and 12 out of the TAU/CT group, leaving 66 for cross-over analysis. Seven in the CT/TAU group completed CT before dropping out making 73 available for experimental medicine analyses. Attention, response inhibition, and working memory were assessed before and after CT and TAU.

Results: Children were more likely to improve with CT than TAU (27/66 v. 13/66, McNemar p = 0.02). Consistent with the experimental medicine hypotheses, responders improved on all tests of executive function (p = 0.009–0.01) while non-responders improved on none (p = 0.27–0.81). The degree of clinical improvement was predicted by baseline and change scores in focused attention and working memory (p = 0.008). The response rate was higher in inattentive and combined subtypes than hyperactive-impulsive subtype (p = 0.003).

Conclusions: Targeting cognitive dysfunction decreases clinical symptoms in proportion to improvement in cognition. Inattentive and combined subtypes were more likely to respond, consistent with targeted pathology and clinically relevant heterogeneity within ADHD

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Psychoneuroendocrinology. 2021 Sep;131.

LACK OF ASSOCIATION BETWEEN SEVERITY OF ADHD SYMPTOMS AND SALIVARY OXYTOCIN LEVELS.

Boyle D, Levi-Shachar O, Gvirts HZ, et al.

Impairments in the reactivity of Oxytocin (OT) system were associated with interpersonal difficulties in children with ADHD. The current study aimed to explore the correlation between symptoms severity and salivary OT levels at different time-points in children with ADHD. Symptoms severity was assessed in 50 children with ADHD (28 males, mean age 9.42 ± 1.65) using the Swanson, Nolan and Pelham Questionnaire-IV (SNAP-IV) and the Strengths and Difficulties Questionnaire (SDQ). Salivary OT levels were measured at baseline, as well as 15 min after positive social interaction. There was no statistical correlation between severity of ADHD and salivary OT levels in each of the time points. We conclude that impairments in the reactivity of the OT system in children with ADHD, associated with interpersonal impairments, might be a distinct aspect of the clinical picture, differentiated from the levels of inattentive, hyperactive/impulsive or behavioral symptoms

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Psychoneuroendocrinology. 2021 Sep;131.

HAIR CORTISOL CONCENTRATION AND NEUROCOGNITIVE FUNCTIONS IN PRESCHOOL CHILDREN AT RISK OF DEVELOPING ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Mann C, Schloß S, Cosan A, et al.

Objective: Sex differences have been shown in the relation between hair cortisol concentration (HCC) and ADHD symptoms. As an extension of these findings, we analyze whether a child's sex modulates the associations between HCC and ADHD-related neurocognitive functions.

Methods: A community-based sample of 122 children was tested at age 4–5 (T1) and 8 (T2) years. At T1 and T2, ADHD symptoms were assessed with clinical parent interviews and parent and teacher

questionnaires. Neurocognitive functions (i.e. T1: inhibitory control, working memory (WM), T2: verbal and performance intelligence (IQ-p)) were assessed using (neuro-)psychological tests. At T1, HCC was analyzed in the most proximal 3 cm scalp hair segment using luminescence immunoassay.
Results: Exclusively in boys, low HCC correlated with low WM and IQ-p. The sex-by-HCC interaction effect on WM was significant. In boys, HCC completely explained the links of ADHD inattention symptoms with WM and IQ-p, respectively.
Conclusion: Results suggest a specific neurocognitive/endocrine profile in preschool boys at risk of developing ADHD, comprising hypocortisolism combined with memory and attention deficits

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Psychoneuroendocrinology. 2021 Sep;131.

MOTHER'S HAIR CORTISOL AND SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN HER PRESCHOOL CHILD.

Cosan AS, Schloß S, Vasen Z, et al.

Children with attention deficit hyperactivity disorder (ADHD) require increased caregiver assistance and supervision, and their parents have shown high perceived parenting stress. Hence, physiological adjustment processes in the caregivers, involving the hypothalamic-pituitary-adrenal axis, seem plausible. We analyzed the association between maternal hair cortisol concentration (HCC) and symptoms of ADHD in preschool-aged children. 150 mothers of 4–5-year-old children participated in the study. To determine the HCC, the first scalp-near 3 cm hair segment was used. ADHD symptoms of the child were measured using teacher- and parent-report questionnaires and a clinical interview with the mother. When controlling for several putative confounders, teacher-reported ADHD symptoms were significantly positively associated with mothers' HCC. No associations of HCC with the mother-reported ADHD symptoms of the child emerged. It is possible that teacher-reported ADHD symptoms of the child reflect relevant ADHD symptoms more validly. As our study is the first on this issue, cross-validation is needed

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Psychophysiology. 2021 Sep;58.

EXPLORING AUTONOMIC REGULATION IN CHILDREN WITH ADHD WITH AND WITHOUT COMORBID ANXIETY DISORDER THROUGH THREE SYSTEMATIC LEVELS OF CARDIAC VAGAL CONTROL ANALYSIS: REST, REACTIVITY, AND RECOVERY.

Robe A, Pasarelu CR, Dobrean A.

Autonomic nervous system (ANS) dysregulation, characterized by reduced vagally mediated Heart Rate Variability (HRV), has been associated with Attention-Deficit/ Hyperactivity Disorder (ADHD). This study investigated the dynamic vagal modulation of cardiac output in response to shifts in environmental demands in children and adolescents with ADHD, with and without a comorbid anxiety disorder. High-frequency HRV (HF-HRV) measures were obtained from 46 children and adolescents ranging from 6 to 17 (M = 9.38; SD = 2.31) years old, during three successive experimental conditions: a baseline recording followed by a sustained attention task, and a post-task recovery period. Findings support the reliability of the d2 Test, a cancelation test of attention and concentration, to induce parasympathetic withdrawal and extend prior work on 'vagal flexibility'. Further, these findings suggest a pattern of group differences in ANS functioning in children with ADHD, with and without a comorbid anxiety disorder. Only the ADHD without comorbid anxiety group showed a normative autonomic response to the cognitive challenge (reduced HF-HRV). The participants did not display an adaptive process of restoration following the cognitive challenge; the HRV suppression was prolonged during post-task recovery period, suggesting that ANS responded as if the cognitive stressor was still present. The current paper covers and discusses theoretical implications for the abnormalities in neurophysiological functioning and the different physiological responses in the two ADHD subtypes

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Res Dev Disabil. 2021 Nov;118:104063.

THE RELATIONSHIP BETWEEN INTERNALIZING PROBLEMS AND ACUTE EXERCISE DURATION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: THE ROLE OF FRONTAL ALPHA ASYMMETRY.

Chueh TY, Hsieh SS, Tsai YJ, et al.

BACKGROUND: Frontal alpha asymmetry (FAA) has been associated with the regulation of certain types of internalizing psychopathologies, and is affected by acute aerobic exercise (AE). However, no previous studies have examined the association between FAA and internalizing problems or the effects of acute exercise on FAA in children with ADHD.

AIMS: This study had two objectives. First, it aimed to examine the relationship between FAA and internalizing behaviors in children with ADHD. Second, it sought to investigate the differential effects of acute AE (30 and 50 min) on FAA.

METHOD: Participants were assigned to one of the following three groups: 50 min of AE, 30 min of AE, and a control group. Resting electroencephalogram (EEG) data were recorded before and after their respective treatments. EEG data from 43 participants were analyzed to investigate the association between pre-test FAA and internalizing problems as assessed by Child Behavior Checklist scores. Additionally, EEG data from 46 participants were analyzed to examine the effects of acute AE on post-test FAA while controlling for pre-test FAA.

RESULTS: Pre-test FAA was found to be significantly negatively associated with internalizing problems, with both hemispheres contributing to this association. Regarding the effects of acute exercise, the 50-minute AE group had highest post-test FAA, reflected by the increased relative left-side frontal activity.

CONCLUSIONS: These findings suggest that FAA is a biological marker of internalizing symptoms in children with ADHD, and a 50-minute session of AE can effectively modulate FAA

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Research on Child and Adolescent Psychopathology. 2021 Sep;49:1165-78.

CONDITIONAL LEARNING DEFICITS IN CHILDREN WITH ADHD CAN BE REDUCED THROUGH REWARD OPTIMIZATION AND RESPONSE-SPECIFIC REINFORCEMENT.

De Meyer H, Tripp G, Beckers T, et al.

When children with ADHD are presented with behavioral choices, they struggle more than Typically Developing [TD] children to take into account contextual information necessary for making adaptive choices. The challenge presented by this type of behavioral decision making can be operationalized as a Conditional Discrimination Learning [CDL] task. We previously showed that CDL is impaired in children with ADHD. The present study explores whether this impairment can be remediated by increasing reward for correct responding or by reinforcing correct conditional choice behavior with situationally specific outcomes (Differential Outcomes). An arbitrary Delayed Matching-To-Sample [aDMTS] procedure was used, in which children had to learn to select the correct response given the sample stimulus presented (CDL). We compared children with ADHD (N = 45) and TD children (N = 49) on a baseline aDMTS task and sequentially adapted the aDMTS task so that correct choice behavior was rewarded with a more potent reinforcer (reward manipulation) or with sample-specific (and hence response-specific) reinforcers (Differential Outcomes manipulation). At baseline, children with ADHD performed significantly worse than TD children. Both manipulations (reward optimization and Differential Outcomes) improved performance in the ADHD group, resulting in a similar level of performance to the TD group. Increasing the reward value or the response-specificity of reinforcement enhances Conditional Discrimination Learning in children with ADHD. These behavioral techniques may be effective in promoting the learning of adaptive behavioral choices in children with ADHD

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Sch Psychol. 2021 Sep;36:358-66.

COMPARING THE INITIAL IMPACT OF COVID-19 ON BURDEN AND PSYCHOLOGICAL DISTRESS AMONG FAMILY CAREGIVERS OF CHILDREN WITH AND WITHOUT DEVELOPMENTAL DISABILITIES.

Chafouleas SM, Iovino EA.

The current COVID-19 pandemic is presenting challenges for families (Cluver et al., The Lancet, 2020), which may be exacerbated for caregivers of children with developmental disabilities (DDs; Center on the

Developing Child, Stress, hope, and the role of science: Responding to the coronavirus pandemic, 2020). The purpose of this study was to explore caregiver burden and psychological distress among caregivers of children with DD as compared to caregivers of typically developing children across the United States as a result of COVID-19. Between 2 weeks and 1 month following COVID-19-related school closures, a total of 460 caregivers from across the U.S. completed an online survey via Qualtrics; recruitment and initial survey completion occurred simultaneously. Of the total sample of eligible participants (N = 407), 225 were the primary caregiver of a child with autism spectrum disorder (ASD)/attention-deficit/hyperactivity disorder (ADHD) and 182 were the primary caregiver of a child without ASD/ADHD. Participants across groups indicated varying levels of exposure to COVID-19 and an impact of COVID-19 at the community and individual or family levels. However, caregivers of children with ASD/ADHD reported significantly higher levels of burden, depression, anxiety, and stress. Overall, findings are consistent with anecdotal and preliminary reports that all caregivers are experiencing COVID-19-related challenges, with caregivers of children with ASD/ADHD experiencing even greater challenges, particularly with regard to burden and psychological distress

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Sch Psychol. 2021 Sep;36:313-24.

THE SHORT-TERM IMPACT OF REMOTE INSTRUCTION ON ACHIEVEMENT IN CHILDREN WITH ADHD DURING THE COVID-19 PANDEMIC.

Lupas KK, Mavrakis A, Altszuler A, et al.

There is nationwide concern that the abrupt transition to remote instruction in response to the Coronavirus disease (COVID-19) pandemic will have detrimental impacts on student learning. As a uniquely vulnerable group within schools, students with disabilities like attention deficit hyperactivity disorder (ADHD) may be at enhanced risk for these negative outcomes. The present study features a unique examination of achievement scores, collected for two Cohorts (2018–2019, 2019–2020) of students with ADHD. By collecting achievement data in both the fall and spring for each Cohort, direct comparisons between changes in achievement for Cohort One (2018–2019) can be made to those in Cohort Two (2019–2020). Analyses summarized remote learning practices, within-group changes in achievement data over time for Cohort Two, and between-group differences in score changes over time for Cohorts One and Two. Teachers used a variety of remote learning approaches, including videoconferencing and independently completed assignments. Student achievement scores in both Cohorts significantly improved from fall to spring. No significant differences were found in score growth between the Cohorts, indicating that the move to remote instruction did not have a differentially negative impact on Cohort Two. Implications focus on the promise of well-delivered remote instruction, and the need to examine individual factors (such as poor internet access) that may exacerbate the risk of students with disabilities receiving remote instruction

Impact and Implications—There is nationwide concern that the rapid move to remote instruction during the COVID-19 pandemic will have long-lasting negative impacts on our youth. This study demonstrated that children with attention and behavioral difficulties did not show a substantial decrease in academic achievement following three to 4 months of remote instruction. These results present the short-term impact of remote instruction; future work must address whether continuing to deliver school remotely impacts students with disabilities

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Sinapse. 2020;20:170-80.

PSYCHIATRIC PRESENTATION OF CHILDHOOD MULTIPLE SCLEROSIS: SYSTEMATIC LITERATURE REVIEW.

Duarte L, et al.

Introduction: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system that also affects children and adolescents. The association between psychopathology and MS is frequent in adults, but there is little research on this comorbidity in childhood. The aim of this work was to make a systematic literature review on psychopathology as an initial presentation of pediatric MS.

Methods: A search was performed on the PubMed and Embase databases, using the terms multiple sclerosis child* [AND] psychiatr* [AND/OR] presenting symp-tom. Of the 84 results obtained, 3 articles whose

title or summary were considered adequate, were selected. From these articles bibliographic references, 2 additional articles were included.
Results: Five articles were reviewed. Heilñ et al (1995) described the case of a 15-year-old adolescent who presented with manic symptoms accompanied by cognitive difficulties. Clinical investigation found changes compatible with the diagnosis of MS. Lopez-Meza et al (2005) described the case of an 11-year-old girl who, after an appar-ent herpetic encephalitis, developed a psychopathological picture of disturbed impulse control and affective symptoms, of progressive worsening. At the age of 21, a diagnosis of MS was made. Treadwell-Deering et al (2007) described a case of a 14-year-old teenager with attention deficit hyperactivity disorder, who developed psychotic symptoms with poor response to therapy, difficulties in speech, fine motor skills and attention, being subsequently diagnosed with MS. Tapos and Sivaswamy (2013) described a case of a 16-year-old teenager with a previous diagnosis of schizoaffective disorder with poor response to therapy, exhibiting a slight spasticity of the lower limbs, ataxia and dysar-thria, which subsequently allowed the diagnosis of MS. Ackerman (2017) described a case of a 16-year-old teenager, a regular cannabinoid consumer, who developed atypical psychotic symptoms lasting several months and was later diagnosed with MS.
Discussion: The possibility of psychiatric symptoms arising in the context of clinical conditions that do not typically include psychiatric manifestations is often overlooked. Children and adolescents with psychopathological symptoms must undergo careful anamnesis, neurological examination and, if indicated, imaging studies. It is essential to raise the awareness of clinicians who work directly with these young people

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Sleep. 2021;44:A242.

RESTLESS SLEEP AND OTHER COMORBIDITIES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kapoor V, Ferri R, Stein M, et al.

Introduction: The etiology of restless sleep has recently been identified as secondary to various medical and sleep conditions. Parents of children with ADHD complain of restless sleep and sleep disturbances in their children. We aimed to assess restless sleep causes in our patient population with ADHD and establish the prevalence of restless sleep disorder (RSD), as recently defined.
Methods: A retrospective study of children with ADHD who underwent polysomnography was carried out. Diagnostic and descriptive information collected for each patient included age, sex, polysomnographic parameters, sleep disorders, psychiatric comorbidities, and medications.
Results: Sixty-six PSGs were reviewed. The mean age of children was 11.6 (-¦3.6 SD) years; 17 were female and 49 were male. Parents of 54 (81.1%) children had concerns of restlessness during sleep; 47 (71.2%) children had obstructive sleep apnea, 17 (25.8%) had PLMS 5/hour, 13 (19.7%) had RLS, 6 (9.1%) had RSD, 27 (41%) had depression or anxiety, 5 (7.6%) had insomnia.
Conclusion: In a pediatric sleep medicine referred group of patients with ADHD, who are known to have significant sleep and psychiatric comorbidities, obstructive sleep apnea, RLS, and RSD were found to be the most prevalent sleep disorders, whereas depression and anxiety were the most common psychiatric disorders. Complaint of secondary restless sleep seems to be common, while primary restless sleep disorder was seen in approximately 9% of children. The results of this study aid pediatricians and child psychiatrists in screening children with ADHD for associated sleep disorders

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Sleep. 2021;44:A298-A299.

SLEEP ARCHITECTURE AND SLEEP PROBLEMS IN ADOLESCENTS AND YOUNG ADULTS WITH AND WITHOUT ADHD: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Marten F, Keuppens L, Baeyens D, et al.

Introduction: During the past years, an increasing number of articles has focused on comparing sleep in youths with and without ADHD. However, so far no meta-analysis has been conducted summarizing the findings. Therefore, the current study assesses sleep architecture (i.e. the basic sleep structure), sleep problems, and sleep hygiene. Sleep was assessed both subjectively and objectively and the two groups were compared on multiple variables.

Methods: Two researchers independently performed a literature search (1980-2020). Studies using a case-control design comparing sleep in youths (12-25 years) with and without ADHD were included. Study quality was evaluated using the Newcastle-Ottawa Scale. Standardized mean differences were calculated for each outcome domain being reported by at least two studies.
Results: 10379 publications were screened, resulting in 11 studies and 52 effect sizes (nADHD=2377, ncontrol=21687). These effect sizes were summarized into 7 objective and 11 subjective variables measuring sleep. Two objective sleep variables were significantly worse in the ADHD group; total sleep time (z=2.16, p=.03) and sleep onset latency (z=2.39, p=.02). The two groups did not differ on sleep efficiency, sleep onset/offset time, and time in bed. Comparing the groups on subjective variables resulted in the same pattern, with total sleep time (z=21.27, p<.001) being significantly shorter in the ADHD group, and sleep onset latency (z=15.39, p<.001) and wake after sleep onset (z=13.50, p<.001) being significantly longer. Additionally, the ADHD group reported a significantly lower sleep efficiency (z=20.15, p<.001) and subjective sleep satisfaction (z=3.50, p<.001). Wake time and number of awakenings during the night were not significant. Youths with ADHD also reported significantly more sleep problems, including insomnia (z=6.38, p<.001), daytime sleepiness (z=26.68, p<.001) and sleep disturbances (z=8.00, p<.001). Due to only two studies measuring it, with a focus on different variables, sleep hygiene could not be included.
Conclusion: In general, youths with ADHD have a disrupted sleep architecture and experience more sleep problems compared to their typically developing peers. Consequently, sleep assessment should become a routine part during the diagnostic process of ADHD. Additionally, more research is needed focusing on sleep architecture and sleep hygiene, and on the development of a sleep intervention for youths with ADHD

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Sleep. 2021;44:A246-A247.

LONGITUDINAL ASSOCIATION BETWEEN NREM SLEEP DEPTH AND AROUSABILITY WITH ADHD AND INTERNALIZING DISORDERS IN ADOLESCENCE.

Ricci A, Fernandez-Mendoza J, He F, et al.

Introduction: Sleep depth decreases in the transition from childhood to adolescence, even in typically developing (TD) youth. However, it remains unknown whether this developmental trajectory in NREM sleep depth differs across adolescents with psychiatric/behavioral disorders.
Methods: We analyzed the sleep EEG of 392 subjects aged 5-12 at baseline and 12-22 at follow-up (45.2% female, 23.2% racial/ ethnic minority), of whom 246 were TD adolescents (controls), 62 were diagnosed with a psychiatric/behavioral disorder and were taking stimulant, anti-depressant, anxiolytic, sedative and/or antipsychotic medications, and 84 were un-medicated. NREM sleep depth was measured at both time points using the odds ratio product (ORP), which provides a standardized continuous EEG measure of NREM sleep depth/arousability (higher ORP reflects lighter NREM sleep). General linear models examined mean differences between groups on the percent change in ORP between baseline and follow-up (+öORP) while adjusting for sex, race/ethnicity, age, BMI and AHI at follow-up, and PSG system, psychiatric/behavioral disorders, psychoactive medications and ORP at baseline as well as time-to-follow-up.
Results: Overall, medicated (80.4%, 95%CI=66.2-94.6) and un-medicated (66.1%, 95%CI=53.0-79.1) subjects showed a higher +öORP compared to controls (52.2%, 95%CI=40.0-64.5, p<0.01 and p<0.05, respectively) but did not differ between each other (p=0.134). Specifically, un-medicated subjects with ADHD (n=56) showed a higher +öORP (77.3%, 95%CI=62.4-92.1) compared to controls (p<0.01), while subjects with ADHD on stimulant medication (n=36) did not differ (66.1%, 95%CI=48.9-93.2) from controls (p=0.268) or from un-medicated ADHD subjects (p=0.303). Subjects with internalizing disorders on psychoactive medications (n=29) showed a higher +öORP (104.9%, 95%CI=82.8-127.0) compared to controls (p<0.01) and to un-medicated subjects (n=27) with internalizing disorders (60.1%, 95%CI=36.8-83.3, p<0.01), who did not differ from controls (p=0.772).
Conclusion: The greater increase in ORP in the transition to adolescence in un-medicated youth with ADHD suggests that decreased NREM sleep depth may be a biomarker of the disorder. In contrast, the greater increase in ORP in medicated youth with internalizing disorders suggests that psychoactive medications impact NREM sleep depth in these children as they transition to adolescence. These data have important implications for sleep EEG studies that include medicated and un-medicated youth with comorbid psychiatric disorders

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Sleep. 2021;44:A245.

THE ASSOCIATION OF CIRCADIAN RHYTHMS WITH COGNITIVE FUNCTIONING IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Li X, Shea KSC, Wong CKD, et al.

Introduction: Disrupted circadian rhythms is associated with impaired cognitive function. Although circadian rhythm disturbances are commonly seen in individuals with attention-deficit hyperactivity disorder (ADHD), whether their cognitive functioning is thus affected remains unclear. This study aimed to examine the associations of circadian-related parameters with different cognitive abilities in children with ADHD.

Methods: Fifty-seven children with ADHD were recruited into this study (age range: 6-12 years, 66.7% male). They were assessed by parent-report questionnaires on sleep problems (Children's Sleep Habits Questionnaire, CSHQ), and ADHD symptoms (Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour Scale). Actigraphic data collected for seven consecutive days were analyzed using parametric and nonparametric methods. Cognitive functioning was assessed with Continuous Performance Test (CPT) for sustained attention, Letter-digit test for processing speed, Digit Span test and N-back task for working memory, Tower of London test for planning skills and Bergs Card Sorting Test for set-shifting ability. The relationship between circadian parameters and cognitive performance was analyzed using multiple regression while controlling for age, sex, ADHD medication, the day of cognitive assessment (school days vs non-school days), total sleep time, and CSHQ total score.

Results: Increased activity during the most active 10-h period of the day (St. +¦ = 0.39, p = 0.012) was related to more omission errors on CPT, and later onset of the least active 5-h period of the day (St. +¦ = 0.44, p = 0.004) was associated with longer correct reaction time on CPT. Lower relative amplitude was associated with poorer performance on Digit Span (St. +¦ = 0.33, p = 0.042). No significant associations were found between the circadian-related parameters and the performance on other tasks measuring processing speed and executive functions.

Conclusion: Circadian rest-activity rhythms (blunted rest-activity rhythms, higher daytime activity, and later onset of nocturnal rest) were associated with cognitive functioning in ADHD children. Future longitudinal studies are needed to explore the long-term impact of circadian rhythm disturbances and the effects of circadian-focused intervention on cognitive functioning in ADHD children

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Sleep. 2021;44.

PROSPECTIVE EXAMINATION OF ADOLESCENT SLEEP PATTERNS AND BEHAVIORS BEFORE AND DURING COVID-19.

Becker SP, Dvorsky MR, Breaux R, et al.

Study Objectives: To prospectively examine changes in adolescent sleep before and during the COVID-19 pandemic in adolescents with and without ADHD.

Methods: Participants were 122 adolescents (ages 15-17; 61% male; 48% with ADHD). Parents reported on adolescents' sleep duration and difficulties initiating and maintaining sleep (DIMS); adolescents reported on sleep patterns, sleep duration, delayed sleep/wake behaviors, and daytime sleepiness before (September 2019 to February 2020) and during (May-June 2020) COVID-19. Adolescents also reported on their health behaviors, COVID-19-related negative affect, and difficulties concentrating due to COVID-19.

Results: Parents reported adolescents had more DIMS during COVID-19 than before COVID-19, with clinically elevated rates increasing from 24% to 36%. Both bedtimes and waketimes shifted later during COVID-19, and adolescents reported more delayed sleep/wake behaviors. Adolescents also reported less daytime sleepiness and longer school night sleep duration during COVID-19. In considering differences between adolescents with and without ADHD, adolescents with ADHD did not experience an increase in school night sleep duration and were less likely to obtain recommended sleep duration during COVID-19. In the full sample, controlling for ADHD status, COVID-19-related sadness/loneliness was associated with increases in DIMS, and spending less time outside and more COVID-19-related worries/fears were associated with increases in delayed sleep/wake behaviors during COVID-19.

Conclusions: COVID-19 had negative and positive impacts on adolescent sleep. Adolescents with ADHD did not experience the benefit of increased school night sleep duration during COVID-19 like adolescents without ADHD. Negative affect and health behaviors may be useful intervention targets for reducing negative impacts of COVID-19 for adolescent sleep

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Sleep Med. 2021;87:77-84.

SHORTER RAPID EYE MOVEMENT SLEEP DURATION IN CHILDREN WITH ATTENTION-DEFICIT /HYPERACTIVITY DISORDER: THE IMPACT ON QUALITY OF LIFE.

Darweesh AED, El Beh KA, Hashem MM, et al.

Objectives: The relationship of sleep with attention deficit hyperactivity disorder (ADHD) remains complex and unclear. The current study aimed to compare the subjective and objective sleep parameters among children with and without ADHD. Moreover, to address the effect of sleep parameters on the quality of life (QoL).

Methods: We assessed 42 participants who were children with ADHD (aged 6ΓÇô12 years), with predominant combined presentation (23), compared to 42 healthy children, who underwent a sleep study assessment subjectively (the Children's Sleep Habits Questionnaire), and objectively (one-night Polysomnographic recording). Also, parents completed the pediatric quality of life inventory (PedsQL-P).

Results: Children with ADHD had more subjective sleep problems. ADHD patients also had a significant decrease in total sleep time and sleep efficiency, spending more time in wake and N1 sleep stages. Moreover, they had significantly lower rapid eye movement (REM)sleep duration and less duration of deep sleep stages. Multivariate regression analysis showed that REM sleep duration was the most contributing and predictive factor to QoL and school function impairment.

Conclusion: Children with ADHD have a significantly lower sleep quantity and poor sleep quality. In addition, short REM sleep duration independently contributes to further deterioration in different areas of QoL

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Soc Sci Med. 2021 Sep;284:114232.

"WHY CAN'T YOU SIT STILL?"THE EFFECT OF DAILY PHYSICAL ACTIVITY ON CHILDHOOD INATTENTION/HYPERACTIVITY AND THE EDUCATIONAL GENDER GAP.

Chen K, Phipps S.

Despite the compelling evidence of the long-run consequences of childhood inattention/hyperactivity and harmful side effects of stimulant medication, relatively little is known about accessible non-pharmacological options to reduce inattentive/hyperactive behaviours. This study evaluates the effect of daily exercise on inattentive/hyperactive behaviours among young children by leveraging evidence from a quasi-experiment generated when 3 Canadian provinces adopted mandatory requirements for all students in grades 1 through 6 to participate in 20-30Â min of daily physical activity at school between 1994 and 2009. By exploiting plausibly exogenous variations in the timing of implementation and duration of physical activity mandated as well as over 20,000 observations on a sample of nationally representative children, our difference-in-differences estimates indicate that brief bouts of daily exercise at school effectively reduce inattention/hyperactivity in children - with the beneficial effect enhanced by the duration of exercise mandated. Importantly, most of the exercise effect is concentrated on boys. Since boys' higher rates of inattention/hyperactivity contribute to the explanation for boys' lagging academic motivation and achievement, we argue that providing more scope for physical activity during the school day might be a feasible policy option not only for reducing inattentive/hyperactive behaviours, but also for helping to close the educational gender gap in the longer run

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Soc Sci Med. 2021 Sep;284.

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Soc Sci Med. 2021;289.

NEGOTIATING ADHD: PRAGMATIC MEDICALIZATION AND CREOLIZATION IN URBAN INDIA.

Slagboom MN, et al.

Although a growing number of studies have demonstrated differences in responses to ADHD-like behaviours, very few studies have focused on theorizing diversity in the way ADHD is framed and approached globally. To contribute to the study of medicalization in a global context, this study examines the discursive field in which care professionals explain and treat ADHD among children in metropolitan India and addresses the need for an analytic framework to grasp the variations in the way ADHD is understood and approached. Building on the concepts of pragmatic medicalization and creolization, we study ADHD discourses in India asking What is at stake and What matters most? In this mixed methods study, 64 care professionals regularly involved in assessing ADHD-like behaviour completed an online Q-sort, and 21 professionals participated in face-to-face interviews. The Q-data were subjected to factor analysis. The interviews were analyzed using qualitative content analyses. Our study identified six distinct ADHD discourses, which showed that care professionals combine explanatory and treatment models. Professionals adapt their explanations and treatments of ADHD to parents worries regarding academic performance, family prestige, stigma and side effects of allopathic medicine. Our findings indicate that an awareness of local concerns and adjustments to structural opportunities can diversify how ADHD-like behaviour is framed and responded to. This study demonstrates that medicalization operates between the emerging institutions of care and the everyday concerns of families and care professionals and reveals the need to examine conflicting stakes as drivers of diverse responses to ADHD diagnosis and treatment in India and the rest of the world

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Transl Psychiatry. 2021 Sep;11:493.

DO SHAPES HAVE FEELINGS? SOCIAL ATTRIBUTION IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Vandewouw MM, Safar K, Mossad SI, et al.

Theory of mind (ToM) deficits are common in children with neurodevelopmental disorders (NDDs), such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), which contribute to their social and cognitive difficulties. The social attribution task (SAT) involves geometrical shapes moving in patterns that depict social interactions and is known to recruit brain regions from the classic ToM network. To better understand ToM in ASD and ADHD children, we examined the neural correlates using the SAT and functional magnetic resonance imaging (fMRI) in a cohort of 200 children: ASD (N=76), ADHD (N=74) and typically developing (TD; N=50) (4-19 years). In the scanner, participants were presented with SAT videos corresponding to social help, social threat, and random conditions. Contrasting social vs. random, the ASD compared with TD children showed atypical activation in ToM brain areas-the middle temporal and anterior cingulate gyri. In the social help vs. social threat condition, atypical activation of the bilateral middle cingulate and right supramarginal and superior temporal gyri was shared across the NDD children, with between-diagnosis differences only being observed in the right fusiform. Data-driven subgrouping identified two distinct subgroups spanning all groups that differed in both their clinical characteristics and brain-behaviour relations with ToM ability

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Translational Pediatrics. 2020;9:S104-S113.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: DIAGNOSTIC CRITERIA, EPIDEMIOLOGY, RISK FACTORS AND EVALUATION IN YOUTH.

Cabral MDI, Liu S, Soares N.

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in childhood with persistence into adulthood. It has a multifactorial etiology. Its chronicity, if diagnosis is missed or delayed, will result in significant negative impact on the individualΓÇÖs overall functioning and development. With the revised diagnostic criteria released in 2013 by the American Psychiatric Association, established standards of clinical practice continue to be applicable and valuable in the diagnosis and management of ADHD. In older children and adolescents, it is important to differentiate what is developmentally appropriate from problematic as ADHD has high correlation with poor outcomes, comorbidities, and low quality of life

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Translational Pediatrics. 2020;9:S114-S124.

NON-PHARMACOLOGIC MANAGEMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: A REVIEW.

Shrestha M, Lautenschleger J, Soares N.

Attention-deficit/hyperactivity disorder (ADHD) is a very common neurobehavioral disorder that affects children and adolescents with impact that persists beyond adolescence into adulthood. Medication and non-pharmacological treatments are evidence-based interventions for ADHD in various age groups, and this article will elaborate on the psychosocial, physical and integrative medicine interventions that have been studied in ADHD

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Tunis Med. 2021;99:380-82.

PICA IN AN ADOLESCENT WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER RESPONSIVE TO METHYLPHENIDATE.

Bourgou S, Sahli L, Sarhan A, et al.

We report the case of a boy 12-years old diagnosed with Pica and ADHD (combined type) according to DSM-5 criteria. A past diagnosis of disinhibited attachment disorder was also retained. Methylphenidate 40 mg daily was prescribed. The ADHD and pica symptoms improved within 3 weeks. The scholar results improved. The patient didn't engage in any pica behavior during the followship

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Turkish Journal of Medical Sciences. 2021;51:2107-11.

THE STUDY OF TAU AND PHOSPHO TAU PROTEIN LEVELS IN ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Sarao-lu H, et al.

Background/aim: Attention deficit and hyperactivity disorder (ADHD) is a widespread neurodevelopmental disorder that begins in childhood and has negative consequences throughout adult life. The etiology and pathogenesis of ADHD are still unclear. Tau protein is a soluble microtubule-related protein expressed by neurons and localized in the cytoplasm as well as axons. Tau protein provides stability of microtubule in two ways: phosphorylation and isoforms. The excessive phosphorylation of Tau separates the protein from the microtubule, thus making it unstable. In this study, we aimed to investigate whether there is a relationship between serum Tau protein and phospho Tau (p-Tau181) levels and ADHD occurrence.

Materials and methods: This study included 26 male children aged 7ΓÇô12 years with newly diagnosed ADHD, who had previously not used any medication for ADHD, and 26 male healthy children. Serum Tau and p-Tau181 concentrations were performed by enzyme-linked immunosorbent assay (ELISA).

Results: In patients, the Tau levels were not significantly different from those of the controls; the p-Tau181 levels were significantly higher than those of the controls.

Conclusion: We concluded that high p-Tau181 might be associated with the progression of ADHD and cognitive changes in ADHD

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Vaccines. 2021;9.

FACTORS RELATED TO CAREGIVER INTENTIONS TO VACCINATE THEIR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AGAINST COVID-19 IN TAIWAN.

Tsai CS, Hsiao RC, Chen YM, et al.

The aims of this study were to examine the proportion of caregivers who were hesitant to vaccinate their children with attention-deficit/hyperactivity disorder (ADHD) against coronavirus disease 2019 (COVID-19) and the factors related to caregiver intentions to vaccinate their children against COVID-19. In total, 161 caregivers of children with ADHD were recruited in this study. The caregivers completed an online questionnaire to provide data regarding their intention to vaccinate their children against COVID-19, concerns about the effectiveness and safety of vaccines, unfavor-able family attitudes toward vaccines, and children's medication use for ADHD and comorbid psy-chopathology. The factors related to caregiver intentions to vaccinate their child were examined using linear regression analysis. The results indicated that 25.5% of caregivers were hesitant to vaccinate their children with ADHD, and 11.8% refused to vaccinate their children against COVID-19. The caregivers concerns about the safety of vaccines and children's regular use of medication for ADHD were negatively associated with caregiver intentions to vaccinate, whereas the children's comorbid conduct or oppositional defiant problems were positively associated with the caregiver intentions to vaccinate. An intervention that enhances caregiver intentions to vaccinate their children with ADHD against COVID-19 by addressing the related factors found in this study is war-ranted

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Vision Research. 2021 Sep;186:52-58.

CAPTURING ATTENTION IMPROVES ACCOMMODATION: AN EXPERIMENTAL STUDY IN CHILDREN WITH ADHD USING MULTIPLE OBJECT TRACKING.

Molina R, Redondo B, Molina-Carballo A, et al.

The present study was aimed at assessing the impact of manipulating the attentional load using a multiple object tracking (MOT) task on the dynamics of the accommodative response in children with attention deficit hyperactivity disorder (ADHD). The pupil size was recorded to assess the effectiveness of the experimental manipulation, and the role of ADHD medication was also explored. The accommodative and pupil dynamics (magnitude and variability) were monitored with an open-field autorefractometer (WAM-5500) in 41 children with ADHD (24 non-medicated and 17 medicated) and 21 non-ADHD controls, while they performed the MOT task with four different levels of complexity (i.e., tracking zero, one, two, or three targets). We found that increasing the attentional load caused a heightened accommodative response, showing a negative association between MOT complexity and accommodative lag in children with ADHD and non-ADHD controls. Complementarily, the pupil size increased as a function of task complexity, confirming a successful experimental manipulation. The stability of accommodation was insensitive to the attentional manipulation, but it differed between groups. Specifically, non-medicated children with ADHD exhibited a greater variability of accommodation in comparison to controls. Increasing the attentional load is associated with a reduction in the accommodative lag in children with ADHD and controls. Our findings show that the allocation of attention plays an important role in the dynamics of the accommodative response, which may be of relevance in the diagnosis and treatment of accommodative deficits in children with and without ADHD

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World Psychiatry. 2021;20:417-36.

RISK AND PROTECTIVE FACTORS FOR MENTAL DISORDERS BEYOND GENETICS: AN EVIDENCE-BASED ATLAS.

Arango C, Dragioti E, Solmi M, et al.

Decades of research have revealed numerous risk factors for mental disorders beyond genetics, but their consistency and magnitude remain uncer-tain. We conducted a "meta-umbrella" systematic synthesis of umbrella reviews, which are systematic reviews of meta-analyses of individual studies, by searching international databases from inception to January 1, 2021. We included umbrella reviews on non-purely genetic risk or protective factors for any ICD/DSM mental disorders, applying an established classification of the credibility of the evidence: class I (convincing), class II (highly suggestive), class III (suggestive), class IV (weak). Sensitivity analyses were conducted on prospective studies to test for temporality (reverse causation), TRANSD criteria were applied to test transdiagnosticity of factors, and A Measurement Tool to

Assess Systematic Reviews (AMSTAR) was employed to address the quality of meta-analyses. Fourteen eligible umbrella reviews were retrieved, summarizing 390 meta-analyses and 1,180 associations between putative risk or protective factors and mental disorders. We included 176 class I to III evidence associations, relating to 142 risk/protective factors. The most robust risk factors (class I or II, from prospective designs) were 21. For dementia, they included type 2 diabetes mellitus (risk ratio, RR from 1.54 to 2.28), depression (RR from 1.65 to 1.99) and low frequency of social contacts (RR=1.57). For opioid use disorders, the most robust risk factor was tobacco smoking (odds ratio, OR=3.07). For non-organic psychotic disorders, the most robust risk factors were clinical high risk state for psychosis (OR=9.32), cannabis use (OR=3.90), and childhood adversities (OR=2.80). For depressive disorders, they were widowhood (RR=5.59), sexual dysfunction (OR=2.71), three (OR=1.99) or four-five (OR=2.06) metabolic factors, childhood physical (OR=1.98) and sexual (OR=2.42) abuse, job strain (OR=1.77), obesity (OR=1.35), and sleep disturbances (RR=1.92). For autism spectrum disorder, the most robust risk factor was maternal overweight pre/during pregnancy (RR=1.28). For attention-deficit/hyperactivity disorder (ADHD), they were maternal pre-pregnancy obesity (OR=1.63), maternal smoking during pregnancy (OR=1.60), and maternal overweight pre/during pregnancy (OR=1.28). Only one robust protective factor was detected: high physical activity (hazard ratio, HR=0.62) for Alzheimer's disease. In all, 32.9% of the associations were of high quality, 48.9% of medium quality, and 18.2% of low quality. Transdiagnostic class I-III risk/protective factors were mostly involved in the early neurodevelopmental period. The evidence-based atlas of key risk and protective factors identified in this study represents a benchmark for advancing clinical characterization and research, and for expanding early intervention and preventive strategies for mental disorders

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Changes in Sleep Patterns and Disorders in Children and Adolescents with Attention Deficit Hyperactivity Disorders and Autism Spectrum Disorders during the COVID-19 Lockdown

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Abstract: Background. The COVID-19 lockdown determined important changes in the sleep of a large percentage of the world population. We assessed the modifications of reported sleep patterns and disturbances in Italian children and adolescents with autism spectrum disorders (ASD) or attention deficit hyperactivity disorders (ADHD), compared to control children, before and during the COVID-19 lockdown in Italy. Methods. Parents of 100 ASD, 236 ADHD patients, and 340 healthy children filled out an anonymous online survey and a modified version of the Sleep Disturbance Scale for Children (SDSC), advertised via social media, to evaluate sleep patterns and disturbances of their children before and during the lockdown. Results. Before the lockdown, bedtime and risetime were not different between the three groups. During the lockdown, ADHD children tended to have a later bedtime and risetime than ASD and controls, while ASD children tended to maintain similar bedtime and risetime. Overall, during the lockdown, a reduced sleep duration significantly differentiated clinical groups from controls. Anxiety at bedtime, difficulties in falling asleep, and daytime sleepiness increased in all groups during the lockdown. Hypnic jerks, rhythmic movement disorders, night awakenings, restless sleep, sleepwalking, and daytime sleepiness increased in ASD and ADHD patients, in particular. Conclusions. This is the first study comparing sleep habits and disorders in ASD and ADHD during the lockdown showing specific differences consistent with the core characteristics of two neurodevelopmental disorders.

Keywords: sleep; ADHD; ASD; COVID-19

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1. Introduction

The general confinement from the COVID-19 pandemic and the consequent school closure, interruption of contacts with family members and friends, as well as reduced social and leisure activities, has brought unparalleled modifications to the lifestyle of children and adolescents, with important repercussions on their mental state and behaviors [1].

In particular, COVID-19 lockdown resulted in important changes in sleep habits and sleep disorders in a large portion of the world's population of all ages [2–6]. The increase in sleep difficulties was often associated with higher levels of psychopathological symptoms or decreased quality of life [3,7,8].

In face of a great amount of literature on the young and adult general population, only a few studies were conducted on sleep patterns or disturbances of the clinical population, especially children and adolescents with autism spectrum disorder (ASD) [9] and attention-deficit/hyperactivity and impulsive disorders (ADHD) [10], despite their frequent sleep disturbances and altered sleep patterns, independently by COVID-19 [11]. Since sleep

patterns significantly changed during the lockdown in typically developing children and adolescents [2,5,6,12], similar or even worse changes in subjects with ADHD and ASD could be expected. Several studies [9,10,13–17] reported a high percentage of patients with ASD or ADHD that changed their sleep with a significant worsening of sleep quality and disturbances during the lockdown. Specifically, ASD children showed significant worsening of sleep disturbances, sleep duration, and sleep quality [14,15] and an increase in bedtime resistance, delay in falling asleep, and night awakenings [17]. Children with ADHD showed an alteration of sleep patterns in 85% of cases [16] and, unlike their healthy peers in the control group that experienced an increase in school night sleep duration, they did not benefit from the COVID-19 lockdown [13].

Significant changes in sleep habits and disturbances in children with ADHD or ASD and adolescents during the lockdown have been reported by other studies. Since ADHD and ASD are two neurodevelopmental disorders with different symptoms, we could have expected that sleep changes would reflect specific clinical traits characterizing these two populations. To the best of our knowledge, no study has compared these two disorders for their sleep patterns and disturbances during the COVID-19 lockdown, thus, the aim of this study was to evaluate the different responses of these two clinical conditions in terms of sleep patterns and sleep disturbances.

2. Materials and Methods

2.1. Participants

Parents of Italian children and adolescents completed an online survey, advertised via social media, for a limited time window (from 7th May to 15th June 2020), targeting children aged 4 to 18 years. ASD and ADHD children and adolescents had been diagnosed by a child and adolescent psychiatrist of the Child and Adolescent Mental Health Services, before the survey, and were being followed at the same center. The survey was developed and conducted following the guidelines set by the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [18]. From a total of 5825 respondents, we identified ADHD and ASD patients and selected randomly a sample of typically developing subjects matched for age and sex with the clinical groups.

In total, 100 ASD (16 females, 16% and 84 males, 84%), 236 ADHD patients (44 females, 18.6% and 192 males, 81.4%), and 340 controls (58 female, 17.1% and 282 males, 82.9%) were enrolled in the analysis.

In Italy, the COVID-19 lockdown started on March 2020 with important restrictions that included school closure, limited activities for businesses and factories, and movement restrictions. The strict lockdown in Italy lasted for almost three months, with the progressive reopening of several activities in mid-June 2020. Italian schools reopened in September 2020, with some limitations.

There was no monetary or credit compensation for participating in the study. The study protocol was approved by the Ethics Committee of the Department of Developmental and Social Psychology of the Sapienza University of Rome and was conducted in accordance with the Declaration of Helsinki.

2.2. Measures

A specific questionnaire was arranged for the survey. The first section was devoted to the collection of demographic data (age, gender, caregiver education, region of Italy). A second section was organized to gather information on sleep arrangement and schedule during weekdays and during weekends (bedtime, risetime, sleep latency, sleep duration, co-sleeping). All these questions were asked in order to evaluate differences between before and during the lockdown period. A third section of the survey was related to family composition, work of parents during the lockdown, online lessons for children and adolescents, screen exposure time (excluding the hours for lessons), use of over-the-counter or prescription drugs for sleep. Caregivers completed a modified version of the Sleep Disturbance Scale for Children (SDSC) [19].

Retrospective questions were used to estimate perceived changes across two time periods: from "before the lockdown" (i.e., in the last month before the outbreak) to "during the lockdown" (i.e., in the seven days prior to filling out the survey).

The SDSC was originally validated on a sample of 6- to 16-year-old healthy children from the general population [19] but was also used for younger children [20,21]. We grouped questions related to sleep-disordered breathing into one question and selected, in total, 13 items in order to facilitate the compilation by parents.

2.3. Data Analysis

Descriptive statistics were applied to characterize sociodemographic variables, sleep patterns, and sleep disturbances. Data were reported as frequencies and percentages for comparisons between the groups. The McNemar's test was performed to compare sleep patterns and sleep disturbances before and during the lockdown. "Before-during" bedtime and risetime were recorded within three categories based if maintained, delayed, or anticipated and sleep duration if maintained, increased, or reduced. Chi-square tests were conducted to compare changes in sleep patterns, sleep schedule, and sleep disturbances before and during lockdown, within and between the groups. Fisher's exact test was applied when appropriate.

For all comparisons, p-values less than 0.05 were considered to be statistically significant. Statistical analyses were performed using the SPSS software release 17.0 (SPSS INC, Chicago, IL, USA).

3. Results

Demographics of the sample are reported in Table 1.

Table 1. Demographics of the three groups of children enrolled in this study.

Gender	ADHD	ASD	Controls
Total	236	100	340
Gender			
F	44 (18.6%)	16 (16.0%)	58 (17.1%)
M	192 (81.4%)	83 (83.0%)	282 (82.9%)
Age			
4–5 years	23 (9.7%)	24 (24.0%)	57 (16.8%)
6–12 years	155 (65.7%)	47 (47.0%)	192 (56.5%)
13–18 years	58 (24.6%)	29 (29.0%)	91 (26.8%)
Respondent			
Mother	221 (93.6%)	91 (91.0%)	315 (92.6%)
Father	14 (5.9%)	9 (9.0%)	3 (0.9%)
Grandparent	1 (0.4%)	0 (0.0%)	22 (6.5%)
Education level of respondent			
Graduation	79 (33.6%)	41 (41.0%)	169 (49.9%)
High schools	123 (52.3%)	49 (49.0%)	142 (41.9%)
Middle schools	27 (11.5%)	9 (9.0%)	26 (7.7%)
Elementary schools	6 (2.6%)	1 (1.0%)	2 (0.6%)
Family income			
Low	45 (19.2%)	17 (17.0%)	45 (13.5%)
Middle	183 (78.2%)	79 (79.0%)	258 (77.2%)
High	6 (2.6%)	4 (4.0%)	31 (9.3%)
Siblings			
Only child	80 (34.0%)	38 (38.4%)	86 (25.3%)
2 children	128 (54.5%)	45 (45.5%)	191 (56.2%)
3 children	24 (10.2%)	14 (14.1%)	51 (15.0%)
≥4 children	3 (1.3%)	2 (2.0%)	12 (3.5%)

In all three groups, there was a prevalence of males. Most of the parents providing data on their child's sleep habits were mothers and most families had a middle income.

3.1. Comparison of Sleep Patterns in the Three Groups before and during Lockdown

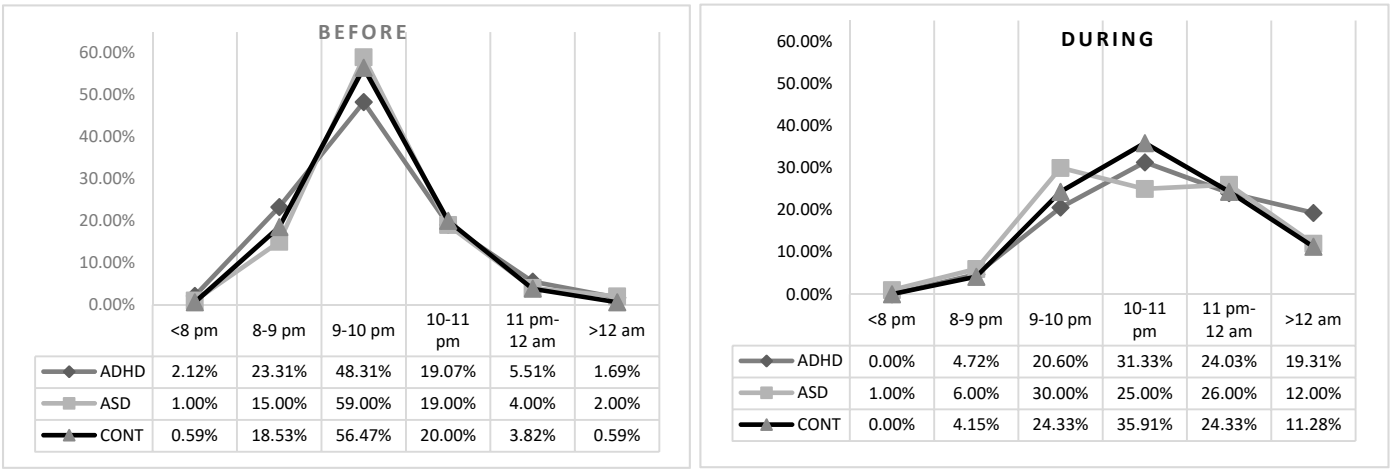
3.1.1. Bedtime

Before lockdown, no differences were found for bedtime during weekdays in the three groups. During lockdown, no differences were found between the two clinical groups, but the ADHD group that had a higher percentage of children going to bed after 12 a.m. than controls and the ASD group had a lower percentage of children going to bed between 10 to 11 p.m. than controls (Table 2; Figure 1).

Table 2. Comparison between bedtime in weekdays before and during lockdown in the three groups.

				ADHD vs. ASD		ADHD vs. Controls		ASD vs. Controls	
	ADHD	**ASD**	**Controls**	χ^2	p	χ^2	p	χ^2	p
Bedtime WD before									
<8 p.m.	5 (2.1%)	1 (1.0%)	2 (0.6%)	-	NS *	-	NS *	-	NS *
8–9 p.m.	55 (23.3%)	15 (15.0%)	63 (18.5%)	2.937	NS	1.950	NS	0.660	NS
9–10 p.m.	114 (48.3%)	59 (59.0%)	192 (56.5%)	3.216	NS	3.730	NS	0.202	NS
10–11 p.m.	45 (19.1%)	19 (19.0%)	68 (20.0%)	0.000	NS	0.077	NS	0.049	NS
11 p.m.–12 a.m.	13 (5.5%)	4 (4.0%)	13 (3.8%)	-	NS *	0.918	NS	-	NS *
>12 a.m.	4 (1.7%)	2 (2.0%)	2 (0.6%)	-	NS *	-	NS *	-	NS *
Bedtime WD during									
<8 p.m.	0 (0.0%)	1 (1.0%)	0 (0.0%)	-	NS *	-	NS	-	NS *
8–9 p.m.	11 (4.7%)	6 (6.0%)	14 (4.2%)	0.236	NS	0.106	NS	0.602	NS
9–10 p.m.	48 (20.6%)	30 (30.0%)	82 (24.3%)	3.446	NS	1.090	NS	1.330	NS
10–11 p.m.	73 (31.3%)	25 (25.0%)	121 (35.9%)	1.350	NS	1.284	NS	4.122	**0.042**
11 p.m.–12 a.m.	56 (24.0%)	26 (26.0%)	82 (24.3%)	0.146	NS	0.007	NS	0.115	NS
>12 a.m.	45 (19.3%)	12 (12.0%)	38 (11.3%)	2.638	NS	7.153	**0.007**	0.040	NS

WD = weekday. Significant differences at $p < 0.05$ are in bold. * Fisher's exact test was applied.



(**a**) (**b**)

Figure 1. Bedtime before (**a**) and during (**b**) lockdown in the tree groups.

3.1.2. Risetime

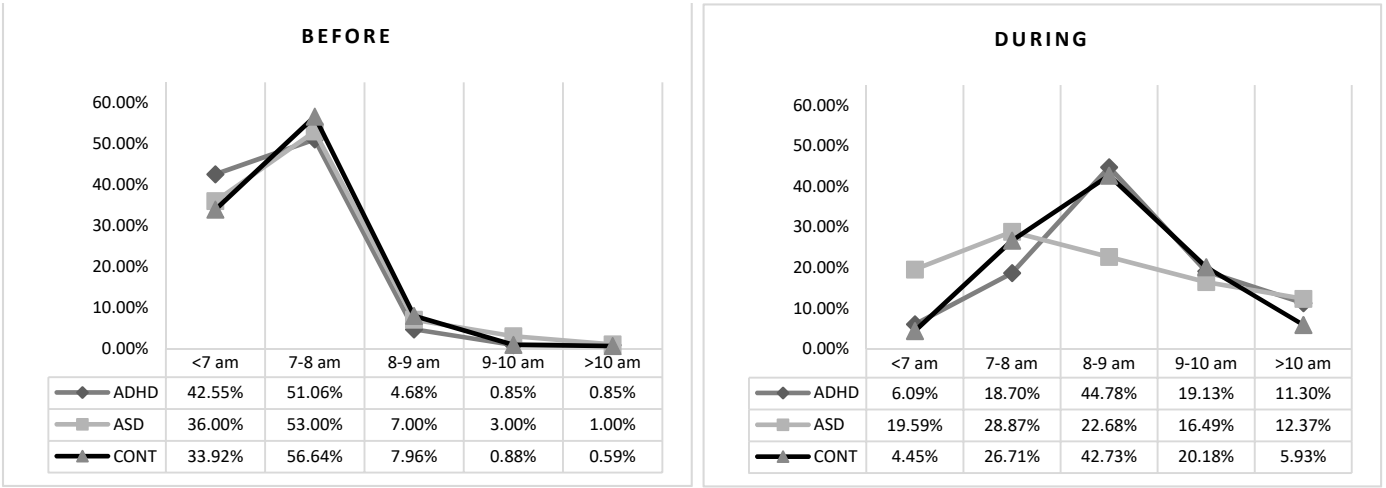
Similarly, before lockdown, no differences were found for risetime during weekdays, probably due to common school schedules (Table 3; Figure 2).

During lockdown, the lack of obliged risetime led to the appearance of important differences: 19.6% of ASD children continued to wake up before 7 a.m., whereas only 6.1% of ADHD and 4.45% of the control group stayed in this time slot. Most ADHD children and controls (44.8% and 42.8%, respectively) woke up between 8 and 9 a.m., whereas ASD children's risetime during lookdown was more uniformly distributed in the early morning hours (Table 3; Figure 2). Both clinical groups had a significantly higher percentage of children with risetime after 10 a.m. than controls.

Table 3. Comparison between risetime in weekdays before and during lockdown in the three groups.

				ADHD vs. ASD		ADHD vs. Controls		ASD vs. Controls	
	ADHD	**ASD**	**Controls**	χ^2	p	χ^2	p	χ^2	p
Risetime WD before									
<7 a.m.	100 (42.6%)	36 (36.0%)	115 (33.9%)	1.249	NS	4.412	**0.036**	0.148	NS
7–8 a.m.	120 (51.1%)	53 (53.0%)	192 (56.6%)	0.105	NS	1.738	NS	0.414	NS
8–9 a.m.	11 (4.7%)	7 (7.0%)	27 (8.0%)	0.742	NS	2.421	NS	0.101	NS
9–10 a.m.	2 (0.9%)	3 (3.0%)	3 (0.9%)	-	NS *	-	NS *	-	NS *
> 10 a.m.	2 (0.9%)	1 (1.0%)	2 (0.6%)	-	NS *	-	NS *	-	NS *
Risetime WD during									
<7 a.m.	14 (6.1%)	19 (19.6%)	15 (4.5%)	13.70	**0.000**	0.754	NS	23.901	**<0.001**
7–8 a.m.	43 (18.7%)	28 (28.9%)	90 (26.7%)	4.152	**0.042**	4.886	**0.027**	0.177	NS
8–9 a.m.	103 (44.8%)	22 (22.7%)	144 (42.7%)	14.11	**<0.001**	0.234	NS	12.891	**<0.001**
9–10 a.m.	44 (19.1%)	16 (16.5%)	68 (20.2%)	0.316	NS	0.095	NS	0.655	NS
>10 a.m.	26 (11.3%)	12 (12.4%)	20 (5.9%)	0.076	NS	5.287	**0.021**	4.569	**0.033**

WD = weekday. Significant differences at $p < 0.05$ are in bold. * Fisher's exact test was applied.



(**a**) (**b**)

Figure 2. Risetime before (**a**) and during (**b**) lockdown in the tree groups.

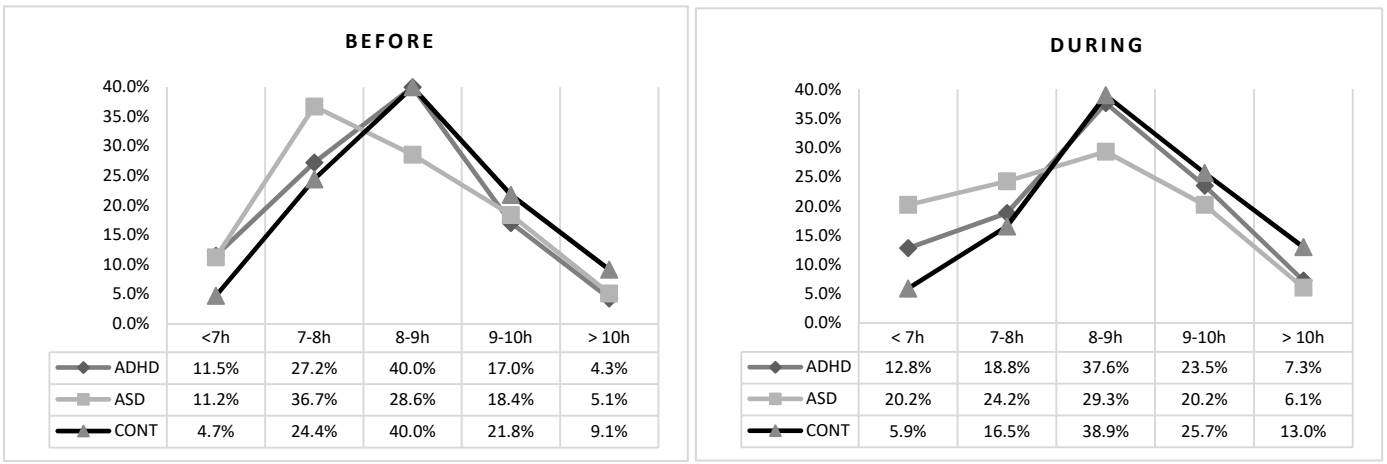
3.1.3. Sleep Duration

Before lockdown, both clinical groups, when compared to controls, had a significantly higher percentage of children sleeping less than 7 h (Table 4, Figure 3). Moreover, the ASD group showed a lower percentage of children sleeping between 8 to 9 h/night than the ADHD and control groups.

Table 4. Comparison between sleep duration in weekdays before and during lockdown in the three groups.

				ADHD vs. ASD		ADHD vs. Controls		ASD vs. Controls	
	ADHD	**ASD**	**Controls**	χ^2	p	χ^2	p	χ^2	p
Sleep duration WD before									
<7 h	27 (11.5%)	11 (11.2%)	16 (4.7%)	0.005	NS	9.241	**0.002**	5.588	**0.018**
7–8 h	64 (27.2%)	36 (36.7%)	83 (24.4%)	2.971	NS	0.582	NS	5.838	**0.016**
8–9 h	94 (40.0%)	28 (28.6%)	136 (40.0%)	3.891	**0.049**	0.000	NS	4.242	**0.039**
9–10 h	40 (17.0%)	18 (18.4%)	74 (21.8%)	0.087	NS	1.967	NS	0.529	NS
> 10 h	10 (4.3%)	5 (5.1%)	31 (9.1%)	0.115	NS	4.961	0.026	1.626	NS
Sleep duration WD during									
<7 h	30 (12.8%)	20 (20.2%)	20 (5.9%)	2.971	NS	8.326	**0.002**	18.888	**<0.001**
7–8 h	44 (18.8%)	24 (24.2%)	56 (16.5%)	1.266	NS	0.501	NS	3.062	NS
8–9 h	88 (37.6%)	29 (29.3%)	132 (38.9%)	2.110	NS	0.104	NS	3.066	NS
9–10 h	55 (23.5%)	20 (20.2%)	87 (25.7%)	0.435	NS	0.347	NS	1.238	NS
>10 h	17 (7.3%)	6 (6.1%)	44 (13.0%)	0.157	NS	4.752	**0.029**	3.627	NS

WD = weekday. Significant differences at $p < 0.05$ are in bold.



(**a**) (**b**)

Figure 3. Sleep duration before (**a**) and during (**b**) lockdown in the tree groups.

During lockdown, no differences in sleep duration were found between the two clinical groups while both clinical groups had a significantly higher percentage of children sleeping less than 7 h than controls (Table 4; Figure 3).

3.2. Comparison of Sleep Patterns during Lockdown

ADHD children showed a higher percentage of delaying and a lower percentage of maintaining weekday bedtime than ASD and controls and tended to delay risetime during weekday and weekend more than ASD but not than controls (Table 5). Sleep duration changes were not different between the ADHD and ASD groups, while controls showed a higher percentage of children who maintained the same sleep duration. Compared to controls, both clinical groups increased the weekday and weekend sleep latency during the lockdown (Table 6).

Table 5. Comparison of weekday–weekend bedtime and risetime in the three groups.

	Delayed	Advanced	Maintained	χ^2	p	χ^2	p	χ^2	p
Bedtime WD									
ADHD	188 (80.7%)	0	45 (19.3%)	19.947	**<0.001**	9.824	**0.007**	4.845	NS
ASD	58 (58%)	1 (1%)	41 (41%)						
Controls	235 (69.7%)	3 (0.9%)	99 (29.4%)						
Bedtime WE									
ADHD	98 (42.4%)	5 (2.2%)	128 (55.4%)	2.280	NS	5.621	NS	1.875	NS
ASD	44 (44.4%)	5 (5.1%)	50 (50.5)						
Controls	124 (36.8%)	20 (5.9%)	193 (57.3%)						
Risetime WD									
ADHD	192 (81.4%)	3 (1.3%)	34 (14.8%)	22.444	**<0.001**	6.602	NS	20.606	**<0.001**
ASD	59 (60.8%)	7 (7.2%)	31 (32%)						
Controls	256 (76.2%)	2 (0.6%)	78 (23.2%)						
Risetime WE									
ADHD	136 (58.6%)	41 (17.7%)	55 (23.7%)	33.333	**<0.001**	2.199	NS	43.600	**<0.001**
ASD	31 (31%)	13 (13%)	56 (56%)						
Controls	216 (63.9%)	46 (13.6%)	76 (22.5%)						

WD = weekday; WE = weekend. Significant differences at $p < 0.05$ are in bold.

Table 6. Comparison of weekday–weekend sleep duration and sleep latency in the three groups.

				ADHD vs. ASD		ADHD vs. Controls		ASD vs. Controls	
	Increased	Decreased	Maintained	χ^2	p	χ^2	p	χ^2	p
Sleep duration WD									
ADHD	80 (34.3%)	59 (25.3%)	94 (40.3%)	5.318	NS	16.165	**<0.001**	7.214	**0.027**
ASD	22 (22.4%)	25 (25.5%)	51 (52%)						
Controls	101 (29.8%)	49 (14.4%)	189 (55.8%)						
Sleep duration WE									
ADHD	49 (21.3%)	51 (22.2%)	130 (56.5%)	0.914	NS	24.650	**<0.001**	22.627	**<0.001**
ASD	17 (17%)	25 (25%)	58 (58%)						
Controls	78 (23.1)	26 (7.7%)	233 (69.2%)						
Sleep latency WD									
ADHD	103 (48.4%)	0 (0%)	110 (51.6%)	5.195	NS	7.190	**0.027**	12.058	**0.002**
ASD	41 (57.7%)	1 (1.4%)	29 (40.8%)						
Controls	116 (31.1%)	1 (0.3%)	196 (62.6%)						
Sleep latency WD									
ADHD	117 (51.6%)	2 (0.9%)	110 (48.0%)	4.181	NS	9.416	**0.009**	14.101	**<0.001**
ASD	49 (61.3%)	2 (2.5%)	29 (36.3%)						
Controls	127 (38.5)	7 (2.1%)	196 (59.4%)						

WD = weekday; WE = weekend. Significant differences at $p < 0.05$ are in bold.

3.3. Comparison of the Prevalence of Sleep Disorders in the Three Groups before and during Lockdown

3.3.1. Intragroup Comparison

During lockdown, we observed an increased prevalence of several sleep disorders, especially in the two clinical groups (Supplementary Table S1).

A significant increase in anxiety at bedtime and daytime sleepiness was found in all the three groups: anxiety at bedtime increased from 15.3% to 23.7% in ADHD children ($p = 0.007$), from 12.0% to 22.0% in the ASD group ($p = 0.006$), and from 5.6 to 11.2% in controls ($p = 0.003$).

Difficulty in falling asleep increased in the two clinical groups: from 27.1% to 39.0% in the ADHD group ($p = 0.001$), and from 23.0% to 35.0% in the ASD group ($p = 0.029$).

Prevalence of sleepwalking increased significantly only in the ADHD and control groups, from 0.4% to 5.9% (p = 0.000) for ADHD and from 0.0% to 2.4% (p = 0.000) for controls.

Nightmares increased in all the three groups but significantly only in controls, from 4.7% to 10.3% (p = 0.003). Daytime sleepiness increased from 12.3% to 19.9% in the ADHD group (p = 0.005), from 4.0% to 15.0% in the ASD group (p = 0.003) and from 4.4% to 7.9% in the control group (p = 0.029).

The only significant decrease in sleep disorders was found for bruxism in ADHD children that diminished from 16.5% to 11.0% (p = 0.015).

3.3.2. Intergroup Comparison

While before lockdown there was no difference between the clinical groups and controls, during lockdown difficulties in falling asleep significantly increased in the two clinical groups resulting in a significant difference with the control group.

Anxiety at bedtime, hypnic jerks, rhythmic movement disorder, and night awakenings were found to be significantly higher in the clinical groups than in controls, both before and during lockdown.

Restless sleep and snoring/apnea were significantly higher in both clinical groups than in controls (in ASD, only during lockdown) (Table 7).

Table 7. Comparison of sleep disorders before and during lockdown in the three groups.

					ADHD vs. ASD		**ADHD vs. Control**		**ASD vs. Control**	
		ADHD %	**ASD %**	**CONT %**	χ^2	p	χ^2	p	χ^2	p
Difficulties falling asleep	before	64 (27.1%)	23 (23.0%)	72 (21.2%)	0.621	NS	2.727	NS	0.152	NS
	during	92 (39.0%)	35 (35.0%)	65 (19.1%)	0.474	NS	27.726	**<0.001**	11.099	**0.001**
Anxiety at bedtime	before	36 (15.3%)	12 (12.0%)	19 (5.6%)	0.607	NS	15.070	**<0.001**	4.831	**0.028**
	during	56 (23.7%)	22 (22.0%)	38 (11.2%)	0.118	NS	16.073	**<0.001**	7.687	**0.006**
Hypnic jerks	before	30 (12.7%)	11 (11.0%)	14 (4.1%)	0.192	NS	14.583	**<0.001**	6.830	**0.009**
	during	39 (16.5%)	12 (12.0%)	13 (3.8%)	1.117	NS	27.366	**<0.001**	9.640	**0.002**
Rhythmic movement dis.	before	10 (4.2%)	7 (7.0%)	5 (1.5%)	1.116	NS	4.204	**0.040**	8.906	**0.003**
	during	14 (5.9%)	9 (9.0%)	7 (2.1%)	1.037	NS	5.950	**0.015**	10.625	**0.001**
Night awakenings >2	before	29 (12.3%)	10 (10.0%)	11 (3.2%)	0.358	NS	17.667	**0.000**	7.780	**0.005**
	during	34 (14.4%)	18 (18.0%)	21 (6.2%)	0.693	NS	10.926	**0.001**	13.373	**0.000**
Restless sleep	before	80 (33.9%)	28 (28.0%)	75 (22.1%)	1.120	NS	9.928	**0.002**	1.521	NS
	during	83 (35.2%)	34 (34.0%)	71 (20.9%)	0.042	NS	14.517	**0.000**	7.318	**0.007**
Snoring/apneas	before	19 (8.1%)	8 (8.0%)	13 (3.8%)	0.000	NS	4.745	**0.029**	2.966	NS
	during	22 (9.3%)	9 (9.0%)	12 (3.5%)	0.009	NS	8.416	**0.004**	5.088	**0.024**
Sleepwalking	before	1 (0.4%)	3 (3.0%)	0 (0.0%)	-	NS *	-	NS *	-	**0.011** *
	during	14 (5.9%)	7 (7.0%)	8 (2.4%)	0.137	NS	4.858	**0.028**	5.068	**0.024**
Sleep terrors	before	3 (1.3%)	0 (0.0%)	4 (1.2%)	-	NS *	-	NS *	-	NS *
	during	4 (1.7%)	4 (4.0%)	2 (0.6%)	-	NS *	-	NS *	-	**0.026** *
Bruxism	before	39 (16.5%)	7 (7.0%)	31 (9.1%)	5.393	**0.020**	7.160	**0.007**	0.439	NS
	during	26 (11.0%)	11 (11.0%)	21 (6.2%)	0.000	NS	4.355	**0.037**	2.666	NS
Nightmares	before	28 (11.9%)	2 (2.0%)	16 (4.7%)	-	**0.003** *	10.118	**0.001**	-	NS *
	during	42 (17.8%)	5 (5.0%)	35 (10.3%)	9.560	**0.002**	6.771	**0.009**	2.621	NS
Daytime sleepiness	before	29 (12.3%)	4 (4.0%)	15 (4.4%)	-	**0.026** *	12.249	**0.000**	-	NS *
	during	47 (19.9%)	15 (15.0%)	27 (7.9%)	1.128	NS	17.839	**0.000**	4.459	**0.035**

Significant differences at $p < 0.05$ are in bold. * Fisher's exact test was applied.

Compared to controls, sleepwalking was more prevalent in the ASD group, both before and during lockdown, while sleep terrors were more prevalent only during lockdown.

The prevalence of bruxism and nightmares was significantly increased in children with ADHD compared to ASD and controls, both before and during lockdown.

On the other hand, no differences were found between ASD and controls in the prevalence of nightmares and bruxism (Table 7).

Daytime sleepiness was higher in ADHD than in control children, both before and during lockdown, and slightly more prevalent in ASD than in controls during lockdown (Table 7; Figures S1 and S2).

4. Discussion

The lockdown experience significantly impacted sleep patterns and disturbances of children and adolescents with ADHD and ASD, as well as of controls. As also indicated by other studies [5,6,12], sleep is one of the more impaired domains during the COVID-19 lockdown, independently by mental health condition and age and it is known that sleep problems in ASD and ADHD patients may worsen daytime behavior and functioning, as well as increase parental distress [11]. We found, in both clinical groups, a higher percentage of subjects that reported a reduced sleep duration and an increased sleep latency than controls. ASD patients showed less changes in weekday-weekend risetime than both ADHD and controls, while children with ADHD reported higher delays in bedtime than the other groups. Our findings are supported by specific studies on these two clinical groups and controls [2,16], reporting delayed bedtime in children with ADHD [10,17] and a reduced sleep duration in both ADHD and ASD [9,10,13,15,22].

Although changes of lifestyle caused by the lockdown affected both clinical groups and controls, generally children and adolescents with ADHD showed greater instability of their sleep schedule and increased delay in weekday sleep schedule, when compared to ASD and controls, during lockdown. This finding, according to the night-to-night variability in the sleep–wake patterns reported by several comparative studies in children with ADHD compared to typically developing children [23–25], supports the consideration that the "variability" of sleep patterns, represents a distinctive marker of the ADHD condition.

Since ADHD patients' functioning is strongly dependent on environmental changes, in agreement with other studies [10,26], our findings confirm that sudden lifestyle changes caused by the pandemic lockdown impacted the sleep and behavior of ADHD patients more than on those of ASD patients or controls. Conversely, children and adolescents with ASD seemed to be less vulnerable to the effects of prolonged isolation, showing a higher stability in bedtime and risetime than both ADHD and controls, probably linked to the stereotyped and fixed behavior of these children, since inflexibility and insistence on sameness are hallmark characteristics of ASD [15].

The significantly decreased sleep duration in the ADHD group, compared to controls, is supported by the study by Becker et al. [13], suggesting that ADHD patients did not benefit from the COVID-19 lockdown, unlike their healthy peers of the control group that experienced an increase in school days night sleep duration and were more likely to obtain recommended sleep duration during COVID-19. Similarly, Mutluer et al. [15] reported a decrease in the number of hours ASD children slept from before to during COVID-19. Finally, our findings agree with those by Bruni et al. [2] who reported a general stable sleep duration among healthy children, with only a small but significant increase during lockdown.

We found an increase in several sleep disorders during the lockdown: some disorders increased in all the three groups, such as anxiety at bedtime and daytime sleepiness while difficulties in falling asleep hypnic jerks, rhythmic movement disorder, night awakenings, restless sleep, sleepwalking, and daytime sleepiness increased especially in patients with ASD and ADHD. Interestingly, at baseline, ADHD children resulted to have increased bruxism, nightmares, and daytime sleepiness than their ASD peers, while during the lockdown ASD and ADHD children and adolescents had a similar prevalence of all sleep disturbances, with the exception of nightmares that were more frequent in ADHD children.

Very few studies have been published on the impact of the COVID-19 lockdown on sleep disorders of patients with ASD and ADHD. Regarding the sleep disorders of ASD patients during the pandemic, our results are in agreement with those by Türkoğlu et al. [17] that reported an increase in difficulties (and delay) in falling asleep, and anxiety at bedtime; in contrast, we did not find an increase in night awakenings, but we observed an increase in daytime sleepiness. Similarly, Lugo-Marin et al. [14] reported a deterioration in sleep quality in 56% of 100 ASD patients (children and adults). Very few studies have examined sleep disorders of ADHD youths during COVID-19. In a sample of 241 youth (aged 6–15 years) with ADHD in China, 48% of parents indicated that COVID-19 had not changed

their child's sleep, with 20% indicating that sleep had worsened, and 32% indicating that sleep had improved. Becker et al. [13] reported less improvement of daytime sleepiness in ADHD adolescents compared to their healthy peers of the control group.

Several sleep symptoms that we found increased in our ASD and ADHD children have been recognized to be an expression of a psychological distress condition [27,28] strictly related to the pandemic.

Altogether, our findings confirm a great distress susceptibility in both clinical children due to the sudden changes of lifestyle imposed by the lockdown experience that determined a vulnerability of their sleep–wake patterns. The different sleep pattern alterations in the two clinical groups might be linked to their core traits defining two distinct disorders: children with ASD, that tended to maintain their sleep–wake schedule, were less vulnerable due to the stereotyped behavior and insistence on sameness while children with ADHD, that showed greater changes in sleep–wake patterns, were more vulnerable, due to their innate behavior instability, swift changes in mood, and low frustration tolerance.

We have to consider that the interruption of social relationships, the reduction in physical activities as well as the academic and normal working activities, had an impact on sleep. In parallel, other studies showed a strong impact of lockdown on affective domains, highlighting mainly an increase in depression symptoms (for ADHD see Melegari et al., 2021) [26]. Further studies focused on the lockdown impact on both sleep patterns and affective states in these clinical populations should contribute to explain their reciprocal interaction. Some limitations of this study need to be considered, such as the sample size (although relatively large for this condition) and sampling only respondents from a single country; thus, results may not be fully generalizable to other countries. In addition, the predetermined sample size to adequately reduce the risk of type II error was not achieved. Furthermore, most subjectively reported elements of the SDSC should be interpreted with caution due to potential parental misinterpretation in ASD subjects that are often non-verbal. Although the survey was conducted after only a few days from the end of the strict lockdown and in the presence of lighter restrictions, we cannot exclude a memory bias of the parents. Finally, we should consider that self-selection bias is inherent with the online survey methodology employing nonprobability sampling. On the other hand, a strength of the study is that examined similarity or differences in sleep pattern changes using the same instruments and the same temporal window of investigation.

5. Conclusions

To our knowledge, this is the first study comparing sleep habits and disorders in two neurodevelopmental disorders, ASD and ADHD, highlighting the differences in sleep patterns and disorders between these two different clinical populations, both at baseline and during the COVID-19 lockdown. It will be important to examine whether changes in sleep persist over time, continue to change, or return to the pre-COVID-19 levels as the pandemic continues.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/brainsci11091139/s1, Supplementary Table S1. Sleep disorders before and during lockdown in the three groups. Figure S1: Sleep disorders in the three groups before lockdown, Figure S2: Sleep disorders in the three groups during lockdown.

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RESEARCH ARTICLE

WILEY

Quality of life improvement in children with attention-deficit hyperactivity disorder reduces family's strain: A structural equation model approach

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Abstract

Objectives: The objective of the study is to analyse how the quality of life of children diagnosed with attention-deficit/hyperactivity disorder (ADHD) impacts the relationship between disease severity and family burden.

Method: The data collected by a longitudinal, observational study involving 1478 children with ADHD residing in 10 European countries (aged 6 to 18 years) were analysed to evaluate the relationships between ADHD severity, the children's quality of life and family burden.

Results: The disorder's severity directly and indirectly affected the children's health-related quality of life (HRQoL) and family burden. The degree of family burden was modulated by the children's HRQoL.

Conclusions: One of the primary causes of the stress experienced by parents of children with ADHD is their perception of the child's reduced HRQoL and not the symptom severity itself. Efforts to minimize symptom severity cannot alone reduce family burden.

KEYWORDS
ADHD, children, family burden, health-related quality of life

1 | INTRODUCTION

Attention Deficit Hyperactivity disorder (ADHD) is one of the most common childhood neurobehavioural conditions (Boyle et al., 2011). ADHD symptoms usually become more evident in school-aged children, are more frequent in boys than in girls and tend to persist into adulthood (Centers for Disease Control and Prevention, 2013). The prevalence range reported is quite wide (from 0.2% to 34.5%), and heterogeneity in the methodological approaches used have contributed to these differences (Polanczyk et al., 2015). When case definition is based on a clinical evaluation, the overall ADHD prevalence is 2.9% (range: 1.1–16.7) (Reale & Bonati, 2018). The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) defines core ADHD symptoms as difficulty in paying attention, inability to focus and to control behaviour and being hyperactive. Symptoms such as these, which can only lead to a significant impairment at school (Spencer, 2006) and in the activities of daily life (Pineda et al., 1998),

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ADORE, ADHD observational research in Europe; CGAS, children's global assessment scale; CGI-S, clinical global impression-severity; CHIP-CE, child health and illness profile-child edition; CSDR, Clinical Study Data Request; DSM, Diagnostic and Statistical Manual of Mental Disorders; FSI, Family Strain Index; GFI, goodness of fit index; HRQoL, health-related quality of life; IQR, interquartile range; PSI-SF, Parenting Stress Index Short Form; RMSEA, root mean square error of approximation; SD, standard deviation; SDQ, Strengths and Difficulties Questionnaire; SEM, structural equation model; SRMS, standardized root mean square residual.

often persist into adolescence and adulthood, causing personal, social, occupational and even leisure time dysfunctions (Resnick, 2005).

According to the American Psychiatric Association, the severity of symptoms is pivotal for diagnosing and establishing the severity of the disorder (American Psychiatric Association, 2013). The clinical picture is frequently (in approximately 75% of cases) complicated by other mental disorders or multiple comorbid mental disorders (in approximately 60%) that adversely affect the prognosis and may necessitate specific therapeutic measures (Banaschewski et al., 2017). In short, ADHD symptoms result in a complex pattern of behaviours characterized by inattention and or impulsivity and hyperactivity leading to increased demands on parents' time and contributing to their level of stress (Heath et al., 2014). Although families of children with ADHD usually face more challenging caregiver situations, their children's difficult behaviours may undermine parents' confidence and well-being with respect to their caregiving role (Counts et al., 2005).

Several studies have confirmed that ADHD severity has an important impact on family strain (Breen & Barkley, 1988; Harrison & Sofronoff, 2002; Mash & Johnston, 1983). A significant positive correlation was found between the severity of the disorder, measured using the Children's Global Assessment Scale (CGAS) scores, and parent's' stress scores, measured using the Parenting Stress Index Short Form (PSI-SF) (Narkunam et al., 2014). The findings emerging when instruments other than the PSI-SF were used (Johnson & Reader, 2002) likewise suggest that an optimal management of a child diagnosed with ADHD requires more than just minimizing the core symptoms; other interventions, for both the child and the parents, are needed to reduce family burden (Narkunam et al., 2014).

It has been found that health-related quality of life (HRQoL) is lower in ADHD children compared with that in healthy children (Danckaerts et al., 2010), and the same has been reported for the members of their families (Dey et al., 2019). The severity of the symptoms may increase the impact of ADHD on the children's HRQoL and family distress (Cappe et al., 2017). Treatments (pharmacological and/or psychological) may have a positive effect, even if it may be only short lived and negligible, on HRQoL of both children and parents (Bundgaard Larsen et al., 2020; Coghill, 2010).

The current study set out to analyse the data of a longitudinal observational multi-country study focusing on children with ADHD in the attempt to evaluate the association between the symptom severity, the HRQoL of the children and the family burden.

We hypothesized that children's HRQoL can mediate the impact of ADHD severity on family burden.

Key messages

- The symptoms of children with attention-deficit/hyperactivity disorder (ADHD) dynamically contribute to generating high levels of distress in their parents.
- The parents' emotional distress can be explained by multiplicity of factors, including symptom severity.
- A sizable part of family strain is attributable to the child's health-related quality of life (HRQoL).
- Some interventions should be designed to alleviate parents' burden.

2 | METHODS

2.1 | Participants and procedure

We submitted a research proposal through the Clinical Study Data Request (CSDR) website (https://clinicalstudydatarequest.com) to gain access to the original data sets of the ADHD Observational Research in Europe (ADORE) project (Ralston & Lorenzo, 2004), a prospective, non-interventional study involving 1478 children with hyperactive/inattentive/impulsive symptoms but not yet formally diagnosed with ADHD. The children were observed by 244 investigators residing in 10 European countries: Austria, Denmark, France, Germany, Iceland, Italy, the Netherlands, Norway, Switzerland and the United Kingdom. Patient recruitment was begun in June 2003 and completed in December 2004. After submitting a signed data sharing agreement, we were furnished with access to anonymized patient-level data and supporting documentation in a secure data access system, known as the SAS Clinical Trial Data Transparency system.

2.2 | Measures

2.2.1 | Time lived in the disorder

Children with ADHD symptomatology who had never been formally diagnosed with the disorder were eligible to participate in the study. As symptoms can arise at different ages, time of onset might influence their severity and therefore the children's quality of life. The time lived in/with the disorder was defined as the length of time between the onset of the first symptoms and enrolment in the study.

2.2.2 | Treatment

The children with more severe symptoms were receiving pharmacological; psychological; occupational; or speech therapy, educational interventions in school, psychomotor/physiotherapy or herb/homoeopathy; some were being taught relaxation techniques or were undergoing electroencephalogram biofeedback or hypnosis; others were simply following a diet. Treatment variable was dichotomized as received (at least one type) and not received (none).

2.2.3 | Severity and impairment

The evaluation of the children with ADHD took into consideration a wide range of factors in the attempt to establish a

complete psychopathological profile. The following scales were utilized to assess the children's emotional, psychological and social status:

- The CGAS, a numeric scale used by clinicians to rate the general functioning of a child. Scores range from 1 (*most impaired*) to 100 (*best level of adaptive functioning*) (Kratochvil et al., 2007; Schaffer et al., 1983). A CGAS score of >70 is generally accepted to indicate good overall functioning and a score of <60 indicates poor functioning that will generally require intervention;
- The Clinical Global Impression-Severity (CGI-S) scale, another numeric scale used by clinicians to learn more about the patient's global functioning. Scores range from 1 (*normal*, *not at all ill*) to 7 (*very severely ill*) (Busner & Targum, 2007). A score of 4 indicates moderately ill and a score of 5 indicates markedly ill;
- The ADHD Rating Scale IV Edition (ADHD-RS-IV) is a validated instrument to assess ADHD symptoms; each of its 18 items corresponds to one of the items on the Diagnostic and Statistical Manual of Mental Disorders, IV edition (DSM-IV) diagnostic criteria (DuPaul et al., 1998). The patient's parent responds to the scale's items during a semi-structured interview with a clinician. Severity is rated on a 4-point Likert scale ranging from 0 (*never or rarely*) to 3 (*very often*), with higher scores indicative of greater ADHD-related behaviour;
- The parent-reported version of the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997), a brief psychopathology screening tool that consists of 25 items regarding five subscales: emotional symptoms, conduct problems, hyperactivity-inattention, peer relationship problems and prosocial behaviour. Only the hyperactivity-inattention subscale was considered in the present study. A score <6 identifies 'normal' subjects;
- The patient's comorbidities were also investigated. The pathologies considered were anxiety, asthma, bipolar disorder, conduct disorder, coordination problems, depression, epilepsy, learning disorder, obsessive compulsive disorder, oppositional defiant disorder, psychosis, tics and Tourette's syndrome. For anxiety, depression, conduct disorder and oppositional defiant disorder, the investigator was requested to assess severity in single-item questions in Likert scale format; for other problems, the investigator was requested to simply state if the problem is present in single-item questions (Ralston & Lorenzo, 2004). Comorbidity variable was defined as the number of comorbid disorders reported by the investigator.

These five scores were transformed into dichotomous variables using validated cut-offs (CGAS ≤ 40: serious/severe problems; CGI ≥ 5: markedly ill or worse; number of comorbidities ≥ 1; ADHD-RS-IV ≥ 41; SDQ-hyperactivity≥8). (Döpfner et al., 2006; Overgaard et al., 2019; Reale et al., 2017) and then they were used to define the 'child's severity and impairment' latent factor. Higher scores in 'child's severity and impairment' latent factor indicate more severe health conditions.

2.2.4 | Quality of life

Children's HRQoL was assessed using the Standard Parent Report Form of the Child Health and Illness Profile-Child Edition (CHIP-CE). The 76 items on the questionnaire examine all aspects of a child's life and primarily his/her family and school life that could affect his/her HRQoL (Riley et al., 2006).

The scores on the five domains (i.e., satisfaction, comfort, resilience, risk avoidance and achievement), which range from 0 (*worst*) to 5 (*best*), were used to measure the 'Quality of life' factor. Higher scores indicate better quality of life.

2.2.5 | Family strain

The stress and pressure on the parents and families of ADHD children were assessed using the Family Strain Index (FSI). The FSI includes two 'emotional' items, which measure the affective and emotional stress associated with being a caregiver of a child with ADHD, and four 'restriction' items, assessing those limitations in the family's social activities resulting from living with a child with this disorder (Riley et al., 2006). Parents were asked to rate the frequency of each item over the past four weeks on a 5-point Likert scale: 0 (*never*), 1 (almost never), 2 (*sometimes*), 3 (*almost always*) and 4 (*always*). A total score was obtained by summing the scores of the six items (possible range 0–24); higher scores indicate more emotional distress or interruption of normal activities due to the child's problems.

2.3 | Data analysis

The social, demographic and clinical variables were summarized using descriptive statistics: categorical variables are presented as percentages; continuous variables as mean and standard deviation (SD) or median and interquartile range (IQR), according to the normality assumption, which was tested using the Shapiro–Wilk test.

Pearson's correlation was calculated to verify the association between the five variables considered to assess ADHD severity and impairment: CGAS, CGI-S, ADHD-RS-IV and SDQ scores, as well as the number of comorbidities.

A structural equation model (SEM) approach was used to examine the relationships between family strain; the child's severity/impairment and quality of life; and the effect of the child's sex, treatment and time lived in the disorder. The hypothesized relationships are represented in Figure 1. Observed variables are indicated by squares, latent variables by circles and effects by arrows. The observed variables of CGAS, CGI, ADHD-RS-IV, comorbidities and SDQ contributed to the latent construct 'Child's severity and impairment'; the scores on the five CHIP-CE domains (i.e., satisfaction, comfort, resilience, risk avoidance and achievement) defined the latent construct 'child's quality of life'.

Missing data were imputed using the full information maximum likelihood method of the CALIS procedure (Yung & Zhang, 2011),

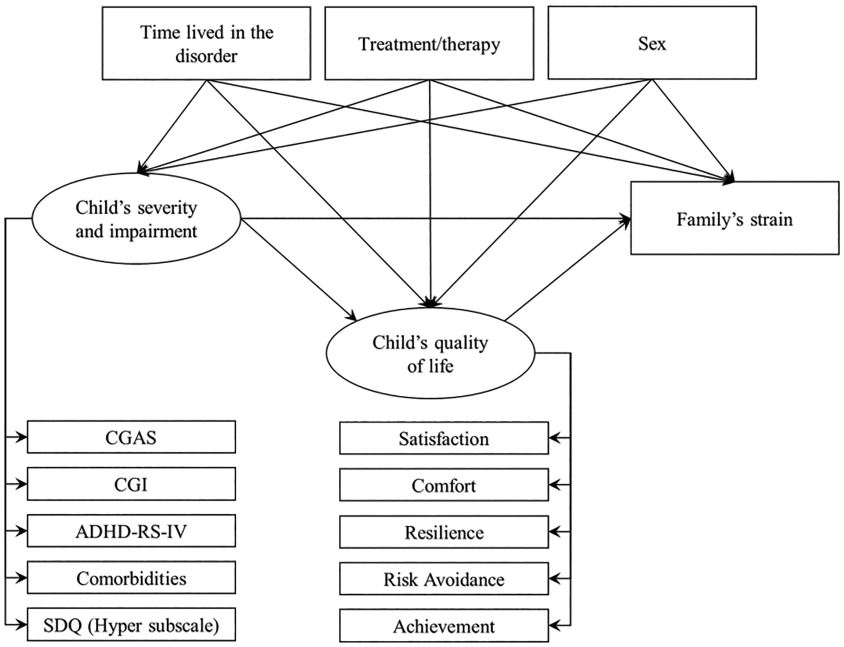

FIGURE 1 Hypothesized structural model for child's severity and quality of life, and family's strain. ADHD, attention-deficit/hyperactivity disorder; CGAS, Children's Global Assessment Scale; CGI, clinical global impression; SDQ, Strengths and Difficulties Questionnaire

which has been shown to be superior to ad hoc methods for treating incomplete observations (Muthén et al., 1987) for both normal (Enders & Bandalos, 2001) and nonnormal distributions (Enders, 2001).

The following goodness-of-fit indices and thresholds were used: the standardized root mean square residual (SRMS, <0.08), the root mean square error of approximation (RMSEA, <0.08) and the goodness of fit index (GFI, ≥0.90). All analyses were performed using SAS version 9.4.

3 | RESULTS

The sociodemographic characteristics of the 1478 children with ADHD who participated in the study are outlined in Table 1. The majority of the participants were male (84.10%) and between the ages of 6 and 9 (67.13%) years. The age of the child when his/her parents first became aware of the hyperactive/inattentive symptoms/problems was younger than 5 years for 44.58% of the participants.

The mean scores on the subscales of the CHIP-CE score range between 2.9 (achievement domain) and 4.0 (comfort domain), showing a deviation from a standard population, while the mean FSI score was 10.4 (SD = 5.4), indicating a moderate level of emotional distress or interruption of normal activities due to the child's problems. The mean CGAS score was 55.2 (SD = 10.6), indicating that the child's functioning was variable and that there were sporadic difficulties or symptoms in several but not all social areas. The mean CGI score was 4.4 (SD = 0.9), denoting overt symptoms causing noticeable, but modest, functional impairment or distress; the symptom level probably warranted medication.

The CGAS and CGI scores were significantly correlated to one another ($r = -0.537$) and to the number of comorbidities, the ADHD-RS-IV score and the SDQ hyperactivity score, with Pearson's coefficients falling into the low to moderate range (absolute values between 0.274 and 0.382) (Table 2).

The standardized structural coefficients of the model depicted in Figure 1 are presented in Table 3. A good model–data fit was found (SRMSR = 0.0498, RMSEA = 0.0824 and GFI = 0.9307).

Data analysis uncovered that symptom severity was influenced by both the time lived in the disorder and the treatment utilized. The longer a child lived with the disorder, in fact, the more his/her symptoms worsened. Moreover, the children with more severe symptoms had a higher probability of receiving some treatment or therapy, which did not, however, significantly improve their quality of life. Treatment had only an indirect effect on the children's HRQoL, which was mediated by symptom severity. The children who received treatment of some kind were those who displayed more severe symptoms and therefore whose HRQoL was lower.

The severity of symptoms and impairments strongly affected the life of the whole family: the symptom severity produced the strongest observed effect on the child's quality of life (−0.7530) and a direct and indirect effect on family strain. The family's burden increased proportionally with the worsening of symptoms (total effect = 0.6273), primarily due to the mediating effect of the child's quality of life (indirect effect = 0.4339). The finding suggests that the stress experienced by parents is mainly caused by their perception of their child's reduced quality of life rather than by symptom severity itself.

4 | DISCUSSION

The aim of this study was to investigate the interrelationships between the severity of the symptoms of ADHD, the child's HRQoL and family burden. Some studies have reported that the severity of a

child's ADHD symptoms and the parents' perception of his/her impairment across emotional, cognitive and behavioural domains are a source of anxiety for them (Graziano et al., 2011). The current study set out to investigate these variables in the effort to gain greater insight into the causes and effects of the child's HRQoL and family burden.

As expected (Reale et al., 2017), ADHD severity and impairment were found to be key factors affecting the children and their families' lives. Indeed, in agreement with previous investigations, the findings of the present study strongly suggest that worse symptoms were associated, on the one hand, with worse HRQoL (Coghill & Hodgkins, 2016; Klassen et al., 2004) and, on the other, with higher parenting stress (Cappe et al., 2017; Muñoz-Silva et al., 2017).

The model used here made it possible to confirm these direct effects of ADHD severity and impairment as well as to identify its indirect effect on family burden. Indeed, what emerged was the mediating role of the children's HRQoL, which in turn negatively affected parental stress.

This result highlights the parents' growing perception of their children's low HRQoL and of their own helplessness and sense of loss

TABLE 1 Participant characteristics

	% of sample	N
Age at baseline, years		1445
6–9	67.13	
10–12	22.00	
13–17	10.87	
Age at first awareness, years		1310
0–4	44.58	
5–6	30.15	
7–9	19.70	
10–17	5.57	
Prescribed pharmacotherapy (yes)	3.26	1473
Prescribed psychotherapy (yes)	18.37	1475
Other prescribed treatment (yes)	43.79	1459
Sex (male)	84.10	1453

	Median [IQR]	[Range]	N
CGAS	55.0 [11.0]	[30–92]	1206
CGI	4.0 [1.0]	[1–7]	1472
Number of comorbidities	3.0 [2.0]	[0–7]	1473
ADHD-RS	36.0 [13.0]	[7–54]	1476
SDQ	9.0 [3.0]	[4–37]	1459
CHIP-CE: satisfaction domain	3.6 [0.8]	[1.27–5.00]	1464
CHIP-CE: comfort domain	4.0 [0.6]	[2.27–5.00]	1463
CHIP-CE: resilience domain	3.7 [0.6]	[1.95–4.89]	1467
CHIP-CE: risk avoidance domain	3.6 [0.9]	[1.29–4.92]	1462
CHIP-CE: achievement domain	2.9 [0.8]	[1.00–4.80]	1414
Family strain (FSI)	10.0 [8.0]	[0–24]	1444

Abbreviations: ADHD-RS, attention-deficit/hyperactivity disorder Rating Scale; CGAS, Children's Global Assessment Scale; CGI, clinical global impression; CHIP-SE, Child Health and Illness Profile-Child Edition; FSI, Family Strain Index; IQR, interquartile range; SDQ, Strengths and Difficulties Questionnaire.

TABLE 3 Standardized estimated parameters for the structural model: direct, indirect and total effects

	Direct	Indirect	Total
Effects on child's severity			
Time lived in the disorder	0.1114*	—	0.1114*
Treatment/therapy	0.1123*	—	0.1123*
Sex	0.0264	—	0.0264
Effects on child's QoL			
Child's severity	−0.7530*	—	−0.7530*
Time lived in the disorder	−0.1006*	−0.0838*	−0.1844*
Treatment/therapy	0.0416	−0.0846*	−0.0430
Sex	0.0046	−0.0198	−0.0152
Effects on family's strain			
Child's QoL	−0.5763*	—	−0.5763*
Child's severity	0.1934*	0.4339*	0.6273*
Time lived in the disorder	−0.0057	0.1278*	0.1221*
Treatment/therapy	−0.0481*	0.0465	−0.0016
Sex	0.0163	0.0139	0.0302

Abbreviation: QoL, quality of life.
*$p < 0.0001$.

TABLE 2 Pearson's correlation between the five indices (CGAS, CGI, number of comorbidities, ADHD-RS-IV and SDQ) considered to assess ADHD severity and impairment

	CGAS	CGI	Number of comorbidities	ADHD-RS-IV	SDQ
CGAS		−0.537 ($n = 1204$)	−0.274 ($n = 1202$)	−0.285 ($n = 1206$)	−0.342 ($n = 1195$)
CGI	−0.537 ($n = 1204$)		0.300 ($n = 1468$)	0.335 ($n = 1470$)	0.382 ($n = 1453$)
Number of comorbidities	−0.274 ($n = 1202$)	0.300 ($n = 1468$)		0.172 ($n = 1471$)	0.274 ($n = 1454$)
ADHD-RS-IV	−0.285 ($n = 1206$)	0.335 ($n = 1470$)	0.172 ($n = 1471$)		0.495 ($n = 1457$)
SDQ	−0.342 ($n = 1195$)	0.382 ($n = 1453$)	0.274 ($n = 1454$)	0.495 ($n = 1457$)	

Note: All the correlation coefficients are statistically significant ($p < 0.0001$).
Abbreviations: ADHD-RS-IV, attention-deficit/hyperactivity disorder Rating Scale IV Edition; CGAS, Children's Global Assessment Scale; CGI, clinical global impression; SDQ, Strengths and Difficulties Questionnaire.

(Galloway & Newman, 2017). In the light of these findings, it is clear that health care systems should invest in programmes aiming not only to reduce symptom severity in children diagnosed with ADHD but also to improve their well-being and quality of life. The efficacy of pharmacological treatments in managing ADHD core symptoms has long been recognized (Kaplan & Sadock, 1988), and some psychosocial interventions have recently proven to be effective. Parent training programmes could also help to teach parents how to manage their children's challenging behaviours (Bundgaard Larsen et al., 2020; Coates et al., 2015; Zwi et al., 2011). The present study found that psychosocial measures had only scarce effects on the HRQoL of ADHD patients (Danckaerts et al., 2010; Kousha & Abbasi Kakrodi, 2019) and medication also had a limited effect (Coghill & Hodgkins, 2016). In fact, some treatments had only a weak, indirect effect on the HRQoL.

Long-term comparative studies have investigated a variety of pharmacological and/or nonpharmacological treatments utilized to aid ADHD children manage their behaviour and parents deal with their stress. Further studies are necessary to identify what characteristics, besides symptom severity, are usually found in the patients who benefit from those treatments.

4.1 | Limitations and strengths

The study presents some limitations. First, data regarding some parameters were missing, although for a small proportion of patients, which has not introduced bias thanks to the estimation method adopted. Second, the contribution of each participating country was different and not proportional to the target national population. This implies that our findings refer to a general European population of 6–17 years old ADHD patients and their families.

As far as its strengths are concerned, the study examined the data of a sizable number of patients, and it used a large battery of well-known, reliable scales/questionnaires to evaluate the patients' neuropsychiatric status. The consistency and reliability of the ADORE data set used in the present work have, moreover, been assessed by several studies. (Döpfner et al., 2006; Ralston & Lorenzo, 2004).

The impact that ADHD and its severity has on the children and their parents' well-being warrants further study. Efforts in any case to help these families need to be two sided: the children require help to manage their symptoms and the parents need to learn better parenting skills and perhaps even more importantly to deal with their feelings of guilt and anxiety.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly available but can be requested from the Clinical Study Data Request (CSDR) website (https://clinicalstudydatarequest.com). To obtain access to anonymized patient-level data and supporting documentation in a secure data access system, it is necessary to submit a research proposal and sign a data sharing agreement.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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The Virtual City Paradigm™ for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study

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Navigation is a complex process, requiring target localization, route planning or retrieval, and physical displacement. Executive functions (EFs) such as working memory, inhibition and planning are fundamental for succeeding in this complex activity and are often impaired in Attention Deficit and Hyperactivity Disorder (ADHD). Our aim was to analyze the feasibility of a new ecological navigation task, the Virtual City paradigm™ (VC™) to test visuo-spatial memory and EFs in children with ADHD. Visuo-spatial short and working memory, inhibition and planning skills were tested with standardized tasks. The VC™, a new paradigm developed by our group, used the Virtual Carpet™ technology, consisting of a virtual town with houses, streets and crossroads projected on the ground. It includes a motion capture system, tracking body movement in 3D in real time. In one condition, children were required to walk through the city and reach a sequence of houses. In the other, before walking, they had to plan the shortest path to reach the houses, inhibiting the prepotent response to start walking. The results show a good feasibility of the paradigm (feasibility checklist and ad hoc questionnaire), being ecological and motivating. VC™ measures of span positively correlated with visuo-spatial short and working memory measures, suggesting that VC™ heavily relies on efficient spatial memory. Individual subject analyses suggested that children with ADHD may approach this task differently from typically developing children. Larger samples of ADHD and healthy children may further explore the specific role of EFs and memory, potentially opening new avenues for intervention.

Keywords: visuo-spatial memory, executive functions, navigation, ADHD, children, neurodevelopmental disorders

INTRODUCTION

Spatial navigation is certainly one of the most complex neural functions in humans and one that is absolutely vital to everyday life. Retrieving locations and paths, planning routes to distant destinations, ascertaining one's location in space, drawing and reading maps, are all daily navigational tasks. A lack of navigation skills may impair one's ability to find things, reach targets, avoid obstacles, and return home. It may lead to complete dependence on others, or even to death, if experienced in a dangerous environment. In spite of a large amount of studies on navigation deficits in patients with neurological deficits (1–5), the availability of validated diagnostic tools for navigation disorders is still extremely limited. In addition, there are no studies assessing navigation in patients with neurodevelopmental disorders, as Attention Deficit and Hyperactivity Disorder (ADHD).

Traditionally, spatial navigation has been assessed by means of paper mazes, in manual space and not requiring locomotion. Only recently, novel tests for the assessment of navigation have been created and validated in adults and children (6, 7). The Magic Carpet is such a test and has been validated both in typically developing children and in children with cerebral palsy (8). It is derived from the Walking Corsi Test (9–11) and assesses locomotor navigation via the same procedure of the Corsi Block-Tapping Test for short-term visual-spatial memory, but translated from manual into locomotor space. By analyzing the errors made on the Magic Carpet (6, 8, 12) it has been possible to gain insight into the cognitive strategies used by different groups at different ages and to formulate hypotheses on the development of human navigation. However, the Magic Carpet did not allow measuring the kinematics of the trajectory, nor also the head direction as an index of gaze direction, as was done previously in the study of Belmonti (8) in typically developing children and children with Cerebral Palsy, capturing body motion during task execution.

The Virtual City paradigm (VC™) has therefore been developed in collaboration with the group in Paris of A. Berthoz [see (13)]. It is implemented using the Virtual Carpet™ experimental design (7, 14, 15), with the aim of assessing real locomotor navigation in a controlled laboratory space and under specific experimental conditions, allowing for grading of task difficulty and analysis of different neuropsychological functions. The nature of processes necessary for successfully completing such locomotor navigation tasks, such as egocentric and allocentric strategies, have been analyzed in the literature, both in adults (16–18) and in children (6, 8, 19, 20).

This new and ecological way of testing neuropsychological functions and cognitive strategies, in a motivating context, suitable for children with neurodevelopmental disorders, can be potentially highly informative for understanding executive functions (EFs) and memory in children with ADHD, for whom such functions are specifically challenging.

ADHD is a neurodevelopmental disorder with persistent inattention and/or hyperactivity/impulsivity, present in at least two life contexts, associated with significant social and academic impairment and with onset before 12 years of age (21). According to the Diagnostic and Statistical Manual of Mental Disorders – Fifth edition (DSM-5, 2013) (21), there are three ADHD presentations: predominantly inattentive, predominantly hyperactive/impulsive and combined. ADHD is one of the most prevalent childhood disorders with a worldwide prevalence of around 7%, with problems persisting into adulthood (22).

ADHD has a high heterogeneity at the clinical, genetic and neurocognitive levels (23). Children and adolescents with ADHD have been shown to consistently display differences in brain structure and function with respect to typically developing peers. Review of neuroimaging data indicate alterations prevalently in fronto-striatal, fronto-parieto-temporal, fronto-cerebellar and fronto-limbic networks, according to different neuropsychological and clinical phenotypes [for a review of neuroimaging studies see (24–26)]. At the cognitive level, ADHD is associated with a wide range of neuropsychological deficits, the most frequently reported being deficits in inhibition, memory, temporal discounting, decision making and timing, indicating that these constitute key cognitive domains, with EFs being heavily studied (27, 28). There are indications however that children and adolescents with ADHD may fall in distinct neuropsychological subgroups, displaying some but not all of the key cognitive deficits (29).

Among deficits in several cognitive areas, working memory, that is the function of actively holding in mind and manipulating information relevant to a goal, has received much attention (30, 31), also for tailoring rehabilitation (32). Visual-spatial short memory has been found to be more impaired than verbal short-term memory, and memory difficulties have been reported both at the level of storage and of active control/updating components in central executive tasks (33). Indeed, visual-spatial working memory may be thus a leading candidate endophenotype for ADHD.

Response inhibition is fundamental when alternative courses of thoughts or actions (planned or already initiated) have to be inhibited to allow the emergence of goal-directed behavior, and its deficit is associated with impulsive behaviors, a core DSM-5 diagnostic feature of ADHD. Reward-delay impulsivity has been explored with a meta-analytic method to examine differences in children and adolescents with and without ADHD (34), showing that youths with ADHD exhibited moderately increased impulsive decision-making compared to controls.

Deficits in planning abilities are also frequently reported in ADHD. A meta-analysis examined performance and latency measures in five tower planning task variants in 41 studies including ADHD, to calculate between-group effect sizes, and found moderate-magnitude planning deficits (35). Children with ADHD responded more quickly on planning tasks when compared to normal peers.

It has been also proposed that cognitive impairments in ADHD may result from both central controlled processes and more automatic information processes (36), with reciprocal functional interactions between subcortical regions and higher-order brain networks (37). The automatic processes, underpinned by dynamic subcortical circuits (including superior

TABLE 1 | Demographic and clinical data of the ADHD sample.

n.	Age (yrs;mo)	Sex	Adhd presentation	Specific learning disability	Intelligence (WISC-IV indices)			
					VCI	PRI	WMI	PSI
1	7;11	M	Combined		104	98	82	68
2	7;3	F	Combined		116	93	82	56
3	9;6	M	Combined		120	106	121	123
4	8;0	M	Combined		100	91	61	53
5	8;2	M	Combined		104*	96**	NA	NA
6	9;5	M	Combined		120	93	97	94
7	7;10	M	Combined		90	80	79	82
8	8;11	M	Combined	Yes	108	100	94	94
9	9;8	F	Combined	Yes	98	89	79	94
10	13;8	M	Combined	Yes	122	108	112	74
11	12;10	M	Combined	Yes	96	102	82	94
12	8;5	M	Combined		100	91	70	85
13	8;0	F	Combined		112	126	94	79
14	10;7	M	Combined		114	124	103	118
15	9;3	M	Combined		132	113	94	88
16	8;9	F	Combined	Yes	114	100	91	71
17	10;7	M	Combined		106	124	94	79
18	12;8	M	Inattentive	Yes	112	119	103	123
19	13;1	M	Inattentive		108	104	94	88
20	12;3	M	Inattentive		120	122	103	79
21	8;8	F	Inattentive	Yes	128	91	85	82
22	10;3	M	Inattentive	Yes	108	91	82	109

*VCI Verbal Comprehension Index; PRI Perceptual Reasoning Index; WMI Working Memory Index; PSI Processing Speed Index; *Verbal Intelligence quotient and **Performance Intelligence quotient at WPPSI-III at 6;8 years; NA not applicable.*

culliculus, pulvinar, and basal ganglia), may play a pivotal role in pathological distractibility of ADHD, representing "biological shortcuts," which may bypass more complex systems, such as those involved in strategic planning (37, 38). Following this model, deficits in executive functions may be due, at least partly, to deficits in this automatic processing, leading to higher cognitive loads and limited resources available for EFs (39). Structural differences in subcortical structures in individuals with ADHD compared with those without this diagnosis may support this model.

Based on these considerations, the VC™ paradigm was intended as a new and more ecological tool for assessing cognitive processes which are challenging for children with ADHD, as focused attention, memory, planning and inhibition, especially when they have to be recruited together as is the case in real-life situations.

The aim of this brief research report was to analyze, in a group of school-aged children diagnosed with ADHD, the feasibility of a navigation approach transferred to the VC™ paradigm and its capacity to explore and measure the cognitive strategies used by these children during a visuo-spatial memory task. The feasibility study was thus specifically intended for this clinical population with significant impairments in these areas of cognitive functioning, which were also tested with classical neuropsychological tasks.

METHODS

Subjects

The feasibility study included a clinical group of drug-naïve children with a diagnosis of ADHD, recruited in our third-level hospital of Child and Adolescent Neurology and Psychiatry. All participants underwent a multi-dimensional assessment, and diagnoses were made according to the DSM 5 (21), based on clinical history and a structured interview, Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL) (40). The inclusion criteria were: (1) Diagnosis of ADHD; (2) Drug naïvité for stimulant treatment and any other pharmacotherapy; (3) Absence of intellectual disability; (4) Absence of comorbid conditions, except for Specific Learning Disabilities-SLD- (DSM 5); (5) Verbal intelligence of 85 or above (Wechsler Scales) (41, 42) to ensure full comprehension of the verbal instructions of the VC™ paradigm; (6) Absence of any visual (non-corrected) or gait problems.

Twenty-two patients aged 7–13 years were recruited (mean 9;8 years; sd 1;9 years; males $n = 17$; 77%), all eligible to be included in the study. ADHD presentation was 77% combined ($n = 17$) and 23% inattentive ($n = 5$), 36% displaying comorbid SLD ($n = 8$). Mean verbal intelligence was 110.5 (sd 10.6). Demographic and clinical data for the entire sample of 22 participants is presented in **Table 1**.

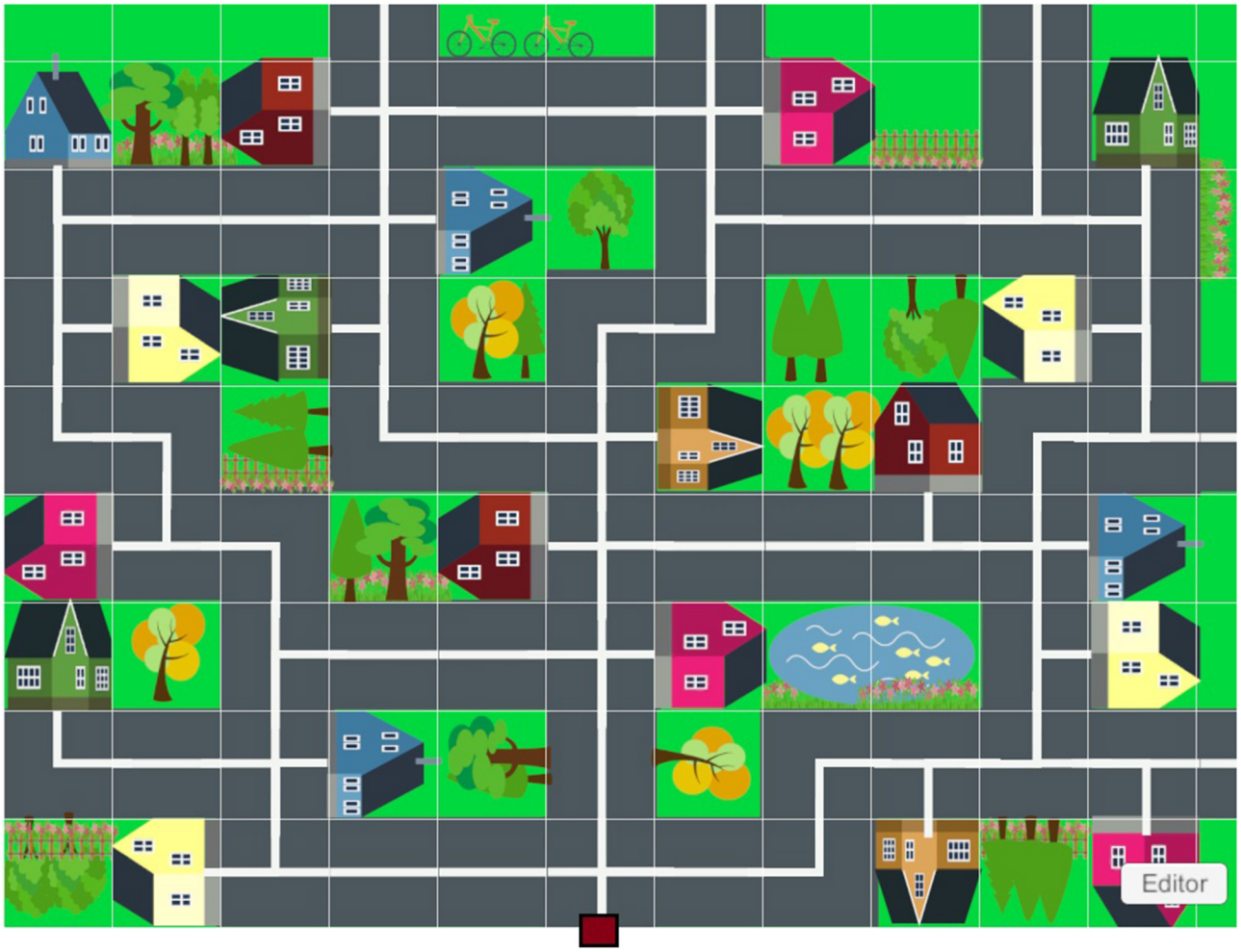

FIGURE 1 | VC™ projection on the ground. The red square indicates the starting position.

This study complied with the Declaration of Helsinki and was approved by the Regional Pediatric Ethical Committee (n.175/2019). Parents and children signed a written consent form (for children, in a child friendly format).

Procedures and Measures

The experimental design was divided into two assessments administered to each child: the VC™ paradigm and neuropsychological tasks, both testing visuo-spatial memory and EFs. The VC™ paradigm and neuropsychological tests were carried out at different times of the same day or on two different days (no longer than a week apart), in order to reduce the fatigue effect as much as possible. Order of assessments was randomized with half of the participants starting with the VC™ paradigm and the other with the neuropsychological evaluation, in the majority of cases. Duration of the entire VC™ paradigm ranged from 40 to 50 min in a single session although for some children, due to variability in collaboration, duration could be longer. Subsequently, the psychologists (BDL and MCC) who administered the task, filled out a feasibility VC™ questionnaire created ad hoc. The duration of the neuropsychological assessment was 1 h on average in one single session but varied again as a function of degree of collaboration.

The experimental set up and the procedures were the following:

The Virtual City Paradigm™

The VC™ is a projected virtual town on the floor, consisting of 20 houses, street lanes and crossings (**Figure 1**), created on Unity 5.5.1© platform. Two projectors were installed and connected to a computer so as to project the town on an off-white carpet (2.6 m × 3.2 m) in a dark laboratory space. The child had to move around the virtual town to reach the houses which flickered (the targets). Houses flickered either in a sequence, or all together. For tracking the trajectory of the child, the motion capture system (HTC® Vive and Steam© software), included two handheld three-dimensional space (3D) motion sensors applied one on the head (fixed on a bike helmet worn by the child) and one on

the trunk (fixed on a belt worn by the child) (see (13)) and two infrared cameras allowing tracking of body movement in 3D in real time (see videos in the **Supplementary Material**).

The VC™ paradigm included three different conditions in which the number of houses to be reached (span level), the sequence order, flicker duration, and the instructions varied.

1 City Pointing: While keeping the starting position, the child was asked to point (with a laser pointer) each house as it flickered (for 2.5 s). The sequence of flickering houses was randomized and the houses' order was set so that no contiguous houses flickered in a sequence. This procedure allowed assessing efficacy of visual search abilities in a large space and visuo-spatial span. If the child correctly pointed to at least 80% of the houses, the other conditions were administered.
2 City Following: A given number of houses was made to flicker in sequence. The child was asked to remain in the starting position and observe each house as it flickered (for 2.5 s). Then the child was asked to walk on the streets to reach each house in the same order he/she had seen them flickering. The sequences were randomized and the houses' order set with a mathematical algorithm to ensure both easy sequences (the houses are near to each other and not too many rotations are needed to reach the next one) and some difficult ones (i.e., more distant houses and more rotations). There was a maximum of five span levels (from the starting level of two houses for all subjects up to a level of six houses). Criterion for success on any given level was three out of five trials correct and in case of failure, five additional trials for the same level were presented before proceeding with the third condition. Similarly to the Corsi Block Tapping test, a span measure was obtained, but for this paradigm it was the longest sequence reached by the subject (even if the three out of five criterion was not met).
3 City Planning: The child was asked to observe the houses that were flickering simultaneously while keeping the starting position, and then to walk on the streets to reach the houses he/she had seen flickering. The specific instruction was to plan the shortest path. There was a maximum of three span levels (from a span of two to a span of four) each with 10 trials, with the starting span level being the span level reached in the second condition. Flickering duration for each span level was respectively 7.4, 11.3, and 13.1 s.

The cognitive strategies needed to complete the VC™ tasks could be the following: a first encoding phase in which the subject mentally encoded the spatial distribution of the houses and eventually the temporal sequence of their presentation. This encoding may be perturbed in ADHD due to a deficit in selective attention and/or spatial memory. For this reason, a control condition was added (City Pointing), to ensure that children do indeed pay attention to all houses in the town as they flicker; a second recall phase in which before starting the task, the subject had to mentally rehearse the encoded representation of the flickering houses' spatial distribution and to generate the trajectory. Both phases imply spatial short- and long-term memory and inhibition, intended, the latter, as the capacity to inhibit the prepotent response to start walking in the town before having generated a trajectory or the shortest path as in the City Planning condition; finally, when the subject navigated the town, he/she needed to update the mental trajectory of the houses he/she had generated. That is, he/she had to represent the position of the houses relative to his actual position in the town and no longer the one relative to the starting position in which he/she had originally encoded them. This phase could tax the updating component of spatial memory (working memory).

In addition to the span measure, the VC™ paradigm provides kinematics data on the movement trajectory of each subject. In particular, the HTC© Vive system and Steam© software allows both to generate the target positions (i.e., the houses) in the virtual environment (calibration procedure) and to record the trajectories of each child during navigation. The calibration procedure was performed by the psychologist (BDL) who positioned herself over each target house following a standard order, enabling to configure the global navigational array and to set the houses' positions in a cartesian coordinate system by triggering the 3D motion sensor.

To record the trajectory of the children, the system detected the locomotion during the experimental sessions and computed, for specific time frames (in ms), head and trunk sensor positions on X, Y, and Z axes, and rotation angles with respect to the X, Y, Z axes direction. These data were treated using Matlab 2021 to yield parameters such as trunk and head position and rotation in the horizontal plane, trunk and head velocity, acceleration, and stops during the trajectory. Further details on automatic kinematic data analysis are reported in (13).

Neuropsychological Assessment

Visuo-spatial short-term memory/working memory tasks in the reaching space included the Corsi Block Tapping task forward and backward (43) and a computerized block tapping task, the Spatial Span Task (CANTAB®) (44). The span measure was the longest sequence correctly retrieved. The Digit span WISC-IV subtests-forward and backward- served as a control verbal measure of spatial memory. Parents and children filled out a pilot questionnaire on everyday visuo-spatial and navigation abilities (Santa Barbara Sense of Direction Scale-Parent and Child Version: p-CBSOD and c-CBSOD) adapted by Murias et al. (45) (see **Supplementary Material 1**).

The Stop Signal Task (CANTAB®) (44) was administered as a measure of response inhibition. It is a go-no-go task adapting the time interval between the go stimulus and the stop stimulus to the performance of the subject providing as the outcome measure, the estimate of time during which an individual can successfully inhibit the response 50% of the time. The Tower of London (46) was administered as a measure of planning expressed in terms of total decision time, execution time and number of rule violations. As an ecological measure of EFs, parents filled out the Behavior Rating Inventory of Executive Function - Second Edition (BRIEF-2) (47) on their children's abilities for inhibition, working memory, monitoring and self-monitoring, shift, planning and emotional regulation.

Feasibility Assessment

The feasibility of the VC™ paradigm was investigated with two measures, an *ad-hoc* questionnaire on acceptability and usability filled out by the two experimenters (BDL and MCC) and a feasibility checklist. The questionnaire (see **Supplementary Material 2**), conforming to the standard definitions of usability (48–50) and acceptability (51, 52) [for a review study see (53)], consisted of 14 questions ranked on a 5-point Likert scale (1 most negative, 5 most positive). The feasibility checklist with criteria for success, based on a literature review (see **Supplementary Material 2**, **Table 1**), consisted of nine outcome measures grouped in four areas specific for the VC™ (accessibility, training motivation, technical smoothness, and training compliance) and 5 for the entire study design and procedures (participation willingness, participation rates, loss to follow-up, assessment timescale and assessment procedures).

RESULTS

Feasibility Analyses

Feasibility questionnaire data and checklist measures were available for 21/22 subjects. Feasibility questionnaire results for usability and acceptability revealed a prevalence of positive responses, indicating a satisfactory feasibility of the VC™ paradigm. For usability (6 questions), there were 74/126 responses graded as 5 and 29/126 as 4. For acceptability (8 questions), there 73/168 graded as 5 and 44/168 as 4.

Feasibility criteria were met for all measures both for the VC™ (accessibility 91%; compliance 91%; technical smoothness 32%; motivation 14%) and for the entire study design and procedures (participation willingness 95%; participation rates 4%; missing data: VC™ and neuropsychological assessment 13%; time scale 91%; procedure 91%).

VC™ Span Level and Neuropsychological Measures

The VC™ span level and neuropsychological measures were available for 18 out of 22 subjects due to 1 drop-out because parents refused to continue the study, 1 to technical sensors problems, and 2 for failure to complete the entire VC™ in a single session. Missing data (either Tower of London or WISC-IV digit span) concerned three subjects.

Group data will be presented first and then data from two 10 year-old children with ADHD deemed exemplary. A typically developing 10 year-old child served as a comparison subject.

Statistical analyses were computed with RStudio version 2020 for Windows (www. R-project.org). Preliminary Spearman correlation analyses were computed between the VC™ span and neuropsychological measures. The span level of the City Following condition, intended as the longest sequence reached (but not passed), was compared with the raw data of the different neuropsychological measures (Corsi Span, CANTAB© Spatial Span, CANTAB© Stop Signal, Tower of London, BRIEF-2) and with the standard WISC-IV Digit Span scores.

As expected, there was significant correlation between the VC™ span level and both the Corsi forward ($r = 0.67$, $p = 0.002$) and backward spans ($r = 0.60$, $p = 0.008$). In addition, there was a significant positive correlation between the VC™ span and the backward digit span ($r = 0.57$, $p = 0.01$). Age correlated significantly with the VC™ span level ($r = 0.70$, $p = < 0.001$). A significant negative correlation was found between c-SBSOD and VC™ span level ($r = -0.70$, $p = 0.001$). No other significant correlation was observed with other neuropsychological test measures (Tower of London and CANTAB© span and inhibition) and questionnaire measures (BRIEF-2, p-SBSOD).

Individual VC™ Trajectories and Neuropsychological Data

Based on trajectories analyses, a qualitative description of the behavior during VC™ performance is presented for two children with ADHD (subject 22, Inattentive and subject 17 Combined, **Table 1**), and the comparison subject. **Figure 2** compares the trajectories of the same sequence (span level 3, trial 3) in the City Following condition, where the child is asked to reach three houses flickering in an easy sequence.

In **Figure 2A**, the child with Combined ADHD performed the trial correctly by reaching the 3 target houses in the right order. However, he reached the first and second target houses, then stopped, not remembering the exact position of the third target house. He therefore returned to the starting position, looked around (as indicated by the red arrows), then he presumably remembered the position of the third target house and headed toward it. In **Figure 2B**, the child with Inattentive ADHD failed the task. The child started from the initial position and correctly reached the first and second houses. He then reached a wrong house, then stopped, looked around, understood that he had failed and thus proceeded to reaching another (incorrect) house. From **Figure 2B**, this child's head movements, shown by red arrows, indicate a high distractibility of the subject, given his frequent deviation from the trajectory and they do not predict the following movement directions. **Figure 2C** shows that the comparison child reached the target houses in the right order with a linear locomotion trajectory. The head movements did not deviate from the path when linear, while they were anticipatory when body rotations were necessary, predicting the following movement directions. Neuropsychological assessment data of the two children with ADHD and the comparison subject revealed some important qualitative differences. They concern not only visuo-spatial memory abilities (Corsi span forward and backward), but also EFs, a core deficit of ADHD children. Specifically, with regards to the parent report questionnaire BRIEF-2, the cognitive regulation abilities (Cognitive Regulation Index) were much poorer in the children with ADHD than in the control, with T scores in the clinical/borderline range. Tower of London performance indicated significant difficulties only in the Inattentive presentation. Such skills could be crucial for carrying out the task, and include planning, working memory and self-monitoring. CANTAB© and SBSOD (child and parent report) data were not available for the comparison subject and thus are not presented.

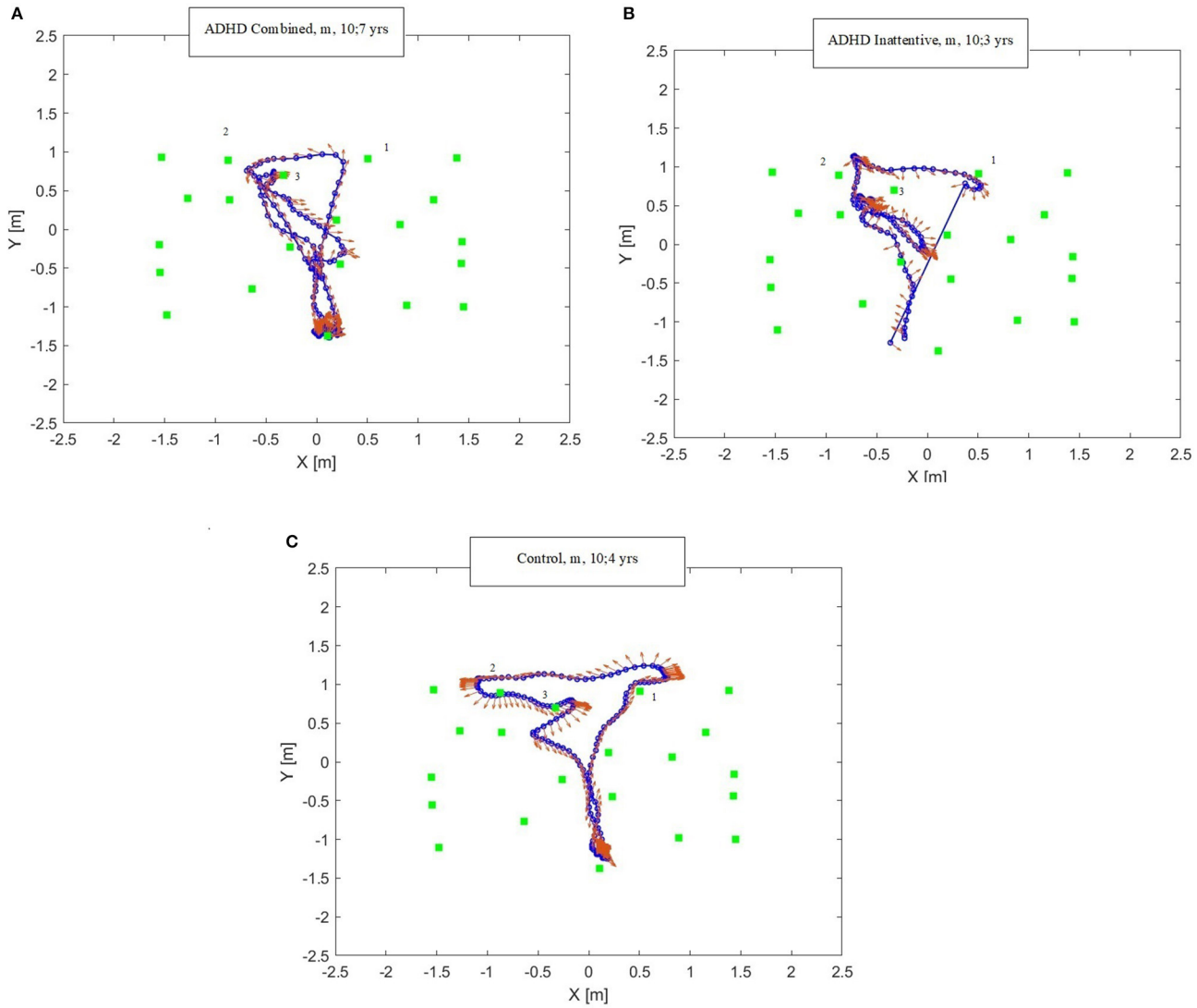

FIGURE 2 | (A–C) Trajectories at the VC™ paradigm of two children with ADHD and one control child. Blue lines and circles: motion trajectories; Red arrows: head direction with respect to the trajectory; Green squares: house position with sequence number on top. X and Y axes indicate the sensors' position in the navigational array (meters). **(A)** trajectory of a combined type ADHD child, male, aged 10;7 years; **(B)** trajectory of an inattentive type ADHD child, male, aged 10;3 years; **(C)** trajectory of a control subject, male, aged 10;4 years.

DISCUSSION

Feasibility

The primary aim of the study was to evaluate the feasibility of the VC paradigm™ for assessing visual-spatial memory and EFs in a navigation task in children with ADHD. The results from the *ad-hoc* feasibility questionnaire indicated satisfactory usability and acceptability. Regarding usability, the device could be used efficiently with no need for external technical support, with intuitive hardware and software instructions, the sensors being non-invasive and the entire device not posing any danger to the child. Concerning acceptability, the VC™ proved to be a motivating and playful task for children, potentially informing clinical practice, recruiting different cognitive strategies than the neuropsychological tests presented in peri-personal space. The VC™ appeared to be a more ecological assessment measure as it investigates the skills required in daily life. However, some technical issues with the motion sensors limited correct data acquisition. This could be due to the high level of hyperactivity combined with the sensors' high sensitivity, both interfering with the position acquisition by the cameras. The feasibility checklist highlighted a good compliance, as the great majority of the subjects performed the entire task and within the designated time frame. The children were also very motivated and reported a limited effort in carrying out the task. Concerning the feasibility of the entire study design and procedures, the participation rate was extremely high, as none of the participants except one dropped out of the study.

Correlations Between Virtual City™ Span and Neuropsychological Measures

Significant associations were found between VC™ span - Following condition- and verbal and visuo-spatial memory abilities. A larger correlation was found between the VC ™ span and the Corsi Block Tapping test. No associations were found between the VC™ span (Following condition) and EF measures differently than expected from the literature (6, 8). The VC™ span was the sole measure to be analyzed, while other available parameters such as head deviation from the trunk, latency and kinematic parameters may offer new insights into the role of EFs. Furthermore, the EF measures chosen may not have been sensitive enough. The negative correlation between the Child SBSOD questionnaire and the VC™ span was unexpected. Better perception for one's spatial orientation abilities was associated with lower VC™ span. This could be due to difficulty in fully understanding the questions, as well as to a reduced awareness of one's own deficits.

Performance Differences in ADHD Subjects Compared With the Control Child

The trajectory analyses of ADHD and control subjects reveal some qualitative differences in spatial navigation behavior which may be associated with the deficits displayed by children with ADHD.

Although the child with combined ADHD performed the sequence correctly, the locomotor pathway was non-linear. In fact, this child went back to the starting point possibly to rehearse the trajectory previously encoded. This suggests that he recruited an egocentric storing strategy less functional than an allocentric one. This return-to-start behavior has been described in adults (54) in a "virtual starmaze" task and accounted for as "a mixed strategy." During navigation, sensory stimuli can be encoded in spatial reference frames centered on the sensory organs (egocentric) or in an allocentric reference frame, with allocentric spatial encoding strategy introducing a substantial computational simplification, acquired later in childhood and probably subsumed by EFs (7). Since executive dysfunction is one of the core deficits of ADHD, these children may have difficulties in activating an allocentric strategy to store the targets. The child with inattentive ADHD showed the worst performance, being highly distractible, failing the sequence, following a linear path (he did not return to the starting point), with head and trunk not moving in the same directions.

Given the novelty of this complex navigation paradigm, tapping processes beyond executive functions, it is premature to interpret the preliminary results in terms of specific models or hypotheses on attentional/executive dysfunctions in ADHD. Further analyses on the planning trajectories and on the pattern of responses of typically developing children could provide insights on the role of automatic processes which could be preponderant in approaching this task in ADHD but also in younger children.

Infact, no age-matched control group was recruited for this study. However, as already highlighted, this is a feasibility study aimed at analyzing usability and acceptability of a new way of testing cognition in navigation in a clinical population with significant impairments in cognitive functions tapped in the VC™ paradigm. A study on typically developing children will be conducted, matched to a larger group of children with ADHD for analyzing if there are specific patterns of behavior which characterize this clinical population, as suggested by the preliminary trajectories' analyses. To better understand the cognitive processes involved in the VC™ task, further investigations will be necessary, taking into account parameters other than span such as decision time, head deviation from trajectory, to name the most relevant that have been studied in other navigational tasks. These indicators could clarify the role and nature of EFs that did not clearly emerge in this feasibility study, but are certainly involved in such a challenging navigational task. Further neuropsychological assessments could be advantageous as to allow disentangling specific cognitive processes which may be pivotal for understanding how children approach this ecological yet complex task.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Regional Pediatric Ethical Committee (n.175/2019), Tuscany region, Italy. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

BDL: methodology, investigation, resources, data curation, writing—original draft, and writing—review and editing. VB: conceptualization, methodology, formal analysis, and writing—review and editing. PB: methodology, formal analysis, supervision, writing original draft, and writing—review and editing. MCC: formal analysis, investigation, resources, and writing—review and editing. AC: methodology, software, validation, data curation, and writing—review and editing. GM: methodology, supervision, resources, and writing—review and editing. AT: methodology, resources, and writing—review and editing. MZ: resources, data curation, visualization, and formal analyses. GC: conceptualization, supervision, writing, review and editing, and funding acquisition project administration. AB: methodology, conceptualization, formal analysis, supervision, writing, and review and editing. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.708434/full#supplementary-material

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ORIGINAL PAPER

Examining Temporal Cognition in Preschoolers With Attention Deficit Hyperactivity Disorder: Insights From Parent–Child Interactions

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Abstract

Increasing evidence supports the existence of time-related impairments in school-aged children and adults with Attention-Deficit/Hyperactivity Disorder (ADHD), but this deficit has not yet been investigated in preschoolers with ADHD. The aim of the current study was to determine the extent to which time-related impairments can be identified within the context of parent–child interactions in preschoolers with ADHD. Participants for this study included 29 children with ADHD and 34 typically developing (TD) children (63.5% male; $M_{age} = 4.77$, $SD = 0.65$; 82.5% Hispanic/Latinx), and their parents. A ten-minute play session was video-recorded for each parent-child dyad. The verbal interactions were transcribed and coded for words/expressions related to the categories of time (e.g., "later", "tomorrow"), as well as mathematics (e.g., "two more", "some"), and space (e.g., "here/there", "behind"). The proportion of tokens (total number of terms) and types (different terms) of each category was calculated in relation to the total verbal production for each individual (i.e., parents and children separately), and differences between groups were analyzed. Results indicated that compared to TD children, children with ADHD showed a poorer vocabulary of time-related words ($d = 0.63$), whereas similar rates between groups were found for the math- and space-related words. Correlation analyses revealed significant associations between the types of time-related words used by children, and problems with attention and executive functioning. These results offer some evidence for not only the presence of time-related deficits in preschoolers with ADHD, but also the association between time-related deficits and impairments in cognitive functioning.

Keywords Time processing deficit · Time-related words · Attention-Deficit/Hyperactivity Disorder · Preschool · Parent–child interaction

Highlights

- Time-related impairments characterize individuals with ADHD, but they have never been investigated in preschoolers with ADHD.
- A poorer vocabulary of time-related words was found in preschoolers with ADHD, compared to controls.
- Preschoolers with ADHD and controls showed similar rates of math- and space-related words.
- Significant associations between the types of time-related words used by children, and problems with attention and executive functioning, were identified.

The capability of processing and estimating time, also definable as sense of time or temporal cognition (Zakay & Block, 1997), is a fundamental and complex function in human beings: individuals need to keep track of temporal durations of inner and outer events, for developing a sense of their own story and for interacting efficiently with the surrounding environment (Grondin, 2010). Increasing evidence supports the existence of time-related impairments in individuals with Attention-Deficit/Hyperactivity Disorder

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(ADHD; Hart et al., 2012; Noreika et al., 2013; Toplak et al., 2006). ADHD is a neurodevelopmental disorder characterized by inattention and/or hyperactivity/impulsivity, associated with poor social, behavioral, and academic outcomes (American Psychiatric Association, 2013; Currie & Stabile, 2004; Ros & Graziano, 2018). Theoretical models of neuropsychological functioning, such as the triple pathway model, recognizes that individuals with ADHD have deficits in timing, inhibition and delay (Sonuga-Barke et al., 2010). Alterations in temporal cognition may represent a primary cause of key symptoms in ADHD, and the assessment of time estimation skills has been recently hypothesized to be a potential useful method for differential diagnosis, distinguishing between confirmed cases of ADHD and other psychiatric disorders characterized by symptoms similar to that of ADHD (Walg et al., 2017).

Time-Related Skills in Preschoolers

Literature on temporal cognition and time comprehension in typically developing preschoolers offer insights that are meaningful for the purposes of the present study. A sense of time is exhibited as early as infancy, and improvements in temporal skills are observed between 3 and 10 years of age (Droit-Volet, 2013). By age 5, children's time processing skills are associated with short-term memory span and the development of attention and executive functioning (EF; Zélanti & Droit-Volet, 2011), working memory and information processing speed (Droit-Volet & Zélanti, 2013). More specifically, a recent study in 4-year-old children demonstrated the association between time comprehension and the ability to delay gratification, such that preschoolers who performed at chance level in a time estimation task, showing scarce comprehension of the time concept, had more difficulty waiting during a delay-of-gratification task (Zmyj, 2018).

Time processing difficulties can be identified with both behavioral tasks (e.g., time reproduction, time estimation, time discrimination; Plummer & Humphrey, 2009; Smith et al., 2002) and self- or proxy-report questionnaires (e.g. "It's About Time" questionnaire; Barkley, 1998). However, preschool children are often not aware of the passage of time and its relevance since time judgments are context-dependent at this age (Droit-Volet, 2013). For this reason, use of experimental tasks for assessing time processing, in which explicit time judgment are required, can lead to an inaccurate estimation of children's time-processing skills. However, when the duration of daily activities is in question, children are able to accurately judge the length of temporal intervals as early as 3–5 years (Friedman, 1990).

One way for investigating temporal cognition, not yet applied to children with ADHD, is through analysis of caregiver-child verbal interactions to identify abnormal patterns in the use of time-related terms. Play sessions in which the child interacts with his/her caregiver, are ecologically valid situations in which spontaneously produced language can be observed. A similar approach has been used, to investigate the use of temporal terms in children from different socio-economic backgrounds (Rosemberg et al., 2014). As pointed out by this last study, children's understanding of time concept is not directly observable. Language allows individuals to conceptualize the abstract aspects of temporality. By analyzing linguistic production, it is possible to identify indicators of understanding of time concept, such as the time-related terms produced in verbal interactions (Rosemberg et al., 2014). Because children acquire linguistic terms for describing time-related concepts during the preschool years (Busby Grant & Suddendorf, 2014), 4–5 years of age is an optimal period for investigating this issue. At this stage of development, children are able to produce time-related terms such as temporal (e.g., always) or sequential (e.g., after) adverbs, adverbial phrases (e.g. in the afternoon), and nouns referring to time (e.g., minutes; Busby Grant & Suddendorf, 2014; Rosemberg et al., 2014).

To date and to the best of our knowledge, the literature has not directly analyzed the association between the use of temporal terms by children and their actual time-related skills. However, a few recent studies could shed some light on this topic. For example, Tobia et al. (2019) analysed the predictive power of a questionnaire investigating preschoolers' "sense of time" on time processing tasks. Results demonstrated a significant association between teachers' reported "sense of time" and tasks of time reproduction and time discrimination both concurrently and longitudinally (Tobia et al., 2019). This finding is noteworthy because the majority of the items on the "sense of time" teacher questionnaire related to the use of temporal terms and time-related speech (e.g., spontaneous references to durations in their speech), thus supporting the existence of an association between use of temporal terms and performance in time processing tasks. Furthermore, it has been hypothesized, starting from studies investigating how children learn temporal terms (e.g., Tillman et al., 2017), that the use of temporal terms in children's language provides the primary source of the temporal reasoning system (Tillman, 2019).

Time-Related Skills in Children with ADHD

Time processing deficits characterize the profile of ADHD in school-aged children (Houghton et al., 2011; Huang et al., 2012; Meaux & Chelonis, 2003; Smith et al., 2002; Walg et al., 2015), potentially affecting daily routines, home and school activities, and social relations. However, despite many results reflecting time-related deficits in ADHD, these

findings are equivocal, and some studies have reported no significant temporal or timing deficits in this population (e.g., Brown & Vickers, 2004).

Despite the increasing evidence of time processing deficits in older children and adults with ADHD, there is limited research examining these processes as early as preschool. Some evidence comes from the administration of the Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P; Gioia et al., 2003), containing a Plan/Organized subscale that assesses behaviors related to time management, estimation of time and organization of steps directed to a goal. Preschoolers with ADHD score significantly worse on the Plan/Organized scale when compared to typically developing controls (Mahone & Hoffman, 2007). However, considering the inconsistent validity of the BRIEF subscales (Spiegel et al., 2017), Mahone and Hoffman's (2007) result may reflect general self-regulation problems in preschoolers with ADHD, rather than a difficulty specifically related to time management. Similarly, Marks et al. (2005) assessed memory of time in preschoolers with ADHD and found that children with ADHD demonstrated significantly weaker temporal sequencing performance compared to typically developing peers. However, results indicated weaker observed performance may be a byproduct of deficits in nonexecutive abilities, and not directly related to a specific memory of time deficit. The well-known deficits in working memory, attention, speed of processing (Kalff et al., 2005; Mahone & Hoffman, 2007), and delayed gratification (Pauli-Pott & Becker, 2011) in preschoolers with ADHD support the expectation of finding weaker time-related skills in this population. Furthermore, deficits in time processing skills may be associated with deficits in EF and symptoms of ADHD (Zélanti & Droit-Volet, 2011).

Math- and Space-Related Difficulties in Children with ADHD

Underachievement in students with ADHD has been identified across both the literacy and mathematics domains (Barry et al., 2002), with particularly severe problems in learning mathematics. However, these deficits have been partly interpreted as consequences of poor attention and EF, associated with ADHD and essential skills for determining mathematical knowledge and procedures (Zentall, 2007). Considering the developmental path of learning skills in children with ADHD, deficits in mathematical learning become progressively larger with age, with discrepancy between IQ scores and achievement in mathematics increasing in older students (Nussbaum et al., 1990). However, little is known about the mathematical skills of preschoolers with ADHD. The investigation of math-related words during play interaction can be an indirect way to investigate the onset of such learning difficulties among young children (Anderson, 1997; Blevins-Knabe & Musun-Miller, 1996).

One cognitive process associated with mathematical skills as early as preschool is spatial ability (Cornu et al., 2018; Verdine et al., 2014). Visuo-spatial deficits have been identified in some samples of children with ADHD. In particular, children with ADHD performed more poorly on tasks assessing visuo-spatial working memory (Alloway & Stein, 2014; Westerberg et al., 2004) and on the spatial tasks of the WISC-R and WISC-V (Bonafina et al., 2000; Raiford et al., 2015). However, visuo-spatial difficulties dissipate in early adolescence (Westerberg et al., 2004), and data on preschoolers are still limited.

The Present Study

To date, no research has directly investigated time-related difficulties in children aged 4-5 years with ADHD. As Pauli-Pott and Becker (2011) suggested, it is important to isolate time windows suitable for an early reliable assessment of the deficits associated with ADHD. This study contributes to the literature by investigating the time-related deficit characterizing ADHD in preschoolers through the analysis of parent–child interactions. In the past, some studies observed language production during interactions between parents and children with ADHD, mainly for investigating the use of language to guide and control children's behavior (Bindman et al., 2013) or analyzing children's pragmatic language abilities (Camarata & Gibson, 1999). Thus, it is possible to investigate the role of parents' linguistic input in relation to key features of ADHD through the analysis of the verbal interactions between parents and their children. Analyzing both children's and parents' production of time-related words will therefore clarify the extent to which caregiver linguistic input relates to children with ADHD's time-processing difficulties. Poor time-related language in children with ADHD, in a situation in which the linguistic input by their parents is adequate, will offer evidence in favor of a time processing deficit in ADHD independent from environmental influences.

The primary aim of the present study was to examine temporal cognition in a sample of preschoolers with ADHD, compared to typically developing peers. We investigated this issue by observing parent-child play interactions and analyzing the use of time-related words in spontaneous verbal production. We hypothesized that verbal interactions between children with ADHD and their parents would contain a weaker set (in terms of quantity and diversity) of time-related terms, compared to typically developing peers, whereas similar quantity and diversity were expected for math- and space-related words. Difficulties related to these domains may indeed emerge later in development, as a

consequence of poor EF (Zentall, 2007). This result would offer some evidence in favor of an early time-related deficit as a neuropsychological marker in children with ADHD (Sonuga-Barke et al., 2010), and would support the existence of this deficit in the preschool age group. Furthermore, this would be the first investigation of temporal cognition obtained by the analysis of spontaneous verbal production during child-parent play interactions in children with ADHD. The consideration of parents' utterances would determine if time-related language in children with ADHD is associated to time-related expressions used by their parents.

The secondary aim was to examine the associations between the time-, math- and space-related words and core features or impairments that characterize ADHD in preschoolers (e.g., symptom severity, EF, and academic and cognitive functioning). Past studies with typically developing children suggest links between time and EF, as well as attentional skills (Zélanti & Droit-Volet, 2011). The current study will expand such works by examining these associations in preschoolers with ADHD. Deficits in academic functioning, higher rates of hyperactivity and attention problems, as well as weaker EF characterize the profile of children with ADHD (Kalff et al., 2005; Mahone & Hoffman, 2007). Furthermore, attention and EF are related to both temporal cognition (Zélanti & Droit-Volet, 2011) and mathematical ability (Zentall, 2007). Thus, we expected greater time-related word production would be associated with fewer attention problems, better academic performance, and better EF.

Method

Participants

The sample included 29 children with ADHD (79.30% males, mean age = 4.85 ± 0.56 years old) and 34 TD (50% males, mean age = 4.71 ± 0.72 years old) children. Sample demographics and screening variables for both groups are described in Table 1. For each participant, a parent was involved including 28 mothers and 1 father of children with

Table 1 Participants' demographic and screening variables

	ADHD ($N = 29$)	TD ($N = 34$)
Child sex (% male)	79.30	50.00*
Child age (mean)	4.85 (0.56)	4.71 (0.72)
Child ethnicity (%Hispanic/Latino)	79.30	85.30
Child prime language (%)		
English only	44.80	29.40
Spanish only	6.90	2.90
English and Spanish	44.80	64.70
Other	3.40	2.90
Caregiver age (mean)	35.83 (6.43)	35.91 (4.82)
Caregiver level of education[a] (mean)	4.69 (1.26)	5.00 (0.89)
Child full scale IQ (Mean)	96.45 (14.45)	108.15 (10.60)**
BASC-2 hyperactivity T-score parent (mean)	71.10 (12.71)	43.97 (7.26)**
BASC-2 attentional problems T-score parent (mean)	65.65 (7.87)	45.68 (6.79)**
BASC-2 hyperactivity T-score teacher (mean)	68.76 (2.28)	N/A
BASC-2 attentional problems T-score teacher (mean)	61.52 (1.25)	N/A
BRIEF plan/organize T-score (Mean)	66.41 (14.41)	47.38 (11.23)**
BRIEF global executive functioning T-score (mean)	73.00 (13.77)	44.12 (7.81)**
Head–toes–knees–shoulders total score	14.21 (14.09)	27.41 (12.10)**
WJ-III achievement standard score (Mean)	104.68 (16.06)	117.94 (11.27)**
Total number of tokens produced by children	342.83 (141.53)	382.59 (149.57)
Total number of tokens produced by parents	730.03 (207.98)	757.15 (217.38)
Total number of types produced by children	158.55 (45.72)	176.85 (49.39)
Total number of types produced by parents	256.76 (44.62)	277.21 (54.34)

Note: ADHD Attention-Deficit/Hyperactivity Disorder, *BASC-2* Behavior Assessment System for Children, 2nd Edition, *BRIEF* Behavior Rating Inventory of Executive Function.

*$p < 0.01$ significant group differences, **$p < 0.001$ significant group differences.

[a]1 = Some high school, 2 = High school graduate, 3 = Some college, 4 = Associates degree, 5 = College graduate (bachelor degree), 6 = Advance graduate (masters, MBA, MD, Ph.D, JD).

ADHD and 28 mothers and 6 fathers of TD children. Parents of children in the two groups were balanced for age and level of instruction (see Table 1).

Participants were recruited via brochures, radio and newspaper ads, involving local preschools and mental health agencies, open houses, and parent workshops. A total of 78 families responded, 40 of whom indicated having children with behavioral problems. A screening appointment was scheduled for all 78 families, and written informed consent was provided by the primary caregivers of all the participants. Due to technical problems with the transcription of child-parent interactions, 6 children in the group of children with behavioral concerns were excluded from the sample. For the selection of the ADHD group, the following criterion were applied to the remaining 34 children initially identified as having behavioral problems, leading to a sample of 30:

(a) Meeting DSM-IV criteria for a diagnosis of ADHD ($n = 21$),

(b) Meeting DSM-IV criteria for a diagnosis of oppositional defiant disorder (ODD) *plus* having clinically significant levels of hyperactivity or inattention ($n = 7$) as indicated by:

(b1) at least 6/9 items of Inattention or Hyperactivity/Impulsiveness scored as "Pretty much" and "Very much" on the parent version of the Disruptive Behavior Disorder Rating Scale (DBD; Pelham et al., 1992),

(b2) a T-score of 60 or higher on the Hyperactivity and Attention Problems subscales of the parent/teacher BASC-2 (Reynolds & Kamphaus, 2004) or

(c) Showing hyperactivity *and* inattention symptoms as indicated by the (b1) criteria ($n = 2$).

The diagnosis of ADHD or ODD (criterion a/b) was obtained through a parent structured interview (Diagnostic Interview Schedule for Children Version IV; Shaffer et al., 2000) and parent and teacher rating scales (Pelham et al., 1992) based on standard practice recommendations (Pelham et al., 2005) by a psychologist. According to these criterion, four participants were excluded from the ADHD group.

Children included in the typically developing (TD) group did not meet DSM-IV criteria for any developmental disorder and could not have had elevated levels of hyperactivity or inattention symptoms as indicated by

(a) a Hyperactivity *and* Attentional problems T-score <60 on the parent BASC-2 (Reynolds & Kamphaus, 2004), and
(b) less than 6/9 items of Inattention and Hyperactivity/Impulsiveness scored as "Pretty much" and "Very much" on the parent version of the Disruptive Behavior Disorder Rating Scale (DBD; Pelham et al., 1992).

According to these criterion, four children were excluded from the TD group.

Finally, IQ was measured through the administration of the Wechsler Preschool and Primary Scale of Intelligence–Forth Edition (WPPSI-4; Wechsler, 2012), conducted by doctoral level graduate students under the supervision of a licensed psychologist (third author). All children were required to have a full scale IQ score of 70 or higher for inclusion in the current study. According to this criteria, one additional participant was excluded from the ADHD group, resulting in a final sample of 29 children with ADHD.

In terms of compensation, families who participated in this study were provided individualized feedback regarding their children's academic performance while those in the ADHD group were also eligible to receive a summer treatment intervention (Graziano et al., 2014) at a subsidized cost.

Procedure

Two 5-minute play sessions were video-recorded for each parent-child dyad. In one session, parents were instructed to direct the play session (parent directed interaction; pdi), choosing the games and the game-rules; in the other session, children were encouraged to lead the game (child directed interaction; cdi). These CDI and PDI play sessions are routinely done in parent training research, specifically parent–child interaction therapy (PCIT; Hembree-Kigin & McNeil, 2013). The play sessions were transcribed and coded for identifying words and expressions related to time, mathematics, and space. Time words/expressions included temporal adverbs (e.g., "later", "always"), temporal adverbial expressions (e.g., "in the evening", "for a minute"), and nouns denoting time (e.g., "week"). Temporal terms were identified based on past research investigating time-related words in preschoolers (Busby Grant & Suddendorf, 2014; Rosemberg et al., 2014). Mathematics words and expressions were derived congruent with past research analyzing math-related activities and discourses in parent-child and teacher-child interactions (Anderson, 1997; Blevins-Knabe & Musun-Miller, 1996; Klibanoff et al., 2006). Mathematics words/expressions included number words, expressions describing quantities (e.g., "all", "some of"), manipulation of quantities (e.g., "two more"), and terms describing shape attributes (e.g., "bigger", "small"). Space words/ expressions included terms referring to the location of objects and people (e.g., "here/there", "far/near", "behind") consistent with previous studies (Anderson, 1997; Ferrara et al., 2016).

All videos were transcribed into the CHAT (CHILDES system) format (MacWhinney, 2000). The total number of words/expressions in the time, math, and space categories (tokens) and the different terms within a category (types) were determined for both children and parents by a trained developmental psychologist. For the 20% of participants (Syed & Nelson, 2015), tokens and types for the three

categories were independently coded by a second observer, showing very good to excellent reliability (r's = 0.83-0.94). The second observer was trained by a developmental psychologist based on the math, space, time coding scheme described above. The percentages of tokens and types in each category, in relation to the total tokens and types of words produced by each individual, were then calculated.

Florida International University institutional review board approved the project.

Measures

Behavioral Functioning

Within the ADHD and TD samples, parents and teachers competed the Behavior Assessment System for Children, 2nd Edition (BASC-2; Reynolds & Kamphaus, 2004). The BASC-2 is a widely-used tool that assesses emotional and behavioral domains. For the purposes of this study, the Hyperactivity and the Attention Problems T-scores were used ($\alpha s = 0.93$–0.95; Reynolds & Kamphaus, 2004). This instrument proved to have adequate concurrent and predictive validity (see Pelham et al., 2005).

Parents within the ADHD and TD samples also completed the Disruptive Behavior Disorder (DBD) Rating Scale (Pelham et al., 1992) to measure symptoms of ADHD. Each symptom of ADHD is rated on a 4-point frequency scale from 0 ("not at all") to 3 ("very much"). For the purposes of the present study, the Inattention ($\alpha = 0.93$) and Hyperactivity/Impulsivity ($\alpha = 0.93$) scales were used (Pelham et al., 1992); more information on DBD validity and reliability can be found in Pelham et al. (2005).

Executive Functioning (EF)

Parents of children of both groups completed the Behavior Rating Inventory of Executive Function–Preschool version (BRIEF-P; Gioia et al., 2003). The BRIEF-P assesses five clinical scales (inhibit, shift, emotional control, working memory, and plan-organize). Higher scores on clinical scales/composites are indicative of weaker EF skills. The plan/organize subscale ($\alpha = 0.90$) and the global composite score ($\alpha = 0.98$) were used as measures of EF; validity based on convergence or divergence with a variety of measures and on internal factor structure was proven (Gioia et al., 2003).

Children were administered the head–toes–knees–shoulders task (HTKS; Ponitz et al., 2008). HTKS is a widely-used measure of EF, suitable for preschoolers. In this task, children are required to follow a set of behavioral rules paired with conflicting behavioral responses. There are two parts to the task, each with 10 trials. Prior to each part, children are given a set of rules (e.g., "touch your head" and "touch your toes"), such that the child must respond with the opposite behavior. In the second part, a new set of rules is added (i.e., shoulders and knees). Children received two points for a correct response, one point for a self-corrected response, or zero points for an incorrect response, with a total possible score of 40. Higher scores indicate better EF performance. Examinations of the HTKS revealed 3-month test–retest reliability above 0.90 (Ponitz et al., 2008), good concurrent validity with parents' ratings of attention and inhibitory control (Ponitz et al. 2009), and validity in a sample of children with externalizing behavior problems (Graziano et al., 2015).

Academic functioning and IQ

Children were administered six subsets from the Woodcock–Johnson Test of Achievement, 3rd Edition (WJ-III, Woodcock et al., 2001). The six subsets (i.e., applied problems, calculation, writing samples, letter-word identification, passage comprehension, spelling) were standardized and combined to create an academic achievement composite score ($\alpha = 0.85$ on our sample), such that higher scores indicated better academic achievement. Median reliability coefficients for the subtests were .80 or higher (Woodcock et al., 2001). Extensive evidence of content, construct, and concurrent validity of the WJ-III is reported in the test's manual (Woodcock et al., 2001).

The full-scale IQ was obtained through the administration of the WPPSI-4 (Wechsler, 2012) for the age range 4:0–7:7. Reliability values have been found to be between the good ($\alpha = 0.86$) to excellent ($\alpha = \geq 0.90$) range, with FSIQ having 0.96 as internal consistency and 0.93 as test–retest reliability (Syeda & Climie, 2014). The WPSSI-4 also shows good content validity and internal structure (Syeda & Climie, 2014).

Data Analyses

All analyses were conducted using Statistical Package for the Social Sciences, version 25 (SPSS 25). Preliminary analyses investigated any associations among the dependent variables and demographics, as well as any difference in the global number of tokens and types produced by children and parents in the two groups during interactions. MANOVAs were then conducted to investigate the differences between children with ADHD ($n = 29$) and TD children ($n = 34$) in parents' tokens and types used for each semantic category (i.e., time, math, space). Finally, correlation analyses on the entire sample were conducted to determine if the variables of interest (tokens and types) were associated with demographic variables (parents' educational level, children's IQ), ADHD-related symptoms (Hyperactivity and Attentional problems subscales of the BASC-2; Reynolds & Kamphaus, 2004); children's EF (measured with

the BRIEF; Gioia et al., 2003, and via the HTKS task; Ponitz et al., 2008); and children's academic functioning (WJ-III; Woodcock et al., 2001).

Results

Preliminary Analyses

Preliminary analyses examined any potential associations between demographic variables and the study's outcomes. There were no significant associations between demographics and the study's dependent variables. In particular, no sex differences emerged, $ts(61) = -1.705–1.963$, $ps = 0.054–0.737$. However, as seen in Table 1, a significant difference in IQ was found between children with ADHD and TD. For this reason, IQ was included as a covariate in subsequent analyses. No significant differences between groups were found in the total number of tokens and types produced by children and parents in the interactions, $ts(61) = 0.503–1.614$, $ps = 0.112–0.617$. Additionally, associations between child and parent types and tokens were examined (see Table 2). For both parents and children, a significant correlation between types and tokens within each category emerged; therefore, tokens and types of each category were included together as dependent variables in subsequent MANCOVAs.

Analyses of verbal production

Children

The results of the MANCOVAs run for the time category, revealed a significant multivariate effect of Group, $F(2, 59) = 3.67$, $p = 0.03$; $\eta^2 = 0.11$, and a non-significant effect of the covariate, $F(2, 59) = 1.77$, $p = 0.18$; $\eta^2 = 0.06$. Children with ADHD produced a significantly lower proportion of types of time-related terms compared to TD children, $F(1, 60) = 4.45$, $p = 0.04$, $d = 0.63$, whereas time-related tokens were similar across groups, $F(1, 60) = 1.03$, $p = 0.31$; $d = 0.21$. On the contrary, for both the math and space categories, the MANCOVAs lead to non-significant multivariate results for both Group, $F(2, 59) = 0.19$, $p = 0.83$; $\eta^2 = 0.01$ and $F(2, 59) = 0.05$, $p = 0.95$; $\eta^2 = 0.002$ respectively, and for the covariate, $F(2, 59) = 0.35$, $p = 0.71$; $\eta^2 = 0.01$ and $F(2, 59) = 0.78$, $p = 0.46$; $\eta^2 = 0.03$ respectively. Figure 1 represents the percentage of children's types and tokens in each category.

Table 2 Pearson correlations for types and tokens in the time, math and space categories, for (a) children and (b) parents

(a) Children	Math tokens	Time tokens	Space tokens	Math types	Time types
Time tokens	−0.02	–			
Space tokens	−0.07	−0.10	–		
Math types	0.88**	0.07	−0.10	–	
Time types	−0.004	0.86**	−0.15	0.02	–
Space types	−0.06	−0.06	0.73**	−0.09	−0.06
(b) Parents					
Time tokens	0.38**	–			
Space tokens	0.51**	0.32*	–		
Math types	0.71**	0.16	0.05	–	
Time types	−0.06	0.54**	−0.17	0.08	–
Space types	0.07	0.09	0.57**	−0.10	0.001

*$p < 0.05$; **$p < 0.01$.

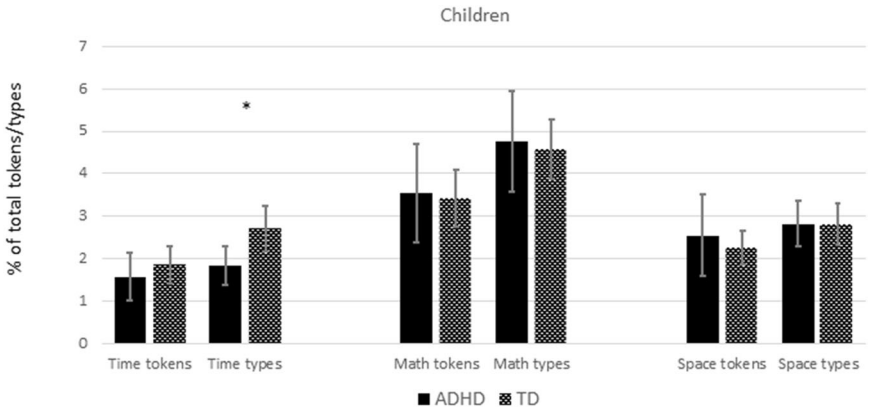

Fig. 1 Percentage of tokens and types in the time, math and space categories, produced by children with ADHD and with typical development (TD). *$p < 0.05$

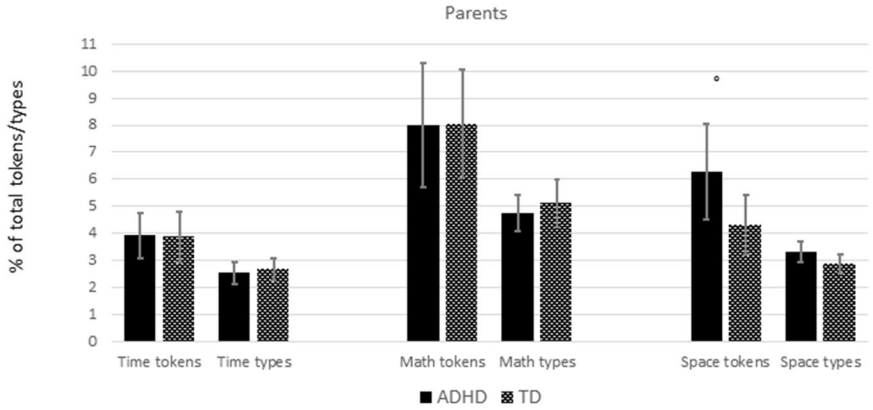

Fig. 2 Percentage of tokens and types in the time, math and space categories, produced by parents of children with ADHD and with typical development (TD). °$p = 0.052$

Parents

The analysis of parent's verbal production showed a non-significant effect of Group for all the categories considered: time-related terms, $F(2, 60) = 0.25$, $p = 0.78$; $\eta^2 = 0.01$, math-related terms, $F(2, 60) = 0.42$, $p = 0.66$; $\eta^2 = 0.01$, and space-related terms, $F(2, 60) = 2.13$, $p = 0.13$; $\eta^2 = 0.07$. It should be noted that, when looking at the univariate effects, a marginal significant effect of Group was found for the space-related tokens, $F(1, 61) = 3.92$, $p = 0.052$; $d = 0.50$, with parents of children with ADHD showing a higher number of words produced within the space category. The percentage of parents' types and tokens in each category are presented in Fig. 2.

Correlational Analyses

Pearson correlations between types and tokens in the time, math and space categories, and children's ADHD symptoms, executive functioning, and academic and cognitive functioning were performed.

Demographic factors

There were no significant associations between children's age, caregivers' level of instruction and the study's dependent variables.

ADHD symptoms

As seen in Table 3, children's time types were significantly correlated with parent rated attention problems, $r = -0.34$, $p = 0.006$. Children who showed more time types demonstrated less attention problems. No other child or parent tokens or types were significantly associated with ADHD symptoms.

Executive functioning

As seen in Table 3, children displaying a greater number of time types were reported by parents as having less EF problems as indicated by the BRIEF Plan-Organize Scale and Global Executive Functioning Composite, $r = -0.28$, $p = 0.029$ and $r = -0.31$, $p = 0.012$, respectively. Correlations between parent's verbal production and children's executive functioning variables revealed that more tokens of space-related words produced by parents was associated with weaker EF performance on the HTKS task, $r = -0.26$, $p = 0.04$.

Academic and cognitive functioning

As shown by Table 3, no significant correlations were found between children's verbal production and their academic and cognitive functioning. A significant correlation emerged between parent's tokens of space-related words and children's IQ, $r = -0.32$, $p = 0.01$, with greater use of space-related words by parents being related to lower child IQ.

Discussion

This study was primarily aimed at analyzing temporal cognition in preschoolers with ADHD, considering the lack of research on this topic. The language production—i.e., total number of terms within the time, math and space categories (tokens), and the diversity of these terms (types)—was examined during parent-child play interactions. Play sessions are ecologically valid situations which minimize problems related to the request of explicit time judgments to such young children (Droit-Volet, 2013). Results indicated that preschoolers with ADHD produced fewer types of time-related words and expressions compared to TD peers, whereas no group differences were found for math- and space-related terms. The secondary aim of the current study was to examine the associations between children's and parents' language production and children's ADHD symptoms, executive functioning, and academic and cognitive functioning. We found that a higher number of time-related types produced by children was linked to lower parent-rated attentional problems and lower executive functioning problems. Furthermore, more tokens

Table 3 Pearson correlations between types and tokens in the time, math and space categories, demographics and children's screening measures for (a) children and (b) parents

(a) Children		Time tokens	Math tokens	Space tokens	Time types	Math types	Space types
Demographics	Caregiver level of instruction	0.03	0.05	−0.06	−0.09	0.04	0.05
	Child's age	0.04	−0.11	0.04	0.04	−08	0.03
ADHD symptoms	BASC-2 hyperactivity	−0.06	0.02	0.10	−0.23	0.07	0.02
	BASC-2 attentional problems	−0.17	−0.04	0.10	−0.34**	0.002	0.02
Executive functioning	BRIEF plan-organize	−0.17	−0.10	−0.01	−0.28*	−0.09	−0.04
	BRIEF global executive functioning	−0.16	−0.01	0.04	−0.31*	0.03	−0.02
	HTKS	0.07	−0.07	−0.18	0.20	−0.02	−0.17
Academic and cognitive functioning	WJ-III achievement	0.13	0.04	−0.05	0.25	0.08	0.04
	IQ	0.03	0.07	−0.16	0.16	0.08	−0.06
(b) Parents							
Demographics	Caregiver level of instruction	0.05	0.18	−0.01	−0.01	0.06	0.09
	Child's age	−0.06	−0.22	−0.07	−0.06	−07	0.09
ADHD symptoms	BASC-2 hyperactivity	−0.10	−0.13	0.03	−0.10	−0.09	0.05
	BASC-2 attentional problems	−0.04	−0.07	0.19	−0.11	−0.10	0.19
Executive functioning	BRIEF plan-organize	−0.04	−0.02	0.17	−0.16	−0.10	0.10
	BRIEF global executive functioning	−0.05	0.03	0.22	−0.15	−0.08	0.12
	HTKS	−0.13	−0.15	−0.26*	−0.12	0.01	−0.20
Academic and cognitive functioning	WJ-III achievement	0.05	−0.06	−0.22	0.15	0.07	−0.22
	IQ	−0.23	−0.11	−0.32*	−0.07	−0.02	−0.14

Note: BASC-2 Behavior Assessment System for Children, 2nd Edition, *BRIEF* Behavior Rating Inventory of Executive Function, *HTKS* Head–toes–knees–shoulders task, *WJ-III* Woodcock–Johnson Test of Achievement, 3rd Edition.

$^{**}p < 0.01$; $^{*}p < 0.05$.

of space-related words produced by parents were associated with weaker EF performance showed by children on the HTKS task. Math-related words were not associated with ADHD symptoms, executive functioning, or academic and cognitive functioning. The implications of our findings are discussed below.

Our primary result, namely fewer types of time-related words used by children with ADHD relative to their TD peers, suggests that the time processing impairments characterizing ADHD (Noreika et al., 2013) emerge as early as the preschool age. The current study found early time processing deficits in children with ADHD in the quality (i.e., heterogeneity) of time-related language production, but not quantity. Furthermore, this gap between children with ADHD and TD was found exclusively for time-related words, as no significant differences emerged for words in the math- or space-categories. This is the first direct evidence of deficits in temporal cognition of children with ADHD as young as preschool.

The lower heterogeneity of time-related words found in preschoolers with ADHD could be related to the linguistic input received by their parents. In fact, it is expected that children's use of words and verbal expressions is closely tied to the communicative input they receive by their caregivers (e.g., Tomasello, 2009), especially for time-related words (Hudson, 2006; Levy & Nelson, 1994). However, the present study showed weaker production of time-related terms in children with ADHD compared to TD children in a context in which all parents produced similar amounts of temporal terms. This suggests that fewer types of temporal terms used by children with ADHD likely do not lie in the linguistic input they receive from their primary caregivers, rather are influenced by other variables. Considering the hypothesis that identifies time processing deficits as an independent neuropsychological component, and as an endophenotype of ADHD (Hwang-Gu & Gau, 2015; Sonuga-Barke et al., 2010), the reduced heterogeneity of temporal terms in preschoolers with ADHD may reflect this specific and early feature of ADHD. Also, it has been hypothesized that the use of temporal terms in young children could support the development of the temporal reasoning system (Tillman, 2019), and the assessment of children with a questionnaire investigating, among other time-related skills, their use of temporal terms, has been

found to be predictive of time processing skills measured with behavioral tasks (Tobia et al., 2019). This literature supports an important role the use of time-related words could have in the development of time-related skills. Furthermore, considering children with ADHD underperformed TD peers only in time-related terms, rather than all three categories, this result cannot be considered the consequence of the recognized comorbidity between ADHD and language deficits (Tirosh & Cohen, 1998).

Another result of the present study is the lack of differences found between the ADHD and TD groups in children's use of math and spatial words, which may be also related to the young age of our sample. In accordance with this interpretation, some studies showed that math difficulties in children with ADHD are a consequence of their attentional and EF deficits, and tend to emerge when children are exposed to academic requests during the school years (Zentall, 2007). A similar path has been demonstrated for space-related problems, which become stronger with age when compared to TD's skills (Westerberg et al., 2004). It is therefore possible that impairments in language production related to the math and space domains would emerge in the following years, but may not yet be detectable in preschoolers. Alternatively, it is also possible that math- and space-related deficits in ADHD would never affect children's language production but would emerge only in their performance in behavioral tasks and learning. Consistent with this hypothesis, the current study identified lower academic achievement in children with ADHD.

Secondary aim of this study was analyzing the association between the time-, math- and space-related words and core features characterizing ADHD, specifically EF and achievement. The current study only found significant associations between children's types of time-related terms and attention problems and executive functioning. These findings are consistent with past research showing the association of time processing with attention skills and EF (Droit-Volet & Zélanti, 2013; Zélanti & Droit-Volet, 2011). Our findings contribute to this emerging literature by demonstrating that a language measure of temporal cognition is correlated with attention and EF in young children. Additionally, the current study offers indirect evidence that a profile of high inattention and low EF, typical of ADHD, is associated with a weaker temporal cognition, corroborating the group differences found in the present sample of preschoolers.

As it relates to our analyses of parents' verbal production, we found a marginal effect in terms of higher use of space-related words by parents of children with ADHD. This may be a function of a greater use of commands as a way to manage their children's behavior. In fact, past studies have shown more frequent use of verbal direction and commands during interactions between caregivers and children with ADHD, compared to TD (Danforth et al., 1991). The present study's correlation analyses are partially in line with this interpretation. More tokens of space-related words were produced by parents of children with weaker EF and a lower IQ. Unexpectedly, parents' education level was not related to their verbal production categories. Considering past research demonstrating mothers with higher SES using longer utterances and more types of words when they talk to their children (Hoff, 2003), we expected significant correlations of parents' verbal production with this variable. However, the production of terms within the categories considered in the present study seems to be linked to children-level variables, more than to parents' education.

Many studies investigating time-related difficulties in children with ADHD used wide age-ranges and included only school-aged and older children (e.g., Houghton et al., 2011; Smith et al., 2002). The present study is the first investigation of temporal cognition, in terms of time-related verbal production, in preschoolers with ADHD. This responds to the need to clarify time periods for reliable assessments of specific deficits associated with ADHD (Pauli-Pott & Becker, 2011). In fact, our results suggest that the preschool years are an optimal developmental period for investigating time-related difficulties. Beyond the assessment of such time-related difficulties, time processing skills should be taken into consideration when planning early interventions to facilitate everyday functioning for children with cognitive impairments (Janeslätt et al., 2009). The individuation of time-related difficulties in children with ADHD as young as 4, suggests preschoolers may benefit from interventions aimed at improving time processing skills. This can be done, for example, by explicitly helping parents teach their children the meaning and appropriate use of time-related words and concepts, and by suggesting strategies for planning and time estimation, as bases of time management (e.g., Leech et al., 2019; Marlowe, 2000).

This study has some limitations. First, the use of a unique measure for assessing time-related difficulties, namely the verbal production within the time category, needs further validation. Indeed, future studies should include multiple measures of temporal cognition of preschoolers, such as targeted questionnaires for parents and teachers (e.g., Sense of time questionnaire; Tobia et al., 2018) as well as behavioral measures suitable for young children (e.g., temporal bisection tasks; Droit-Volet & Zélanti, 2013). Obtaining such a multimethod assessment is critical towards validating the role of time-related words produced by children as an index of their temporal cognition. Second, the small sample size of the study and the higher percentage of males in the ADHD compared to the TD group are significant limitations. Future studies should include a larger number of children per group, as well as samples properly matched for sex, to maximize power. Furthermore, a larger sample would allow to analyze possible differences in time-related skills in subgroups of children with ADHD, such as those with only-ADHD or ADHD *and* ODD, and to confirm effects that we found as only marginal (i.e.,

higher use of space-related words by parents of children with ADHD). Also, larger samples would allow to examine how contextual factors influence various aspects of parent–child interactions, included the use of temporal terms. Third, the majority of the sample was Hispanic/Latinx, which limits the generalizability of the results. To examine the extent to which our findings are applicable to non-Hispanic/non-Latinx children, these should be replicated in samples of preschoolers that differ in ethnicity. However, most studies on time-related impairments in school-aged children with ADHD involve non-Hispanic/Latinx white (Noreika et al., 2013); therefore, results of the present study offer some new evidence on time impairments in Hispanic/Latinx children with ADHD. Finally, to disentangle the direction of time related impairment and associated variables (ADHD symptoms and EF), a longitudinal study would be needed.

Despite these limitations, the current study has strengths. This study is the first to identify time related impairments in preschoolers with ADHD based upon expressed language. It is also the first to detect these deficits within the context of parent–child interactions, previously not investigated for this purpose within ADHD populations. Additionally, our study showed that significant associations between temporal cognition, attentional skills and EF can be identified in children as early as preschool. More work is needed, with future directions examining whether time-related deficits can be identified in preschoolers using multiple methods and exploring the developmental path of time processing impairment. Lastly, it will be important to examine whether multimodal early intervention programs that are effective with preschoolers with ADHD and their parents, such as the Summer Treatment Program for Pre-Kindergarteners (STP-Prek; Graziano & Hart, 2016), can also indirectly improve children's time-related skills, or whether focused ancillary interventions are needed to address this underlying impairment.

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Compliance with Ethical Standards

Conflict of Interest The authors declare no competing interests.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (Florida International University) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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SCIENTIFIC INVESTIGATIONS

The impact of lockdown on sleep patterns of children and adolescents with ADHD

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Study Objectives: The current study examined the impact of home confinement (lockdown) because of the COVID-19 pandemic on the sleep patterns of children and adolescents with attention-deficit hyperactivity disorder (ADHD).

Methods: Nine hundred ninety-two parents of children and adolescents with ADHD filled out an anonymous online survey through the ADHD family association website. The survey investigated the sleep patterns and disturbances (using a modified version of the Sleep Disturbance Scale for Children) and screen exposure time before and during lockdown.

Results: During lockdown, 59.3% of children and 69.4% of adolescents with ADHD reported a change of bedtime, with a significant increase in patients with ADHD who went to sleep at 11 PM or later. Sleep duration, in contrast, resulted in 2 opposing processes with more children and adolescents sleeping either less than 6 hours/night or 10–11 hours/night. Among children and adolescents, respectively, 19.9% and 22% slept less than they did before lockdown, whereas 21.4% and 27.4% slept for more hours. Bedtime delay and decreased sleep duration were associated with an increase in screen time exposure. Moreover, patients with ADHD reported an increase in sleep disturbances when compared to their previous condition, mainly including difficulties falling asleep, anxiety at bedtime, night awakenings, nightmares, and daytime sleepiness.

Conclusions: Lockdown impacted sleep-wake rhythms by strengthening the maladaptive sleep patterns reported in usual-life conditions in children and adolescents with ADHD.

Key words: COVID-19, attention-deficit hyperactivity disorders, sleep-wake patterns, sleep disorders, children, adolescents

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Children and adolescents with attention-deficit hyperactivity disorder are easily intolerant of forced restrictions and rules, which may result in them being particularly vulnerable to the lockdown experience and showing alterations of their sleep patterns. Furthermore, the limitations of activities and relationships because of lockdown may cause an increase in screen exposure time that may affect the sleep of patients with attention-deficit hyperactivity disorder.

Study Impact: Our findings highlight that lockdown impacted sleep-wake rhythms by strengthening the maladaptive sleep patterns reported in usual-life conditions in children and adolescents with attention-deficit hyperactivity disorder and significantly delayed bedtime and increased daytime screen exposure particularly in patients who reduced their sleep duration. The increase in sleep disturbances, mainly difficulties falling asleep, anxiety at bedtime, night awakenings, nightmares, and daytime sleepiness may further affect daytime functioning in children and adolescents with attention-deficit hyperactivity disorder.

INTRODUCTION

The lockdown restrictions for the COVID-19 pandemic has caused critical physical and mental health problems in the entire population because of social isolation and the impossibility of engaging in varied and satisfying activities.[1,2] One of the most frequently reported consequences caused by the confinement regards the alteration of sleep-wake rhythms in children, adolescents, and their families.[3,4] Considering the crucial role that sleep plays on developmental processes, the individuation of the impact of confinement on sleep-wake patterns and sleep disturbances has represented a crucial field of investigation for child and adolescent psychiatrists.

Based on previous studies, 2 important factors have associated the altered sleep patterns in children and adolescents and the adult population with lockdown: stress and anxiety linked to COVID-19 infection,[5] and the increased use of media and screen exposure because of the greatly reduced possibility of alternative activities.[3]

Most studies have been conducted on the general population, although it is reasonable to expect that patients with developmental disorders might be a population at higher risk.

Children and adolescents with attention-deficit hyperactivity disorder (ADHD) are often intolerant of forced restrictions and of accepting rules.[6] Therefore, changes imposed by lockdown with a lack of specific rhythms (school, sports, or leisure activities) can potentially promote critical variations in their sleep

patterns. Moreover, because the restrictions significantly limit pleasant activities, the consequent use of social media and television may represent an important aspect that interferes with a regular sleep schedule.[3,7] Understanding the impact of lockdown on the sleep of children and adolescents with ADHD and evaluating the factors that promote unhealthy changes represent a research area of high priority.

Therefore, the aims of this study were (1) to assess sleep patterns and sleep disturbances in Italian children and adolescents with ADHD confined at home during the COVID-19 pandemic, as compared to their sleep habits before confinement; and (2) to identify the relationship between screen exposure time and sleep patterns during the lockdown period.

METHODS

Participants

A total of 992 participants (male = 847 [85.4%], female = 145 [14.6%]; mean age, 11.52 years; standard deviation, 3.17) completed the survey. All parents with a child or adolescent who was diagnosed with ADHD by a child and adolescent psychiatrist were informed of the survey through the Italian ADHD Family Association website.

The total sample can be considered as representative for the entire Italian territory with a participation of all regions, 20 metropolitan cities, and 78.3% (72/92) of the Italian provinces. Data reported in this study were part of a wider research project designed with multiple purposes regarding the psychological impact of home confinement in Italy. There was no monetary or credit compensation for participating in the study. The study was approved by the Ethics Committee of the Department of Developmental and Social Psychology, Sapienza University, Rome and was conducted in accordance with the Declaration of Helsinki.

Procedures

An anonymous online survey to be completed by parents was arranged for this study to evaluate the effect of lockdown on sleep patterns and disturbances and on the use of social media and total daily screen exposure time in children and adolescents with ADHD.

Data were collected with a survey advertised through the national ADHD Family Association website, for a limited time window (from June 4–June 21, 2020), targeting patients with ADHD aged 5 to 18 years. Before accessing the survey, parents were asked to read the written consent form and to agree to participate in the study. Informed consent represented a required field for advancing in the compilation of the questionnaire.

The questions investigated sleep habits (duration and bedtime) and sleep disturbances to evaluate the differences before and during lockdown, along with the demographic information of the parent completing the survey (sex, caregiver education) and family composition. Moreover, screen exposure time (2–3 hours/day, half of the day, most of the day), excluding the hours spent for online lessons, and device preferences (video games, internet, television, mobile phones) were also assessed.

Instruments

The Sleep Disturbance Scale for Children by Bruni, Ottaviano, et al[8] investigates the occurrence of sleep disturbances based on 26 items in a Likert-type scale, with values 1–5 (higher numerical values reflect a higher clinical severity of symptoms). For the purpose of this study and to facilitate the compilation of responses by parents, we selected specific questions to evaluate the prevalence before and during lockdown. Some questions were grouped into 1 (ie, sleep-disordered breathing) and other questions, not relevant for the time period, were excluded. The final questionnaire was composed of 13 items.

Statistical analyses

Descriptive statistics were applied to characterize sociodemographic variables, sleep patterns, and sleep disturbances. Data were reported as frequencies and percentages. The McNemar nonparametric χ^2 test was used to compare sleep patterns and sleep disturbances and the use of social media, before and during lockdown.

To assess the changes occurring during lockdown, bedtime and sleep duration were recoded into 3 categories: bedtime was classified as delayed, anticipated, or no change, and sleep duration was classified as increased, decreased, or no change; a cross-tabulation analysis was then conducted between bedtime, sleep duration and screen exposure time.

The χ^2 test was used to compare children vs adolescents on sleep patterns and sleep disturbances during the lockdown. For all comparisons, P values < .05 were considered as statistically significant. Statistical analyses were performed using SPSS software release 17.0 (SPSS Inc., Chicago, IL).

RESULTS

The total sample was composed of 528 children (441 male (83.5%), 87 female (16.5%); age range, 5–11.11 years; mean age, 9.1 years; standard deviation, 1.63) and 464 adolescents (406 male (87.5%), 58 female (12.5%); age range, 12–17.1 years; mean age, 14.3 years; standard deviation, 1.92]. The sex composition of the 2 age groups was not statistically different ($\chi^2 = 3.130$; $P = .077$).

The family economic status of the entire sample was high in 3%, middle in 75.2%, and low in 21.8%. Mothers were the main compilers of the survey (88.6%).

As for the education level, the majority of compilers had a graduate (29%) or high school degree (52.6%); middle school was reported by 17.9% and elementary school by 0.5%. The family composition was reported as follows: parents with 1 offspring member, 31.3%; parents with 2 offspring members, 51.9%; parents with 3 offspring members, 13.3%; and parents with ≥ 4 offspring members, 3.5%.

During lockdown, we found a significant delay of bedtime in both children and adolescents: There was a significant reduction in the number of patients with ADHD who went to bed at 8–10 PM, with an increase in the number of patients with ADHD who went to bed at 11 PM or later (**Table 1**). Compared to children, there was a higher percentage of adolescent patients who went to bed ≥ 12 AM and a lower percentage at 8–10 PM and 10–11 PM (**Table 1**).

Table 1—Comparison of bedtime before and during lockdown in children and adolescents with ADHD and age groups comparison.

Bedtime		Before, n (%)	During, n (%)	χ^2	*P* <	C vs A	
						χ^2	*P* <
8–10 PM	C	452 (85.6)	165 (31.2)	285.003	.0001	42.3877	.0001
	A	239 (51.5)	64 (13.8)	169.140	.0001		
10–11 PM	C	66 (12.5)	176 (33.3)	66.006	.0001	10.135	.001
	A	151 (32.5)	112 (24.1)	7.482	.006		
11 PM–12 AM	C	7 (1.3)	136 (25.8)	117.871	.0001	0.330	NS
	A	49 (10.6)	127 (27.4)	38.006	.0001		
≥ 12 AM	C	5 (0.9)	41(7.8)	34.028	.0001	98.449	.0001
	A	22 (4.7)	152 (32.8)	126.068	.0001		

A = adolescents; ADHD = attention-deficit hyperactivity disorder; C = children; NS = not significant.

Bedtime was delayed in 59.3% (313/528) of children and 69.4% (322/464) of adolescents, and no change was reported by 40.7% (215/528) of children and 29.7% (138/464) of adolescents. Only 0.9% (4/464) of adolescents advanced their bedtime (**Figure 1**).

In contrast, with regard to sleep duration, we found trends in the opposite directions. There was an increased percentage of patients who slept < 6 hours/night (with higher rates in adolescents) and a higher rate of participants who slept ≥ 10–11 hours/night (with higher rates in children), whereas the percentage of patients who slept 8–9 hours per night decreased (**Table 2**).

During lockdown, sleep duration changed in 41.3% of children and in 49.4% of adolescents; in particular, sleep duration decreased in 19.9% and 22%, increased in 21.4% and 27.4%, and was maintained in 58.7% and 50.6% of children and adolescents, respectively (**Figure 2**).

Figure 3 reports the interaction between bedtime and sleep duration, showing that among patients who delayed bedtime, a high percentage of children (77.9%) and adolescents (82.7%) increased sleep duration but also that a high percentage of children (83.8%) and adolescents (89.2%) decreased sleep duration, and 44.2% of children and 53.6% of adolescents did not change sleep duration.

Figure 4 shows that among participants who did not change their bedtime, 22.1% of children and 15.7% of adolescents increased sleep duration, 16.2% of children and 9.8% of adolescents decreased sleep duration, and 55.8% of children and 46% of adolescents maintained the same sleep duration (**Figure 4**).

Finally, among 4 (0.9%) adolescents who anticipated bedtime, 2 increased sleep duration, 1 reduced it, and 1 maintained the same sleep duration.

Both children and adolescents with ADHD significantly increased the use of leisure screen time during lockdown, with the exception of the use of television (**Table S1** in the supplemental material). Age group comparison highlighted that children made greater use of television and that adolescents spent more time with the internet and their mobile phone (**Table S1**). Overall, we observed that 64.2% of children and 72% of adolescents spent half or most of the time/day in front of a screen.

Figure 1—Bedtime changes during lockdown.

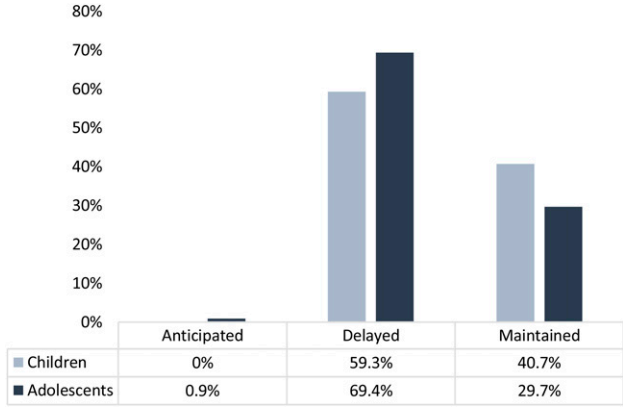


Table 3 reports the cross-tabulation between screen exposure time and delayed and maintained bedtime. Adolescents with bedtime delay used screen time most of the day at a significantly higher percentage than those who maintained the same bedtime. Conversely, children and adolescents who maintained their bedtime used screen time for 2–3 hours per day at a significantly higher percentage.

Table 4 includes the cross-tabulation between screen exposure time and sleep duration. Children and adolescents with a decreased sleep duration used screen time most of the day at a significantly higher percentage than those who maintained or increased sleep duration. Conversely, children and adolescents who maintained the same sleep duration used screen time for 2–3 hours per day at a significantly higher percentage.

Based on the Sleep Disturbance Scale for Children, during lockdown, both children and adolescents with ADHD showed an increase of sleep disturbances mainly related to falling asleep, anxiety at bedtime, night awakenings, and daytime sleepiness when compared to previous conditions (**Table 5**). In comparing the different age groups, we found that children reported an increase in nightmares, anxiety at bedtime, and bruxism, whereas adolescents showed an increase in daytime sleepiness (**Table 5**).

Table 2—Comparison of sleep duration before and during lockdown in children and adolescents with ADHD and age groups comparison.

Hours		Before, n (%)	During, n (%)	χ^2	*P* <	C vs A	
						χ^2	*P* <
< 6	C	14 (2.7)	28 (5.3)	—	.004*	18.604	.0001
	A	26 (5.6)	61 (13.1)	21.811	.0001		
6–7	C	78 (14.8)	85 (16.1)	.371	NS	5.590	.018
	A	132 (28.4)	102 (22)	5.923	.015		
8–9	C	318 (60.2)	269 (50.9)	12.909	.0001	2.991	NS
	A	271 (58.4)	210 (45.3)	20.112	.0001		
10–11	C	114 (21.6)	139 (26.3)	4.608	.032	10.680	.001
	A	31 (6.7)	82 (17.7)	30.120	.0001		
≥ 12	C	4 (0.8)	7 (1.3)	—	NS*	—	NS†
	A	4 (0.9)	9 (1.9)	—	NS*		

*McNemar binomial distribution. †χ^2 Fisher test in interage group comparison. A = adolescents; ADHD = attention-deficit hyperactivity disorder; C = children; NS = not significant.

Figure 2—Sleep duration changes during lockdown.

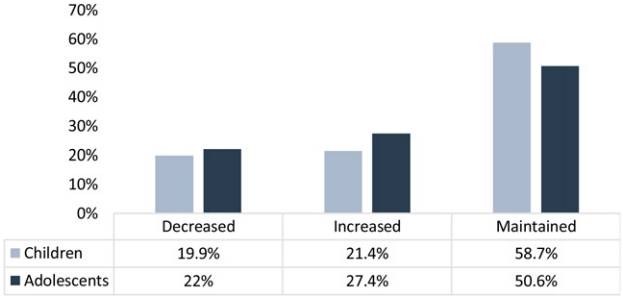
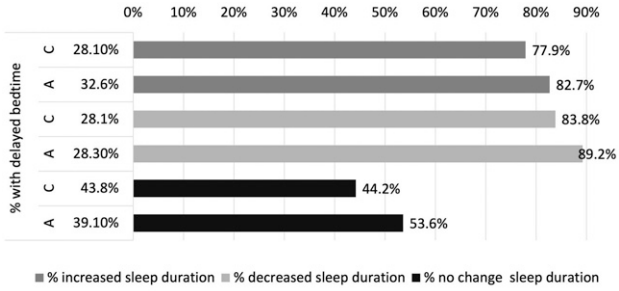


Figure 3—Cross-tabulation between bedtime delay and sleep duration.



A = adolescents, C = children.

Daytime sleepiness in patients who delayed their bedtime vs those who maintained their bedtime was significantly prevalent in children (60/313 = 19.2% vs 26/215 = 12.1%; $\chi^2 = 4.681$; $P = .031$) and in adolescents (113/322 = 35.1% vs 27/138 = 19.6%; $\chi^2 = 15.934$; $P < .001$). Furthermore, daytime sleepiness in patients who reduced their sleep duration vs those who maintained their sleep duration increased in children (29/105 = 27.6% vs 39/310 = 12.6%; $\chi^2 = 11.066$; $P = .004$) and in adolescents (44/102 = 43.1% vs 48/235 = 20.4%; $\chi^2 = 15.934$; $P < .001$). Interestingly, adolescents who increased their sleep duration (49/127 = 38.6%) also showed higher daytime sleepiness than those who maintained their sleep duration.

No differences were found for cosleeping (children, 23.7% vs 24.8%; adolescents, 7.8% vs 7.3%) and for the use of over-the-counter products for sleeping (children, 18% vs 19.5%; adolescents, 21.3% vs 21.1%).

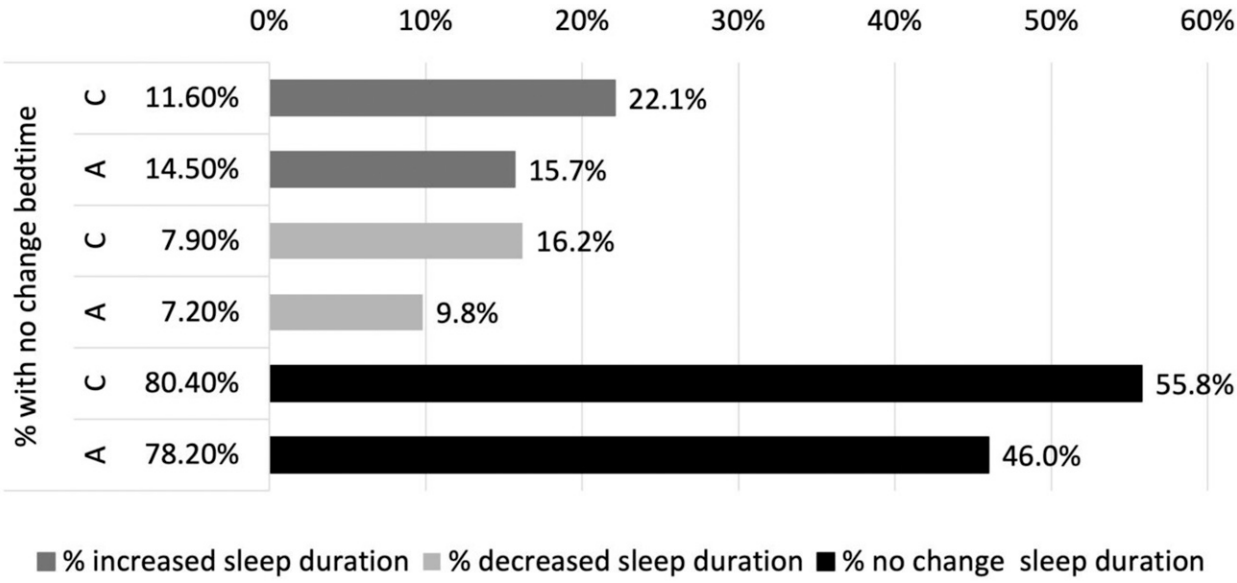
DISCUSSION

Our results show that lockdown restrictions for the COVID-19 pandemic affected the sleep-wake rhythm of patients with ADHD, disrupting in a dramatic way the previous habits of bedtime and sleep duration. Approximately 60% of children and 70% of adolescents reported a delay in their bedtime, and approximately 40% of children and 50% of children and adolescents also showed a significant change in their sleep duration. These percentages are higher than those reported among children and adolescents without ADHD.[7] Moreover, as reported in other studies in children and in the adult general population,[3,9,10] our results show that the delay of bedtime and reduced sleep duration were related with the increased time of screen exposure.

In general, accordingly with several reports conducted in preschool children[11] and in older children and adults,[3,12] the lockdown condition causes the disruption of previous sleep-wake habits, independently by age and mental health condition. Altogether, the lockdown seems to be a reinforcing factor of the maladaptive sleep habits and the instability of the sleep-wake system that have already been reported in patients with ADHD in general.[13] Different studies have reported an increase of sleep duration in children and adolescents without ADHD during lockdown,[5,12,14] probably because home confinement allowed a better alignment with their sleep requirements.[15,16]

Our findings provide further critical information and highlight that both children and adolescents who delayed bedtime

Figure 4—Cross-tabulation between maintained bedtime and sleep duration.



A = adolescents, C = children.

Table 3—Cross-tabulation of screen time use and bedtime.

	Screen Time								
	Most of the Day			Half-Day			2–3 H		
	% (n)	χ^2	*P*	% (n)	χ^2	*P*	% (n)	χ^2	*P*
Children									
Bedtime delayed	36.1 (113/313)	1.384	.239	33.5 (105/313)	4.304	.038	24.6 (77/313)	7.757	.005
Bedtime maintained	31.2 (67/215)	—	—	25.1 (54/215)	—	—	35.8 (77/215)	—	—
Adolescents									
Bedtime delayed	56.2 (181/322)	16.433	.0001	23.6 (76/322)	1.717	.424	13 (42/322)	29.422	.0001
Bedtime maintained	36.2 (50/138)	—	—	18.1 (25/138)	—	—	34.1 (47/138)	—	—

Table 4—Cross-tabulation of screen time use and sleep duration.

	Screen Time								
	Most of the Day			Half-Day			2–3 H		
	% (n)	χ^2	*P*	% (n)	χ^2	*P*	% (n)	χ^2	*P*
Children									
Duration increased	36.3 (41/113)	14.529	.001	29.2 (33/113)	0.271	.873	26.5 (30/113)	8.460	.015
Duration maintained	28.4 (88/310)	—	—	31.0 (96/310)	—	—	33.5 (104/310)	—	—
Duration decreased	48.6 (51/105)	—	—	28.6 (30/105)	—	—	19.0 (20/105)	—	—
Adolescents									
Duration increased	53.5 (88/127)	15.934	.0001	23.6 (30/127)	0.325	.850	13.4 (17/127)	15.884	.0001
Duration maintained	41.7 (98/235)	—	—	21.7 (51/235)	—	—	26.8 (63/235)	—	—
Duration decreased	64.7 (66/102)	—	—	20.6 (21/102)	—	—	10.8 (11/102)	—	—

Table 5—Comparison of sleep disturbances before and during lockdown in children and adolescents with ADHD and age groups comparison.

		Before, n (%)	During, n (%)	χ^2	*P* <	C vs A	
						χ^2	*P* <
Difficulty falling asleep	C	130 (24.6)	247 (46.8)	77.780	.0001	0.005	NS
	A	152 (32.8)	216 (46.6)	24.951	.0001		
Anxiety at bedtime	C	103 (19.5)	166 (31.4)	38.828	.0001	34.334	.0001
	A	56 (12.1)	72 (15.5)	5.114	.024		
Hypnic jerks	C	80 (15.2)	97 (18.4)	4.830	.028	3.807	.051
	A	59 (12.7)	64 (13.8)	0.485	NS		
Rhythmic movements	C	33 (6.3)	42 (8.0)	—	.078*	7.218	.007
	A	13 (2.8)	18 (3.9)	—	NS*		
> 2 awakenings/night	C	50 (9.5)	94 (17.8)	31.879	.0001	3.310	NS
	A	36 (7.8)	63 (13.6)	13.796	.0001		
Restless sleep	C	223 (42.2)	214 (40.5)	0.985	NS	2.584	NS
	A	160 (34.5)	165 (35.6)	0.254	NS		
Snoring/apnea	C	33 (6.3)	31 (5.9)	—	NS*	0.630	NS
	A	41 (8.8)	33 (7.1)	—	NS*		
Sleepwalking	C	38 (7.2)	46 (8.7)	—	NS*	5.381	.020
	A	29 (6.3)	23 (5)	—	NS*		
Sleep terrors	C	28 (5.3)	27 (5.1)	—	NS*	5.044	.025
	A	10 (2.2)	11 (2.4)	—	NS*		
Bruxism	C	91 (17.2)	82 (15.5)	1.939	NS	10.932	.001
	A	60 (12.9)	40 (8.6)	12.033	.001		
Nightmares	C	80 (15.2)	132 (25)	27.094	.0001	25.891	.0001
	A	49 (10.6)	57 (12.3)	1.633	NS		
Daytime sleepiness	C	61 (11.6)	86 (16.3)	6.940	.008	27.824	.0001
	A	90 (19.4)	141 (30.4)	26.882	.0001		

*Binomial distribution. A = adolescents; ADHD = attention-deficit hyperactivity disorder; C = children; NS = not significant.

showed either an increased or a decreased sleep duration. However, only the participants with ADHD who delayed bedtime and decreased sleep duration reported an increased time of screen exposure. It is noteworthy that in other studies in children and in the adult general population,[3,8,9] delayed bedtime was related to screen exposure but sleep duration remained unchanged or increased.

Furthermore, we observed an increase in daytime sleepiness that was related, in both age groups, with a bedtime delay and a decrease of sleep duration. In adolescents, we also saw an increase in daytime sleepiness that was associated with an increase in sleep duration.

This finding is alarming considering that in Italy, regular academic activities at school have been interrupted for adolescents, and the persistence of this condition could represent a risk factor for the stabilization of disrupted sleep patterns and screen addiction. A further critical data point is the increase of sleep disturbances recorded during the lockdown. Under normal conditions, several studies reported a high prevalence of parent-reported sleep disturbances in school-aged children with ADHD,[17–19] with approximately one-third of children who experienced chronic sleep-onset insomnia,[20] night awakenings, restless sleep, and difficult morning awakening.[13,17,21–23] Our findings highlight that lockdown also increased the vulnerability to sleep disturbances common among children and adolescents with ADHD, with the aggravating circumstance of anxiety at bedtime and nightmares presumably linked to worries about COVID-19 infection.

Some limitations of this study must be acknowledged. First, we did not specifically evaluate the influence of psychiatric comorbidity, and therefore we cannot exclude the influence of psychiatric comorbidity on habits and sleep disorders. Second, although the survey was conducted after only a few days from the end of strict lockdown and in the presence of lighter restrictions, we cannot exclude a memory bias of the parents. Nevertheless, the large sample size of our study, representative of the Italian population with ADHD, makes us confident that our findings reflect the impact of the lockdown experience on the sleep patterns of this population. The major challenge after the pandemic will be to identify its sequelae and to assess whether patients with ADHD will experience long-term disrupted sleep habits. It is crucial that sleep concerns be part of research initiatives aimed at mitigating the consequences of COVID-19 pandemic–related restrictions in children and adolescents with ADHD.

ABBREVIATION

ADHD, attention-deficit hyperactivity disorder

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DISCLOSURE STATEMENT

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