NEWSLETTER

INDICE:

BIBLIOGRAFIA ADHD GIUGNO 2021

Am J Epidemiol. 2021 Jun;190:1047-55.

THE EFFECT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER ON PHYSICAL HEALTH OUTCOMES: A 2-SAMPLE MENDELIAN RANDOMIZATION STUDY.

Leppert B, Riglin L, Wootton RE, et al.

Attention-deficit/hyperactivity disorder (ADHD) is associated with a broad range of physical health problems. Using different research designs to test whether ADHD has a causal role in these associations is important because comorbid health problems increase the serious social and economic impacts of ADHD. We used 2-sample Mendelian randomization (MR) to infer causal relationships between ADHD and previously implicated physical health conditions. Different MR methods were used to test the robustness and plausibility of our findings. Consistent findings underwent bidirectional and multivariable MR. We found evidence of ADHD having a causal effect on childhood obesity (odds ratio = 1.29, 95% confidence interval: 1.02, 1.63) and coronary artery disease (odds ratio = 1.11, 95% confidence interval: 1.03, 1.19) with consistent results across MR approaches. There was additional MR evidence for a bidirectional relationship between ADHD and childhood obesity. The relationship with coronary artery disease attenuated when controlling for childhood obesity. There was little evidence for inferring a causal effect on other cardiometabolic, autoimmune, allergic, and neurological diseases. Our findings strengthen the argument for effective treatment of children with ADHD, and suggest that clinicians who manage ADHD need to be aware of the risk of childhood obesity to reduce future risks of coronary artery disease

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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.

Anal Methods. 2021 Jun;13:2434-41.

DETERMINATION OF ATOMOXETINE LEVELS IN HUMAN PLASMA USING LC-MS/MS AND CLINICAL APPLICATION TO CHINESE CHILDREN WITH ADHD BASED ON CPIC GUIDELINES.

Xia Y, Guo HL, Hu YH, et al.

The Clinical Pharmacogenetic Implementation Consortium (CPIC) guidelines for personalized atomoxetine therapy are based on the CYP2D6 genotype information and the peak plasma concentrations of atomoxetine. Therefore, a highly rapid, sensitive, and reproducible method is critical for the clinical implementation of the guidelines. In this study, an LC-MS/MS approach was developed and validated for the determination of atomoxetine levels in human plasma using atomoxetine-d3 as the internal standard. Samples were prepared by simple protein precipitation method with MeOH. The analyte was separated using a Kinetex C18 column (2.1 mm × 50 mm, 2.6 μm, Phenomenex) with a flow rate of 0.25 mL min-1, using a gradient elution. A MeOH and water solution containing 5 mM ammonium acetate and 0.1 mM formic acid (pH 6.26) was used as the mobile phase and successfully solved the problem of inconsistent retention time between the plasma samples and the solution samples of atomoxetine. Detection was performed under positive-electrospray-ion multiple reaction-monitoring mode using the 256.4 → 43.8 and 259.3 → 47.0 transitions for atomoxetine and atomoxetine-d3, respectively. Linearity was achieved using an extremely wide range, from 0.500 to 2000 ng mL-1 in plasma. The intra- and inter-batch precision and accuracy, dilution accuracy, recovery, and stability of the method were all within the acceptable limits and no matrix effect was observed. With a complex needle wash solution containing ACN : MeOH : isopropanol : H2O (4 : 4:1 : 1, v/v/v/v), carryover contamination was eliminated successfully. This method was successfully implemented on pediatric patients with attention-deficit/hyperactivity disorder and provided valuable information to enable clinicians to do dose selection and titration

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Biol Psychol. 2021 May;162.

SOCIAL AND NON-SOCIAL GAZE CUEING IN AUTISM SPECTRUM DISORDER, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND A COMORBID GROUP.

Seernani D, Ioannou C, Damania K, et al.

Recent trends in literature, along with the changes to the Diagnostic and Statistical Manual (DSM), make it imperative to study Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) together, in order to better understand potential aetiological commonalities between these highly comorbid disorders. The present study examines social cueing, a highly studied construct in ASD, and intra-subject variability (ISV), a potential endophenotype of ADHD, in four groups of typically developing (TD), ADHD, ASD- (ASD without ADHD), ASD+ (ASD with ADHD) participants (N = 85) aged 10–13 years. Results showed that social cueing is intact in the 'pure' ASD group when task expectations are clear. The ADHD group showed faster saccadic reaction times, no increased ISV and a pattern of viewing comparable to the TD group. However, the ASD + group showed a differences in processing style and ISV. A secondary analysis gives evidence of non-additive effects of the ASD and ADHD factors. (PsycInfo Database Record (c) 2021 APA, all rights reserved)

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BMC Psychiatry. 2021 Jun;21:316.

ADHD SYMPTOMATOLOGY OF CHILDREN WITH CONGENITAL HEART DISEASE 10 YEARS AFTER CARDIAC SURGERY: THE ROLE OF AGE AT OPERATION.

Czobor NR, Ocsovszky Z, Roth G, et al.

Background: The aim of the present study was to investigate the differences in ADHD symptomatology between healthy controls and children who underwent cardiac surgery at different ages.

Methods: Altogether, 133 children (54 patients with congenital heart disease undergoing first cardiac surgery under 3 years of age, 26 operated at the age of 3 or later, and 53 healthy controls) were examined. Patients completed the Youth Self Report (YSR), while their parents completed the Child Behaviour Checklist (CBCL) and the ADHD Rating Scale-IV.

Results: Children receiving surgery for the first time under the age of 3 years were more likely diagnosed with cyanotic type malformation and have undergone to a greater number of operations. However, ADHD symptoms of those treated surgically at or above 3 years of age were more severe than that of the control group or those who were treated surgically at a younger age. The control group and those treated surgically below the age of three did not differ across any of the ADHD symptom severity indicators.
Conclusions: The age at the time of cardiac surgery might be associated with later ADHD symptom severity - with lower age at operation associated with better outcomes. Further, adequately powered studies are needed to confirm these exploratory findings and investigate the moderators of this relationship.

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BMJ Open. 2021 Jun;11:e050541.

ADJUVANT EFFECTS OF VITAMIN A AND VITAMIN D SUPPLEMENTATION ON TREATMENT OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A STUDY PROTOCOL FOR A RANDOMISED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, MULTICENTRIC TRIAL IN CHINA.

Zhou P, Wolraich ML, Cao AH, et al.

INTRODUCTION: Approximately 7.2% of children in the world suffer from attention-deficit/hyperactivity disorder (ADHD). Due to the availability of the osmotic-release oral-system methylphenidate, ADHD currently has a remission rate of up to 30.72%. Nevertheless, it has been reported that patients with ADHD tend to exhibit vitamin A and vitamin D deficiency, which may aggravate the symptoms of ADHD. This study aims to determine the effect of vitamin A and vitamin D supplementation as adjunctive therapy to methylphenidate on the symptoms of ADHD.
METHODS AND ANALYSIS: This is a parallel, prospective, interventional multicentric study. Patients will be enrolled from the southern, central and northern parts of China. A target of 504 patients will be followed for 8 weeks. They will be allocated into three groups (vitamin AD, vitamin D and placebo) and administered the interventions accordingly. Data on changes in the symptoms of ADHD as well as changes in the serum concentrations of vitamin A and vitamin D will be recorded. Both responders and nonresponders based on the sociodemographic and clinical data will also be described to mitigate selection bias.
ETHICS AND DISSEMINATION: This study is performed in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Children's Hospital of Chongqing Medical University, China (approval number: (2019) IRB (STUDY) number 262). The results of the trial will be reported in peer-reviewed scientific journals and academic conferences regardless of the outcomes.
TRIAL REGISTRATION NUMBER: NCT04284059

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BMJ Open. 2021 Jun;11:e049165.

BALANCED GROWTH PROJECT: A PROTOCOL OF A SINGLE-CENTRE OBSERVATIONAL STUDY ON THE INVOLVEMENT OF THE VESTIBULAR SYSTEM IN A CHILD'S MOTOR AND COGNITIVE DEVELOPMENT.

Van HR, Deconinck FJA, Wiersema JR, et al.

INTRODUCTION: The involvement of the vestibular system in the motor and higher (cognitive) performances of typically developing or vestibular-impaired children is currently unknown or has only scarcely been explored. Interestingly, arguments for an interaction between vestibular, motor and cognitive functions in children can also be supported by research on children known for their difficulties in motor and/or cognitive processing (eg, children with neurodevelopmental disorders (NDD)), as they often present with vestibular-like characteristics. Therefore, in order to elucidate this interaction, and to increase the understanding of the pathophysiology and symptomatology of vestibular disorders and NDD in children, the Balanced Growth project was developed. It includes the following objectives: (1) to understand the association between motor skills, cognitive performances and the vestibular function in typically developing school-aged children, with special focus on the added value of the vestibular system in higher cognitive skills and motor competence; (2) to investigate whether a vestibular dysfunction (with/without an additional auditory disease) has an impact on motor skills, cognitive performances and motor-cognitive interactions in children and (3) to assess if an underlying vestibular dysfunction can be identified in school-aged children with NDD, with documentation of the occurrence and characteristics of vestibular dysfunctions in this group of children using an extensive vestibular test battery.

METHODS AND ANALYSIS: In order to achieve the objectives of the observational cross-sectional Balanced Growth study, a single-task and dual-task test protocol was created, which will be performed in three groups of school-aged children (6-12 years old): (1) a typically developing group (n=140), (2) (audio) vestibular-impaired children (n=30) and (3) children with an NDD diagnosis (n=55) (ie, autism spectrum disorder, attention deficit/hyperactivity disorder and/or developmental coordination disorder). The test protocol consists of several custom-made tests and already existing validated test batteries and includes a vestibular assessment, an extensive motor assessment, eight neurocognitive tests, a cognitive-motor interaction assessment and includes also additional screenings to control for potential confounding factors (eg, hearing status, intelligence, physical activity, etc).
ETHICS AND DISSEMINATION: The current study was approved by the ethics committee of Ghent University Hospital on 4 June 2019 with registration number B670201940165 and is registered at Clinical Trials (clinicaltrials.gov) with identifier NCT04685746. All research findings will be disseminated in peer-reviewed journals and presented at vestibular as well as multidisciplinary international conferences and meetings.
TRIAL REGISTRATION NUMBER: NCT04685746

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BMJ Open. 2021 Jun;11:e045868.

LINKING COHORT-BASED DATA WITH ELECTRONIC HEALTH RECORDS: A PROOF-OF-CONCEPT METHODOLOGICAL STUDY IN HONG KONG.

Gao L, Leung MTY, Li X, et al.

OBJECTIVES: Data linkage of cohort-based data and electronic health records (EHRs) has been practised in many countries, but in Hong Kong there is still a lack of such research. To expand the use of multisource data, we aimed to identify a feasible way of linking two cohorts with EHRs in Hong Kong.
METHODS: Participants in the 'Children of 1997' birth cohort and the Chinese Early Development Instrument (CEDI) cohort were separated into several batches. The Hong Kong Identity Card Numbers (HKIDs) of each batch were then uploaded to the Hong Kong Clinical Data Analysis and Reporting System (CDARS) to retrieve EHRs. Within the same batch, each participant has a unique combination of date of birth and sex which can then be used for exact matching, as no HKID will be returned from CDARS. Raw data collected for the two cohorts were checked for the mismatched cases. After the matching, we conducted a simple descriptive analysis of attention deficit hyperactivity disorder (ADHD) information collected in the CEDI cohort via the Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour Scale (SWAN) and EHRs.
RESULTS: In total, 3473 and 910 HKIDs in the birth cohort and CEDI cohort were separated into 44 and 5 batches, respectively, and then submitted to the CDARS, with 100% and 97% being valid HKIDs respectively. The match rates were confirmed to be 100% and 99.75% after checking the cohort data. From our illustration using the ADHD information in the CEDI cohort, 36 (4.47%) individuals had ADHD-Combined score over the clinical cut-off in the SWAN survey, and 68 (8.31%) individuals had ADHD records in EHRs.
CONCLUSIONS: Using date of birth and sex as identifiable variables, we were able to link the cohort data and EHRs with high match rates. This method will assist in the generation of databases for future multidisciplinary research using both cohort data and EHRs

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British Journal of Educational Psychology. 2021 Jun;91:755-74.

TRAJECTORIES OF ACADEMIC ACHIEVEMENT FOR STUDENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lawrence D, Houghton S, Dawson V, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is associated with negative social and occupational outcomes across the life course. However, there has been limited population-based research that quantifies the impact of ADHD on academic achievement and academic trajectories.
Aims: To compare academic performance and academic trajectories of students with ADHD with students without a mental disorder.
Sample: Data were drawn from Young Minds Matter, a national population-based sample of 6,310 Australian children and adolescents aged 4–17 years. Using linked achievement test data, the academic performance and trajectories of 327 students with ADHD were compared with those of 3,916 students without a mental

disorder. Methods: Survey data were combined with scores on national standardized tests for literacy and numeracy over an 8-year period.
Results: In Year 3, students with ADHD were on average 1 year behind students with no mental disorder in reading and numeracy, and 9 months behind in writing. In Year 9, the gaps were much larger with students with ADHD on average 2.5 years behind in reading, 3 years behind in numeracy, and 4.5 years behind in writing.
Conclusions: Students with ADHD have substantially lower achievement in reading, writing, and numeracy. Writing was the most adversely affected domain. For example, in Year 9 students with ADHD were on average writing at a Year 5 level. Children and adolescents with ADHD need substantial support to manage inattention, impulsivity, and hyperactivity. Skilled remediation in literacy and numeracy is required throughout all school years

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Child Adolesc Psychiatr Clin North Am. 2021 Apr;30:349-60.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND THE DYSREGULATION OF EMOTION GENERATION AND EMOTIONAL EXPRESSION.

Blader JC.

Individuals with attention-deficit/hyperactivity disorder (ADHD) frequently experience strong reactions to emotionally evocative situations. Difficulties modulating anger and other upsets have clinically significant behavioral consequences. Those with ADHD may have anomalies in emotion generation, emotion expression, or both that predispose to these problems. The association between ADHD and emotion dysregulation raises Important clinical and research issues, including possible heterogeneity in the mechanisms by which they are related. Although first-line treatments for ADHD often help to resolve emotional dysregulation symptoms as well, the evidence base for widespread practice of combination pharmacotherapy remains sparse. Psychosocial treatments that engage processes underlying emotional dysregulation are in development

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Child Psychiatry Hum Dev. 2021 Jun;52:355-64.

A LATENT CLASS ANALYSIS OF PERCEIVED NEIGHBORHOOD CONDITIONS ASSOCIATED WITH MENTAL DISORDERS AMONG CHILDREN IN THE UNITED STATES.

Li X, Fu Q, Leigh I, et al.

The current study examined the association between perceived neighborhood conditions and common childhood mental disorders in a nationally representative sample of children in the U.S. The data were derived from the 2017 National Survey of Children's Health, including American children aged 6-17 years (N=15,438). Latent class analysis was used to identify subtypes of perceived neighborhood conditions regarding neighborhood physical environment, social capital, and violence. Three classes were identified: Ideal Neighborhood (55.99%); Insufficient Assets (27.38%), and Broken and Unsafe Neighborhood (16.63%). The effects of latent classes on psychiatric outcomes (i.e. attention deficit hyperactivity disorder, depression, anxiety, conduct problem, and any of these four disorders) were examined. Class membership was differentially associated with the mental disorders after adjustment for demographic variables, food insufficiency, and guardian's mental health. The Broken and Unsafe Neighborhood class was associated with greater odds of all childhood psychiatric disorders than the Ideal Neighborhood and Insufficient Assets class. Insufficient Assets class was associated with greater odds of all childhood psychiatric disorders than the Ideal Neighborhood class. The findings suggest that neighborhood-level interventions to decrease children's mental health burdens are critically needed

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Dev Cognitive Neurosci. 2021 Jun;49.

IS THERE ANY INCREMENTAL BENEFIT TO CONDUCTING NEUROIMAGING AND NEUROCOGNITIVE ASSESSMENTS IN THE DIAGNOSIS OF ADHD IN YOUNG CHILDREN? A MACHINE LEARNING INVESTIGATION.

Öztekin I, Finlayson MA, Graziano PA, et al.

Given the negative trajectories of early behavior problems associated with ADHD, early diagnosis is considered critical to enable intervention and treatment. To this end, the current investigation employed machine learning to evaluate the relative predictive value of parent/teacher ratings, behavioral and neural measures of executive function (EF) in predicting ADHD in a sample consisting of 162 young children (ages 4–7, mean age 5.55, 82.6 % Hispanic/Latino). Among the target measures, teacher ratings of EF were the most predictive of ADHD. While a more extensive evaluation of neural measures, such as diffusion-weighted imaging, may provide more information as they relate to the underlying cognitive deficits associated with ADHD, the current study indicates that measures of cortical anatomy obtained in research studies, as well cognitive measures of EF often obtained in routine assessments, have little incremental value in differentiating typically developing children from those diagnosed with ADHD. It is important to note that the overlap between some of the EF questions in the BRIEF, and the ADHD symptoms could be enhancing this effect. Thus, future research evaluating the importance of such measures in predicting children's functional impairment in academic and social areas would provide additional insight into their contributing role in ADHD

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Eat Weight Disord. 2021 Jun;26:1491-501.

RESTRICTIVE EATING DISORDERS IN CHILDREN AND ADOLESCENTS: A COMPARISON BETWEEN CLINICAL AND PSYCHOPATHOLOGICAL PROFILES.

Zanna V, Criscuolo M, Mereu A, et al.

PURPOSE: DSM-5 describe three forms of restrictive and selective eating: Anorexia Nervosa-Restrictive (AN-R), Anorexia Nervosa-Atypical (AN-A), and Avoidant/Restrictive Food Intake Disorder (ARFID). While AN is widely studied, the psychopathological differences among these three diseases are not clear. The aim of this study was to (i) compare the clinical features of AN-R, AN-A, and ARFID, in a clinical sample recruited from a specialized EDs program within a tertiary care children's Hospital; (ii) identifying three specific symptom profiles, to better understand if restrictive ED share a common psychopathological basis.

METHODS: Data were collected retrospectively. Psychometric assessment included: the Children's Depression Inventory (CDI), the Multidimensional Anxiety Scale for Children (MASC), the Child Behavior Checklist (CBCL), and the Eating Disorder Inventory-3 (EDI-3).

RESULTS: A final sample of 346 children and adolescent patients were analyzed: AN-R was the most frequent subtype (55.8%), followed by ARFID (27.2%) and AN-A (17%). Patients with ARFID presented different features from AN-R and AN-A, characterized by lower weight and medical impairment, younger age at onset, and a frequent association with separation anxiety and ADHD symptoms. EDI-3 profiles showed specific different impairment for both AN groups compared to ARFID. However, no differences was detected for items: 'Interpersonal Insecurity', "Interoceptive Deficits", "Emotional Dysregulation", and "Maturity Fears".

CONCLUSIONS: Different ED profiles was found for the three groups, but they share the same general psychopathological vulnerability, which could be at the core of EDs in adolescence.

LEVEL OF EVIDENCE: III. Evidence obtained from case-control analytic studies

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Ecotoxicol Environ Saf. 2021 Sep;220:112391.

A CROSS-SECTIONAL SURVEY OF PRESCHOOL CHILDREN: EXPLORING HEAVY METAL EXPOSURE, NEUROTRANSMITTERS, AND NEUROBEHAVIOURAL RELATIONSHIPS AND MEDIATION EFFECTS.

He B, Wang Y, Li S, et al.

Background: Exposure to heavy metals has been considered harmful and can cause cognitive deficits in preschool children.

Objective: To investigate the possible mediation effect of neurotransmitters on the relationship of heavy metal exposure with neurobehaviour.

Methods: The levels of blood heavy metals and neurotransmitters, along with the neurobehavioural scores, were determined in preschool children. Multiple linear regression was used to assess the relationship

between heavy metals, neurotransmitters, and neurobehavioural scores. Furthermore, the mediating role of neurotransmitters was investigated.
Results: An interquartile range (IQR) increase in lead (6.10 µg/L) was associated with a decrease of 8.52%, 30.06%, and 20.10% for Glutamic acid (Glu), Glycine (Gly), and gamma-aminobutyric acid (GABA), respectively. An IQR increase in arsenic (19.37 µg/L) was associated with an increase of 6.32% and 2.09% for Gly and GABA, respectively. Further, an IQR increase in zinc (15.58 µg/L) was associated with an increase of 1.44% for Ser, whereas the IQR increase was associated with a decrease of 2.14%, 2.24%, and 1.89% for Glu, Gly, and GABA, respectively. An IQR increase in selenium (38.75 µg/L) was associated with an increase of 1.88% for GABA. Moreover, both Glu and Gly decreased by 2.87% for an IQR increase in manganese (16.92 µg/L). An IQR increase in mercury (15.22 µg/L) was associated with a decrease of 2.43% for Ser, but the IQR increase was associated with an increase of 4.99% and 3.09% for Gly and GABA, respectively. It was found that Glu and Serine (Ser) have a significant linear relationship with conduct score and impulsivity-hyperactivity index, and that there was a significant linear relationship between Ser and the learning disability index. GABA and conduct score and attention-deficit hyperactivity disorder (ADHD) index have a significant linear relationship. There is a significant linear relationship between Gly and conduct, anxiety, ADHD, and impulsivity-hyperactivity index. The results of the mediating effect analysis indicated that Ser, Glu, Gly, and GABA have a specific mediating effect between blood heavy metals and neurobehaviour.
Conclusion: We showed the mediating effect of neurotransmitters. The current study may provide valuable information regarding the prevention and management of metal-related neurological disorders in preschool children

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Environ Int. 2021 Aug;153:106523.
EARLY-LIFE ENVIRONMENTAL EXPOSURE DETERMINANTS OF CHILD BEHAVIOR IN EUROPE: A LONGITUDINAL, POPULATION-BASED STUDY.
Maitre L, Julvez J, LÃ³pez-Vicente M, et al.
BACKGROUND: Environmental exposures in early life influence the development of behavioral outcomes in children, but research has not considered multiple exposures. We therefore aimed to investigate the impact of a broad spectrum of pre- and postnatal environmental exposures on child behavior.
METHODS AND FINDINGS: We used data from the HELIX (Human Early Life Exposome) project, which was based on six longitudinal population-based birth cohorts in Europe. At 6-11Â years, children underwent a follow-up to characterize their exposures and assess behavioral problems. We measured 88 prenatal and 123 childhood environmental factors, including outdoor, indoor, chemical, lifestyle and social exposures. Parent-reported behavioral problems included (1) internalizing, (2) externalizing scores, using the child behavior checklist (CBCL), and (3) the Conner's Attention Deficit Hyperactivity Disorder (ADHD) index, all outcomes being discrete raw counts. We applied LASSO penalized negative binomial regression models to identify which exposures were associated with the outcomes, while adjusting for co-exposures. In the 1287 children (mean age 8.0Â years), 7.3% had a neuropsychiatric medical diagnosis according to parent's reports. During pregnancy, smoking and car traffic showing the strongest associations (e.g. smoking with ADHD index, aMR:1.31 [1.09; 1.59]) among the 13 exposures selected by LASSO, for at least one of the outcomes. During childhood, longer sleep duration, healthy diet and higher family social capital were associated with reduced scores whereas higher exposure to lead, copper, indoor air pollution, unhealthy diet were associated with increased scores. Unexpected decreases in behavioral scores were found with polychlorinated biphenyls (PCBs) and organophosphate (OP) pesticides.
CONCLUSIONS: Our systematic exposome approach identified several environmental contaminants and healthy lifestyle habits that may influence behavioral problems in children. Modifying environmental exposures early in life may limit lifetime mental health risk

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Environ Int. 2021 Sep;154:106549.

PREGNANCY EXPOSURE TO ORGANOPHOSPHATE ESTERS AND THE RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN THE NORWEGIAN MOTHER, FATHER AND CHILD COHORT STUDY.

Choi G, Keil AP, Richardson DB, et al.

BACKGROUND: Organophosphate esters (OPEs) are a class of flame retardants in common use. OPEs can easily leach from materials, resulting in human exposure. Increasing concentrations have been reported in human populations over the past decade. Recent studies have linked prenatal OPE exposure to hyperactivity and attention problems in children. Such behaviors are often found among children with attention-deficit hyperactivity disorder (ADHD), however, no study has investigated OPEs in relation to clinically assessed ADHD.

OBJECTIVE: To evaluate prenatal exposure to OPEs as risk factors for clinically assessed ADHD using a case-cohort study nested within the Norwegian Mother, Father, and Child Cohort Study (MoBa).

METHODS: We included in the case group 295 ADHD cases obtained via linkage with the Norwegian Patient Registry, and the sub-cohort group 555 children sampled at baseline, irrespective of their ADHD case status. Prenatal concentrations of OPE metabolites were measured in maternal urine collected at 17 weeks of gestation, and included diphenyl phosphate (DPHP), di-n-butyl phosphate (DNBP), bis (2-butoxyethyl) hydrogen phosphate (BBOEP), and bis (1,3-dichloro-2-propyl) phosphate (BDCIPP). We estimated risk ratios and the corresponding 95% confidence intervals [95% CI] using logistic regression, adjusting for season of urine collection, child sex, birth year, and maternal depression, education, and sum of urinary di(2-ethylhexyl) phthalate metabolites (DEHP) concentration during pregnancy. To assess the overall impact of simultaneously decreasing exposure to all chemical constituents of an OPE-phthalate mixture, quantile based g-computation was implemented. The mixture constituents included OPE and phthalate metabolites commonly detected in our study. In all models, we considered effect measure modification by child sex and polymorphisms in genes encoding paraoxonase 1 (PON1) and cytochrome P450 (P450) enzymes. Mediation analysis was conducted using thyroid function biomarkers estimated from maternal blood collected at 17 weeks of gestation.

RESULTS: DPHP was detected in nearly all samples (97.2%), with a higher geometric mean among the case group (0.70 μg/L) as compared to the sub-cohort (0.52 μg/L). DNBP was commonly detected as well (93.8%), while BBOEP (52.9%) and BDCIPP (22.9%) were detected less frequently. A higher risk of ADHD was observed in children with greater than median exposure to DPHP during pregnancy (risk ratio: 1.38 [95% CI: 0.96, 1.99]), which was slightly higher among girls (2.04 [1.03, 4.02]) and children of mothers with PON1 Q192R genotype QR (1.69 [0.89, 3.19]) or PON1 Q192R genotype RR (4.59 [1.38, 15.29]). The relationship between DPHP and ADHD (total risk ratio: 1.34 [0.90, 2.02]) was partially mediated through total triiodothyronine to total thyroxine ratio (natural direct effect: 1.29 [0.87, 1.94]; natural indirect effect: 1.04 [1.00, 1.10]; 12.48% mediated). We also observed an elevated risk of ADHD in relation to BDCIPP detection during pregnancy (1.50 [0.98, 2.28]). We did not observe notable differences in ADHD by DNBP (0.88 [0.62, 1.26]) or BBOEP (1.03 [0.73, 1.46]) during pregnancy. Simultaneously decreasing all constituents of common-detect OPE-phthalate mixture, specifically DPHP, DNBP, and 6 phthalate metabolites, by a quartile resulted in an ADHD risk ratio of 0.68 [0.64, 0.72].

CONCLUSION: Prenatal exposure to DPHP and BDCIPP may increase the risk of ADHD. For DPHP, we observed potential modification by child sex and maternal PON1 Q192R genotype and partial mediation through maternal thyroid hormone imbalance at 17 weeks gestation

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Epidemiology. 2021 Jul;32:583-90.

TERM BIRTH WEIGHT AND NEURODEVELOPMENTAL OUTCOMES.

Cortese M, Moster D, Wilcox AJ.

BACKGROUND: Preterm birth is an important risk factor for neurodevelopmental disabilities. The vast majority of these disabilities occur, however, among term births. The role of fetal growth restriction specifically among term babies has been incompletely described.

METHODS: We conducted a population-based study of term birth weight and its link to a range of neurodevelopmental outcomes using Norwegian health registries. To remove the influence of preterm birth, we restricted our analyses to 1.8 million singleton babies born during a narrow range of term gestational age (39-41 weeks). Babies with malformations were excluded. We adjusted analyses simply for year of birth, as

further adjustments for sex, parity, maternal age, smoking, marital status, immigrant status, and parental education had trivial influence. An additional sibling analysis controlled for unmeasured family-based confounding.
RESULTS: The risk of neurodevelopmental disabilities at term steadily increased at birth weights lower than 3.5 kg. Using the category of 3.5-3.9â€‰kg as the reference, the odds reached 25-fold for cerebral palsy at the smallest weights (95% confidence interval 8.0, 79), 16-fold for vision/hearing disability (4.0, 65), 11-fold for intellectual impairment (6.9, 17), 7-fold for schizophrenia (1.0, 50), 5.4-fold for epilepsy (2.6, 12), and 3.5-fold for autism spectrum (1.3, 9.4) and behavioral disorders including attention-deficit hyperactivity disorder (2.1, 5.4). Associations remained robust with sibling controls. CONCLUSIONS: Reduced fetal growth is a powerful predictor of a wide variety of neurodevelopmental disabilities independent of preterm delivery

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Epilepsy Behav. 2021 Aug;121:108037.
CLINICAL AND ELECTROPHYSIOLOGICAL PREDICTORS OF BEHAVIORAL DISORDERS IN PATIENTS WITH BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES.
Özgen Y, GÃ¼ngÃ¶r M, Kutlu M, et al.
PURPOSE: Long-term seizure and developmental outcomes of benign childhood epilepsy with centrotemporal spikes (BECTS) are thought to be good. Studies have shown that behavioral disorders may accompany BECTS. We aimed to investigate the frequency of behavioral disorders in patients with BECTS and evaluate their relationship to epilepsy features.
METHODS: Data for 41 patients with BECTS followed up at our clinic between December 2019 and June 2020 were analyzed. Behavioral disorders and intelligence were evaluated by the Turgay Diagnostic and Statistical Manual of Mental Disorders 4th Edition - Disruptive Behaviour Disorders Rating Scale and Wechsler Intelligence Scale for Children Revised, respectively. Patients with a diagnosis of BECTS were divided into 2 groups: children with a behavioral disorder and children without a behavioral disorder. Demographic characteristics, clinical and electroencephalography (EEG) findings, and intelligence level were compared between the two groups.
RESULTS: Twelve of the patients (29%) were classified as having attention-deficit/hyperactivity disorder (ADHD) and 2 (5%) were classified as having oppositional defiant disorder (ODD). The age at seizure onset was earlier in patients with behavioral disorders (p=0.023). Bilateral interictal epileptic discharges (IEDs) were more common in children with behavioral disorders than children without behavioral disorders (p=0.039). The most preferred antiseizure medication was carbamazepine, followed by levetiracetam and valproic acid. The intelligence score of the patients with BECTS was in the normal range in both groups. The total, verbal, and performance scores were lower in patients with a behavioral disorder than in patients without a behavioral disorder, but there was no statistically significant difference between the two groups.
CONCLUSION: Behavioral disorders may be present in approximately one-third of patients with BECTS. Early onset of seizures and the presence of bilateral IEDs may be risk factors for behavioral disorders in children with BECTS

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Georgian Med News. 2021 May;91-95.
NEUROLOGICA DISORDERS OF CHILDREN LIVING IN ECOLOGICALLY AFFECTED REGION OF GEORGIA.
Chochia A, Geladze N, Gogberashvili K, et al.
Article discussed the clinical evidence of children with attention deficit hyperactivity disorder (ADHD) living in different regions with polluted air. We have revealed the correlation between severity of neurological impairment and level of Hg, Pb, Zn and Cu in blood of children of three different age group (2-5y, 6-9 y and 10-13y). According to our results we found correlation between living area and level of xenobiotics and essential microelements. Thus we have concluded that beyond the level of xenobiotics and essential microelements in child's blood their primary and secondary role in the development of neurological disorders in regions of various anthropogenic impact has to be considered

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Int J Environ Res Public Health. 2021 May;18.

EVENT-BASED PROSPECTIVE MEMORY DEFICIT IN CHILDREN WITH ADHD: UNDERLYING COGNITIVE FACTORS AND ASSOCIATION WITH SYMPTOMS.

Costanzo F, Fucà E, Menghini D, et al.

Event-based prospective memory (PM) was investigated in children with Attention deficit/hyperactivity disorder (ADHD), using a novel experimental procedure to evaluate the role of working memory (WM) load, attentional focus, and reward sensitivity. The study included 24 children with ADHD and 23 typically-developing controls. The experimental paradigm comprised one baseline condition (BC), only including an ongoing task, and four PM conditions, varying for targets: 1 Target (1T), 4 Targets (4T), Unfocal (UN), and Reward (RE). Children with ADHD were slower than controls on all PM tasks and less accurate on both ongoing and PM tasks on the 4T and UN conditions. Within the ADHD group, the accuracy in the RE condition did not differ from BC. A significant relationship between ADHD-related symptoms and reduced accuracy/higher speed in PM conditions (PM and ongoing trials), but not in BC, was detected. Our data provide insight on the adverse role of WM load and attentional focus and the positive influence of reward in the PM performance of children with ADHD. Moreover, the relation between PM and ADHD symptoms paves the road for PM as a promising neuropsychological marker for ADHD diagnosis and intervention

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Int J Environ Res Public Health. 2021 May;18.

VALIDATION OF THE ITALIAN VERSION OF THE BEHAVIORAL INHIBITION QUESTIONNAIRE (BIQ) FOR PRESCHOOL CHILDREN.

Agostini F, Benassi M, Minelli M, et al.

Behavioral Inhibition (BI) is a temperamental trait characterized by fear and wariness in reaction to new and unfamiliar stimuli, both social and non-social. BI has been recognized as possible forerunner of anxiety disorders, especially social anxiety and phobia; therefore, its assessment is clinically relevant. The present study aimed to examine the psychometric properties of the Italian adaptation of the Behavioral Inhibition Questionnaire (BIQ), which measures BI in preschool children. The BIQ was completed by 417 Italian parents (230 mothers, 187 fathers) of 270 preschoolers aged 3-5. Confirmatory factor analysis showed a good internal validity: the factorial structure was corresponding to the original six-factor version. Results showed excellent internal consistency, significant item-total correlations, good inter-rater reliability, convergent validity (by correlating the BIQ with the Italian Questionnaires of Temperament-QUIT, the Anxiety-Shy Conner's Scale and the Laboratory Temperament Assessment Battery) and discriminant validity (i.e., no correlation with Conners' ADHD scale). Significant correlations emerged between BI indexes and total BIQ scores of parents and maternal (but not paternal) versions of the questionnaire. Altogether, the results are promising and consistent with previous validation studies, suggesting the BIQ as a reliable and valid measure for evaluating parents' perception of BI in Italian preschoolers

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Int J Environ Res Public Health. 2021 May;18.

PRELIMINARY STUDY OF ADHD BIOMARKERS IN ADULTS WITH FOCUS ON SERUM IRON AND TRANSCRANIAL SONOGRAPHY OF THE SUBSTANTIA NIGRA.

Bahn GH, Lee SM, Hong M, et al.

As previous studies have reported abnormalities in the iron indices of peripheral blood and hyperechogenicity of the substantia nigra (SN) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD), we aimed to examine the same in adults with ADHD using transcranial Doppler sonography (TCS). In addition, we compared the iron indices and TCS findings before and after methylphenidate (MPH) treatment. A total of 39 participants aged â‰¥19 years (13 patients and 26 healthy controls) were recruited from Kyung Hee University Hospital between October 2018 and September 2019. All subjects were clinically evaluated based on the ADHD diagnostic criteria in the DSM-5, the Adult ADHD Self-Report Scale, and the Diagnostic Interview for ADHD in Adults (DIVA-5). Further, the iron indices including serum iron, ferritin, and mean platelet volume were determined. Additionally, TCS focused on the midbrain and echogenicity of the SN was conducted. Follow-up for all items was conducted for five ADHD patients after MPH treatment. Patients with ADHD had significantly lower education levels (number of years) than controls. There were no statistically

significant differences in serum iron indices or the echogenic area between ADHD and control groups. Further, there were no significant changes in iron indices or TCS findings after MPH medication. Unlike previous studies, this study showed no differences between patients with ADHD and controls. Therefore, it is important to determine if these null findings were due to different target populations (children vs. adults) or other factors, including ADHD subtypes

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Int J Environ Res Public Health. 2021 May;18.

RISK OF RESPIRATORY INFECTIOUS DISEASES AND THE ROLE OF METHYLPHENIDATE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY.

Li DJ, Chen YL, Hsiao RC, et al .

Children with attention-deficit/hyperactivity disorder (ADHD) are commonly affected by medical illness. The aim of the present study was to explore the risks of contracting respiratory infectious diseases (RIDs), including upper and lower RIDs and influenza, in children with ADHD. We also examined whether methylphenidate has a protective effect regarding the risk of contracting RIDs among children with ADHD who have a history of methylphenidate treatment. Children in the Taiwan Maternal and Child Health Database from 2004 to 2016 were included in the present study. Upper and lower RIDs, influenza, ADHD, age, sex, and records of methylphenidate prescription were identified. A Cox proportional hazards regression model was used to estimate the significance of the risk of RIDs among children with ADHD in comparison with that among children without ADHD after adjustment for sex and age. The self-controlled case series analysis was conducted to examine the protective effect of methylphenidate treatment against RIDs. In total, 85,853 children with ADHD and 1,458,750 children without ADHD were included in the study. After controlling for sociodemographic variables, we observed that children with ADHD had significantly higher risks of upper RIDs, lower RIDs, and influenza infection than did those without ADHD. Among the children with ADHD who had a history of methylphenidate treatment, the risk of contracting RIDs was lower during the methylphenidate treatment period than during the nontreatment period. Children with ADHD had a higher RID risk than those without ADHD. Methylphenidate might reduce the risk of RIDs among children with ADHD who have a history of methylphenidate treatment

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Int J Environ Res Public Health. 2021 May;18.

PARENTAL AGE AND THE RISK OF ADHD IN OFFSPRING: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Min X, Li C, Yan Y.

Evidence has suggested that parental age at birth is a risk factor of offspring attention deficit/hyperactivity disorder (ADHD). We conducted a meta-analysis of observational studies investigating the association between parental age and offspring ADHD. We conducted a systematic search that followed the recommended guidelines for performing meta-analyses on PUBMED, EMBASE, and Web of Science up to 8 April 2021. We calculated pooled risk estimates from individual age with and without adjusting for possible confounding factors. Dose-response analysis for parental age and ADHD risk was performed. Eleven studies were selected in this meta-analysis, which included 111,101 cases and 4,417,148 participants. Compared with the reference points, the lowest parental age category was associated with an increased risk of ADHD in the offspring, with adjusted odds ratios (ORs) of 1.49 (95% confidence intervals (95%CI) 1.19-1.87) and 1.75 (95%CI 1.31-2.36) for the mother and father, respectively. The highest parental age was statistically insignificant, with adjusted ORs of 1.11 (95%CI 0.79-1.55) and 0.93 (95%CI 0.70-1.23) for mother and father separately. Dose-response analysis indicated a non-linear relationship of parental age with offspring ADHD, with the lowest ADHD risk at 31-35 years old. The results of this meta-analysis support an association between young parental age and the risk of ADHD. More high-quality studies are needed to establish whether the association with parental age is causal

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Int J Environ Res Public Health. 2021 May;18.

SOCIAL ANXIETY IN VICTIMIZATION AND PERPETRATION OF CYBERBULLYING AND TRADITIONAL BULLYING IN ADOLESCENTS WITH AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Liu TL, Hsiao RC, Chou WJ, et al.

Victimization and perpetration of cyberbullying and traditional bullying are prevalent among adolescents with autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). The aims of this study were to examine the role of social anxiety in victimization and perpetration of cyberbullying and traditional bullying in adolescents with ASD and ADHD in Taiwan. A total of 219 adolescents with ASD and 287 adolescents with ADHD aged 11-18 years and their caregivers were recruited from the child psychiatry outpatient clinics into this study. The associations of social anxiety with victimization and perpetration of cyberbullying and traditional bullying were examined using logistic regression analysis. The results indicated that after the effects of sex, age, and autistic social impairment were controlled, social anxiety increased the risk of being a victim of cyberbullying (Odds Ratios (OR) = 1.048; 95% Confidence Interval (CI): 1.013-1.084), a victim of traditional bullying (OR = 1.066; 95% CI: 1.036-1.097), and a perpetrator of traditional bullying (OR = 1.061; 95% CI: 1.027-1.096) in adolescents with ASD. After the effects of sex, age, and ADHD symptoms were controlled for, social anxiety increased the risk of being a victim of traditional bullying in adolescents with ADHD (OR = 1.067; 95% CI: 1.039-1.096). Social anxiety was significantly associated with several forms of bullying involvement in adolescents with ASD and ADHD and warrants being considered into prevention and intervention programs for bullying involvement

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J Affect Disord. 2021 Aug;291:359-67.

A NOVEL MULTIDIMENSIONAL QUESTIONNAIRE FOR THE ASSESSMENT OF EMOTIONAL DYSREGULATION IN ADOLESCENTS: REACTIVITY, INTENSITY, POLARITY AND STABILITY QUESTIONNAIRE-YOUTH VERSION (RIPOST-Y).

Sesso G, Milone A, Drago F, et al.

BACKGROUND: The failure to regulate emotions, namely emotional dysregulation (ED), is a relevant construct in adolescent psychiatry, in terms of prognostic and developmental implications. We developed and validated a novel self-report questionnaire for the assessment of ED, the RIPoSt-Y, both in clinical and non-clinical samples.

METHODS: Items selection and subscales construction were conducted on healthy controls (n=374), while test-retest reliability was evaluated in a subsample (n=72); internal consistency was examined both in the control group and in two clinical samples, respectively including patients with Bipolar Spectrum Disorders (BSD; n=44) and ADHD (n=34). Construct, concurrent and convergent validity were also assessed.

RESULTS: Thirty-one items were finally retained, and three subscales were identified (Affective Instability, Emotional Reactivity, Interpersonal Sensitivity). Test-retest was significant for each subscale with moderate-to-good correlations, and internal consistency showed good-to-excellent coefficients. Construct validity was supported by significant differences between patients and controls and gender-related differences. Concurrent validity was confirmed through significant associations with two subscales of the CHT-Q, while convergent validity proved to be significant with the CBCL/YSR dysregulation-profile. Cut-offs were also computed to discriminate clinically significant scores of ED.

LIMITATIONS: The use of a school-based survey to recruit controls could have biased our results; gender distributions between clinical and non-clinical samples were significantly different.

CONCLUSIONS: Our novel questionnaire proved to be a valid and reliable tool able to assess the presence of ED in youths and to characterize this fundamental construct in its multidimensional facets

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J Affect Disord. 2021 Jul;290:292-99.

RISK FACTORS FOR PRE-ADOLESCENT ONSET SUICIDAL BEHAVIOR IN A HIGH-RISK SAMPLE OF YOUTH.

Zelazny J, Stanley B, Porta G, et al .

OBJECTIVE: To identify risk factors for preadolescent onset suicidal behavior compared with adolescent/young adult onset suicidal behavior in a longitudinal sample of youth with parental history of mood disorders.

METHODS: The sample includes 545 youth who were age 21 years or less at the time of their baseline assessment. Participants underwent baseline and yearly study assessments. Observations were censored at the time point closest to the first episode of suicidal behavior for youth with suicidal behavior and at the time of last observation for youth without suicidal behavior. Youth were categorized into 3 groups: first onset of suicidal behavior before the age of 13 (n = 32), first onset of suicidal behavior between the ages of 13-21 (n = 51) and those without suicide related behaviors (nÂ =Â 462). ANOVA, Chi-square, Fisher's exact test and multinomial regression were used to test the hypotheses.
RESULTS: Significant predictors of preadolescent onset suicidal behavior were diagnosis of depressive disorder (RRR = 11.41, p<.001) and diagnosis of ADHD (RRR = 2.86, p = .02). Adolescent onset was predicted by diagnosis of depressive disorder (RRR = 4.12, p = .008), female sex (RRRÂ =Â 2.68, pÂ =Â .02) and self-reported suicidal ideation (RRR = 1.48, p = .004).
LIMITATIONS: These results are most applicable to offspring of parents with significant mood disorders.
CONCLUSIONS: The strongest predictor of suicidal behavior in both groups was a diagnosis of depressive disorder, and the risk was nearly 3 times higher in preadolescents. ADHD was a significant predictor only for preadolescents, while female sex and self-reported suicidal ideation predicted suicidal behavior in adolescents

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J Atten Disord. 2021 Jul;25:1199-206.
EARLY PREGNANCY RISK AMONG ADOLESCENTS WITH ADHD: A NATIONWIDE LONGITUDINAL STUDY.
Hua MH, Huang KL, Hsu JW, et al.
Objective: ADHD potentially leads to risky sexual behaviors, and is considered a major risk factor for early pregnancy (EP). However, the association between ADHD and subsequent EP remains unknown.
Method: Seven thousand five hundred five adolescents with ADHD and 30,020 age- and sex-matched individuals without ADHD were enrolled from 2001 to 2009 and were followed until the end of 2011. Adolescents who developed any pregnancy (at age 30 years) or EP (at age <20 years) during the follow-up period were identified.
Results: Adolescents with ADHD were found to be prone to pregnancy (hazard ratio [HR] = 1.27) and EP (HR = 2.30) compared with those without ADHD. Long-term ADHD medication use was related to a lower risk of subsequent any pregnancy (HR = 0.72) and EP (HR = 0.69).
Conclusion: Adolescents with ADHD had an increased risk of any pregnancy and EP compared with their non-ADHD counterparts. Long-term ADHD medication use was associated with a lower subsequent EP risk

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J Atten Disord. 2021 Jul;25:1302-10.
EYE VERGENCE RESPONSES DURING AN ATTENTION TASK IN ADULTS WITH ADHD AND CLINICAL CONTROLS.
Jiménez EC, Avella-Garcia C, Kustow J, et al.
Objective: ADHD patients show poor oculomotor control and recent studies show that attention-related eye vergence is weak in ADHD children. We aimed to assess vergence as a potential diagnostic biomarker for ADHD in adults.
Method: We assessed the modulation in the angle of vergence while performing an attention task (N = 144), comparing the results for adults previously diagnosed with ADHD (N = 108) with age-matched clinical controls (N = 36).
Results: Significant differences in eye vergence response modulation between clinical controls and ADHD patients were documented. Diagnostic test accuracy was 79%.
Conclusion: In combination with an attention task, eye vergence responses could be used as an objective marker to support the clinical diagnosis of adult ADHD

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J Atten Disord. 2021 Jul;25:1295-301.

AMPHETAMINE-DEXTROAMPHETAMINE AND PREGNANCY: NEONATAL OUTCOMES AFTER PRENATAL PRESCRIPTION MIXED AMPHETAMINE EXPOSURE.

Rose SJ, Hathcock MA, White WM, et al.

Objective: A retrospective cohort study was performed to evaluate whether birthweight was less among infants of women taking amphetamine-dextroamphetamine during pregnancy at our academic institution.

Method: We identified mother-infant pairs with documented exposure to amphetamine-dextroamphetamine in pregnancy from 2005 through 2015. Patients were matched 2:1 with unexposed controls. Charts were reviewed for known causes of intrauterine growth restriction. Analysis of birthweight used generalized estimating equation blocking on matching. Medical histories were analyzed with (2) test or Fisher's exact test.

Results: We identified 53 exposed mother-infant pairs. The difference in mean birthweight of infants exposed to amphetamine-dextroamphetamine versus those not exposed was 26.9 g, which is not significant (95% confidence interval [CI] = [-141, 195 g]; p = .75). A significant difference was noted for exposed versus unexposed mothers for comorbid psychiatric illness and history of substance abuse (p < .001).

Conclusion: With a limited sample size, our study suggests no significant difference in birthweight

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J Atten Disord. 2021 Jun;25:1146-59.

GAMIFIED ATTENTION TRAINING IN THE PRIMARY SCHOOL CLASSROOM: A CLUSTER-RANDOMIZED CONTROLLED TRIAL.

Kirk HE, Spencer-Smith M, Wiley JF, et al.

Objective: This randomized controlled trial evaluated the efficacy of attention training delivered in class on cognitive attention processes, inattention, hyperactivity, working memory, and numeracy in primary school children.

Method: Eight classes (n = 98 children; 5-9 years) were cluster randomized to gamified attention training, a placebo program, or a no-contact control condition. Assessments were conducted at baseline, immediately after the 5-week intervention (posttraining), and 6 months later (follow-up).

Results: Posttraining, attention training was associated with reduced inattention and hyperactivity within the classroom compared with controls, and reduced hyperactivity at home compared with the no-contact control. At follow-up, reduced hyperactivity within the classroom compared with the no-contact control persisted. No effects of training on cognitive attention processes, working memory, and numeracy were observed posttraining.

Conclusion: Classroom-based attention training has select benefits in reducing inattention and hyperactivity, but may not promote gains in cognitive or academic skills in primary school children

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J Atten Disord. 2021 Jul;25:1207-14.

DIFFERENTIAL PARENT AND TEACHER REPORTS OF ADHD SYMPTOMS ACCORDING TO THE CHILD'S COUNTRY OF ORIGIN: A QUANTITATIVE STUDY FROM DENMARK EXPLORING THE IMPLICATION FOR DIAGNOSIS.

Sahuric A, HohwÃ¼ L, Bang MK, et al.

Objective: This study aimed to investigate differences in parent- and teacher-reported ADHD symptoms according to the child's country of origin.

Method: We conducted a cross-sectional study of 4,207 nonimmigrant (Danish origin) and 233 immigrant (non-Danish origin) children including ratings of phenotypical ADHD symptoms on the Strengths and Difficulties Questionnaires. The association between ADHD symptoms and country of origin, separately for parents and teachers, was analyzed using multiple logistic regression.

Results: Teachers reported similar numbers of ADHD symptoms for immigrant and nonimmigrant children (odds ratio [OR] = 0.95, confidence interval [CI] = [0.58, 1.54]), whereas immigrant parents were less likely than nonimmigrant parents to report ADHD symptoms (OR = 0.42, CI = [0.21, 0.84]).

Conclusion: Immigrant parents were less likely than nonimmigrant parents to report ADHD symptoms, whereas the teachers reported similar amount of ADHD symptoms in the two groups of children. Our results

emphasize the importance of paying attention to teacher reporting of ADHD symptoms when assessing immigrant children

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J Atten Disord. 2021 Jul;25:1272-83.

MONOAMINERGIC GENETIC VARIANTS, PREFRONTAL CORTEX-AMYGDALA CIRCUIT, AND EMOTIONAL SYMPTOMS IN CHILDREN WITH ADHD: EXPLORATION BASED ON THE GENE-BRAIN-BEHAVIOR RELATIONSHIP.

Liu L, Zhao Q, Yu X, et al.

Objective: This study aimed to explore the association between monoaminergic genetic variants and emotional lability (EL) symptoms in children with ADHD. In addition, genetic effects on prefrontal cortex (PFC)-amygdala functional connectivity (FC) were investigated.

Method: Children with ADHD and controls were genotyped for five monoaminergic genetic variants and were evaluated for EL symptoms. Imaging genetic exploration was conducted with previously reported aberrant PFC-amygdala resting-state functional connectivities (RSFCs) as target features.

Results: A genotypic effect on EL symptoms was only found for NET1-rs3785143, indicating higher EL symptoms in TT genotype carriers than in C-allele carriers. Imaging genetic analyses indicated a marginal effect of NET1-rs3785143 on ADHD-altered FC between the superficial amygdala (SFA) and middle frontal gyrus (MFG). Mediation analysis suggested potential effects of NET1-rs3785143 via RSFC (SFA-MFG) on EL.

Conclusion: NET1 variants might participate in the pathogenesis of EL in children with ADHD by influencing the function of the PFC-amygdala circuit

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J Atten Disord. 2021 Jul;25:1260-71.

DIFFERENTIATING SYMPTOMS OF ADHD IN PRESCHOOLERS: THE ROLE OF EMOTION REGULATION AND EXECUTIVE FUNCTION.

Landis TD, Garcia AM, Hart KC, et al.

Objective: This study examined the extent to which individual differences in executive function (EF) and emotion regulation (ER) were uniquely associated with inattention and hyperactivity symptoms of ADHD, respectively.

Method: Participants included 249 preschool children with at-risk or clinically elevated levels of externalizing behavior problems (EBPs).

Results: Regression analyses were conducted examining the association between EF and ER-as reported by parents/teachers and assessed via child task performance-and hyperactivity and inattention. Even after accounting for IQ, age, sex, and severity of oppositional defiant disorder, greater levels of parent/teacher-reported EF problems and worse EF performance were associated with greater inattention. In addition, better observed ER was associated with lower inattention. Conversely, greater levels of parent/teacher-reported EF problems and worse parent/teacher-reported ER were associated with greater hyperactivity.

Conclusion: Our findings suggest that underlying deficits in EF and ER do differentially relate to ADHD symptoms

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J Atten Disord. 2021 Jul;25:1321-30.

AN OPEN-LABEL TRIAL OF METHYLPHENIDATE TREATING SLUGGISH COGNITIVE TEMPO, INATTENTION, AND HYPERACTIVITY/IMPULSIVITY SYMPTOMS AMONG 6- TO 12-YEAR-OLD ADHD CHILDREN: WHAT ARE THE PREDICTORS OF TREATMENT RESPONSE AT HOME AND SCHOOL?

Firat S, Gul H, Aysev A.

Objective: This study investigated the effects of sluggish cognitive tempo (SCT), other psychiatric symptoms, age, dose, and pretreatment ADHD severity on methylphenidate (MPH) treatment response among ADHD children in both home and school. In addition, the predictors of the MPH-SCT treatment response were examined.

Methods: One hundred eighty-five (6-12 years old) ADHD children who were treated with MPH included in the study.

Results: MPH improved SCT total and SCT-Daydreaming scores both at home and school while improved SCT-Sluggish scores in only school. Higher pretreatment Daydreaming score predicted lower treatment response for inattention (B = .301, p = .002), and higher Daydreaming-Sluggish scores predicted lower treatment response for total ADHD symptoms at school (B = .456, p = .006; B = .888, p = .04, respectively). Also higher oppositional defiant disorder symptoms have negative effects on MPH treatment response in ADHD. Older age positively affected the MPH-SCT treatment response in paternal and teacher ratings.
Conclusion: SCT symptoms have negative effects on MPH treatment response at school

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J Atten Disord. 2021 Jul;25:1240-50.

EARLY PREDICTORS OF DE NOVO AND SUBTHRESHOLD LATE-ONSET ADHD IN A CHILD AND ADOLESCENT COHORT.

Liu CY, Asherson P, Viding E, et al.

Objective: The study aimed to identify early childhood risk factors for de novo and subthreshold late-onset ADHD.
Method: ADHD symptoms were assessed in 9,875 participants from the Twins Early Development Study (TEDS) using the Conners' Parent Rating Scale at ages 8, 12, 14, and 16 years, along with other childhood characteristics and adolescent outcomes. Multinomial logistic regressions were implemented to identify early childhood predictors of late-onset ADHD and childhood-onset persistent ADHD, with non-ADHD controls as the reference category.
Results: Male sex, increased childhood conduct problems, and low socioeconomic status predicted de novo late-onset ADHD. Additional risk factors predicted subthreshold late-onset ADHD and childhood-onset persistent ADHD. Late-onset ADHD symptoms were also accompanied by increased co-occurring behavioral and emotional problems.
Conclusion: Findings of different childhood predictors between subthreshold and de novo late-onset ADHD suggest further investigation into time-varying environmental and biological factors driving psychopathological changes is warranted to fully characterize late-onset ADHD

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J Autism Dev Disord. 2021 Jul;51:2297-307.

RELATIVE FREQUENCY OF PSYCHIATRIC, NEURODEVELOPMENTAL, AND SOMATIC SYMPTOMS AS REPORTED BY MOTHERS OF CHILDREN WITH AUTISM COMPARED WITH ADHD AND TYPICALÂ SAMPLES.

Mayes SD, Calhoun SL, Baweja R, et al.

No study has analyzed the relative occurrence of a broad range of symptoms reported by mothers of children with autism, ADHD-Combined, and ADHD-Inattentive and typical controls. Mothers rated 1436 children with autism, 1056 with ADHD without autism, and 186 controls, 2-17Â years, on 41 internalizing, externalizing, neurodevelopmental, and somatic problems. Most children with autism had symptoms of ADHD, oppositional defiant disorder, disruptive mood dysregulation disorder, and expressive language disorder and almost half had dysgraphia and receptive language disorder. Symptom overlap between autism and ADHD-Combined was high. Clinicians specializing in autism and ADHD must have expertise in evaluating and treating these comorbidities identified as most problematic by mothers in order to relieve family concerns and develop treatment plans relevant to families

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J Autism Dev Disord. 2021 Jun;51:2124-31.

BRIEF REPORT: DELAYED DIAGNOSIS OF TREATABLE INBORN ERRORS OF METABOLISM IN CHILDREN WITH AUTISM AND OTHER NEURODEVELOPMENTAL DISORDERS.

Márquez-Caraveo ME, Ibarra-GonzÃ¡lez I, RodrÃguez-ValentÃn R, et al.

The objective of our study was to evaluate the frequency of treatable inborn errors of metabolism (IEM) in a clinical sample of Mexican children and adolescents with neurodevelopmental disorders (NDD). Amino acids and acylcarnitines in blood samples of 51 unrelated children and adolescents were analyzed by tandem mass spectrometry to detect treatable IEM of small molecules. One patient with isovaleric acidemia and autism spectrum disorder (ASD) and another with beta-ketothiolase deficiency and ASD/intellectual

disability/attention-deficit/hyperactivity disorder (ADHD) were diagnosed, indicating an IEM frequency of 3.9% (1:26 subjects). The high frequency of treatable IEM indicates the need to perform a minimum metabolic screening as part of the diagnostic approach for patient with NDD, particularly when newborn screening programs are limited to a few disorders

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J Eur Acad Dermatol Venereol. 2021 Jul;35:1505-18.

TOPICAL THERAPY OF ATOPIC DERMATITIS WITH A FOCUS ON PIMECROLIMUS.

Luger T, Paller AS, Irvine AD, et al.

Atopic dermatitis (AD) is a chronic and relapsing, inflammatory skin disease characterized by impaired skin barrier function and immune system dysregulation that results in dryness, skin microbiome dysbiosis and intense pruritus. It is highly heterogeneous, and its management is demanding. Patients with AD are at greater risk of comorbidities such as attention-deficit hyperactivity disorder as well as other atopic diseases. Early-onset AD cases typically improve or resolve in late childhood; however, it is proposed that the prevalence of persistent or adult-onset AD is higher than previously thought. Basic therapy consists of emollient application and trigger avoidance, and when insufficient, topical corticosteroids (TCS) are the first-line treatment. However, corticophobia/steroid aversion and TCS side-effects, particularly on sensitive skin areas, lead to low compliance and insufficient disease control. Several long- and short-term randomized controlled and daily practice studies have demonstrated that topical calcineurin inhibitors, such as pimecrolimus, have similar anti-inflammatory effects to low-to-medium strength TCS, reduce pruritus and improve the quality of life of patients. In addition, pimecrolimus does not cause skin atrophy, is steroid-sparing and has a good safety profile, with no evidence for an increased risk of malignancies or skin infections. In general, pimecrolimus cream is well-accepted and well-tolerated, encouraging patient adherence and leading to its use by many physicians as a preferred therapy for children and sensitive skin areas

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J Interpers Violence. 2021 Jun;36:NP6624-NP6642.

PEER VICTIMIZATION IN PREADOLESCENT CHILDREN WITH ADHD IN TURKEY.

Örengül AC, Goker H, Zorlu A, et al.

The present study aims to investigate peer victimization and its relationship with comorbid psychiatric diagnoses and quality of life (QoL) among children with attention deficit hyperactivity disorder (ADHD). Study sample consisted of 66 children with ADHD (mean age = 8.6 Â± 1.1 years) and age- and gender-matched 66 controls (mean age = 8.5 Â± 1.3 years). In self-reports, the ADHD group reported significantly higher rates of victimization and bullying than the non-ADHD group. Verbal and physical forms of victimization and bullying were the most prevalent forms in both groups; however, exclusion from peer groups, which is named as relational bullying, was the most significantly differing type between two groups. QoL parameters did not significantly differ between the children involved in bullying and those not involved, except for the lower physical QoL in victimized children in the control group. In conclusion, peer victimization was significantly more prevalent in the ADHD group than the non-ADHD group. Preventive measures are needed for peer victimization, especially for children with ADHD

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J Psychiatr Res. 2021 Jun;138:246-55.

IMPAIRED THEORY OF MIND AND EMOTION RECOGNITION IN PEDIATRIC BIPOLAR DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Halac E, Ciray RO, Turan S, et al.

Background: Social cognition is impaired in patients with severe mental disorders. We aimed to investigate impairments in social cognition in youth with pediatric bipolar disorder (PBD) through a systematic review of the literature and the meta-analysis.

Method: Following the PRISMA guidelines, we searched in PubMed, Scopus, and Cochrane CENTRAL for studies reporting on the theory of mind (ToM) and emotion recognition (ER) abilities of patients with PBD compared to healthy controls (HC). We conducted a random-effects model meta-analysis for the contrast

between PBD and HC. Subgroup and meta-regression analyses were conducted for demographic and clinical variables as appropriate.
Results: A total of thirteen studies involving 429 patients with PBD and 394 HC were included. Patients with PBD had significantly poorer social cognitive abilities (Hedges' g for ER, g = -0.74, CI = -0.91, -0.57; and for ToM, g = -0.98, CI = -1.41 to -0.55). Subgroup analysis also revealed significant impairment in ER for patients in a euthymic state (g = -0.75). Age, gender, sample size, the severity of mood symptoms, estimated IQ, the frequencies of bipolar-I disorder, attention-deficit hyperactivity disorder, medications, study quality and euthymia did not moderate the difference in meta-regression. Heterogeneity was low in all analyses and there was no evidence for publication bias.
Conclusion: The results of this meta-analysis supported the notion that PBD is associated with a deficit in social cognitive abilities at a medium to a large level. Impairments in social cognition could be an illness-related trait of PBD. Meta-regression results did not find a moderator of the deficits in social cognition.

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J Psychiatr Res. 2021 Jun;138:360-65.

CLINICAL RISK FACTORS, EMOTIONAL REACTIVITY/REGULATION AND SUICIDAL IDEATION IN ELEMENTARY SCHOOL-AGED CHILDREN.

Sheftall AH, Vakil F, Armstrong SE, et al.

Objective: Suicidal behavior (SB) in young children is rare yet in 2019, suicide was the fifth leading cause of death in 5-12-year-old youth. Understanding the risks associated with childhood suicidal ideation (SI) and SB will determine which factors should be targeted for prevention programming. This study examined clinical characteristics and emotional reactivity/regulation (ERR) in children with (SI+) and without (SI-) SI.
Method: One hundred seventeen children, 6-9 years, and one biological parent were enrolled. Children completed interviews concerning SI/SB and parents completed interviews/self-reports about SI/SB, psychiatric distress, and history of abuse/neglect and their child's SI/SB, mental health, and ERR. Independent t-tests and Chi-square analyses using Bonferroni correction were conducted to examine SI group differences. Variables were then screened using forward stepwise logistic regression to determine association with SI + status. The final logistic regression included variables that survived screening procedures only.
Results: Univariate analyses revealed SI + children were more likely to have a parental history of suicide attempt (PH+), higher rates of current psychotropic medication use, higher scores on the CBCL-DSM oriented scales (e.g., ADHD problems), and higher negative affect compared to SI- children. After analytic screening procedures, PH+, anxiety problems, ADHD problems, and anger survived. The final logistic regression revealed PH + status and anxiety problems were associated with SI + status.
Conclusion: Long-term follow-up is needed to determine if these factors are predictive of a first-time suicide attempt in this at-risk group.

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J Psychiatr Res. 2021 Jun;138:301-10.

NEUROPSYCHOLOGICAL PERFORMANCE IN YOUTH WITH OBSESSIVE-COMPULSIVE DISORDER.

Deepthi K, Roopesh BN, Balachander S, et al.

There is a paucity of literature on neuropsychological functions in youth with obsessive-compulsive disorder (OCD). Most studies have small sample sizes and have yielded inconsistent results. A recent meta-analysis failed to identify any significant impairments. We studied neuropsychological functions (attention, verbal fluency, working memory, set-shifting, response inhibition, planning and visuospatial abilities) in a large sample of youth with OCD (n = 97) in comparison with controls who did not have OCD (n = 50). After controlling for the confounding effects (age, sex, severity of depression and anxiety, presence of comorbid attention-deficit hyperactivity disorder, any tic disorder, number of comorbidities, and non-verbal intelligence measured by the standard progressive matrices), the youth with OCD significantly underperformed with large effect sizes compared to controls, only on the test of 'behavioral reversal', measured by the Object Alternation Test (trials to reach criterion $p < 0.001$, Cohen's d = 1.49; perseverative errors $p < 0.001$, Cohen's d = 1.31). Patients also underperformed on a task of planning, but it was statistically insignificant. Certain comorbid disorders, antipsychotic use and age of onset did not influence neuropsychological performance significantly.

Our study demonstrates that youth with OCD may have impaired 'set-shifting' in the form of 'behavioral reversal' and possibly planning, findings broadly consistent with the literature in adults and with the fronto-striatal model of OCD. It is possible that youth may accumulate more neuropsychological impairments over a period, as the illness continues into adulthood

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J Autism Dev Disord. 2021 Jun;51:2004-18.

APPLICATION OF LATENT CLASS ANALYSIS TO IDENTIFY SUBGROUPS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS WHO BENEFIT FROM SOCIAL SKILLS TRAINING.

Dekker V, Nauta MH, Timmerman ME, et al.

With Latent Class Analysis applied on data of 98 children with autism spectrum disorder (ASD) (9–12 years; 17 girls) participating in social skills training (SST) in a randomized controlled trial (Dekker et al. 2019), four subgroups were detected, based on social-communicative skills before, and response patterns to training. Two subgroups improved after SST. Characterizing the subgroups based on participant and intervention characteristics showed that improvement was related to lower parent-reported perceived difficulty of social-communicative skills at start, higher verbal ability, younger age and milder symptoms of ASD and anxiety. The lowest performing non-improving subgroup participated more often in SST without parent/teacher involvement, compared to all other subgroups. Response to SST in ASD seems to vary depending on participant characteristics

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J Child Psychol Psychiatry. 2021 Jun;62:790-97.

AN OBSERVATIONAL STUDY OF EMOTION REGULATION IN CHILDREN WITH TOURETTE SYNDROME.

Hagstrøm J, Spang KS, Vangkilde S, et al.

Background: Explosive outbursts occur in 25%–70% of children with Tourette syndrome (TS) and may cause more distress than the tics themselves. Previous studies have indicated that a comorbid diagnosis of attention-deficit/hyperactivity disorder (ADHD) is associated with emotional dysregulation in TS; however, this relationship has almost exclusively been studied using parent-reported questionnaires.

Methods: We examined emotion regulation (ER) with an observational measure in 150 medication-naïve children aged 7–12 allocated to four groups: Forty-nine children with TS, 23 children with ADHD, 16 children with TS + ADHD, and 62 typically developing controls. We assessed participants' ER ability, as well as parent–child interactions in the context of a complex puzzle task, and coded the observed behavior with the Tangram Emotion Coding Manual (TEC-M). We examined group differences in ER, as well as associations between ER and severity of symptoms pertaining to TS and ADHD.

Results: Children with TS did not differ from controls in their ER ability. However, children with ADHD and TS + ADHD had more problems with ER than those with TS only and controls. Finally, parents of children with ADHD displayed more tension during the experimental task. ER ability was not associated with tic severity nor premonitory urges; however, better ER ability was associated with less severe symptoms of ADHD.

Conclusions: This study is the first to evaluate ER with an observational, clinician-rated measure in a controlled social setting in children with TS. Our findings support earlier questionnaire-based studies by showing impaired ER in children with TS + ADHD, but not in children with TS without comorbidity. These findings inform our understanding of the phenomenology of emotional dysregulation in TS and the role of comorbid disorders.Biology ClassSaturday, 29 May • 10:40–11:20Google Meet joining infoVideo call link: https://meet.google.com/sbh-rehr-bbr

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J Child Psychol Psychiatry. 2021 Jun;62:680-700.

PRACTITIONER REVIEW: PHARMACOLOGICAL TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN CHILDREN AND YOUTH WITH AUTISM SPECTRUM DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Rodrigues R, Lai MC, Beswick A, et al.

Background: Clinically significant attention-deficit/hyperactivity disorder (ADHD) symptoms are common and impairing in children and youth with autism spectrum disorder(ASD). The aim of this systematic review and meta-analysis was to (a) evaluate the efficacy and safety of pharmacotherapy for the treatment of ADHD symptoms in ASD and (b) distil findings for clinical translation.

Methods: We searched electronic databases and clinical trial registries (1992 onwards). We selected randomized controlled trials conducted in participants <25 years of age, diagnosed with ASD that evaluated ADHD outcomes (hyperactivity/impulsivity and inattention) following treatment with stimulants (methylphenidate or amphetamines), atomoxetine, alpha-2 adrenergic receptor agonists, antipsychotics, tricyclic antidepressants, bupropion, modafinil, venlafaxine, or a combination, in comparison with placebo, any of the listed medications, or behavioral therapies. Data were pooled using a random-effects model.

Results: Twenty-five studies (4 methylphenidate, 4 atomoxetine, 1 guanfacine, 14 antipsychotic, 1 venlafaxine, and 1 tianeptine) were included. Methylphenidate reduced hyperactivity (parent-rated: standardized mean difference [SMD] = -.63, 95%CI = -.95,-.30; teacher-rated: SMD = -.81, 95%CI = -1.43,-.19) and inattention (parent-rated: SMD = -.36, 95%CI = -.64,-.07; teacher-rated: SMD = -.30, 95%CI = -.49,-.11). Atomoxetine reduced inattention (parent-rated: SMD = -.54, 95%CI = -.98,-.09; teacher/investigator-rated: SMD = -0.38, 95%CI = -0.75, -0.01) and parent-rated hyperactivity (parent-rated: SMD = -.49, 95%CI = -.76,-.23; teacher-rated: SMD = -.43, 95%CI = -.92, .06). Indirect evidence for significant reductions in hyperactivity with second-generation antipsychotics was also found. Quality of evidence for all interventions was low/very low. Methylphenidate was associated with a nonsignificant elevated risk of dropout due to adverse events.

Conclusions: Direct pooled evidence supports the efficacy and tolerability of methylphenidate or atomoxetine for treatment of ADHD symptoms in children and youth with ASD. The current review highlights the efficacy of standard ADHD pharmacotherapy for treatment of ADHD symptoms in children and youth with ASD. Consideration of the benefits weighed against the limitations of safety/efficacy data and lack of data evaluating long-term continuation is undertaken to help guide clinical decision-making regarding treatment of co-occurring ADHD symptoms in children and youth with ASD.

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J Psychopathol Behav Assess. 2021 Jun;43:376-87.

EVIDENCE FOR A HIGHER-ORDER ESEM STRUCTURE OF ADHD IN A SAMPLE OF CHINESE CHILDREN.

Yi Z, Wang Y, Tan TX.

Exploratory structural equation modeling (ESEM) solutions have been proposed to represent the factor structures of attention-deficit/hyperactivity disorder (ADHD) in recent literature, yet no studies have assessed those structures in Chinese children. The primary aim of this study was to comprehensively examine the factor structures of the Chinese version of the ADHD Rating Scale-IV (ADHD RS-IV): Home Version. Data on 458 Chinese children aged 3–8 years (boys: 246; 54%) were used to test and compare eleven factor models: confirmatory factor analysis (CFA) models (one-factor, two-factor and three-factor), second-order CFA model, bifactor CFA models (two and three specific factors), ESEM models (two-factor and three-factor), second-order ESEM model, and bifactor ESEM models (two and three specific factors). The results showed that, overall, ESEM models displayed better fit than CFA models. Specifically, the second-order ESEM model with three first-order factors best represented of the ADHD factor structure in our sample. In addition, measurement invariance testing results showed that scalar invariance was established across gender, age and informant groups. Implications for future research are discussed

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J Sleep Res. 2021 Jun;30.

CUMULATIVE INCIDENCE AND RELATIVE RISK OF SLEEP PROBLEMS AMONG CHILDREN AND ADOLESCENTS WITH NEWLY DIAGNOSED NEURODEVELOPMENTAL DISORDERS: A NATIONWIDE REGISTER-BASED STUDY.

Hvolby A, Christensen J, Gasse C, et al.

We estimated the absolute and relative risk of sleep problems in children and adolescents with newly diagnosed neurodevelopmental disorders. This was a population-based cohort study of individuals born in Denmark in 1993–2014 and followed in nationwide registers in 2011–2016. We estimated the 5-year cumulative incidence of sleep problems in incident cases of attention-deficit/hyperactivity disorder (ADHD; n = 12,844), autism spectrum disorder (ASD; n = 8,073), oppositional defiant disorder/conduct disorder (ODD/CD; n = 2,234) and epilepsy (n = 3,709). Hazard ratios (HRs) for sleep problems were estimated by Cox regression. The 5-year risk of sleep problems was highest in ADHD (29.2%; 95% CI, 28.4–30.1), ASD (24.2%; 95% CI, 23.1–25.3) and ODD/CD (27.1% 95% CI, 25.0%–29.2%) and lowest in epilepsy (11.3%; 95% CI, 10.2%–12.6%). For ADHD and ASD, sleep problems were more common in females than in males. Furthermore, sleep problems were predicted by high parental socioeconomic status and varied with the geographical region of residence, suggesting that different clinical practices exist across Denmark and that sleep problems may be more likely to go undetected in families of lower socioeconomic position. Compared with individuals without these disorders, the likelihood of sleep problems was increased in individuals with ADHD (HR, 33.81; 95% CI, 32.78–34.87), ASD (HR, 16.77; 95% CI, 16.15–17.41), ODD/CD (HR, 14.73; 95% CI, 13.88–15.64) and epilepsy (HR, 6.01; 95% CI, 5.67–6.37). After mutual adjustment for comorbidity, HRs were attenuated, especially in ASD, ODD/CD and epilepsy when adjusted for ADHD, suggesting that the increased risk of sleep problems in individuals with ASD, ODD/CD and epilepsy is driven largely by comorbid ADHD. (PsycInfo Database Record (c) 2021 APA, all rights reserved)

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J Am Acad Child Adolesc Psychiatry. 2021 Jun;60:745-56.

EFFECTIVENESS OF MOTIVATIONAL INTERVIEWING-ENHANCED BEHAVIOR THERAPY FOR ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED COMMUNITY-BASED TRIAL.

Sibley MH, Graziano PA, Coxe S, et al.

Objective: This study tests the effectiveness of parent-teen psychotherapy for adolescent attention-deficit/hyperactivity disorder (ADHD) (Supporting Teens' Autonomy Daily [STAND]) versus usual care (UC) in 4 community clinics.

Method: A randomized clinical trial was conducted with double randomization of adolescents and therapists to STAND versus UC. Participants were 278 culturally diverse adolescents diagnosed with DSM-5 ADHD at baseline and 82 community therapists. Seven primary outcomes were assessed at baseline (BL), posttreatment (PT; mean = 5.11 months post-BL, SD = 2.26), and follow-up (FU; mean = 9.81 months post-BL, SD = 2.50): inattention (IN; parent/teacher-rated), academics (parent-rated/official records), family functioning (parent/adolescent-rated), and disciplinary records. Treatment engagement indicated consumer fit (eg, number or sessions received, percentage of sessions attended by parent, satisfaction). The impact of treatment on concurrent medication use was also examined. Service delivery features were examined as moderators of outcome.

Results: Intent-to-treat (N = 278) analyses indicated no significant group × time effects. STAND only led to superior outcomes when therapists were licensed (22% of sample) versus unlicensed (parent-rated IN: $p < .001$, $d = 1.08$; parent-rated academic impairment: $p = .010$, $d = 1.17$). Compared to UC, STAND was associated with greater parent participation ($p < .001$, $d = 0.88$) and higher scores on certain indices of parent satisfaction. STAND also was associated with superior medication engagement over time compared to UC (odds ratio = 7.18).

Conclusion: Evidence-based psychosocial treatment for adolescent ADHD did not outperform UC on outcome trajectories despite improving some indices of treatment engagement. STAND requires additional adaptation for community contexts

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J Int Neuropsychol Soc. 2021 May;27:472-83.

A NEW SPIN ON SPATIAL COGNITION IN ADHD: A DIFFUSION MODEL DECOMPOSITION OF MENTAL ROTATION.

Feldman JS, Huang-Pollock C.

Objectives: Multiple studies have found evidence of task non-specific slow drift rate in ADHD, and slow drift rate has rapidly become one of the most visible cognitive hallmarks of the disorder. In this study, we use the diffusion model to determine whether atypicalities in visuospatial cognitive processing exist independently of slow drift rate.

Methods: Eight- to twelve-year-old children with (n = 207) and without ADHD (n = 99) completed a 144-trial mental rotation task.

Results: Performance of children with ADHD was less accurate and more variable than non-ADHD controls, but there were no group differences in mean response time. Drift rate was slower, but nondecision time was faster for children with ADHD. A Rotation × ADHD interaction for boundary separation was also found in which children with ADHD did not strategically adjust their response thresholds to the same degree as non-ADHD controls. However, the Rotation × ADHD interaction was not significant for nondecision time, which would have been the primary indicator of a specific deficit in mental rotation per se.

Conclusions: Poorer performance on the mental rotation task was due to slow rate of evidence accumulation, as well as relative inflexibility in adjusting boundary separation, but not to impaired visuospatial processing specifically. We discuss the implications of these findings for future cognitive research in ADHD

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Med Lett Drugs Ther. 2021 Jun;63:98-100.

VILOXAZINE ER (QELBREE) FOR ADHD.

Anon.

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Medicine (Baltimore). 2021 Jul;100:e26430.

MATERNAL EXPOSURE TO PESTICIDES DURING PREGNANCY AND RISK FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN OFFSPRING: A PROTOCOL FOR SYSTEMATIC REVIEW AND META-ANALYSIS.

Zhu Z, Wang Y, Tang S, et al.

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) is the most common psychiatric disorder in childhood. Studies explored the association of maternal exposure to pesticides during pregnancy with a risk of offspring developing ADHD, but have reported inconclusive results. Here, we will perform a systematic review and meta-analysis of observational studies to assess a possible association between them.

METHODS: This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols. PubMed, Embase, Web of Science, the Cochrane Library, and the PsycINFO will be searched from inception to May 2021. Observational studies investigating the association of maternal exposure to pesticides during pregnancy with a risk of offspring developing ADHD will be considered. The Newcastle-Ottawa Scales or the scale of the Agency for Healthcare Research and Quality will be used to assess the methodological quality of the included studies according to their study design. A fixed or random-effect model will be used to synthesize data depend on the heterogeneity test. STATA version 12.0 will be used to conduct the meta-analysis.

RESULTS: This study will provide a high-quality evaluation of association between maternal exposure to pesticides during pregnancy and risk for ADHD in offspring.

CONCLUSION: This study will present evidence on whether maternal exposure to pesticides during pregnancy is a risk factor for ADHD in offspring

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Medicine (Baltimore). 2021 Jul;100:e26552.

THE LOWEST EFFECTIVE PLASMA CONCENTRATION OF ATOMOXETINE IN PEDIATRIC PATIENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A NON-RANDOMIZED PROSPECTIVE INTERVENTIONAL STUDY.

Sugimoto A, Suzuki Y, Orime N, et al.

Background: Atomoxetine (ATX) is used as a first-line, non-stimulant treatment for attention-deficit/hyperactivity disorder (ADHD), although no studies have systematically examined the relationship

between plasma concentration and clinical efficacy. We conducted this non-randomized prospective interventional study to examine the relationship between plasma concentration of ATX and clinical efficacy.
Methods: Forty-three ADHD pediatric patients received ATX, and the steady-state through plasma concentration of the last daily dose that was maintained for at least 4 weeks were determined by high-performance liquid chromatography.
Results: The receiver operating characteristic curve suggested that when plasma concentration exceeded 64.60 ng/mL, scores on the ADHD-Rating Scale improved by 50% or more (P = .14). Although 6 of the 8 final responders were unresponsive at the initial dose (.72 ± .04 mg/kg [mean ± standard deviation]), they responded after increasing the ATX dose to the final dose (1.52 ± .31 mg/kg). Excluding 7 outlier participants, the concentration was 83.3 ± 32.3 ng/mL in 7 responders and was significantly higher than 29.5 ± 23.9 ng/mL (P < .01) for the 29 non-responders.
Conclusions: These results suggest that a minimum effective plasma concentration of ATX is required to achieve sufficient clinical efficacy. We hypothesized a mechanism that results in the realization of a clinical effect when the plasma concentration exceeds a certain threshold in the potential response group, whereas will not improve even if the plasma concentration is increased in the unqualified non-responder group.

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Nervenarzt. 2021 Jul;92:670-78.

TREATMENT OF DISORDERS OF EMOTION REGULATION IN THE ADOLESCENTS CENTER AT THE CENTRAL INTITUTE OF MENTAL HEALTH.

Hohmann S, Enning F, Trasselli C, et al.

Severe disorders of emotion regulation, e.g. in the context of mental illnesses, such as borderline disorders, attention deficit hyperactivity disorder (ADHD) and complex posttraumatic stress disorder (PTSD), often begin in childhood and adolescence and influence the psychosocial development of those affected, often into adulthood. Professional treatment therefore often requires longer term planning, if possible from aÂ single source. The sectorized structure of the current psychiatric healthcare system, however, makes this process more difficult or is even a hindrance and promotes high hospitalization rates and chronification. The concept of the Adolescents Center for Disorders of Emotion Regulation at the Central Institute of Mental Health functions as a model concept for long-term, cross-sectoral treatment structures. AÂ constant treatment team from child, adolescent and adult psychiatry and psychotherapy provides evidence-based psychotherapy according to the guidelines of dialectical behavior therapy (DBT) for those affected between the ages of 16 and 24 years. Conceptually, inpatient, day care and staged outpatient treatment modules complement each other in order to not only provide psychotherapy to the young patients in this important phase of life but also to accompany and support them in completing school and training, in partnership and independent living

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Neural Plast. 2021 May;2021.

ALTERED FUNCTIONAL CONNECTIVITY IN CHILDREN WITH ADHD REVEALED BY SCALP EEG: AN ERP STUDY.

Chen C, Yang H, Du Y, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental brain disorders in childhood. Despite extensive researches, the neurobiological mechanism underlying ADHD is still left unveiled. Since the deficit functions, such as attention, have been demonstrated in ADHD, in our present study, based on the oddball P3 task, the corresponding electroencephalogram (EEG) of both healthy controls (HCs) and ADHD children was first collected. And we then not only focused on the event-related potential (ERP) evoked during tasks but also investigated related brain networks. Although an insignificant difference in behavior was found between the HCs and ADHD children, significant electrophysiological differences were found in both ERPs and brain networks. In detail, the dysfunctional attention occurred during the early stage of the designed task; as compared to HCs, the reduced P2 and N2 amplitudes in ADHD children were found, and the atypical information interaction might further underpin such a deficit. On the one hand, when investigating the cortical activity, HCs recruited much stronger brain activity mainly in the temporal and frontal regions, compared to ADHD children; on the other hand, the brain network showed atypical enhanced long-range connectivity between the frontal and occipital lobes but attenuated connectivity

among frontal, parietal, and temporal lobes in ADHD children. We hope that the findings in this study may be instructive for the understanding of cognitive processing in children with ADHD

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Neuropsychopharmacology. 2021 Jun;46:1300-06.

FUNCTIONAL CONNECTIVITY DURING FRUSTRATION: A PRELIMINARY STUDY OF PREDICTIVE MODELING OF IRRITABILITY IN YOUTH.

Scheinost D, Dadashkarimi J, Finn ES, et al.

Irritability cuts across many pediatric disorders and is a common presenting complaint in child psychiatry; however, its neural mechanisms remain unclear. One core pathophysiological deficit of irritability is aberrant responses to frustrative nonreward. Here, we conducted a preliminary fMRI study to examine the ability of functional connectivity during frustrative nonreward to predict irritability in a transdiagnostic sample. This study included 69 youths (mean age = 14.55 years) with varying levels of irritability across diagnostic groups: disruptive mood dysregulation disorder (n = 20), attention-deficit/hyperactivity disorder (n = 14), anxiety disorder (n = 12), and controls (n = 23). During fMRI, participants completed a frustrating cognitive flexibility task. Frustration was evoked by manipulating task difficulty such that, on trials requiring cognitive flexibility, "frustration" blocks had a 50% error rate and some rigged feedback, while "nonfrustration" blocks had a 10% error rate. Frustration and nonfrustration blocks were randomly interspersed. Child and parent reports of the affective reactivity index were used as dimensional measures of irritability. Connectome-based predictive modeling, a machine learning approach, with tenfold cross-validation was conducted to identify networks predicting irritability. Connectivity during frustration (but not nonfrustration) blocks predicted child-reported irritability ($\rho = 0.24$, root mean square error = 2.02, $p = 0.03$, permutation testing, 1000 iterations, one-tailed). Results were adjusted for age, sex, medications, motion, ADHD, and anxiety symptoms. The predictive networks of irritability were primarily within motor-sensory networks; among motor-sensory, subcortical, and salience networks; and between these networks and frontoparietal and medial frontal networks. This study provides preliminary evidence that individual differences in irritability may be associated with functional connectivity during frustration, a phenotype-relevant state

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Neuroscience. 2021 Jul;466:248-57.

THE IMPACT OF ATTENTION DEFICIT-HYPERACTIVITY DISORDER SYMPTOM SEVERITY ON THE EFFECTIVENESS OF TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) ON INHIBITORY CONTROL.

Nejati V, Movahed AM, Nitsche MA.

The present study aimed to assess the impact of transcranial direct current stimulation (tDCS) on different domains of inhibitory control in children with mild or severe ADHD symptoms. Twenty-four children with ADHD, in two groups with severe and mild symptoms, received anodal or sham tDCS over the right dorsolateral prefrontal cortex (dlPFC) during performing inhibitory control tasks. A significant main effect of stimulation condition was found that was limited to the circle tracing task, and the incongruent condition of the flanker task. Moreover, the main effects of stimulation condition and group were non-significant, but their interaction was significant for No-Go accuracy. The results suggest that the right dlPFC has a crucial role in ongoing inhibition in children with ADHD, and that tDCS has a partially symptom severity-dependent effect on inhibitory control. These findings are discussed in connection with severity-dependent psychopathology

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Occup Ther Int. 2021;2021:5564364.

CLINICIANS' VIEWS ON THE NEED FOR CULTURAL ADAPTATION OF INTERVENTION FOR CHILDREN WITH ADHD FROM THE ULTRAORTHODOX COMMUNITY.

Golos A, Mor R, Fisher O, et al.

Culture is a core context within occupational therapy, with a recent literature emphasizing the importance of cultural competence, as well as culturally sensitive assessment and intervention. The recent literature has indicated the efficacy of the Cognitive-Functional intervention (Cog-Fun) for children with ADHD among the general Israeli population, yet no studies to date have examined the necessity of cultural adaptations for minority groups. The current study examines the necessity of adapting the intervention protocol and process

to the Ultraorthodox (UO) population, as perceived by occupational therapists. The study included 28 occupational therapists certified to use the Cog-Fun intervention, who reported using this approach with UO children. Participants responded to an online questionnaire developed for this study, regarding characteristics of the UO population and necessary adaptions to the Cog-Fun intervention process and protocol. Findings were analyzed using descriptive statistics and qualitative content analysis. Results of the study point to the necessity of addressing various features of the UO community, including daily routines and habits, cultural values, knowledge regarding ADHD, and accessibility of information. Participants also reported a need to adapt the graphic content of the intervention materials. The qualitative data expanded on the perceptions of the participants through four main themes: (a) knowledge regarding ADHD diagnosis and intervention; (b) perceptions and attitudes regarding ADHD diagnosis and medication; (c) factors affecting communication between the OT, parents, and teachers; and (d) adapting the intervention protocol to habits, routines, and lifestyle of UO families. This study has direct implications for therapists utilizing the Cog-Fun with UO children and may also provide insights relevant to occupational therapists using other treatment approaches with children from this culture, as well as other minority or traditional groups. Furthermore, this study may serve as an important addition to the limited literature describing cultural adaptations of evidence-based interventions

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Res Dev Disabil. 2021 Jul;114:103983.

PSYCHOLOGICAL DISTRESS AND BURDEN AMONG FAMILY CAREGIVERS OF CHILDREN WITH AND WITHOUT DEVELOPMENTAL DISABILITIES SIX MONTHS INTO THE COVID-19 PANDEMIC.

Iovino EA, Caemmerer J, Chafouleas SM.

The COVID-19 pandemic has created unique challenges for family caregivers of children with developmental disabilities (DD). The purpose of this study was to conduct a 6-month follow-up on the experiences of caregiver burden and psychological distress among caregivers of children with autism (ASD) and/or attention deficit hyperactivity disorder (ADHD) during COVID-19 pandemic, compare their experiences to caregivers of children without DD, and test the interaction between opportunities for self-care and caregiver burden and psychological distress. Results indicated caregivers of children with ASD/ADHD continued to report significantly higher levels of psychological distress and caregiver burden compared to caregivers of children without DD. Counter to study hypotheses decreased opportunities to engage in self-care as a result of the pandemic predicted higher levels of psychological distress and caregiver burden for caregivers of children without DD, whereas only caregiver burden was moderated by self-care for caregivers of children with ASD/ADHD. Overall, the COVID-19 pandemic is continuing to negatively impact the psychological health of family caregivers of school-age children. In general, greater challenges are presented for caregivers of children with ASD/ADHD, but they seem to be more resilient to some COVID-19 challenges than caregivers of children without DD

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Research on Child and Adolescent Psychopathology. 2021 Jun;49:697-710.

EVALUATING THE VIABILITY OF NEUROCOGNITION AS A TRANSDIAGNOSTIC CONSTRUCT USING BOTH LATENT VARIABLE MODELS AND NETWORK ANALYSIS.

Eadeh HM, Markon KE, Nigg JT, et al.

The relational structure of psychological symptoms and disorders is of crucial importance to mechanistic and causal research. Methodologically, factor analytic approaches (latent variable modeling) and network analyses are two dominant approaches. Amidst some debate about their relative merits, use of both methods simultaneously in the same data set has rarely been reported in child or adolescent psychopathology. A second issue is that the nosological structure can be enriched by inclusion of transdiagnostic constructs, such as neurocognition (e.g., executive functions and other processes). These cut across traditional diagnostic boundaries and are rarely included even though they can help map the mechanistic architecture of psychopathology. Using a sample enriched for ADHD (n = 498 youth ages 6 to 17 years; M = 10.8 years, SD = 2.3 years, 55% male), both approaches were used in two ways: (a) to model symptom structure and (b) to model seven neurocognitive domains hypothesized as important transdiagnostic features in ADHD and associated disorders. The structure of psychopathology domains was similar across statistical approaches

with internalizing, externalizing, and neurocognitive performance clusters. Neurocognition remained a distinct domain according to both methods, showing small to moderate associations with internalizing and externalizing domains in latent variable models and high connectivity in network analyses. Overall, the latent variable and network approaches yielded more convergent than discriminant findings, suggesting that both may be complementary tools for evaluating the utility of transdiagnostic constructs for psychopathology research

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Research on Child and Adolescent Psychopathology. 2021 Jun;49:763-73.

MATERNAL PARENTING AND TODDLER TEMPERAMENT: PREDICTORS OF EARLY SCHOOL AGE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-RELATED BEHAVIORS.

Joseph HM, McKone KMP, Molina BSG, et al.

Detection of early risk for developing childhood attention-deficit/hyperactive disorder (ADHD) symptoms, inattention and hyperactivity, may be critical for prevention and early intervention. Temperament and parenting are two promising areas of risk, representing potential targets for preventive intervention; however, studies have rarely tested these factors longitudinally using multiple methods and reporters. In a longitudinal sample of 312 low-income boys, this study tested the hypothesis that negative emotionality (NE) and effortful control (EC) in toddlerhood (1.5–3.5 years old) would predict mother- and teacher-reported ADHD-related behaviors at school age (5–7 years old). Direct effects of observed warm, supportive and harsh maternal parenting were tested in relation to ADHD-related behaviors and as moderators of associations between NE and EC and ADHD-related behaviors. Several predictions were supported: 1) Greater maternal-reported toddler NE positively predicted mother-reported ADHD behaviors; 2) Greater observed EC was associated with fewer mother- and teacher-reported ADHD-related behaviors; 3) Warm, supportive parenting predicted fewer teacher-reported ADHD-related behaviors, and harsh parenting predicted more ADHD-related behaviors as reported by parents and teachers; 4) Harsh parenting moderated the association between observed EC and mother-reported ADHD-related behaviors. Together, the findings suggest that lower child EC, lower warm/supportive parenting, and greater harsh parenting in toddlerhood independently signal increased risk for later ADHD-related behaviors; further, the association between low EC and ADHD-related behaviors was amplified in the context of high levels of harsh parenting

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Sci Total Environ. 2021 Sep;786:147371.

THE EFFECTS OF PHTHALATE ESTER EXPOSURE ON HUMAN HEALTH: A REVIEW.

Chang WH, Herianto S, Lee CC, et al.

Phthalate esters (PAEs) are one of the most widely used plasticizers in polymer products and humans are increasingly exposed to them. The constant exposure to PAEs-contained products has raised some concerns against human health. Thus, the impacts of PAEs and their metabolites on human health require a comprehensive study for a better understanding of the associated risks. Here, we attempt to review eight main health effects of PAE exposure according to the most up-to-date studies. We found that epidemiological studies demonstrated a consistent association between PAE exposure (especially DEHP and its metabolites) and a decrease in sperm quality in males and symptom development of ADHD in children. Overall, we found insufficient evidence and lack of consistency of the association between PAE exposure and cardiovascular diseases (hypertension, atherosclerosis, and CHD), thyroid diseases, respiratory diseases, diabetes, obesity, kidney diseases, intelligence performance in children, and other reproductive system-related diseases (anogenital distance, girl precocious puberty, and endometriosis). Future studies (longitudinal and follow-up investigations) need to thoroughly perform in large-scale populations to yield more consistent and powerful results and increase the precision of the association as well as enhance the overall understanding of potential human health risks of PAEs in long-term exposure

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Sleep Med. 2021 Jul;83:241-47.

SCREEN EXPOSURE EXACERBATES ADHD SYMPTOMS INDIRECTLY THROUGH INCREASED SLEEP DISTURBANCE.

Cavalli E, Anders R, Chaussoy L, et al .

OBJECTIVES: The aim of this study was twofold. First, to confirm the deleterious aspect of evening screen exposure in school-aged children, in particular the effect of screens in the bedroom. Second, to explore the three-way association between degree of screen exposure, sleep disturbance, and ADHD symptoms. Solid evidence exists on the link between sleep disturbance and ADHD symptoms, and screen exposure and sleep disturbance. However, no studies have formally assessed the impact of screen exposure on ADHD symptoms in children, as a function of sleep disturbance.

METHODS: Parents of 374 French children (201 girls, 173 boys, mean age of 10.8± 2.8 years old) completed the Sleep Disturbance Scale for Children (SDSC), the Attention-Deficit/Hyperactivity Disorder (ADHD) Rating Scale, and a questionnaire about their children's screen habits (total hours in the morning, afternoon, and evening per day). Correlational analyses between evening screen exposure, sleep quality and behavioral problems were conducted. Then, formal mediation analyses were run in order to quantify the relationship between variables.

RESULTS: School-aged children with screens in their bedrooms demonstrated more sleep and behavioral problems. Evening TV exposure was associated with higher SDSC and ADHD scores. Furthermore, the Structural Equation Modelling approach confirmed that evening screen exposure is directly associated with more disrupted sleep, which in turn is directly associated with behavioral problems.

CONCLUSIONS: These findings encourage families to avoid putting screens in their children's bedrooms, and limit evening screen exposure. They furthermore demonstrate the importance of taking into account screen exposure time (morning, afternoon, evening) and location (bedroom or elsewhere) in future studies

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ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND SLEEP PROBLEMS IN PRESCHOOL CHILDREN: THE ROLE OF AUTISTIC TRAITS.

Stickley A, Shirama A, Kitamura S, et al.

BACKGROUND: Sleep problems are elevated in children with attention-deficit/hyperactivity disorder (ADHD). However, until now there has been comparatively little research on the role of autistic traits in this association. The current study examined the association between ADHD symptoms and sleep problems in Japanese preschool children and whether autistic traits might also be important for this relationship.

METHODS: Data were analyzed from 1053 children (average age 64.14 months, range 58-71; 50.3% male) that were drawn from the Tama Children's Survey (TCS). Parent-reported information was obtained on ADHD symptoms using the Strengths and Difficulties Questionnaire (SDQ) and autistic traits with the Social Responsiveness Scale Second Edition (SRS-2). Parents also provided information on three different categories of sleep problems experienced by their children - parasomnias, sleep disordered breathing and awakening/daytime problems. Ordinal logistic regression analysis was used to examine the associations.

RESULTS: In analyses adjusted for sociodemographic factors, the mother's mental health and child's emotional problems, compared to children with no ADHD symptoms or autistic traits, children with only ADHD symptoms had significantly increased odds for only one of 11 individual sleep problems - waking in a negative mood. In contrast, children with comorbid ADHD symptoms and autistic traits had elevated odds for five sleep problems with odds ratios ranging from 2.10 (takes time to become alert in the morning) to 3.46 (excessive body movement while sleeping).

CONCLUSIONS: Sleep problems may be especially elevated in children with comorbid ADHD symptoms and autistic traits

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ASSESSING VIOLENCE RISK IN ADOLESCENTS IN THE PEDIATRIC EMERGENCY DEPARTMENT: SYSTEMATIC REVIEW AND CLINICAL GUIDANCE.

Mroczkowski MM, Walkup JT, Appelbaum PS.

INTRODUCTION: Violence risk assessment is one of the most frequent reasons for child and adolescent psychiatry consultation with adolescents in the pediatric emergency department (ED). Here we provide a systematic review of risk factors for violence in adolescents using the risk factor categories from the MacArthur Violence Risk Assessment study. Further, we provide clinical guidance for assessing adolescent violence risk in the pediatric ED.

METHODS: For this systematic review, we used the preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2009 checklist. We searched PubMed and PsycINFO databases (1966-July 1, 2020) for studies that reported risk factors for violence in adolescents.

RESULTS: Risk factors for adolescent violence can be organized by MacArthur risk factor categories. Personal characteristics include male gender, younger age, no religious affiliation, lower IQ, and Black, Hispanic, or multiracial race. Historical characteristics include a younger age at first offense, higher number of previous criminal offenses, criminal history in one parent, physical abuse, experiencing poor child-rearing, and low parental education level. Among contextual characteristics, high peer delinquency or violent peer-group membership, low grade point average and poor academic performance, low connectedness to school, truancy, and school failure, along with victimization, are risk factors. Also, firearm access is a risk factor for violence in children and adolescents. Clinical characteristics include substance use, depressive mood, attention deficit hyperactivity disorder, antisocial traits, callous/unemotional traits, grandiosity, and justification of violence.

CONCLUSION: Using MacArthur risk factor categories as organizing principles, this systematic review recommends the Structured Assessment of Violence Risk in Youth (SAVRY) risk- assessment tool for assessing adolescent violence risk in the pediatric ED

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Z Kinder Jugendpsychiatr Psychother. 2021 Jul;49:284-94.

ADHS - DISORDER CONCEPTS AND THE BEGINNINGS OF PHARMACOTHERAPY IN THE FEDERAL REPUBLIC OF GERMANY AND THE GERMAN DEMOCRATIC REPUBLIC.

Struß N, Stoff H.

ADHS - Disorder concepts and the beginnings of pharmacotherapy in the Federal Republic of Germany and the German Democratic Republic Abstract. After sporadic references before 1900, the concept of attention deficit/hyperactivity disorder became established in the 20th century. The hyperactive and inattentive child then became the focus of neuropediatrics in the wake of the encephalitis lethargica epidemic by clinical presentations of postencephalitic residual conditions. From these patients, physicians distilled a subgroup with an blank neurological history but impressive clinical symptoms. Child psychiatry, which emerged in the middle of the last century, studied these minimally brain-damaged patients, searching for both causes and therapies. The disorder concepts of Reinhart Lempp and Gerhard Göllnitz are significant contributions from the Federal Republic of Germany and the GDR, respectively, which provide revealing insights into the establishment of pharmacotherapy with stimulants in the 1970s

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Zh Nevrol Psikhiatr Im S S Korsakova. 2021;121:55-60.

FEATURES OF THE ORGANIZATION OF SLEEP IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kalashnikova TP, Anisimov GV.

The article presents modern ideas about the clinical features of sleep in children with attention deficit hyperactivity disorder (ADHD), the macrostructure of sleep, its cyclic organization and possible common links in the pathogenesis of sleep disorders and behavioral problems in patients. The relationship between the structure of sleep and impaired executive functions, the level of social maladjustment in patients with ADHD has been proven. Typical of children with ADHD are difficulty in going to sleep and falling asleep for a long time (resistance to sleep time), increased motor activity associated with sleep, including the association of ADHD with Restless legs syndrome (RLS) and periodic leg movement syndrome (PLMS), daytime

sleepiness. The presence of circadian desynchrony in children with ADHD explains the relationship between chronotype, circadian typology, and clinical manifestations of the syndrome. Multidirectional data on the representation of REM sleep by nocturnal polysomnography in children with ADHD depend on age. However, the change in the proportion of REM sleep during the night is considered as a leading factor in the pathogenesis of ADHD manifestations. Various variants of metabolic disorders of melatonin, dopamine, serotonin, aggravated by social jet lag, are considered by the conjugatedcommon pathogenetic mechanisms of sleep disturbance and ADHD. As well as changes in the concentration of iron and ferritin in the blood, which may explain the frequency of RLS and PLMS in children with ADHD. The change in the number of sleep cycles during the night in patients has been demonstrated. Possible strategies for correcting sleep disorders in children with ADHD and their impact on the manifestation of ADHD are discussed

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Article

Event-Based Prospective Memory Deficit in Children with ADHD: Underlying Cognitive Factors and Association with Symptoms

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Abstract: Event-based prospective memory (PM) was investigated in children with Attention deficit/hyperactivity disorder (ADHD), using a novel experimental procedure to evaluate the role of working memory (WM) load, attentional focus, and reward sensitivity. The study included 24 children with ADHD and 23 typically-developing controls. The experimental paradigm comprised one baseline condition (BC), only including an ongoing task, and four PM conditions, varying for targets: 1 Target (1T), 4 Targets (4T), Unfocal (UN), and Reward (RE). Children with ADHD were slower than controls on all PM tasks and less accurate on both ongoing and PM tasks on the 4T and UN conditions. Within the ADHD group, the accuracy in the RE condition did not differ from BC. A significant relationship between ADHD-related symptoms and reduced accuracy/higher speed in PM conditions (PM and ongoing trials), but not in BC, was detected. Our data provide insight on the adverse role of WM load and attentional focus and the positive influence of reward in the PM performance of children with ADHD. Moreover, the relation between PM and ADHD symptoms paves the road for PM as a promising neuropsychological marker for ADHD diagnosis and intervention.

Keywords: ADHD; prospective memory; reward; attention

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1. Introduction

Attention deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by a pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. Manifestations of the disorder must be present in more than one setting such as home and school [1].

ADHD occurs in about 5% of children and adolescents and about 2.5% of adults [2,3]. Besides the primary symptoms of inattention and/or hyperactivity, children and adolescents with ADHD exhibit impairment in a wider range of daily-life and academic domains. For instance, they show great difficulties in organizing and completing activities and in retaining information that they need in certain contexts (e.g., mental arithmetic, task instructions). Moreover, they often forget to perform daily activities, such as writing down homework, doing chores, running errands, returning a toy to a friend, bringing a jacket when going on a school trip [1,4,5].

1.1. Prospective Memory in ADHD

Some of the clinical manifestations of ADHD have been related to impairment in multiple cognitive domains involved in the complex sequence of behaviors required in prospective memory (PM) tasks. PM is the capability to remember to carry out future intentions—for instance, to remember to give someone a message at a certain time (time-based PM)—or event (event-based PM)—for instance, to remember to buy medicine next time you pass a pharmacy [6,7]. Importantly, the appropriate cue for carrying out the planned action is always embedded in ongoing activities (or ongoing tasks) interposed between intention formation and the critical moment of realization. During the execution of a task involving PM activation, the subject has to interrupt the ongoing task to initiate and perform the intended action at the appropriate moment. Mutual interaction between ongoing tasks and PM performances has been documented. Particularly demanding ongoing tasks negatively affect PM performances [8] and, furthermore, a "PM interference effect" [9,10] has been recognized, indicating a decrease in accuracy or speed in an ongoing task when a PM task occurs [11,12].

The neural basis of PM has been traced in the activity of the rostral prefrontal cortex [13,14] in association with other brain regions such as the anterior cingulate gyrus, the precuneus, and the temporal lobe [15–18]. The rostrolateral prefrontal cortex interacts with the putamen to maintain representations of future intentions [19], whereas the connectivity between the anterior prefrontal cortex and the precuneus has been reported to support the top-down sustained monitoring process [20].

PM is a critical issue in children with ADHD, as they often forget to execute their planned actions [21–25]. It has been suggested that PM mediates, at least partially, the relationship between the symptomatology of ADHD and procrastination behavior [26]. Compromised performances on PM tasks were also described in adults with ADHD, in association with a large-scale impairment in planning abilities; importantly, such difficulties have been confirmed not only in laboratory-based PM tasks, but also in naturalistic experimenter-assigned tasks [27,28]. In children with ADHD, the documented hypoactivation of key regions related to PM, in particular, the frontoparietal network [18], may play a role in PM deficits in this population.

Despite consistent findings of the presence of PM deficits in individuals with ADHD, investigations on a possible dissociation between deficits in time-based PM and event-based PM provided more contrasting results. A review by Talbot and Kerns [29] found that, although current literature agrees on the existence of time-based PM deficits in individuals with ADHD, there are inconsistent reports about the performances on event-based PM tasks in this population. Moreover, considering the possible influence of PM tasks on ongoing tasks, the evaluation of the impact of PM tasks on ongoing tasks could provide crucial insights to set up tailored interventions to improve overall functioning. Thus, further investigations on these topics are required.

1.2. Cognitive Factors Underlying Prospective Memory Performance

The cognitive mechanisms mediating performances on PM tasks in children with ADHD have not been extensively investigated. Literature suggests that factors such as working memory (WM) load and attentional focus can modulate PM performances in the general population or other groups of clinical samples. The executive framework of PM development [30] claims that WM supports cue retention and retrieval in PM tasks. Moreover, according to Guynn [11] and Smith [31], the allocation of WM and/or attentional resources is required to monitor the environment for the occurrence of the PM target. WM is required in PM tasks to actively sustain the intention while the individual is involved in the ongoing task; accordingly, WM has been found to be a predictor of PM performance in children and adults [23,32,33]. Thus, the manipulation of WM load in experimental paradigms should influence PM performance, as suggested by a number of studies [34,35]. A recent study conducted in a group of healthy adults found that in the time-based condition, but not in the event-based condition, prospective remembering

was affected by the reduction of WM resources [36]. The role of WM—together with time perception abilities—in PM performance in ADHD has been investigated by Mioni and colleagues [37], but only for time-based PM. The authors found that the relationship between WM abilities, time perception, and time-based PM performance was evident in the control group but not in the ADHD group. However, to our knowledge, there are no studies investigating the role of WM load in event-based PM performances of children with ADHD.

Attention is another crucial factor in the performance of PM tasks. Considering the focus of attention as a possible intervening variable, we can distinguish between focal and non-focal PM targets, which differ in the extent to which the ongoing task guides attention towards the target. PM targets in the center of the attention do not require additional search or monitoring processes for detection [11]. It is conceivable that event-based PM targets arising in the periphery of attention might be less effective in causing retrieval of the action to perform compared to cues arising within the focus of attention. Hicks and colleagues [38] found that if event-based PM targets occur in parts of the environment that are already receiving a good degree of focal processing, then the probability of detection might not be influenced by changes in their features. By contrast, event-based PM targets occurring in the periphery of focal attention can be manipulated to direct attention toward a feature that will trigger recollection of the intention. To date, no data are available on the role of focus of attention in PM performance of children with ADHD.

Another element to take into account when studying PM performances of children with ADHD is the reward amount. Individuals with ADHD exhibit an alteration of reward mechanisms, resulting in an aberrant sensitivity to reinforcement [39]. These alterations have been linked to the concept of delay aversion, which indicates the preference for small immediate rewards over large, delayed rewards [40,41]. Thus, it is conceivable that the number of rewards has a role in modulating PM performances of children with ADHD: in particular, an increased amount of reward should positively affect their performances. However, this hypothesis has never been tested in PM tasks.

Ascertaining the presence of an event-based PM deficit and its cognitive characteristics in children with ADHD could also have important consequences for clinical work. According to the current version of the Diagnostic and Statistical Manual of Mental Disorders [1], the diagnosis of ADHD is a strictly clinical process based on the assessment of an individual's behaviors and features; reliable diagnosis cannot be made using standardized instruments. Studies investigating the neuropsychological profile of individuals with ADHD failed to produce consistent results concerning their cognitive profile [42]. Moreover, it has been demonstrated that standardized instruments evaluating executive control are not predictors of ADHD symptoms and long-term outcomes in ADHD [43,44]. For this reason, investigating the presence of a correlation between performance on Prospective Trials and clinical evaluation of children with ADHD could identify new possible clinical markers for such neurodevelopmental conditions.

In summary, given the established deficits in PM of individuals with ADHD, the presence of specific event-based PM impairment in this population should be evaluated in order to better define the possible role of cognitive variables in event-based PM deficits in ADHD and its relation with symptomatology.

1.3. The Current Study

In the present study, we assessed the presence of deficits in event-based PM in children with ADHD. Moreover, to address the role of cognitive variables possibly influencing PM performance in children with ADHD, we tested different hypotheses with specific reference to WM load, type of attentional focus, and amount of reward, which are known to be involved in both PM tasks execution and ADHD manifestations, at least in part. At this aim, we developed a novel experimental procedure consisting of five different conditions: one baseline condition only including the ongoing task, and four PM conditions, including

the ongoing task and concomitant PM tasks, varying for the WM load, the attentional focus, and the reward amount.

We expected that the manipulation of different cognitive factors intervening in the event-based PM performance would help in clarifying the inconsistent reports on event-based PM deficits in the ADHD population. In this view, we predicted that:

(a) Children and adolescents with ADHD would show reduced performance compared to controls in several event-based PM tasks, expressed as reduced accuracy and increased response times for both the ongoing and the PM conditions. We also predicted that their performance would be modulated by the cognitive factors manipulated in the PM tasks.

Considering the possible role of WM and attentional deficit in the ADHD population, we hypothesized the following:

(b) The increase of WM load (number of PM targets) would specifically affect the performance of children with ADHD by reducing the response accuracy and increasing the response times for both the ongoing and the PM task compared to the other PM conditions.

(c) The occurrence of the PM targets outside the central focus of attention would affect the performance of children with ADHD by reducing the response accuracy and increasing the response times for both the ongoing and the PM task compared to the other PM conditions.

Moreover, in light of the documented aberrant sensitivity to reinforcement typical of individuals with ADHD, we hypothesized that:

(d) The increase in reward amount would positively influence the PM performance of children with ADHD in comparison with the other PM conditions.

We also investigated the possible relation between PM performance and the presence of ADHD-related symptoms. This would represent an important achievement to support clinical evaluation. For this reason, event-based PM performance was related to the scores at an extensively used instrument for clinical and research purposes in ADHD. We hypothesized that:

(e) A negative relationship would emerge between PM performance and the ADHD symptoms.

2. Materials and Methods

2.1. Participants

The study included 47 participants, 24 children with ADHD–ADHD group (15 males and 9 females) and 23 typically developing children–CON group (16 males and 7 females), matched for chronological age (CA), intelligence quotient (IQ), and sex distribution. Table 1 describes the characteristics of participants. All participants were Caucasian, middle socioeconomic status children. The imbalance between males and females mirrors the distribution of ADHD, which is more frequent in males than in females with a ratio of approximately 2:1 [1].

Selection criteria included, in addition to clinical diagnosis of ADHD, age between 8 and 13 years, and performances in the normal range on standardized intelligence tests. The age range was defined based on literature indicating that PM ability has been found to be acquired as early as 2 years of age [45] and to increase significantly around 7 and 8 years of age [46,47]. Exclusion criteria included reports of neurological signs and patients undergoing pharmacological treatments, as well as a history of language delay or learning disability.

Table 1. Characteristics of participants.

Measure	ADHD N 24; 15M/9F		CON N 23; 16M/7F			
	M	SD	M	SD	F(1,45)	*p*
CA	10.42	(1.34)	10.15	(1.51)	0.44	0.51
IQ	108.12	(10.05)	112.39	(9.15)	2.31	0.14
CPRS Oppositional	63.35	(15.45)	46.37	(13.96)	13.70	<0.001 *
CPRS Cognitive probl./inattention	75.33	(12.72)	43.79	(5.75)	100.27	<0.0001 *
CPRS Hyperactivity	66.71	(14.40)	45.11	(8.36)	33.66	<0.0001 *
CPRS Anxious	54.09	(13.78)	45.79	(7.15)	5.62	0.02
CPRS Perfectionism	51.52	(11.41)	46.69	(10.70)	1.98	0.17
CPRS Social problems	57.87	(14.17)	46.95	(12.01)	7.20	0.01
CPRS Psychosomatic	58.65	(16.90)	47.68	(7.45)	6.87	0.01
CPRS ADHD index	75.00	(12.12)	46.47	(9.88)	68.90	<0.0001 *
CPRS Global index- Restless-impulsive	67.33	(11.75)	45.42	(8.91)	45.36	<0.0001 *
CPRS Global index-Emotional lability	60.04	(16.82)	48.26	(11.50)	6.71	0.01
CPRS Global index	69.67	(13.78)	45.68	(10.36)	39.68	<0.0001 *
CPRS DSM Inattentive	75.04	(14.44)	45.68	(8.10)	62.69	<0.0001 *
CPRS DSM Hyperactive/impulsive	64.79	(12.60)	46.63	(9.19)	27.73	<0.0001 *
CPRS DSM Total	73.46	(13.27)	44.37	(7.68)	72.00	<0.0001 *

ADHD = group with Attention deficit/hyperacticity disorder; CON = control group; CA = chronological age; IQ = intelligence quotient; CPRS = Conner's Parent Rating Scales; * survived after Bonferroni correction.

Participants with ADHD were recruited at the Child and Adolescent Neuropsychiatry Unit of the Bambino Gesù Children's Hospital in Rome; all of them were children undergoing the visit for the first diagnosis of ADHD. All participants underwent a child psychiatric and neuropsychological examination conducted by experienced developmental psychiatrists and neuropsychologists. The diagnosis was performed with the support of The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS PL), a clinical interview [48], and the administration of the standardized scale Conners' Parent Rating Scales Long Version, Revised (CPRS) [49]. IQ was assessed using the Raven Coloured Progressive Matrices for children aged up to 11 years or the Raven Standard Progressive Matrices for children aged over 11 years [50]. Considering the clinical evaluation, 17 children out of 24 had a diagnosis of ADHD-combined presentation, and the other 7 children had a diagnosis of ADHD-predominant inattentive presentation. Of the participants with ADHD, 66% had at least one comorbid learning disorder. Controls were recruited at a primary and secondary public school in Rome and underwent the same IQ and CPRS-R scale evaluation. ADHD and CON groups did not differ for chronological age [$F(1,45) = 0.44$, $p = 0.51$], IQ [$F(1,45) = 2.31$, $p = 0.14$], and sex distribution [$\chi 2 = 0.26$, $p = 0.61$], but did differ for ADHD symptoms in the CPRS scale, particularly the CPRS total score and Oppositional, Cognitive problems/inattention, Hyperactivity, ADHD Index, Global index-Restless-impulsive, Global index, DSM Inattentive, and DSM hyperactive/impulsive CPRS-R subscales (all $p < 0.001$).

The experimental sessions were carried out after informed consent had been obtained from all participants and their families, and the study had been approved by the local Ethics Committee (process number 1111_OPBG_2016).

2.2. Study Design and Procedure

The PM assessment was administered on two different days. All participants were tested individually in a quiet, well-lit room. Participants received specific instructions for the execution of the experimental tasks and, before starting the test phase, they were asked to repeat the instructions to assure their comprehension. Each task lasted approximately 7 min; the overall experimental session lasted approximately 45 min.

2.2.1. Assessment

The Raven's Standard Progressive Matrices [50] is a 60-item test used to assess mental ability associated with abstract reasoning, considered a nonverbal estimate of fluid intelligence. The test consists of increasingly difficult pattern matching tasks and has little dependency on language abilities.

Conners' Parent Rating Scales-Long Version, Revised (CPRS) [49] are widely used instruments for diagnostic and research purposes in the ADHD field, which can be administered to both parents and teachers. They assess core symptoms as well as symptoms of other behavioral and emotional disorders commonly associated with ADHD (e.g., oppositional behavior), based on DSM-IV-TR criteria [51]. CPRS is a multidimensional questionnaire; items are scored on a four-point Likert scale and divided into two subscales that assess symptoms related to ADHD: restless-impulsive and emotional lability. The scale has a cut-off for elevated (T 65-69) and for very elevated scores ($T \geq 70$), indicating borderline and clinical scores, respectively. The questionnaire compiles scores in each of the following areas: Oppositional/defiant; Cognitive problems/inattention, Hyperactivity, Anxiety, Perfectionism, Social problems, Psychosomatic, ADHD index, Global index-Restless-impulsive, Global index-Emotional lability, Global index, DSM Inattentive, DSM hyperactive/impulsive, DSM Total.

The K-SADS PL is a clinician-administered semi-structured interview used for diagnosing children and adolescents aged 6 to 18 years according to DSM-IV criteria [48]. The screening interview (including the psychosis screen) is administered first; if threshold symptoms are detected during the screen, in-depth supplements for each category of diagnosis (e.g., psychotic disorders) are administered. It assesses both current and past psychopathology.

2.2.2. Experimental Paradigm

The experimental paradigm consisted of one baseline condition (BC) including only the ongoing task, and four PM conditions, including the ongoing task and concomitant PM tasks. Stimuli were similar in visual characteristics but the task to be performed changed.

The ongoing task required the participants to make a semantic decision, pressing two different buttons of a PC keyboard in response to the stimulus appearing at the center of the screen. The PM task required participants to press another key (the space bar) when the PM target appeared. The PM targets, namely the event that marked the prospective task, varied between conditions. In one PM condition, the reward obtained for responses differed from the other conditions.

The four PM conditions were: 1 Target (1T), 4 Targets (4T), Unfocal (UN), and Reward (RE). 1T included only one PM target, presented at the center of the attentional focus (i.e., center of the screen, in correspondence of the fixation point), without reward manipulation; 4T included four different PM targets, at the center of the attentional focus, without reward manipulation; UN included one PM target, outside the center of the attentional focus (i.e., in correspondence of one of the four corners of the screen), without reward manipulation; RE included only one PM target, at the center of the attentional focus, but a reward manipulation occurred. Performance accuracy (proportion of correct responses) and response reaction time (RTs, milliseconds) to the ongoing trials and the PM trials were recorded.

Stimuli and Procedure

The participants were seated in a comfortable chair facing a 15" PC screen on a table about 40 cm away from them. E-Prime 2.0 software (Psychology Software Tools, Sharpsburg, PA, USA) was used to program and run the experiment and to record participants' answers. Each PM condition included 108 ongoing task trials and 12 PM trials, for a total of 120 trials, instead, the BC included only 120 ongoing task trials. The PM target did not appear in the first four trials of a PM condition. Each trial started with a 200 ms fixation point, consisting of a black cross, 12 points Times New Roman, at the center of the screen, followed by the presentation of a task stimulus, appearing for 2 s. Response RTs and accuracy were recorded during the 2-s stimulus presentation. If a correct response was given, a reward stimulus appeared for 1 s immediately after the response; if incorrect or no response was recorded a different reward stimulus (a red cross indicating no reward) appeared.

Stimuli consisted of colored animal images (belonging to two categories: flying, non-flying animals), mean size 8 × 10 cm, located at the center of the screen, 3° × 3° to the fixation point; and four colored plant images, size 5 × 5 cm, located at the four corners of the screen, respectively 45°, 90°, 180°, 360° to the fixation point, in a white background, for a total of 600 images. Per each condition the stimuli varied: a list of 10 animal images (5 flying and 5 non-flying animals) was presented 12 times in the BC, 1T, UN, and RE conditions, while a list of 40 animal images (20 flying and 20 non-flying animals) was presented 3 times in the 4T condition (total of 90 different animal images). When the animal image was repeated, the surrounding set of plant images changed per each presentation. The sets of 4 plant images at the corners were arranged from a pool of 80 different plant images. A list of 40 plant images was chosen per each condition to create 120 combinations of 4 plant images at the corners, with each plant image presented 12 times. Specifically, 50 different new combinations were created, while 70 other combinations were created with a plant image previously associated with other plant images but in different positions. In this way, each plant image was presented associated with the same plant images, but in different positions, only two times (10 combinations), while for the other two times it was presented associated with 2 of the previous plant images. Thus, each animal image was associated with different plant image combinations. The reward stimuli consisted of the image of a yellow star above a bag, with the writing of the score obtained and the count of the points gained up to that moment. In the case of an error, the bag was covered with a red cross.

Each condition was preceded by a learning session, in which participants were given written task instructions and were shown examples of the stimuli in a PowerPoint presentation. For the PM conditions, the PM targets were previously presented in the PowerPoint presentation to be studied. A recognition test followed to be sure that the participant correctly recognized all the PM targets among distractors (different stimuli list from the experimental conditions).

Each experimental condition started after a short familiarization session of a computerized presentation of 10 trials.

The experiment started with the BC condition, and then the four PM conditions were administered in a counterbalanced order between participants.

Baseline Condition

BC only included the ongoing task, for a total of 108 trials randomly presented. Participants were asked to perform a semantic decision task, pressing the "V" button, if an image of a flying animal appeared, and the "N" button if an image of a non-flying animal appeared (Figure 1). Participants received 1 reward point (RP) for every correct answer and no RP for any wrong or omitted answer.

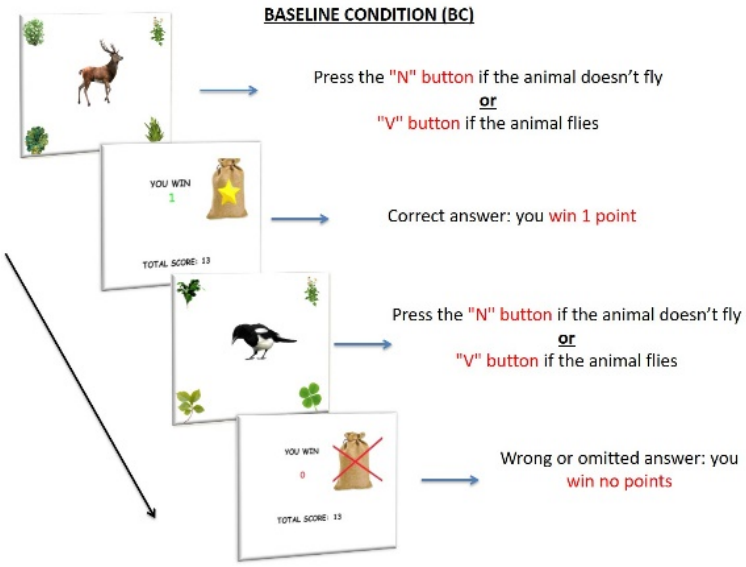

Figure 1. Procedure of Baseline condition (BC). The items consisted of 108 images of an animal located at the center of the screen; images of plants were located at the four corners of the screen. Participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the screen (semantic decision task). Each stimulus appeared for 2 s. Participants received 1 RP for every correct answer and no RP for any wrong or omitted answer.

PM Conditions

In the PM conditions, participants had to execute an event-based PM task (12 trials) while performing the ongoing task (108 trials). Specifically, the ongoing task must be interrupted to be able to carry out the PM task, when the PM target appeared on the screen.

1T. Only one PM target was included, at the center of the attentional focus, without reward manipulation. For the ongoing task, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the screen (ongoing task). However, when a dove—the PM target—appeared at the center of the screen (12 PM trials), participants were required to press the spacebar (PM task), instead of the semantic decision task (Figure 2). They received 1 response point (RP) for every correct answer and no RP for any wrong or omitted answer, in both trials (ongoing and PM trials).

4T. Four PM targets were included, each one presented at the center of the attentional focus, without reward manipulation. For the ongoing task, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared (ongoing task). However, when one of the four PM targets (rabbit, crow, camel, pelican) appeared at the center of the screen (12 PM trials), participants were required to press the spacebar (PM task), instead of the semantic decision task (Figure 3). They received 1 RP for every correct answer and no RP for any wrong or omitted answer, in both trials (ongoing and PM trials).

UN. Only one PM target was included, outside the center of the attentional focus (i.e., in correspondence of one of the four corners of the screen), without reward manipulation. For the ongoing task, participants had to press the "N" button when the image of a non-flying animal appeared and the "V" button when the image of a flying animal appeared on the screen (ongoing task), at the center of the attentional focus (i.e., in correspondence of the fixation point). However, when the cactus plant—PM target—appeared in one of the four corners of the screen (12 PM trials), participants were required to press the spacebar (PM task), instead of the semantic decision task (Figure 4). They received 1 RP for every correct answer and no RP for any wrong or omitted answer, in both trials (ongoing and PM trials).

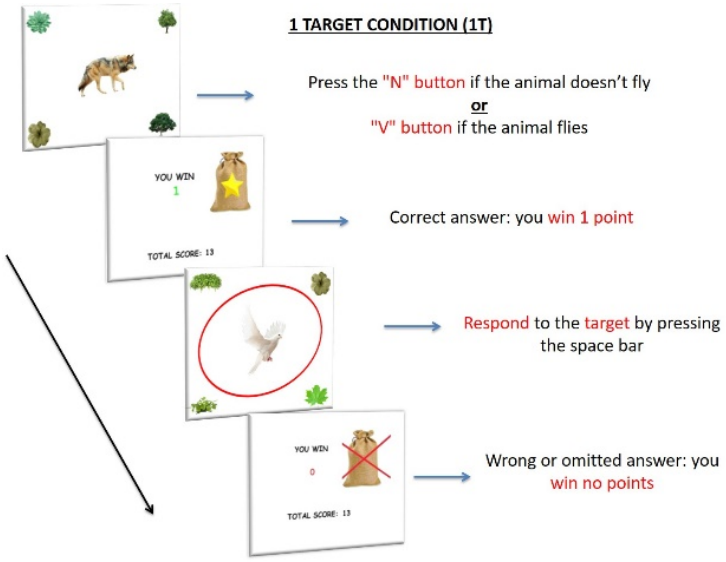

Figure 2. Procedure of 1 Target condition (1T). The items consisted of 120 images of an animal located at the center of the screen; images of plants were located at the four corners of the screen. As in the BC, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the screen (ongoing task). However, when a dove—PM target—appeared on the center of the screen (12 trials), participants were required to press the spacebar (PM task), instead of the semantic decision task. Each stimulus appeared for 2 s. They received 1 RP for every correct answer and no RP for any wrong or omitted answer, in both tasks (ongoing and PM trials).

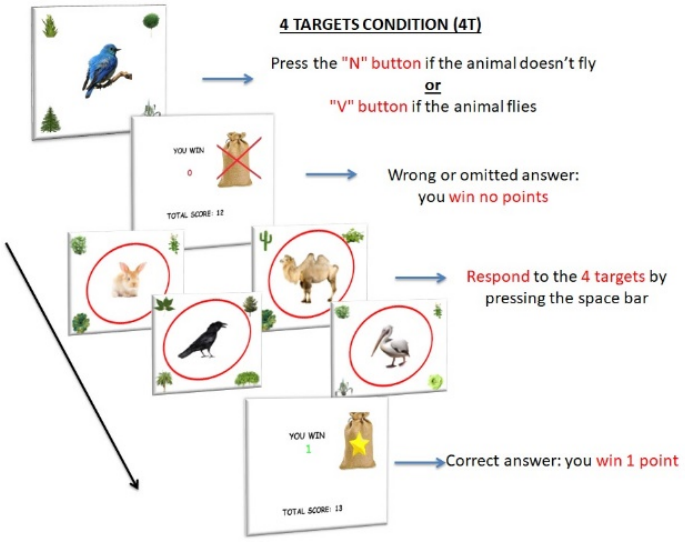

Figure 3. Procedure of 4 Targets condition (4T). The items consisted of 120 images of an animal located at the center of the screen; images of plants were located at the four corners of the screen. As in the BC, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the screen (ongoing task). However, when one of the four PM targets (rabbit, crow, camel, pelican) appeared at the center of the screen (12 trials), participants were required to press the spacebar (PM task), instead of the semantic decision task. Each stimulus appeared for 2 s. They received 1 RP for every correct answer and no RP for any wrong or omitted answer, in both tasks (ongoing and PM trials).

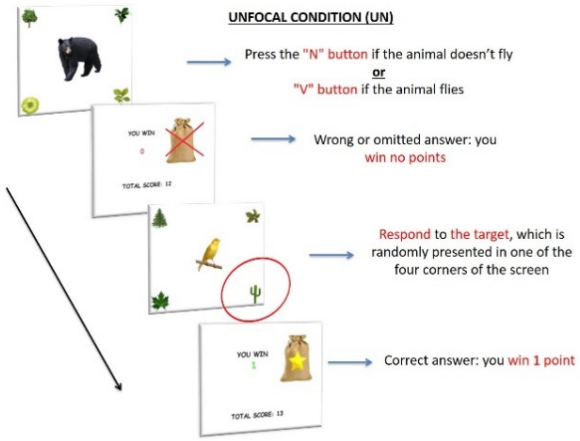

Figure 4. Procedure of Unfocal condition (UN). The items consisted of 120 images of an animal located at the center of the screen; images of plants were located at the four corners of the screen. As in the BC, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the center of the screen (ongoing task). However, when the cactus plant—Prospective target—appeared in one of the four corners of the screen (12 trials), participants were required to press the spacebar (PM task), instead of the semantic decision task. Each stimulus appeared for 2 s. They received 1 RP for every correct answer and no RP for any wrong or omitted answer, in both tasks (ongoing and PM trials).

RE. Only one PM target was included, at the center of the attentional focus, but a reward manipulation occurred. In the ongoing task, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the screen (108 ongoing task trials). However, when a rhinoceros—PM target—appeared at the center of the screen, participants were required to press the spacebar (PM task), instead of the semantic decision task (Figure 5). Differently for the other PM conditions, in the ongoing task trials, they received 1 RP for every correct answer but lost 1 RP for any wrong or omitted answer. Moreover, in the PM trials, they received 50 RP for every correct answer and lost 20 RP for any wrong or omitted answer.

The comparison between the different conditions allowed us to evaluate the contribution of different cognitive variables, with specific reference to the WM load, the type of attentional focus, and the amount of reward, in the PM execution. In particular, 4T differed from 1T only for the number of PM targets, allowing us to evaluate whether the WM load affected event-based PM performance. UN condition differed from 1T only for the location of the PM target (center or corner of the screen), allowing us to evaluate whether the displacement of the PM target out of the attentional focus affected the event-based PM performance. RE condition differed from 1T only for the RP associated with both the ongoing and PM tasks, allowing us to evaluate whether possible changes in motivation, linked to the reward amount, could influence the PM performance.

2.3. Statistical Analyses

The demographic variables were compared through One-way Anovas. A chi-squared test was used to determine the non-parametric variables. To evaluate the effect of the conditions, mixed-design ANOVAs were performed on the mean proportion of accuracy and the mean response RTs separately for the ongoing task trials and the PM trials. For the ongoing task, Group (CON vs. ADHD) was considered as a between-subjects factor and Condition (BC vs. 1T vs. 4T vs. UN vs. RE) as a within-subjects factor; for the PM trials, Group (CON vs. ADHD) was considered as a between-subjects factor and Condition (1T vs. 4T vs. UN vs. RE) as a within-subjects factor.

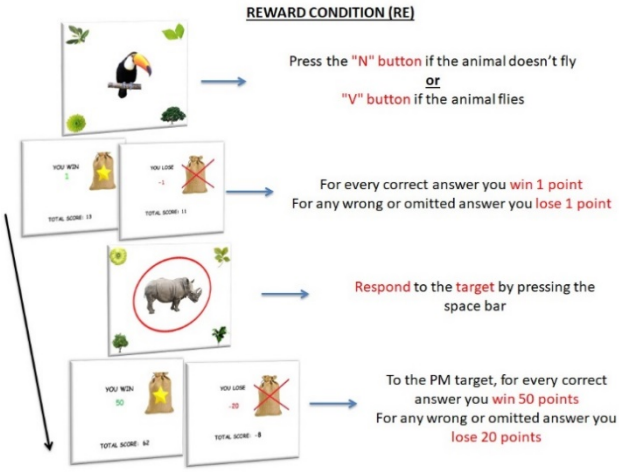

Figure 5. Procedure of Reward condition (RE). The items consisted of 120 images of an animal located at the center of the screen; images of plants were located at the four corners of the screen. As in the BC, participants had to press the "N" button when the image of a non-flying animal appeared on the screen and the "V" button when the image of a flying animal appeared on the screen (ongoing task). However, when a rhinoceros—PM target—appeared at the center of the screen (12 trials), participants were required to press the spacebar (PM task), instead of the semantic decision Table 2 seconds. In the ongoing task, they received 1 RP for every correct answer and lost 1 RP for any wrong or omitted answer. In the PM task, they received 50 RP for every correct PM answer and lost 20 RP for any wrong or omitted PM answer.

Mauchly's test was used to check for a violation of sphericity. The overall level of significance was set at $p < 0.05$. If a violation of sphericity was detected, a Greenhouse–Geisser correction was applied. Post hoc analyses were performed using Bonferroni's test. Partial eta squared (ηp^2) was used to measure effect size. The Pearson correlation was used to test the association between the experimental variables (accuracy and RTs of the ongoing and PM trials of each experimental condition) and the scores obtained on the CPRS global indexes in all groups. A Bonferroni correction for multiple comparisons was applied and, according to the number of comparisons, a different *p*-value was considered statistically significant ($p < 0.0004$).

Table 2. Correlational analysis between the results in the experimental paradigm and the global indexes of the Conner's Parent Rating Scales in both the studied groups.

CPRS	BC		1T				4T				UN				RE			
			Ongoing		PM		Ongoing		PM		Ongoing		PM		Ongoing		PM	
	Acc	Speed	Acc	Speed	Acc	Speed	Acc	Speed	Acc	Speed	Acc	Speed	Acc	Speed	Acc	Speed	Acc	Speed
ADHD Index	−0.19	0.19	−0.38 *	0.38 *	−0.27	0.17	−0.40 **	0.36 *	−0.32 *	0.28	−0.35 *	0.12	−0.32 *	0.29	−0.21	0.31 *	−0.32 *	0.34 *
Global index-Restless-impulsive	−0.13	0.09	−0.26	0.30	−0.12	0.09	−0.30 *	0.26	−0.17	0.19	−0.24	0.17	−0.30	0.24	−0.19	0.23	−0.22	0.33 *
Global index-Emotional lability	−0.03	0.18	−0.14	0.14	−0.20	−0.03	−0.26	0.11	−0.13	0.04	−0.22	0.25	−0.17	0.18	−0.14	0.11	−0.07	0.23
Global index	−0.13	0.08	−0.24	0.31 *	−0.18	0.04	−0.34 *	0.33 *	−0.22	0.20	−0.25	0.21	−0.26	0.24	−0.19	0.24	−0.23	0.26
DSM Inattentive	−0.21	0.22	−0.37 *	0.40 **	−0.26	0.22	−0.40 **	0.39 *	−0.32 *	0.31 *	−0.37 *	0.11	−0.36 *	0.28	−0.23	0.32 *	−0.32 *	0.36 *
DSM Hyperactive/impulsive	−0.18	0.04	−0.37 *	0.16	−0.23	0.06	−0.52 **^	0.21	−0.32 *	0.26	−0.28	0.20	−0.35 *	0.30	−0.33 *	0.26	−0.36 *	0.43 **
DSM Total	−0.18	0.08	−0.34 *	0.28	−0.28	0.12	−0.48 **	0.35 *	−0.34 *	0.36 *	−0.40 **	0.13	−0.45 **	0.36 *	−0.30	0.30	−0.32 *	0.42 **

CPRS = Conner's Parent Rating Scales; BC = baseline condition; 1T = One target condition; 4t = Four-target condition; UN = Unfocal condition; RE = Reward condition; * $p < 0.05$; ** $p < 0.01$; ^survived after Bonferroni correction.

3. Results

3.1. PM Procedure

3.1.1. Ongoing Task—Accuracy

Results showed a significant interaction Group per Condition [F(4,180) = 3.15; $p = 0.02$, $p = 0.03$ with Greenhouse–Geisser correction, $\eta p^2 = 0.07$]. Post hoc analysis revealed that performance of the ADHD group was significantly lower than that of the CON group on the 4T ($p < 0.01$) and UN ($p < 0.01$) conditions, while no difference emerged on the BC, 1T and RE conditions (all $p > 0.1$). Moreover, within-group comparisons showed that participants in the ADHD group had lower accuracy in almost all the PM conditions compared to BC (1T, $p = 0.04$; 4T, $p < 0.01$; UN, $p < 0.001$) with the exception of the RE, to which BC did not differ ($p = 1.00$). In addition, the accuracy on the UN was lower than 1T ($p < 0.01$) and RE ($p < 0.001$) conditions, and the accuracy on the 4T was lower than RE ($p < 0.01$). Conversely, within-group comparisons in the CON group showed no significant differences in accuracy between BC and all PM conditions (all $p > 0.1$). The accuracy on the UN was significantly lower than on the RE ($p = 0.02$). A general Group effect also emerged [F(1, 45) = 12.45; $p < 0.001$, $\eta p^2 = 0.22$] with the ADHD group showing lower accuracy (mean proportion of accuracy 0.91) than the CON group (mean proportion of accuracy 0.97). Finally, a general Condition effect emerged [F(4,180) = 17.7; $p < 0.001$, $p < 0.001$ with Greenhouse–Geisser correction, $\eta p^2 = 0.28$] because all groups showed the lowest accuracy in the UN compared to all other conditions (all $p < 0.01$); moreover ongoing task accuracy on the BC was higher than 1T ($p < 0.05$), 4T ($p < 0.01$) and UN ($p < 0.001$), but not than RE ($p = 1.00$). Figure 6 shows the mean proportion of accuracy in the ongoing task for each condition in the two groups.

3.1.2. Ongoing Task—Speed

The results showed a significant interaction Group per Condition [F(4,180) = 4.18; $p < 0.01$, $p < 0.01$ with Greenhouse–Geisser correction, $\eta p^2 = 0.08$]. However, post hoc analysis showed no significant differences in the mean response RTs between groups for all conditions (all $p > 0.1$), only within-group differences emerged. In particular, participants in the ADHD group were slower in all PM conditions compared to BC (all $p < 0.05$). Furthermore, on the UN, they were slower than all other conditions (all $p < 0.001$) and on the 4T, they were slower than the RE condition ($p = 0.02$). Conversely, in the CON group, no difference emerged between mean response RTs in almost all PM conditions (1T, 4T, RE) and BC (all $p > 0.1$), except for the UN, in which participants were slower than all other conditions (all $p < 0.001$). A general Group effect did not reach significance [F(1, 45) = 3.73; $p = 0.06$, $\eta p^2 = 0.08$] although the ADHD group showed a tendency to be slower (mean response RTs 1021.7 msec) than the CON group (mean response RTs 933.0 msec). Finally, a general Condition effect emerged [F(4, 180) = 100.86; $p < 0.001$, $p < 0.001$ with Greenhouse–Geisser correction, ηp2 = 0.69] because mean response RTs differed in each condition as follows: all groups were slower in the UN (mean response RTs 1320.6 msec) than in the 4T (mean response RTs 991.7 msec) and 1T (mean response RTs 907.9 msec) conditions (all $p < 0.05$), no difference emerged between the 1T and RE (mean response RTs 878.6 msec) conditions ($p > 0.1$), and all groups were slower in RE than BC (mean response RTs 787.8 msec), $p = 0.02$. Figure 7 shows the mean response RTs on the ongoing task for each condition in the two groups.

3.1.3. PM Task—Accuracy

Results showed a significant Group effect [F(1, 45) = 10.59; $p < 0.01$, $\eta p^2 = 0.19$] with the ADHD group showing lower accuracy (mean proportion of accuracy 0.85) than CON group (mean proportion of accuracy 0.93). A general Condition effect also emerged [F (3,135) = 21.78; $p < 0.001$, $p < 0.001$ with Greenhouse–Geisser correction, $\eta p^2 = 0.33$] because all groups showed the lowest accuracy in the UN (mean proportion of accuracy 0.80) and 4T (mean proportion of accuracy 0.85) compared to the other conditions, (all $p < 0.01$—1T

mean proportion of accuracy 0.93, RE mean proportion of accuracy 0.93). Moreover, 1T did not differ from 4T ($p = 0.14$).

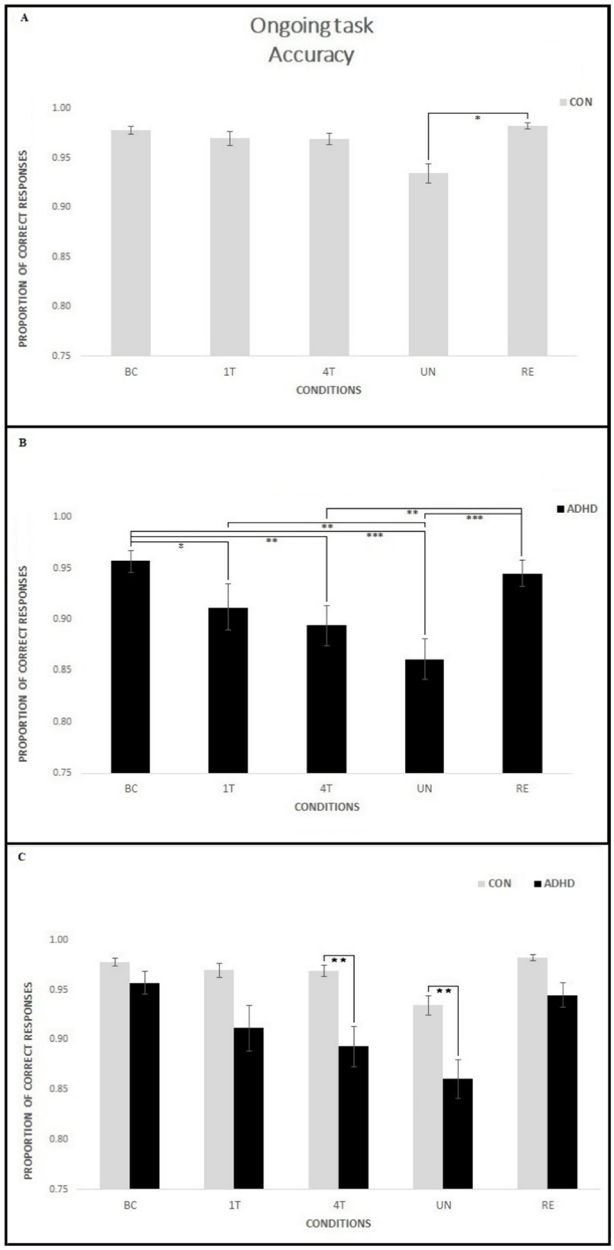

Figure 6. Accuracy on the ongoing task for each condition in the two groups. Within-group comparisons showed that in the CON group (**A**) no significant difference emerged between BC and all the PM conditions; the accuracy on the UN was lower than the RE condition. Conversely, participants in the ADHD group (**B**) showed lower accuracy in almost all the PM conditions compared to BC. 4T and UN conditions were lower than 1T and RE. Between-group comparisons (**C**) showed that the ADHD group performed significantly lower than the CON group on the 4T and UN conditions, while no difference emerged on the BC, 1T, and RE conditions. Asterisks mark significant differences: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Finally, the interaction Group per Condition was significant [F (3,135) = 3.40; $p = 0.02$, $p = 0.04$ with Greenhouse–Geisser correction, $\eta p^2 = 0.07$]. Post hoc analysis revealed that the ADHD group performed significantly lower than the CON group in the 4T ($p = 0.02$) and UN ($p = 0.01$) conditions, while no difference emerged in the 1T and RE conditions

(all $p = 1.0$). Moreover, within-group comparisons showed that participants in the ADHD group showed lower accuracy in the 4T and UN compared to 1T (respectively $p < 0.01$ and $p < 0.001$) and RE (all $p < 0.001$) conditions. Conversely, within-group comparisons in the CON group showed no significant differences between conditions (all $p > 0.1$) except for the UN being lower than RE ($p = 0.02$).

Figure 8 shows the mean proportion of response accuracy on the PM task for each condition in the two groups.

3.1.4. PM Task—Speed

The results showed a significant Group effect [$F(1, 45) = 5.71$; $p = 0.02$, $\eta p^2 = 0.11$] with the ADHD group being generally slower (mean response RTs 1126.1 msec) than CON group (mean response RTs 1015.2 msec). Condition effect also emerged [$F(3,135) = 93.33$; $p < 0.001$, $\eta p^2 = 0.67$], because all groups were slower in response RTs to target stimuli in the 4T and UN compared to 1T and RE conditions (all $p < 0.001$); no difference emerged between the 1T and RE conditions ($p = 0.17$). Finally, no significant interaction Group per Condition emerged [$F (3,135) = 1.45$; $p = 0.23$, $\eta p^2 = 0.03$].

3.2. Correlation Analysis

Results of the correlational analysis between the performance in the experimental paradigm and the global indexes of the CPRS-R were shown in Table 2. As concerns the BC, no significant relationship was shown between each CPRS index and the accuracy or the speed in this condition. Moreover, no relationship was found between the Global index Emotional lability and all experimental variables.

As concerns 1T, some relationships emerged for the ongoing task but not for the PM task. In particular, moderate negative relationships were found between the ongoing task accuracy and the ADHD index, the DSM inattentive, the DSM hyperactive/impulsive, and the DSM Total, i.e., the higher the CPRS score (more symptoms), the lower the accuracy in the ongoing task was (more impaired). An inverse relationship, but in the same direction, was found between the ongoing task response RTs and the score of some CPRS indexes. In particular, a moderate positive relationship emerged with the ADHD index, the Global index, and the DSM inattentive, i.e., the higher the score (more symptoms), the slower the responses were (more impaired).

As concerns 4T, negative moderate to strong relationships emerged between the ongoing task accuracy and all other CPRS indexes, with the exception of the Global index Emotional lability. In addition, a moderate positive relationship emerged between the ongoing task speed and the ADHD index, the Global index, the DSM Inattentive, and the DSM Total. In summary, the higher the CPRS score, the lower the performance in the ongoing task was. A similar relationship was detected in the PM task of the 4T condition, in which the higher the CPRS score in ADHD index, DSM Inattentive, DSM hyperactive/impulsive, and DSM Total, the lower the accuracy on the PM task was. At the same time, the higher the CPRS score in the DSM Inattentive and the DSM Total, the higher the response RTs were.

Elevation in ADHD index, DSM inattentive, and DSM Total negatively correlated with the accuracy in the UN (Ongoing and Prospective trials) and with the performance on the PM Task of the RE (lower accuracy and higher response RTs). Elevation in DSM Hyperactive/impulsive also negatively correlated with PM task accuracy of the UN and with the performance on the RE (lower accuracy on the ongoing and PM tasks, higher response RTs on the PM tasks). DSM Total positively correlated with the response RTs on the PM tasks of the UN. Finally, ADHD index and DSM Inattentive positively correlated with the ongoing task response RTs of the RE condition.

However, after applying Bonferroni correction for multiple comparisons, only the strong negative correlation between DSM Hyperactive/impulsive index and the ongoing task accuracy of the 4T condition survived (see Table 2).

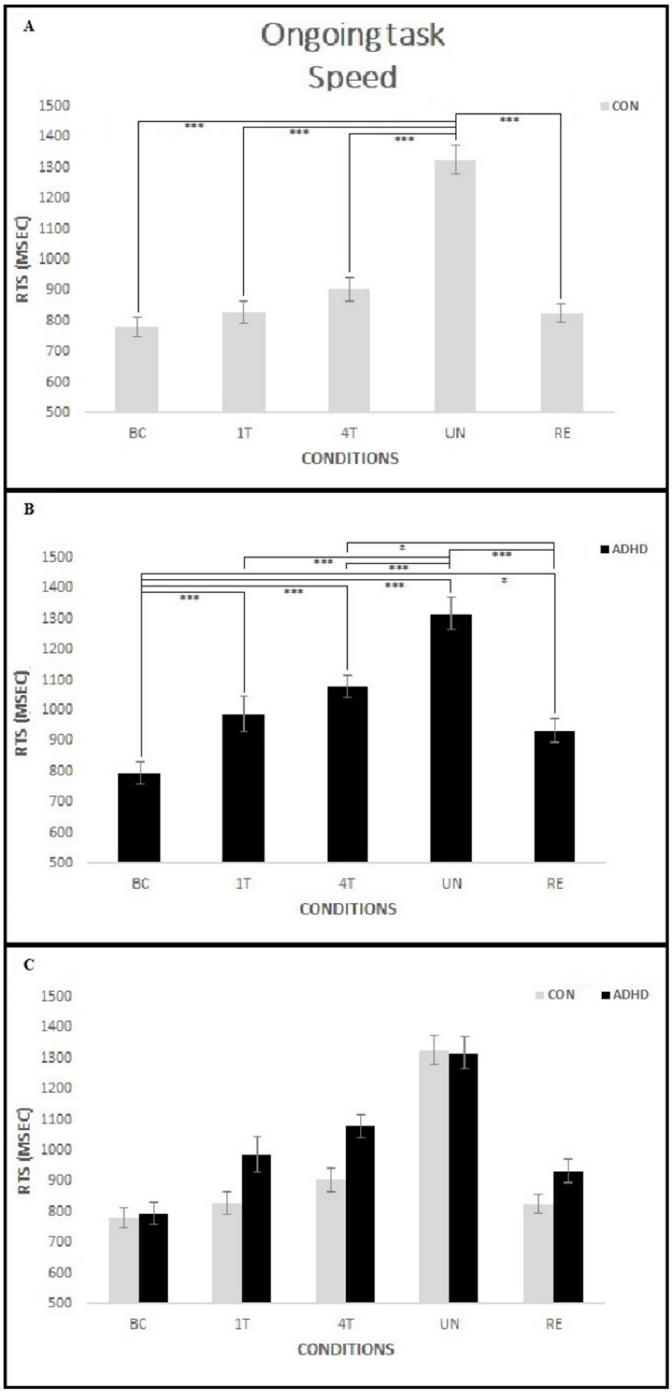

Figure 7. Ongoing task speed for each condition in the two groups. Within-groups differences emerged in the mean response RTs (see **A**,**B**), but no significant differences occurred between groups (**C**). In the CON group (**A**), no difference emerged between the mean response RTs in the BC and almost all PM conditions (1T, 4T, RE), with the exception of the UN, in which they were slower than all other conditions. In the ADHD group (**B**), participants were slower in all PM conditions compared to BC; moreover, as in the CON group, on the UN they were slower than all other conditions. Finally, the mean response RTs on the 4T was slower than the RE condition. Asterisks mark significant differences: * $p < 0.05$, *** $p < 0.001$.

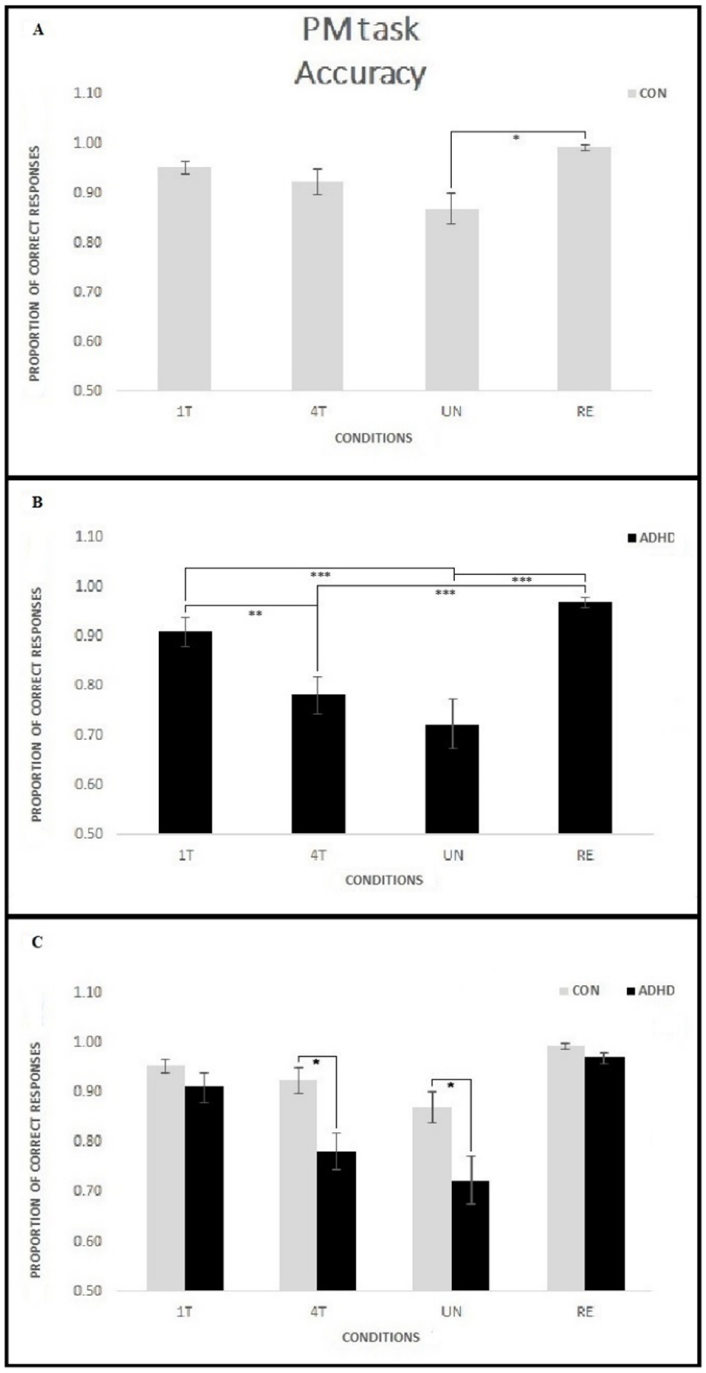

Figure 8. Accuracy on the PM trials for each PM condition in the two groups. Participants in the CON group showed no significant differences between conditions, with the exception of the UN, lower than the RE condition (**A**). Conversely, participants in the ADHD group showed lower accuracy on the 4T and UN conditions compared to 1T and RE (**B**). Moreover, differences between groups emerged because the ADHD group performed significantly lower than the CON group on the 4T and UN conditions (**C**). Asterisks mark significant differences: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

4. Discussion

The current study examined event-based PM in children with ADHD compared to age-, gender- and IQ-matched control participants. We investigated the presence of a possible PM deficit in children with ADHD in terms of impairment in different PM tasks, as well as a possible interfering effect of the PM task on the ongoing task performance. We also evaluated the impact of three cognitive variables (WM load, attentional focus, and

reward sensitivity) on event-based PM performance. Finally, we examined the correlation between event-based PM performance and ADHD symptoms (CPRS scores).

In the ADHD group, a deficit of event-based PM emerged in terms of impaired performance in both ongoing and PM tasks. Indeed, we documented the presence of a marked interfering effect in PM conditions for the ongoing task performance when the PM task was more demanding (4T and UN conditions), resulting in a weakening of response accuracy. We also detected higher reaction times in responding to PM targets for all the PM conditions and reduced accuracy under conditions requiring more cognitive resources (4T and UN). Finally, the correlation between PM performance and CPRS scores revealed a significant relationship between ADHD-related indexes and reduced accuracy/higher reaction times in the PM conditions (ongoing and PM trials), but not in BC. However, the strongest relationships emerged between the DSM Hyperactive/impulsive index and the accuracy on the ongoing task of the 4T (poorer performance associated with more severe symptoms), which is the WM demanding PM condition.

4.1. Event-Based PM Tasks Interfere with Ongoing Task Execution in Children with ADHD

Among children with ADHD, there was a significant tendency to have decreased ongoing task performances, resulting in a weakening of accuracy compared to their BC performance and compared to controls in the 4T and UN conditions. On the contrary, children in the CON group exhibited similar response accuracy for all conditions, thus suggesting that PM tasks did not interfere with their ongoing task performance. Conversely, analysis of the RTs did not detect any difference between groups. However, within-group comparisons revealed that children with ADHD were slower in executing the ongoing task in all PM conditions compared to BC. Conversely, again within-group analysis in the CON group failed to detect differences between response RTs in almost all PM conditions and BC. There was an exception for the UN, where participants were slower than all other conditions, likely because of the cost of the visual searching required to find the PM target. This finding is in line with previous research identifying cue centrality as a variable affecting children's PM performance on typically developing children [52] and, more generally, it is consistent with literature indicating that spared event-based PM performance could be at the cost of ongoing task performance [23,53].

The cost to ongoing task performance in our ADHD group may reflect a described characteristic of individuals with ADHD, who show difficulty in adequately allocating cognitive resources in task performances [54]. A proposed model for ADHD deficit focuses on the imbalance between brain regions involved in higher-order cognitive control and the Default Mode Network, a set of brain regions active during "rest" or during less demanding tasks. The inability to adequately suppress the Default Mode Network while performing a task has been associated with attentional fluctuation and performance deficits in ADHD [55–57]. On the other side, the behavioral neuroenergetics theory of ADHD proposed that the slow processing speed is linked to an insufficient neuronal energy supply, leading to floating performance and diffusion of attention [58]. Thus, our results could be explained in light of these etiological considerations. PM tasks mostly arise in a complex and dynamic environment: children with ADHD perhaps exhibit a less accurate performance on the ongoing task of the 4T condition because of difficulties in distributing cognitive resources when the task is characterized by high levels of cognitive load. Moreover, children with ADHD exhibited a marked worsening of response accuracy on ongoing tasks when the PM target was located on the corner of the screen, outside the focus of attention. This finding is in line with previous literature demonstrating that ongoing task performance is negatively affected by PM tasks involving non-focal PM targets, thus suggesting some degree of capacity sharing between ongoing tasks and PM processing [9].

According to our preliminary hypotheses, WM load and attention focus seem to be crucial variables intervening in performances of children with ADHD, affecting ongoing task performance during event-based PM tasks to a greater extent than in controls, and

having an impact on both accuracy and speed. These variables could therefore be identified as key components influencing event-based PM performance in individuals with ADHD.

4.2. Manipulation of the Reward Positively Influences Ongoing Task Performance in ADHD Children

Children with ADHD exhibited higher response accuracy on ongoing task performance of the RE condition compared to the other PM conditions. Intriguingly, differences in accuracy between the ADHD and CON groups at RE condition did not reach statistical significance. This suggests that the return to the BC performance level in the ADHD group could have been mediated by the manipulation of the reward amount. Of note, the analysis of response accuracy to PM targets revealed that the performance of the CON group was significantly lower in the UN than RE condition, thus confirming that the amount of reward also influences the performance of typically developing children. This is in line with previous findings linking memory function to emotional stimuli associated with the reward mechanism [59,60]. Therefore, consistent with our hypothesis, reward seems to play an important role in supporting the performance of children with ADHD at event-based PM tasks. Again, our results mirrored the clinical manifestation of ADHD. Indeed, it has been documented that individuals with ADHD exhibit high reward sensitivity, namely the reaction and sensitivity to reinforcement, including reward, punishment, and reinforcement schedules [61].

A possible explanation for such disruption in reward processing of individuals with ADHD could be found in the neurobiology of the disorder. Literature reported increased activity in reward regions–such as the ventral and dorsal striatum—in individuals with ADHD responding to reward delivery [62]; moreover, consistent findings indicated that individuals with ADHD have reduced ventral striatal activity in response to reward anticipation [63,64]. It has been proposed that this lower response to anticipated reward could be related to amplified reward-seeking behaviors, correlated with symptoms of hyperactivity/impulsivity, acting as compensation for the reduced ventral striatum activity [63]. Accordingly, individuals with ADHD exhibit the tendency to attribute great weight to immediate rewards and to be particularly prone to frustration in cases of delayed reward [40,64].

Overall, our findings confirm the already established role of reward in cognitive performance not only for children with ADHD but also for typically developing children. Literature documented that reinforcement positively affects the performance of children with ADHD in a stop-signal task [65], in a time reproduction task [66], and ameliorates response inhibition [67]. Our results extend this knowledge to PM performance, providing further insight into novel outcomes for behavioral treatments.

4.3. PM Performance Is Related to ADHD Symptoms

Interestingly, performance in the ongoing task per se was not related to any CPRS score, in the BC. However, the performance in the ongoing task was negatively associated with many ADHD-related symptoms when a PM condition was proposed to participants, thus indicating a modulatory effect of ADHD-related symptoms in the presence of PM tasks. Moreover, the performance on the PM conditions was never associated with the Global index-Emotional lability, which is not a core symptom of ADHD. The most consistent finding was the adverse relation between elevations in many ADHD-related symptoms, such as ADHD index, global index, DSM Inattentive, DSM Hyperactive/impulsive, DSM Total and performance (both accuracy and speed) in ongoing and PM trials of several PM conditions. However, the strongest negative association emerged between the DSM Hyperactive/impulsive index and the ongoing task accuracy on the 4T (WM demanding). Notably, the performance on the ongoing task in the 4T was one of the poorest in the group with ADHD. It could be hypothesized that the severity of ADHD symptoms interferes with resource allocation to the ongoing task, rather than to the PM task [11,31]. In particular, it can be speculated that ADHD symptoms are related to an overall difficulty in distributing

attentional resources, which makes children with ADHD struggling in attending to both ongoing and PM tasks.

These results suggest that the slower reaction times and the lower accuracy in responding to PM targets or during the ongoing task in the PM conditions are associated with core features of ADHD. Thus, the event-based PM performance could be related to ADHD symptoms.

Although preliminary, these findings are quite promising because they pave the way to further examination of PM as a possible neuropsychological variable discriminating between individuals with ADHD and the general population. This is consistent with literature reporting an association between the severity of ADHD symptoms (e.g., hyperactivity) on CPRS and time-based PM difficulties [22]. Extending these findings to event-based PM might have a crucial clinical impact, considering that the diagnosis of ADHD is merely clinical since no objective confirmatory method is currently available. Indeed, the presence of specific behaviors in various contexts represents the most successful method of identifying ADHD and, in spite of the documented presence of structural and functional brain peculiarities [68] and an estimated high heritability of 74% [69], these elements are not diagnostically specific. Moreover, the neuropsychological assessments currently available for ADHD are of little use for diagnostic purposes: the most commonly used neuropsychological batteries and tests proved to be of limited utility for distinguishing individuals with ADHD from the general population, both in childhood [70] and in adulthood [71]. Our results pave the road for further investigations on the identification of an ADHD-specific neuropsychological marker supporting the diagnosis, which would contribute significantly to the identification of such a complex condition and to the setting-up of targeted interventions.

Certain limitations of this study must be underlined. First, the experimental task had limited ecological validity, which could, at least partially, reduce the extendibility of our results to real-life scenarios. Nevertheless, as previously discussed, our findings could mirror some clinical manifestations of ADHD, as also suggested by the documented correlation of the performance in our task with core features of ADHD. Another limitation is the lack of a comprehensive assessment of participants' neurocognitive profiles, which could perhaps reveal the relative impact of important cognitive variables, such as WM abilities, on PM performance in children with ADHD. Thus, further investigations could help to understand the role of individual features in determining the performance at PM tasks in children with ADHD.

5. Conclusions

The current study provides important information about event-based PM functioning in children with ADHD. PM is linked to future orientation and planning, which are essential human features: deficits in PM performances have a number of consequences on daily-life skills and this might partially account for the phenotype of many individuals with ADHD. Thus, the possibility to assess the presence of PM deficits at an early stage represents a fundamental step toward prompt and adequate management of children with ADHD, according to their individual and specific needs.

The evidence for the role of WM load and attentional focus in PM performance of children with ADHD provides further insight into the cognitive system underlying PM impairment in ADHD. Moreover, this finding offers a basis for the setting up of efficient strategies to support children with ADHD in their daily-life activities. More specifically, the ascertainment of PM deficits in children with ADHD represents a crucial starting point for the setting up of tailored interventions. Presently, there is a range of neuropsychological approaches for PM rehabilitation in adults, such as compensatory and remediation strategies [72]. These forms of intervention grounds on two different approaches. The process-based approach targets specific cognitive abilities, such as WM, to improve PM accuracy [73,74]. On the other hand, the strategy-based approach aims to provide a mnemonic strategy to complete a PM task [74]. However, research on PM

rehabilitation in pediatric age is currently limited, with some evidence of efficacy for other neurologic conditions such as traumatic brain injury [72,75]. To the best of our knowledge, specific rehabilitative approaches for PM in children with ADHD have not yet been tested. This could be explained, at least in part, by the fact that PM deficits in this population are considered to be related to impairment in executive functions, motivation abnormalities, and inattention [27,76–78]. It is conceivable then that already existing interventions, based, for instance, on motivational enhancement and the choice of manageable goals [79], might provide some indirect benefit for PM performance in children with ADHD, even though such aspects are not yet considered as outcome variables of available interventions. Further research is required to investigate the feasibility of the existent intervention to ameliorate PM performance in children with ADHD.

Another intriguing aspect to take into account for future research is linked to gender-related differences. Literature, in fact, suggests that task complexity influences response control in children with ADHD in a sexually dimorphic manner: in particular, among the population with ADHD, girls seem to be more prone than males to the interference effects deriving from task complexity [80]. Studies to extend our knowledge about gender-related effects on PM deficits would be an important contribution to understanding the pathophysiology of ADHD.

Finally, our study has significant clinical implications: although we are far from the identification of a neuropsychological marker pathognomonic of ADHD, the correlation of PM deficit with CPRS scores may represent a tool to support clinical diagnostic efficiency of existing evaluation instruments.

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Validation of the Italian Version of the Behavioral Inhibition Questionnaire (BIQ) for Preschool Children

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Abstract: Behavioral Inhibition (BI) is a temperamental trait characterized by fear and wariness in reaction to new and unfamiliar stimuli, both social and non-social. BI has been recognized as possible forerunner of anxiety disorders, especially social anxiety and phobia; therefore, its assessment is clinically relevant. The present study aimed to examine the psychometric properties of the Italian adaptation of the Behavioral Inhibition Questionnaire (BIQ), which measures BI in preschool children. The BIQ was completed by 417 Italian parents (230 mothers, 187 fathers) of 270 preschoolers aged 3–5. Confirmatory factor analysis showed a good internal validity: the factorial structure was corresponding to the original six-factor version. Results showed excellent internal consistency, significant item-total correlations, good inter-rater reliability, convergent validity (by correlating the BIQ with the Italian Questionnaires of Temperament-QUIT, the Anxiety-Shy Conner's Scale and the Laboratory Temperament Assessment Battery) and discriminant validity (i.e., no correlation with Conners' ADHD scale). Significant correlations emerged between BI indexes and total BIQ scores of parents and maternal (but not paternal) versions of the questionnaire. Altogether, the results are promising and consistent with previous validation studies, suggesting the BIQ as a reliable and valid measure for evaluating parents' perception of BI in Italian preschoolers.

Keywords: temperament; behavioral inhibition; anxiety; preschool children; Italian sample; psychometrics; behavioral inhibition questionnaire/BIQ

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1. Introduction

The psychological construct of Behavioral Inhibition to the Unfamiliar (BI) [1] refers to an innate temperamental trait that exists in 10–15% of Caucasian population and can be observed as early as 14 months of a child's age [2]. BI has been originally described as the *"the child's early initial behavioral reactions to unfamiliar people, objects, and contexts, or challenging situations"* (p. 53 in [3]), and concerns a general tendency to be unusually shy and to respond with negative reactivity, fear or withdrawal in unfamiliar situations [4]. The BI trait is in fact characterized by both emotional aspects, such as fear and distress in presence of novelty [5,6], and behavioral aspects, like close proximity to the caregiver, decrease of smiles and vocalizations, freezing, avoidance and reticence in presence of new or unfamiliar stimuli [5,7].

The definition of the temperamental trait of BI requires a distinction from other similar constructs. First, BI should be distinguished from the construct of effortful control, and especially from *inhibitory control*, that is the ability to voluntarily inhibit impulsive behaviors to promote more adequate responses according to the characteristics of the context [8–10], while BI refers to an involuntary process [11]. Second, with regards to *fear* and *anxiety*, BI is obviously a related-fear construct, where fear can be defined as an emotional adaptive response since infancy to unfamiliar stimuli. Fear is expressed according to individual differences and environmental characteristics and only high fear is associated to BI as a

specific temperamental disposition; BI, in turn, has been recognized as a risk factor for the occurrence of later anxiety [12]. BI also differs from *shyness*, which represents wariness and reticence but only refers to socio-evaluative settings; on the contrary, BI refers to a general avoidance of novelty, independently of evaluative situations. Specifically, the BI trait is characterized by the presence of two core components: the response to social stimuli (e.g., stranger adults or peers), and the reaction to nonsocial stimuli (such as new objects, food, physical activity) with risk of injury and uncertainty [13]. The dependent or relatively independent relation between social and nonsocial aspects of BI is still an open debate in literature but, according to the position of Kagan, Snidman and Arcus (1998), these two components would be interdependent from each other. Kagan et al. (1998) highlighted that a young child classified as inhibited might, with experience, diminish the initial reticence with strangers but retain an avoidant style to new objects and unfamiliar places; thus, *"a child can display an avoidant style in any of a number of contexts, but not necessarily all of them"* (p. 1483 in [13]). At the same time, a toddler with high levels of BI could be extremely reticent with adult strangers, but not necessarily so inhibited in a non-social context [14].

The general characteristics of BI tend to remain quite stable over time, although some expressions of the trait could differ according to various contexts, the child's age, gender and cultural values [6]. According to the child's age, the response to social and non-social stimuli may change across development: during infancy, it is more frequent to observe precursors of BI in terms of high negative reactivity, such as negative affect and high motor activity displayed by infants when confronted with novelty [15]. Conversely, during preschool and school ages, inhibited children tend to show avoidance, withdrawal, wariness, disorganization, anxiety when confronted with new stimuli [5,16].

The influence of gender also seems relevant. A meta-analysis of gender differences in temperament by Else-Quest et al. [17] indicated that girls tend to be higher in inhibitory control, shyness and some fearful behaviors, whereas boys are higher in approach-based tendencies such as anger, exuberance, and activity level. Few studies investigated specific gender differences in BI trait during toddlerhood and preschool age [18–20], showing that girls appeared more inhibited than boys, while other studies did not show any gender differences [21–25]. Gagne, Miller and Goldsmith [19] have underlined the contribution of both innate and cultural aspects to explain gender differences in the intensity of BI; however, further studies are needed to deepen this issue.

The influence of cultural factors should also be considered, as levels of BI displayed by children of various cultures may differ [26–30], also according to parents' perception [31]. In particular, a low frequency of inhibition has been observed in Western countries [26,29] and this could be in part explained by the negative connotation these cultural contexts give to shyness and inhibition, considered as socially immature and maladaptive behaviors, while assertiveness and competition are highly promoted and supported [26]. Because most of the measures for BI have been developed in Western countries, the assessment of BI should always consider the specific cultural background of the population investigated.

Following these premises, it is important to highlight the clinical relevance of studying BI; the scientific literature in this field has dedicated much attention to the observation of developmental trajectories in case of high traits of BI, showing an increased risk for anxiety disorders during childhood and adolescence [32–40]. Bayer and collaborators [41] have found that, among inhibited children aged 4, 47.3% of them showed anxiety disorders at 5 years and 40.2% at 6 years. Among the anxiety-related problems associated to high BI, the most frequent are higher rates of social reticence, social rejection, social anxiety and social phobia; cases of selective mutism have also been recognized [42–47]. Indeed, Clauss and Blackford [48] have reported that 40% of children displaying an inhibited profile will develop a social phobia in later childhood or adolescence, compared with the 12% of non-inhibited children.

Based on this evidence, the detection of BI from pre-school age is clinically recommended, in order to support child development and to promote timely intervention when needed. However, given the influence of child age and gender, as well as context and

cultural factors, an early assessment of BI requires reliable and validated instruments to adequately detect this specific construct.

1.1. The Assessment of Behavioral Inhibition

The methods for the assessment of BI most frequently used in early childhood and preschool age are laboratory assessment batteries [49], such as the Behavioral Inhibition Paradigm [50] and Laboratory Temperament Assessment Battery (LAB-TAB) [51]. These procedures consist of a series of new stimuli to which the child is exposed in a limited range of time, such as an adult stranger, unfamiliar peers, and new toys. Laboratory assessments have the advantage of collecting empirical data with a relatively low risk of rater bias [49]. Nevertheless, as no single procedure has been recognized as the gold standard for assessing BI, protocols may vary from study to study and the findings may be difficult to compare [14,52]; furthermore, the laboratory assessments are time intensive, costly, and may not fully capture how individuals act in situations outside the laboratory [53].

To overcome these limits, a useful method of assessment is represented by parent reports. The use of these questionnaires has indeed some advantages: they are timesaving and allow the consideration of parents' perceptions of the child's behaviors across a wide range of situations and longer intervals [22]; additionally, the questionnaires may collect data from different informants (e.g., mothers, fathers, teachers).

Nevertheless, some limits also need to be acknowledged for parent-report questionnaires. There is a tendency to assess caregivers' reports of child BI with instruments originally developed to measure other temperamental dimensions, such as shyness, fear, sociability or introversion/extroversion [6], neglecting the use of the questionnaires specifically developed for BI. Furthermore, another relevant consideration regards the moment of assessment because, as previously described, the expression of BI may vary according to child's age [5,15,16]. For this reason, questionnaires available for infancy, such as Retrospective Infant Behavioral Inhibition Scale (RIBI) [54], could be useful for the detection of precursors, while BI is better measured during childhood.

To our knowledge, only three questionnaires are available for the assessment during preschool age: the first two are the Preschool Behavioural Inhibition Scale (P-BIS) [55] and the Behavioural Inhibition Scale, for children aged 3–6 years (BIS) [56]; both questionnaires focus only on social contexts and neglect BI in non-social situations, therefore their use increases the risk of an overlap between the measurement of social components of BI and shyness. The third questionnaire is the Behavioral Inhibition Questionnaire (BIQ) [21], whose strength is the specific assessment of both social and non-social components of BI; therefore, it would seem a more promising measure compared to P-BIS and BIS.

1.2. The Behavioral Inhibition Questionnaire (BIQ)

The BIQ was originally developed for measuring BI in children aged 3 to 5 years [20] and validated in a sample of 613 mothers, 506 fathers and 585 teachers, representative of the general Australian population. Bishop and colleagues [21] first developed a list of 40 items based on a review of literature on BI characteristics and on existing questionnaires on temperament; ten items were discarded due to poor psychometric properties and the remaining 30 items, after minor changes, constituted the final version of the BIQ. They reflected 3 specific domains: Social Novelty (3 contexts: Unfamiliar adults, Peers, Performance situations), Situational Novelty (2 contexts: Separation and preschool, Unfamiliar situations) and Physical activities with risk of injury (1 context: Physical Challenges).

Statistical analyses found relatively robust psychometric properties both for the parent and the teacher versions. A confirmatory factor analysis supported a 6-factor structure associated to the 6 BI contexts; the authors also found an acceptable internal consistency (almost all Cronbach's α were higher than 0.80). Moderate stability of BI was observed over the twelve-month retest period (all coefficients varied from 0.60 to 0.78 for mothers; from 0.55 to 0.74 for fathers). Moreover, a good agreement among different informants emerged: the mothers' version significantly correlated with fathers' (r = 0.69) and teachers'

versions (r = 0.47), and the fathers' version with the teachers' report (r = 0.43). Furthermore, concurrent and construct validity was satisfactory: a strong association (all r-values > 0.85) was found between BIQ total scores and the Inhibition subscale of the Temperament Assessment Battery for Children–Revised (TABCQ-R [57]); furthermore, BIQ ratings from informants and laboratory observations were significantly correlated (r = 0.25–0.46 for full sample and r = 0.35–0.60 for high- and low-BI groups).

The validity of the BIQ was confirmed by Kim et al. [22] on an American sample of 559 parents of 3-year-old children, reporting findings consistent with the version by Bishop and colleagues [21]. They also found moderate to high convergent and discriminant validity for the parent and teacher versions, using assessment by both self-report measures (Children's Behavior Questionnaire (CBQ) [58] and Child Social Preference Scale (CSPS) [59]) and laboratory tasks (LAB-TAB [51]).

The BIQ was validated in Dutch [4] and Israeli populations [53], confirming its good psychometric properties. Broeren and Muris [4] tested the Dutch version of BIQ (parent form) on 3 age groups of children: 4–7, 8–11 and 12–15 years old. Principal component analysis supported the 6-factor model, as originally suggested by Bishop and colleagues [21]. Overall, they found a good reliability for most of the BIQ subscales (Cronbach's Alpha = 0.79–0.96 in 4–7-year-olds, 0.67–0.95 in 8–11-year-olds, and 0.73–0.95 in 12–15-year-olds). Further, BIQ total scores and Preschool Anxiety Scale-Revised (PAS-R) [60] were substantially correlated (all r > 0.66). More recently, Mernick and colleagues [53] tested the psychometric properties of a Hebrew version of the BIQ in a sample of 227 parents of 4–7-aged children. Good internal consistency (Cronbach's Alpha = 0.94) and 3-month test-retest reliability (r = 0.95) were confirmed. This version also showed a good convergent validity, as BIQ total scores were significantly correlated with the Screen for Child Anxiety Related Emotional Disorders (SCARED) [61] for children aged 4–7 (r = 0.73) and 12–15 (r = 0.71); a good discriminant validity (measured with Revised Conners' Parent Rating Scale-CPRS-R [62] ADHD index) was also found.

To date, the BIQ has been used in multiple fields of research, including investigations on neurophysiological and cognitive substrates of BI [35,63–66] and clinical studies on the risk for the onset of psychopathology [67,68], such as anxiety [36,68–72] and selective mutism [47]. Furthermore, the BIQ has been implemented in several studies for evaluating the efficacy of early interventions directed to inhibited or anxious children [67,73–76]. All these findings seem to provide sufficient evidence for the use of the BIQ as a reliable and valid instrument to detect child BI by assessing adults' perceptions.

In the light of these premises, it is relevant to further contribute to the assessment of the properties of the questionnaire, so that it can be used also in populations different from the original one [21]. Therefore, the aim of the present study was to further investigate the psychometric properties of the BIQ, giving a contribution to the validation of an Italian version of the questionnaire. Specifically, we aimed to evaluate the following psychometric properties: internal validity, internal consistency and inter-rater reliability of the Italian version of BIQ. We also assessed the convergent validity by measuring the correlation with other temperamental measures and we analyzed the discriminant validity by analyzing the divergence between BIQ and attentional difficulties. In addition, we aimed to explore the potential differences in BI traits according to children's gender.

Based on the results by other validation studies of the BIQ [4,22,53], we expected to also find similar good psychometric properties for the Italian version of the questionnaire. If the results would be confirmed, the study would contribute to making available the first questionnaire for the assessment of BI for Italian preschool children, as no other instruments exist, to our knowledge. Furthermore, our results could contribute to enriching the assessment of BI, adding a context belonging to Mediterranean culture, which is different from the cultural backgrounds of the populations of previous validations (Australian, American, Dutch and Hebrew).

2. Materials and Methods

2.1. Participants

Eligible participants were recruited among parents of children attending six kindergartens (18 classrooms) in Bologna and Cesena neighborhoods (Northern Italy). Kindergartens were chosen based on already ongoing collaborations with members of our research team. All parents of the children attending the six kindergartens were invited to take part to a meeting (one for each school) with the researchers, where all the information about the study was given; at the end of the meeting, participation to the study was offered. Participation in the study was voluntary and anonymous. Inclusion criteria were a good comprehension and expression of Italian language in parents, and a lack of disabilities or cognitive impairments in children.

A total of 417 parents (230 mothers and 187 fathers) of 270 children aged from 3 to 6 years (mean age = 4.4, SD = 1.0; 47% males; 42% only child) were included in the study. The sample size was established a priori to have at least five observations for each freely estimated model parameter in CFA analysis [77]. Demographic characteristics of the sample are shown in Table 1.

Table 1. Demographic characteristics of the sample.

Sample Characteristics	Parents (*N* = 417)	Mothers (*N* = 230)	Fathers (*N* = 187)
Age, mean ± SD (range)	38.5 ± 5.4 (26–56)	37.0 ± 4.5 (26–48)	40.4 ± 5.8 (26–56)
Nationality, *n* (%)			
Italian	378 (91%)	209 (91%)	168 (91%)
Foreign	39 (9%)	20 (9%)	16 (9%)
Educational Level, *n* (%)			
Primary	6 (1%)	2 (1%)	4 (2%)
Secondary	117 (29%)	52 (23%)	65 (36%)
High school	201 (50%)	117 (52%)	84 (46%)
University	82 (20%)	54 (24%)	28 (16%)
Marital status, *n* (%)			
Married	275 (68%)	148 (66%)	127 (71%)
Living together	25 (6%)	13 (6%)	12 (7%)
Separated	16 (4%)	11 (5%)	5 (3%)
Single	86 (22%)	52 (23%)	34 (19%)

Note: Differences in sample size were due to missing data.

Of the parents, 91% were Italian, 50% had a high school educational level, and 74% were married/cohabitant. The majority of mothers and fathers were Italian and were married. No significant differences between mothers and fathers were found for nationality ($\chi^2(1) = 0.26$; $p = 0.62$; Phi = 0.03), nor for marital status ($\chi^2(3) = 2.43$; $p = 0.49$; Phi = 0.08). With regard to the level of education, a significant difference was found between mothers and fathers ($\chi^2(3) = 11.14$; $p < 0.05$; Phi = 0.17): although the majority of mothers and fathers had an upper secondary educational level, a higher percentage of mothers had a university degree (24%) compared to the fathers (16%), and 36% of fathers had a lower secondary educational level (compared to 23% of mothers).

To also test the convergent validity by observational measures (selected episodes from Laboratory Assessment Battery (LAB-TAB) Preschool Version), a further sub-sample of 41 parents (23 mothers, 18 fathers) of 23 children (mean age = 4.4; SD = 0.5; 42% males; 65% only child) was recruited from one of the kindergartens included in the study. Unfortunately, it was not possible to recruit a wider sample, due to some practical constraints (e.g., organization difficulties for most of the kindergartens). A priori power analysis was conducted with G*Power [78] to determine the required sample size to test the convergent and discriminant validity. We indicated the Correlation point biserial model, Alpha = 0.05, 1-Beta = 0.80, a medium effect size $r = 0.40$, and we obtained a required sample size of 44 subjects. Multilevel analysis with the school and class variables as random effects and

BIQ total score as the dependent variable was applied to check for potential clustering of the data due to the different schools and different classes included in the study. Results showed no cluster effect for the school variable, considering the Intraclass Correlation Coefficient (ICC = 0.01 with Wald's $Z = 0.75$ and $p = 0.45$), or for the class variable (ICC = 0.02 with Wald's $Z = 0.86$ and $p = 0.39$) on BIQ total scores.

2.2. Procedure and Measures

The project study was approved by the Ethics Committee of the Department of Psychology, University of Bologna, in January 2014.

Parents who participated to the meeting with the researchers and who agreed to participate received a consent form and a set of questionnaires (BIQ, Italian Questionnaires of Temperament (QUIT) [79] and Revised Conners' Parent Rating Scale (CPRS-R) [80]) which were handed out by their child's teacher. All the materials were completed at home and returned to the researchers via the teacher. The presence of BI was also assessed according to observational measures (LAB-TAB) in a subsample of children.

The Behavioral Inhibition Questionnaire (BIQ) [21] consists of 30 items for the parent version, rated on a seven-point Likert scale ranging from 1 (hardly ever) to 7 (most always). Bishop et al. [21] also developed a teacher form, composed of 28 items, but for the aims of the present study we only used the parent version. The BIQ total score ranges from 30 to 180, where higher scores correspond to higher levels of Behavioral Inhibition. Items are included in three specific domains assessing children's behaviors in multiple contexts: Social Novelty (14 items), Situational Novelty (12 items) and Physical Challenges (4 items). Social Novelty refers to the subscales: unfamiliar adults, peers and performing (in front of others), while Situational Novelty is related to the subscales: unfamiliar situations, and separation. Physical Challenges refers to novel physical activities with possible risk of injury.

For the purposes of the study, the original version of the BIQ was translated and cross-culturally adapted according to standard international guidelines as suggested by the International Test Commission [81]. In the first phase, two native Italian speakers, professionals in English translation, translated the items of the original version of the BIQ into Italian, independently. A revision panel of clinical child psychologists and experts in BI assessed the two translations and developed a first synthesized version, which was back-translated into English. Subsequently, the Italian translation, the English back-translation, and the original version were compared and synthesized in a final version. This preliminary version of the BIQ was then submitted to a gender-mixed sample of 20 parents (who were not included in the final sample of this study), in order to find minor changes to improve the readability of the instrument. After receiving the feedback from this sample of parents, the same panel of specialists discussed and approved a final Italian version of the BIQ to undergo an appropriate evaluation of its psychometric properties. The convergent validity of this parent version was evaluated by comparing the BIQ results with the QUIT [79] and LAB-TAB [51].

The QUIT [79] is represented by a sixty-item questionnaire specifically created to assess child temperament from the first month after childbirth to eleven years in the Italian population. It has been developed based on the assumptions of temperament by Thomas and Chess [82] and assesses parent's reports (mother and/or father) on six main temperamental dimensions across four different child's ages: 1–12 months, 13–36 months, 3–6 years (the version used for this study), 7–11 years. The six dimensions are: Physical Activity, Attention, Inhibition to Novelty, Social Orientation, Positive Emotionality, and Negative Emotionality; a high score in a specific dimension refers to a high presence of this dimension in the child's temperament. Each item is rated on a 6-point scale ranging from 1 (hardly ever) to 6 (most always). The 3–6-year version was validated on a sample of 511 parents, showing a moderate to good internal consistency (Cronbach's Alpha = 0.56–0.83); Pearson correlation coefficients between the scales of the questionnaire, completed separately by mothers and fathers, ranged from 0.35 to 0.74, showing a sufficient to good correlation between parents [79]. For the aims of the present study, we were particularly

interested to the QUIT dimensions of Novelty Inhibition, clearly related to BI, and Negative Emotionality, because infant negative affect is a precursor of BI in childhood [12] and it is usually described as an emotional feature of BI [83].

The LAB-TAB Preschool Version [51] is a battery for the assessment of temperament dimensions and consists of 33 episodes evaluating Fear, Distress, Exuberance, Interest/Persistence, Activity Level, Inhibitory Control, and Contentment in children aged 3–6 years. In this study, children were assessed by an adapted version of LAB-TAB for the Italian cultural context, as used in previous studies [84,85]. In order to adequately respond to the aims of the study, we contacted the author of LAB-TAB (Goldsmith) to employ his supervision in the choice and implementation of LAB-TAB. For the comparison of BIQ scores with indicators of BI, the author recommended every child should undergo two episodes of the LAB-TAB procedure: the Stranger Approach (for social components of BI) and the Risk Room (for non-social aspects). The choice of these episodes for the detection of BI was also consistent with previous studies [86–90] and the American validation of the BIQ [22].

The Stranger Approach consists in a "simulation" of a real-life situation. A child, alone in a room, meets a stranger who tries to interact with him/her for about two minutes. The reaction of the child when the stranger approaches him/her is coded. This episode is oriented to detect the social aspects of BI. During the Risk Room episode, the child enters a room with unfamiliar or new toys; initially he/she remains alone to play (phase I), and after 5 min the researcher enters the room asking the child to approach to each toy (phase II). The reaction of the child to each unfamiliar/new object and his/her approach is then coded. This episode is oriented to detect non-social aspects of BI as identified by Kagan and colleagues [91]. Episodes were administered subsequently and only one session of observation was done for every child. All procedures were videotaped; following the LAB-TAB manual, each episode was divided into 20- or 30-s epochs, and specific variables representing the inhibited child's typical behaviors [12,50,91] were coded for each epoch [51]. For the aims of this study, representing an initial validation of the Italian version of the BIQ, we selected specific variables to be coded. For the Stranger Approach, the variables were: (a) Intensity of decrease in activity: represents an apparent or sudden decrease in the activity level of the child during the interaction with the stranger; it includes also freezing behaviors, typical manifestations of inhibited temperament, and was rated on a 4-point scale; (b) Intensity of verbal hesitancy: refers to the hesitancy of the child's answers to the stranger and was rated on a 3-point scale. For the Risk Room episode, the coded variables were: (a) Latency to intentionally touch first object: concerns the interval in seconds before the first definite contact with the first object; (b) Total number of objects touched: includes the number of toys (min. 1–max. 5) explored by the child during the Risk Room episode. All videos were coded by a researcher and clinical child psychologist who had expertise with BI. A second rater coded eight randomly selected videos of LAB-TAB episodes: the inter-rater reliabilities showed acceptable values, ranging from 0.69 to 0.88.

The CPRS-R [62] is a screening tool for the assessment of ADHD symptoms in children aged 3–17 years, by parents' report. High Alpha Coefficients (range 0.75–0.95) showed excellent internal consistency of the CPRS-R. In the present study, we used the Italian version of the Conners Parents Rating Scales Revised, Short Form (CPRS-R:S) [80] that is composed of 27 items, on a 4-point Likert scale ranging from 0 (not at all true) to 3 (very much true). Eight different subscales measure: Oppositional, Cognitive Problems/Inattention, Hyperactivity, Anxious/Shy, Perfectionism, Social Problems, and Psychosomatic; additionally, it is possible to measure a global ADHD index that probes to recognize children/adolescents at risk of ADHD. Because previous literature has underlined a strong association between BI and anxiety and shyness [4,22,41,46,53], in the present study we used scores at Anxious/Shy subscale for detecting convergent validity of the BIQ. Furthermore, we used the ADHD index for the assessment of discriminant validity, as previously done in the validation of Hebrew version of the BIQ [53].

2.3. Statistical Analyses

The data that support the findings of this study are available on request from the corresponding author [MB]. The data are not publicly available due to restrictions (e.g., their containing information could compromise the privacy of research participants). The statistical analyses were conducted using SPSS Statistics (version 26.0; IBM, Chicago, IL, USA) and Analysis of Moment Structures (IBM SPSS Amos, version 26.0; IBM, Chicago, IL, USA) [92] software package.

As a preliminary description of the BIQ, socio-demographic effects on behavioral inhibition were investigated by three univariate ANOVAs that were conducted on the total sample of parents, and separately on the subsamples of mothers and fathers. In all these analyses, educational level, marital status and nationality were considered as between subject factors, the age was the covariate and the BIQ total score was used as dependent variable. These preliminary analyses aimed to describe possible socio-demographic effects on behavioral inhibition. To describe the potential differences that emerged in the parents' BIQ reports between male and female children, three multivariate ANOVAs were conducted on the total sample of parents and on the subsamples of mothers and fathers, considering child's gender as factor and BIQ subscales and total score as dependent variables.

The structural validity of the BIQ was evaluated by means of confirmatory factor analysis (CFA). Taking into account that the data are ordinal and non-normally distributed, the unweighted least squares (ULS) estimation procedure was chosen to perform the CFA. Considering the small sample size of the mother and father subsamples and considering that acceptable sample size to perform CFA analysis requires at least five observations for each freely estimated model parameter [77], CFA analysis was conducted on the total parents' sample ($N = 417$). The closeness of the hypothesized model to the empirical data was evaluated through the following goodness-of-fit indices: the goodness of fit index (GFI, cut-off > 0.95), the normed fit index (NFI, cut-off > 0.95), parsimony normed fit index (PNFI, cut-off > 0.50), the standardized root mean square residual (SRMR, cut-off < 0.1) [93–95]. To test for measurement invariance of the BIQ, we tested the model across the parental role (mothers vs. fathers).

Reliability (internal consistency) was analysed by Cronbach's Alpha on item-total scores in total sample and in mothers and fathers, separately, and by Guttman's split-half coefficient and composite reliability (CR) index. Inter-rater reliability was measured with inter-class correlation index and repeated measure ANOVA with the BIQ total score as dependent variable, the informant (father and mother) as within subject measure and the child's gender as between subject factor (for this analysis we included only those couples mated on the basis of their own child).

To assess the convergent and divergent validity, Pearson's r correlation analysis was applied on the BIQ total scores (separately for the parents' sample, and for father and mother subsamples) with the subscales of the QUIT questionnaire, with the 4 LAB-TAB variables, with the Anxious-Shy score and with ADHD Index measured by CPRS-R.

Discriminant validity was assessed by and Heterotrait-Monotrait Ratio of Correlations (HTMT) index.

3. Results

From the ANOVAs, we found that the age, the educational level, the marital status, and nationality did not affect BIQ score both considering the total sample of parents, and separately for mothers and fathers (all $p > 0.05$).

Descriptive statistics for BIQ subscales and total scores evaluated in children by parents, and separately by mothers and fathers, are shown in Table 2.

Table 2. Estimated means and standard error (SE) for BIQ subscales and total scores assessed in parents, in mothers and in fathers, evaluating males and females.

Factors	Mean	SE	F (1384)	Mean	SE	F (1209)	Mean	SE	F (1174)
	Parents [a]			Mothers [b]			Fathers [c]		
Total BIQ									
Males	89.47	2.06	11.96 **	94.52	3.00	0.09	90.99	2.89	2.24
Females	99.22	1.92	(P.η^2 = 0.03)	95.74	2.82	(P.η^2 < 0.01)	96.81	2.61	(P.η^2 = 0.01)
Total	94.35	1.41		95.13	2.06		93.90	1.95	
Peers									
Males	18.20	0.59	13.15 **	18.80	0.84	4.07 *	17.73	0.82	8.03 **
Females	21.12	0.55	(P.η^2 = 0.03)	21.13	0.79	(P.η^2 = 0.02)	20.87	0.74	(P.η^2 = 0.04)
Total	19.66	0.40		19.87	0.58		19.30	0.55	
Physical Challenges									
Males	10.64	0.31	1.29	10.34	0.42	1.51	10.84	0.45	0.10
Females	11.12	0.29	(P.η^2 < 0.01)	11.05	0.40	(P.η^2 = 0.01)	11.03	0.41	(P.η^2 < 0.01)
Total	10.88	0.21		10.70	0.29		10.93	0.30	
Separation									
Males	12.39	0.49	4.08	14.38	0.71	2.43	12.65	0.66	0.03
Females	13.74	0.46	(P.η^2 = 0.01)	12.87	0.67	(P.η^2 = 0.01)	12.49	0.60	(P.η^2 < 0.01)
Total	13.06	0.33		13.63	0.49		12.57	0.45	
Performance Situations									
Males	12.88	0.41	0.48	13.41	0.56	0.22	13.03	0.59	0.04
Females	13.26	0.38	(P.η^2 < 0.01)	13.05	0.53	(P.η^2 < 0.01)	12.87	0.53	(P.η^2 < 0.01)
Total	13.07	0.28		13.23	0.39		12.95	0.40	
Adults									
Males	12.41	0.42	12.20 **	12.86	0.60	0.80	12.99	0.60	2.79
Females	14.42	0.39	(P.η^2 = 0.03)	13.60	0.57	(P.η^2 < 0.01)	14.34	0.54	(P.η^2 = 0.02)
Total	13.42	0.29		13.23	0.41		13.66	0.41	
Unfamiliar situations									
Males	23.04	0.62	9.30 **	24.72	0.90	0.30	23.76	0.87	1.56
Females	25.64	0.58	(P.η^2 = 0.02)	24.04	0.85	(P.η^2 < 0.01)	25.22	0.78	(P.η^2 = 0.01)
Total	24.34	0.42		24.38	0.62		24.49	0.58	

Note: [a] N = 417; [b] N = 230; [c] N = 187; ** $p < 0.01$; * $p < 0.05$; SE = Standard error; F = F test value; P.η^2 = Partial Eta Squared.

Considering the gender differences, when the analysis was conducted on the whole sample, gender differences were found in "Peers", "Unfamiliar adults", "Unfamiliar situations" and in the BIQ total score (all $p < 0.01$), evidencing higher scores for females compared to males.

3.1. Confirmatory Factor Analysis

To evaluate the BIQ factor structure, four models for parent reports were compared. The first model (Model 1) was a single-factor model in which all items of the questionnaire were loaded onto a single dimension of inhibition. The second model (Model 2) was a three-correlated-factors model where the items of the questionnaire cluster around three domains in which BI occurs (social novelty, situational novelty, and novel physical activities involving minor risk). The third model (Model 3) was a six-correlated-factors model where the items cluster around six contexts that lay within the previous three domains (peer situations, unfamiliar adults, performing in front of others, unfamiliar situations, preschool/separation, and physical challenges). The fourth model (Model 4) was a six-correlated-factors model loading onto one higher-order-factor model, to evaluate whether the covariance between the six first-order factors could be explained by a single

higher-order factor reflecting a general BI. To a descriptive purpose, and considering the possible differences deriving from the different informants, a comparison of the same four estimated models in the mother and father subsamples was performed and is available as Supplementary Materials (see Table S1).

By comparing the four models, Model 4 performed optimally; therefore, we present a full description of the model in the main text, while the other models are described in Supplementary Materials. The fit of Model 4 (six first-order factors, one second-order factor) provided a good fit to the data (Table 3), with a GFI higher than 0.95, a NFI higher than 0.95, a PNFI higher than 0.50 and an SRMR lower than 0.08. Despite that Model 3 was also a well-fitted model, and that the fit indexes were very similar between the two models, the PNFI value was slightly higher than the one associated with the first-order model. Therefore, given that the correlation among the six factors was substantial and that there is theoretical justification to consider a general factor (BI) as a higher-order construct that causes the six lower-order dimensions of BI, we concluded that the higher-order model of the BIQ questionnaire best represented the data of the Italian sample. All the BIQ items loaded significantly to the designated factor, with 27 of the 30 items loading greater than 0.40 (item 4, 14, and 17 loaded below 0.40). The loadings of the six first-order factors onto the second-order factors were also significant (Figure 1). Item 4 ("The child is cautious in activities that involve a physical challenge (e.g., climbing, jumping from a certain height") and item 17 ("The child is hesitant to explore new play equipment") showed the lowest loading to the designated factor (0.39 and 0.23, respectively) and belonged to the same latent variable (Physical challenges), which also was the factor showing the lower loading to the second-order factor (0.41). Additionally, item 14 ("The child is independent") showed a low loading to the designed factor (0.26), but it belonged to the "Unfamiliar situations" latent factor that had the highest loading with the second-order factor (0.99).

Table 3. Fit Indexes for each Model for parents, mother and father reports of Behavioral Inhibition Questionnaire (BIQ).

Model	GFI	NFI	PNFI	SRMR
Parent BIQ				
Model 1: 1 factor	0.93	0.91	0.84	0.09
Model 2: 3 correlated factors	0.95	0.92	0.85	0.08
Model 3: 6 correlated factors	0.97	0.96	0.86	0.06
Model 4: 6 first-order factors. 1 second-order factor	0.97	0.96	0.88	0.06

Note: GFI = Goodness of Fit Index; NFI = Normed Fit Index; PNFI = Parsimony Normed Fit Index; SRMR = Root Mean Square Error of Approximation.

Similar results were obtained performing CFAs on the mother and the father subsamples, separately (see Supplementary Materials Table S1). However, considering the low sample size of each subsample, the results of these two additional CFAs have only a descriptive value.

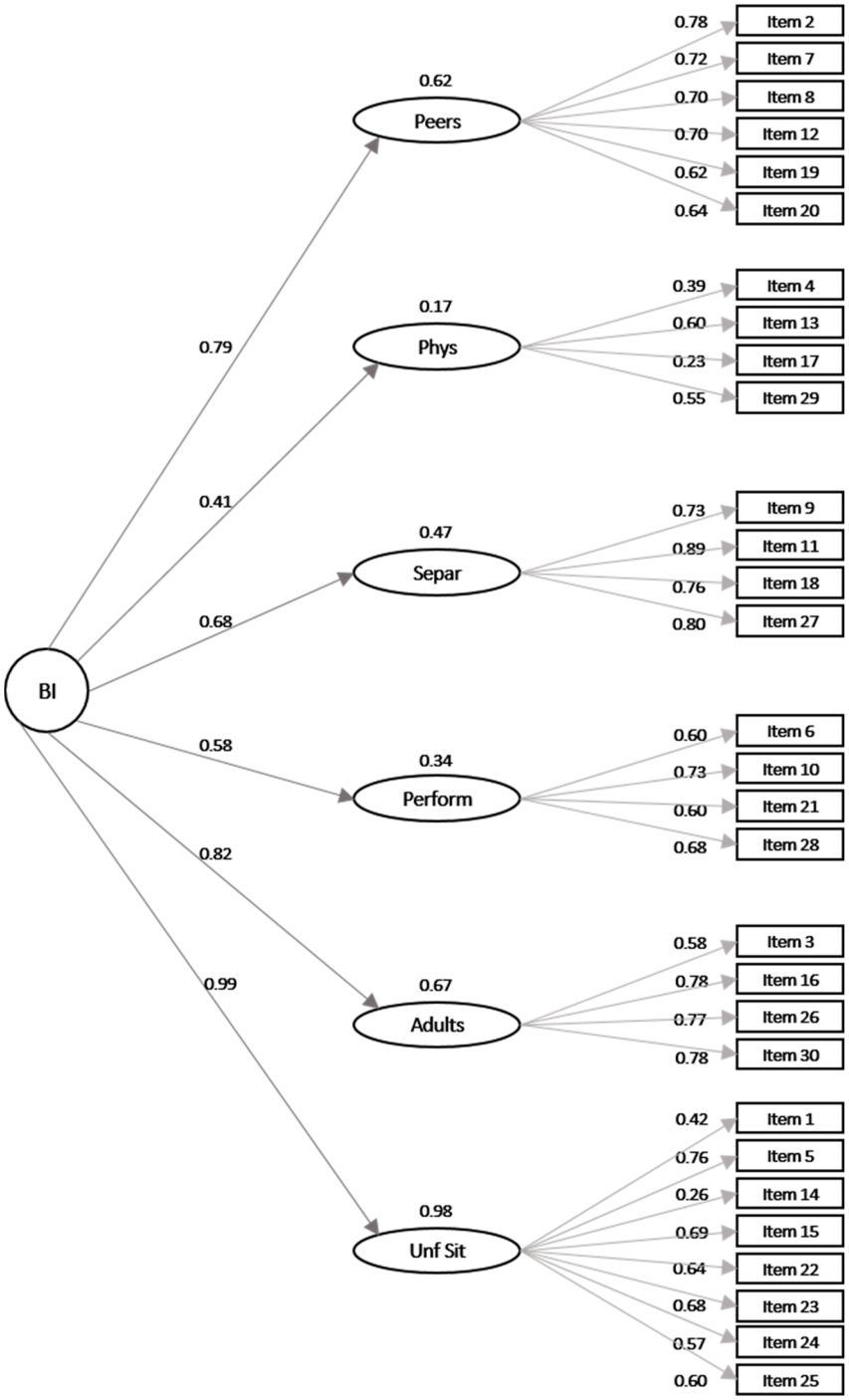

Figure 1. Representation of the standardized parameter estimate in Model 4. Note: BI = Behavioral Inhibition; Phys = Physical challenges; Separ = Separation; Perf = Performance situations; Unf Sit = Unfamiliar situations.

3.2. Measurement Invariance

Configural invariance was tested across groups by requiring the same factor structure across the mother and father groups but allowing the magnitudes of all estimated parameters to vary. Metric invariance was tested across groups by setting factor loadings to be equal across the mother and father groups but allowing other estimated parameters to vary. Both the model to test configural invariance and the model to test the metric invariance showed good fit indices that did not vary significantly from one model to the other. The BIQ scale showed configural and metric invariance across groups (see Table 4).

Table 4. Results of the Measurement Invariance test across parental role groups.

Model	Parental Role (Mothers and Fathers)			
	GFI	NFI	PNFI	SRMR
Configural invariance: Factor structure constrained to be equal	0.97	0.95	0.85	0.06
Metric invariance: Factor loadings constrained to be equal	0.96	0.94	0.88	0.07

3.3. Internal Consistency

BIQ total score showed an excellent internal consistency and a significant item-total correlation for the total sample of parents (Cronbach's Alpha = 0.92; Guttman's split-half coefficient = 0.94; item-total = 0.15–0.71). Similar results were found both for mother (Cronbach's Alpha = 0.92; Guttman's split-half coefficient = 0.95; item-total = 0.15–0.73) and for father (Cronbach's Alpha = 0.90; Guttman's split-half coefficient = 0.94; item-total = 0.13–0.67) subsamples. Only two items showed low correlation with total score (item 4 and item 17). Considering the BIQ subscales, good Alpha coefficients (ranging from 0.75 to 0.87) and good item-total correlations indexes emerged (Table 5), except for the "Physical challenges" subscale, showing a low Alpha coefficient (0.41) and low item-total correlation coefficients (ranging from 0.07 to 0.33). The item 17 had the lowest item-total correlation, showing an Alpha = 0.55 if the item was deleted. Comparable results were obtained for the mother and father forms, separately (Table 5). CR results indicated adequate (CR > 0.70) reliability for all the subscales except for the Physical Challenges subscale (Peers CR = 0.85; Physical Challenges CR = 0.48; Separation CR = 087; Performance Situations CR = 0.75; Adults CR = 0.82; Unfamiliar Situations CR = 0.81).

Table 5. Cronbach's Alphas and Item-Total correlations for parents, and for mothers' and fathers' forms separately.

	Parents		Mothers		Fathers	
	Alpha	Item-Total	Alpha	Item-Total	Alpha	Item-Total
Total BIQ	0.92	0.15–0.71	0.92	0.15–0.73	0.90	0.13–0.67
Peers	0.85	0.56–0.70	0.86	0.57–0.70	0.83	0.50–0.70
Physical Challenges	0.41	0.07–0.33	0.44	0.07–0.35	0.37	0.07–0.34
Separation	0.87	0.69–0.76	0.88	0.72–0.79	0.84	0.63–0.75
Performance Situations	0.75	0.49–0.64	0.75	0.48–0.66	0.74	0.49–0.60
Adults	0.81	0.51–0.71	0.84	0.53–0.73	0.78	0.49–0.68
Unfamiliar Situations	0.80	0.27–0.68	0.83	0.26–0.70	0.76	0.27–0.69

3.4. Inter-Rater Reliability

Mother and father total scores were significantly correlated ($r = 0.63$, $p < 0.001$). Furthermore, mothers and fathers showed a good inter-class correlation index (ICC = 0.77; 95% C.I. = 0.69–0.83). The repeated measures ANOVA, which considered BIQ total scores, showed a non-significant informant effect ($F(1, 161) = 1.48$; $p = 0.23$; Partial $\eta^2 = 0.01$) and a non-significant informant by the child's gender effect ($F(1, 161) = 0.07$; $p = 0.79$; Partial $\eta^2 = 0.00$).

3.5. Convergent, Divergent and Discriminant Validity

Pearson's correlation analysis results concerning convergent validity are shown in Table 6. Significant positive correlations emerged among BIQ total scores and "Novelty Inhibition" and "Negative Emotionality" QUIT subscales for parents, for father and mother subsamples. Additionally, significant negative correlations among BIQ total scores and "Social Orientation", "Positive Emotionality" and "Attention" emerged, again for the main sample and the 2 subsamples. This result was confirmed by significant correlations between BIQ total scores and Anxious-Shy scores evaluated with CPRS-R in the mothers' sample (Pearson's $r = 0.52$; $p < 0.01$), and in the fathers' sample (Pearson's $r = 0.37$; $p = 0.04$).

Table 6. Correlations between BIQ total scores and Italian Questionnaires of Temperament (QUIT) scores.

BIQ Total Score	QUIT Dimensions					
	Social Orientation	Novelty Inhibition	Motor Activity	Positive Emotionality	Negative Emotionality	Attention
Parents [a]	−0.37 **	0.49 **	−0.04	−0.37 *	0.24 **	−0.16 **
Mothers [b]	−0.37 **	0.50 **	0.01	−0.32 **	0.23 **	−0.14 *
Fathers [c]	−0.37 **	0.47 **	−0.12	−0.45 **	0.26 **	−0.21 *

Note: [a] $N = 417$; [b] $N = 230$; [c] $N = 187$; ** $p < 0.01$, * $p < 0.05$.

In addition, to test the convergent validity, Pearson's r correlation indexes between parent BIQ scores and the 4 LAB-TAB variables were calculated (Table 7). Results showed significant correlations in the parents' sample among Intensity of Decrease Activity and BIQ total score, Separation subscale, Unfamiliar adult, and Unfamiliar situations subscales. Moreover, Total Number of Objects Touched showed significant negative correlations with Separation and Unfamiliar adult subscales, whereas Latency to intentionally touch the first object significantly correlated with Unfamiliar adult and Physical challenges subscales.

Table 7. Correlations between BIQ subscales and LAB-TAB indexes.

	LAB-TAB Social Inhibition Indexes		LAB-TAB Non-Social Inhibition Indexes	
BIQ Total Score and Subscales	Intensity of Decrease in Activity	Intensity of Verbal Hesitancy	Total Number of Objects Touched	Latency to Intentionally Touch the First Object
Parents ($N = 41$)				
Total BIQ	0.33 *	0.08	−0.25	0.25
Peers	0.28	−0.03	−0.19	0.09
Physical Challenges	−0.08	−0.04	−0.13	0.32 *
Separation	0.40 **	0.14	−0.38 *	0.21
Performance Situations	0.18	−0.16	−0.25	0.17
Adults	0.36 *	0.13	−0.39 *	0.46 **
Unfamiliar Situations	0.44 **	0.22	−0.19	−0.28
Mothers ($N = 23$)				
Total BIQ	0.39	0.13	−0.26	0.28
Peers	0.28	0.00	−0.10	0.09
Physical Challenges	−0.06	0.17	−0.22	0.39
Separation	0.52 *	0.26	−0.47 *	0.23
Performance Situations	0.10	−0.19	−0.19	0.12
Adults	0.42 *	0.27	−0.42 *	0.47 *
Unfamiliar Situations	0.43 *	0.26	−0.22	0.26
Fathers ($N = 18$)				
Total BIQ	0.34	0.02	−0.27	0.22
Peers	0.31	−0.01	−0.31	0.09
Physical Challenges	−0.02	−0.34	−0.04	0.22
Separation	0.29	−0.00	−0.26	0.20
Performance Situations	0.31	−0.11	−0.31	0.26
Adults	0.29	−0.08	−0.38	0.45
Unfamiliar Situations	0.44	0.16	−0.18	0.20

Note: ** $p < 0.01$, * $p < 0.05$.

Considering only the mothers' sample, Intensity of Decrease Activity correlated with Separation subscale, Unfamiliar adult, and Unfamiliar situations. Furthermore, Total Number of Objects Touched showed significant negative correlations with the subscales, Separation and Unfamiliar adults, while Latency to intentionally touch the first object showed a significant correlation with Unfamiliar Adult.

Globally, these findings indicated a medium magnitude of the associations between parents' reports and observational measures of BI (both social and non-social), as all the significant correlation coefficients ranged from 0.32 to 0.52. However, when considering the fathers separately, no significant correlations were found among LAB-TAB selected variables and BIQ subscales and total score.

Divergent validity was analysed between BIQ total score and ADHD Index measured by CPRS-R, and correlations were calculated. As expected, both mothers' and fathers' samples showed non-significant correlations (Pearson's $r = 0.23$; $p = 0.19$; Pearson's $r = -0.24$; $p = 0.19$, respectively).

HTMT results indicated acceptable discriminant validity according to the HTMT 0.85 criterions (see Table 8).

Table 8. Heterotrait-Monotrait Ratio of Correlations (HTMT) results.

BIQ Subscales	Peers	Phys	Separ	Perform	Adults
Phys	0.40				
Separ	0.54	0.31			
Perform	0.52	0.30	0.31		
Adults	0.64	0.24	0.54	0.62	
Unf Sit	0.76	0.60	0.75	0.48	0.77

Note: Phys = Physical challenges; Separ = Separation; Perf = Performance situations; Unf Sit = Unfamiliar situations.

4. Discussion

The present study aimed to evaluate the psychometric properties of the BIQ in a new cultural context, represented by a population of Italian preschool children. The findings were overall in line with other studies that investigated the operationalization of the BI construct [4,22,53] and also added new insights to former literature.

First, we found a gender effect on BIQ, showing that girls obtained higher scores than boys and confirming part of the previous literature [18–20,47,96]. In our study, this difference emerged particularly when children were exposed to unfamiliar peers, adults, and situations. Nevertheless, when compared to previous studies using the BIQ, our results only partially confirmed those by Bishop et al. [21], who found higher BI in girls only on the Performance Situation and Adults subscales. Furthermore, our results were not in line with the findings by Kim et al. [22] and Vreeke et al. [30], where boys were highly inhibited in Performance and Separation situations compared to girls (while these latter were more inhibited in Physical challenges), nor with those by Mernick et al. [53], who did not find any significant difference. We may consider that, despite the possible influence of methodological issues, the contrasting results reflect the debate in literature about the relationship between gender differences and BI. Globally, the theoretical perspectives on gender effects beyond the findings include, on one hand, the biological theorists, suggesting a prevalent and possible effect of factors (e.g., sex hormones in utero, which would lead to body and brain differences between males and females) existing either prenatally and/or at birth; on the other hand, other researchers suppose that differences are mainly due to gender roles and stereotypes [97]. Again, the context of observation could represent a further influencing factor [98], where girls might be inhibited especially in response to new persons (as emerged in our study), while boys in new environments. Therefore, at present, there is the need to further improve the empirical evidence to fully understand the role of child gender on BI.

Regarding the investigation of main psychometric properties of the Italian BIQ, the findings were in line with the original version and subsequent ones [4,22,53] and globally demonstrated good reliability and validity of this Italian version. CFA showed a good internal validity for the overall sample of parents: results yielded the 6-factor model loading onto a single general dimension of BI as detected by Bishop and collaborators [21] and by Kim et al. [22]. Consistently with these studies, our results seem to confirm BI as a higher-order disposition that is expressed in multiple contexts. It is also of note that, despite our values being less optimal than those resulted in other validations of the BIQ [21,22,53], the items with the lower association scores (#4, #14, #17) were the same as those which emerged also in the study by Kim et al. [22]. These results seem to be especially influenced by the scores of two of the four items that constitute the Physical Challenges subscale: #4-The child is cautious in activities that involve a physical challenge (e.g., climbing, jumping from a certain height.); and #17-The child is hesitant to explore new play equipment. A useful consideration regards the format of these items: in both cases, parents were directly asked to answer about inhibition of their children, suggesting a criticality or a negative judgement when they had to assess their children's reticence. Conversely, more adequate values emerged for the other two items of the same scale (#13-The child is confident in activities that involve physical challenge (e.g., climbing, jumping from heights); #29-The child happily explores new play equipment), suggesting that parents are more prone to assess positive qualities, such as resourcefulness, of their children. The way the items are formulated (negative or positive), therefore, could more heavily influence the Physical Challenges subscale, given that it is composed by fewer items (four) than all the other BIQ subscales. Furthermore, the poorer fit of our model might suggest that this area is particularly critical for the evaluation of Italian children by their parents, therefore further exploration of this subscale would be recommended in future studies.

In addition, for item 14 ("The child is independent"), some considerations are useful: differently from the other items of Unfamiliar situation subscale, this item is somehow generic and does not specify a context of application of the answer (i.e., new situations, new places); therefore, parents could be misled in their interpretation. As suggested by Gartstein [26], Mediterranean parents (i.e., Italian or Spanish populations) are used to highly supporting the preservation of close proximity, while independency is associated to a more individualistic approach, typical in other Western populations.

Taken together, these results suggest some potential critical elements for these items to be used in the Italian context. Nevertheless, considering that our work represents a first validation of the Italian version of the BIQ, these results may be considered overall promising and future studies could further explore the role played by the abovementioned items.

According to the internal consistency of the Italian version of the BIQ, we found excellent results given by significant item-total correlation coefficients, consistently with previous BIQ validation studies [4,22,53]. Nevertheless, low correlation values emerged in Physical Challenges subscale, as already observed by Kim et al. [22] and Mernick et al. [53]. As for CFA, our results could be influenced by item 17, the only one to show low item-total correlations in parents, and mother and father forms. Again, the specificity of the item could have contributed to its weakness for the Italian context.

Our results also indicated adequate convergent and discriminant validity of the Italian BIQ, confirming previous validation studies [4,21,22,53]. Specifically, significant correlations among BIQ total scores and those of QUIT in parents, and mother and father groups, suggested a good convergent validity. As expected, we found that BIQ total scores were significantly correlated with the QUIT Negative Emotionality and Novelty Inhibition subscales, this latter being the most relevant for the BI construct. Significant negative associations emerged also among BIQ scores and the QUIT Social Orientation, Positive Emotionality and Attention subscales. These results may confirm that inhibited children are characterized by low sociability and fewer expressions of positive emotions, such as smiles or laughter [20,22,99]; furthermore, the inverse relationship with attention seems to confirm that the construct of BI is not related to individual voluntary control [11], typical of

the construct of inhibitory control. Among the 6 QUIT subscales, Motor Activity is the only one that showed no significant correlations with the BIQ total scores. Together with the weak psychometric properties observed for the Physical Challenges subscale, this result seems to suggest that the dimension of the motor area is less associated with the parental perception of BI. Prior, Broeren and Muris [4] questioned whether motor activity could sensitively reflect social aspects of BI, hypothesizing that it rather represents a measure of social aspects of anxiety (i.e., fear of body injury or physical danger). Globally, these results might highlight that the inclusion of motor area in the assessment of the BI construct needs to be better investigated and defined in future studies.

The convergent validity of the Italian version of BIQ was confirmed by the significant correlations emerged between BIQ total score and the Anxious-Shy subscale of the CPRS-R. This result was in line with the previous versions of BIQ assessing anxiety [4,53] and shyness constructs [22]; it is also consistent with previous wider literature, where high rates of anxiety disorders were often observed in inhibited children [41,46,100].

The convergent validity was also tested considering observational scores given by LAB-TAB. Results evidenced that children characterized by a high trait of BI, rated by the overall sample of parents, showed a substantial decrease of activity (e.g., muscular tension). Specifically, this reaction emerged in the moment of separation in kindergarten (Separation subscale) or when exposed to unusual situations or strangers (Unfamiliar situation and Unfamiliar adults subscales, respectively), and in correspondence with the BIQ total score. When non-social components of BI were considered, children rated as inhibited, compared to their non-BI peers, touched fewer objects and showed a longer latency to intentionally touch the first object during physical challenges and in unfamiliar situations. These results are partially consistent with those by Kim et al. [22], even if they differently scored LAB-TAB episodes. Overall, our results on external validity are in line with previous literature comparing BI and non-BI children [12,55], showing that inhibition towards new people is associated with non-social indexes of inhibition, such as the number of objects touched by the child. Nevertheless, we did not find associations among LAB-TAB scores and Peers, Physical Challenges and Performance subscales of BIQ. This could be tied to methodological issues, as LAB-TAB being used only on a very limited sample; furthermore, despite we chose the same episodes selected by Kim et al. [22], we used a different coding and this could explain the discrepancy in the results. Therefore, these findings, even if promising, should be further confirmed.

Convergent validity also showed different results in the mother and father samples. Indeed, the results on the overall sample of parents seemed to mainly reflect the mothers' perception. Conversely, we did not find any correlations between father BIQ scores and LAB-TAB indexes, in line with Bishop and colleagues [21], as they also found low associations for father scores regarding convergent validity. We may hypothesize some explanations for these findings: first, it might be possible that fathers, compared to mothers, less frequently observe their children in situations that are likely to trigger BI behavior [21]; they also might be more inclined to capture the child's verbal aspects, such as initiation latency and number of prompts required, whereas mothers may be more sensitive in considering nonverbal features; furthermore, we have to keep in mind more generally that parent reports are influenced by characteristics of personality, mood states and psychopathology [101,102].

In summary, despite moderate correlations between BIQ and LAB-TAB emerging, consistent with previous literature [21,22,102–105], the joint use of self-report and observational procedures seemed to assess dimensions of BI which were not overlapping, suggesting that an integrated method of evaluation, including both observational procedures and parent-report measures, is endorsed when possible [52,106].

Moreover, discriminant validity was confirmed indicating sufficient separation between the BIQ subscales.

Finally, acceptable divergent validity was found, confirming the findings by Mernick et al. [53]. Our results showed that total BIQ was not associated with restless and impulsive behavior, as measured by the ADHD Index of CPRS-R, in both the mother and father samples.

Some limitations of the present study should be considered. First, because it was a first contribution for Italian validation, the partial limited sample size did not allow running more specific and sophisticated analyses. This was particularly evident in the case of convergent validity assessed by LAB-TAB, where only a few indexes were selected, and the sample was very restricted. Second, we focused only on parents, and the perception from other observers was not investigated; nevertheless, it could be useful to also investigate the teachers' perception, as included in the studies by Bishop et al. [21] and Kim et al. [22]. Third, our study was only cross-sectional-based, and we did not examine the stability of the BIQ over time. In addition, the contribution and influence of specific factors like caregiver personality and psychopathology should be included. Lastly, a further validation of the BIQ's Italian version should also explore concurrent and predictive validity. Therefore, future studies are recommended in order to confirm the psychometric characteristics of the BIQ for Italian preschool children.

5. Conclusions

Despite the above-mentioned limitations, to our knowledge this is the only study, up to now, to contribute to the assessment of BI in an Italian sample, and it seems to confirm the promising psychometric properties of the BIQ already uncovered from previous international literature.

Given that the specific cultural factors of a population influence the perception and the expression of the BI trait [26–30], it is important to develop, through accurate validation studies, sensitive instruments for the assessment of BI. Considering the clinical implications of BI for child and adolescent mental health, the availability of a valid tool is of particular relevance for the early identification of children at higher risk for psychopathology and the realization of tailored interventions. Additionally, from a more theoretical point of view, this validation study would support Kagan and colleagues' perspective about BI as a unitary construct which is characterized by an avoidant and fearful behavior towards both social and non-social stimuli [107].

In conclusion, this study provides further evidence of the suitability of the BIQ for the assessment of BI, as it can be easily completed by both mothers and fathers giving, as a result, a reliable measure of BI among Italian preschool children.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ijerph18115522/s1, Table S1: Fit indexes for each model for mother and father reports separately of Behavioral Inhibition Questionnaire (BIQ).

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A novel multidimensional questionnaire for the assessment of emotional dysregulation in adolescents: Reactivity, Intensity, Polarity and Stability questionnaire–youth version (RIPoSt–Y)

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ABSTRACT

Background: The failure to regulate emotions, namely emotional dysregulation (ED), is a relevant construct in adolescent psychiatry, in terms of prognostic and developmental implications. We developed and validated a novel self-report questionnaire for the assessment of ED, the RIPoSt-Y, both in clinical and non-clinical samples.
Methods: Items selection and subscales construction were conducted on healthy controls (n=374), while test-retest reliability was evaluated in a subsample (n=72); internal consistency was examined both in the control group and in two clinical samples, respectively including patients with Bipolar Spectrum Disorders (BSD; n=44) and ADHD (n=34). Construct, concurrent and convergent validity were also assessed.
Results: Thirty-one items were finally retained, and three subscales were identified (Affective Instability, Emotional Reactivity, Interpersonal Sensitivity). Test-retest was significant for each subscale with moderate-to-good correlations, and internal consistency showed good-to-excellent coefficients. Construct validity was supported by significant differences between patients and controls and gender-related differences. Concurrent validity was confirmed through significant associations with two subscales of the CHT-Q, while convergent validity proved to be significant with the CBCL/YSR dysregulation-profile. Cut-offs were also computed to discriminate clinically significant scores of ED.
Limitations: The use of a school-based survey to recruit controls could have biased our results; gender distributions between clinical and non-clinical samples were significantly different.
Conclusions: Our novel questionnaire proved to be a valid and reliable tool able to assess the presence of ED in youths and to characterize this fundamental construct in its multidimensional facets.

1. Introduction

Emotion regulation refers to any strategy that modulates emotion unfolding and shapes the resulting affective and behavioral reactions under distinct conditions (Gross and Jazaieri, 2014; McRae and Gross, 2020; Sheppes et al., 2011). Distinct terms for impaired emotional regulation have been used interchangeably, but Emotional Dysregulation (ED) has been more widely accepted, namely in youth (Faraone et al., 2019). Children with ED exhibit from an early age severe irritability with temper outbursts, mood lability and instability, low tolerance to frustration and low reactivity threshold, inappropriate expression of emotions with excessive intensity, and slow affective normalization (Faraone et al., 2019; Stringaris, 2011), with negative impacts on quality of life and social adjustment (Bunford et al., 2018;

Abbreviations: ADHD, Attention Deficit Hyperactivity Disorder; BD, Bipolar Disorder; BSD, Bipolar Spectrum Disorders; CBCL, Child Behavior Checklist; DP, Dysregulation Profile; ED, Emotional Dysregulation; ODD, Oppositional Defiant Disorder; PD, Personality Disorders; SMD, Severe Mood Dysregulation; YSR, Youth Self Report.

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Lee et al., 2018).

More recent advances are aimed to interpret ED as a neurodevelopmental, early-onset disorder of the regulation of emotions, which is often associated to other psychiatric conditions, strongly affect developmental trajectories and outcomes, including the presence of both internalizing and externalizing comorbidities (Perugi et al., 2016). This latter theoretical framework suggests that ED could be either a shared risk factor for both types of disorder (Stringaris and Goodman, 2009), being strongly associated with them even when adjusting for the association with individual disorders, or else a common key factor for the development of later psychopathology (Caspi, 2000; Haltigan et al., 2018; Holtmann et al., 2011; Lahey et al., 2008), possibly serving as an efficient proxy in clinical applications.

Although ED should be considered a transdiagnostic dimension or an intermediate stage in the development of different mental disorders, its most prominent features of mood lability, emotional reactivity and impulsivity, and overt irritability have been more closely associated with mood disorders, and more specifically with pediatric bipolar disorder (BD) (Wozniak et al., 1995). Between the mid-1990s and early 2000s, mostly in the United States, there was a huge increase of pediatric BD diagnoses, based on the interpretation of chronic irritability and dysregulated emotionality as a developmental expression of early-onset BD (Biederman et al., 2004). Leibenluft et al. (2003) further defined the pediatric BD phenotypes, including, among others, a "broad phenotype", called Severe Mood Dysregulation (SMD), phenotypically different from BD, and characterized by chronic, non-episodic illness, and severe irritability. The debate between episodic and chronic course of ED, defining specific and stable phenotypes, was further developed (Leibenluft et al., 2003b; Masi et al., 2006) and finally prompted a new DSM-5 diagnostic category, called Disruptive Mood Dysregulation Disorder, distinct from the BD spectrum and included within the realm of depression. This new category is still discussed, mostly in terms of boundaries with other mental disorders, particularly attention deficit hyperactivity disorder (ADHD) and Oppositional Defiant Disorder (ODD) (Axelson et al., 2015; Copeland et al., 2013; Mayes et al., 2016).

More specifically, the irritable dimension of ODD shows a strong association with emotionality (Stringaris and Goodman, 2009). Accordingly, the World Health Organization categorized, in the ICD-11 classification system, a chronic irritability within the "irritable" type of ODD, without including DMDD (Evans et al., 2021; Lochman et al., 2015). This solution is supported by longitudinal studies, such as, for instance, the British national survey (n = 7,912) which showed that the "irritable" dimension of ODD significantly predicted emotional disorders at follow-up, particularly depression and anxiety (Stringaris and Goodman, 2009). Consistently, in 80 referred children with disruptive behavior disorders, those with higher scores on a clinical measure of ED at age 8 were at increased risk for presenting mood disorders later in adolescence, and ED was the only significant predictor of a mood disorder at 14 – 15 years (Masi et al., 2015).

Developmental trajectories of psychopathology further clarify the transdiagnostic implications of ED, particularly emotional overreactivity and interpersonal sensitivity, which make individuals hypersensitive to interpersonal stimuli (namely peer rejection), and prone to feeling wounded also for minor critiques or imagined slights, with subsequent hostility and anger (Perugi et al., 2016). These feelings can start early in life, with attachment disorders and separation anxieties, often co-occurring with emotional and behavioral impulsivity, and can persist in adulthood (Perugi et al., 2016). Moodiness, impulsivity, and interpersonal problems are similar to those described in DSM-5 cluster B personality disorder, the different diagnoses depending on the developmental phase, perspective, and moment of observation (Perugi et al., 2011). Reimherr et al. (2010) explored the relationship between the dimensions of ADHD and personality disorders (PD) in adulthood, and found that none of the ADHD-alone patients had a PD compared with 33% of ADHD + ED patients and 68% of ADHD + ED + ODD patients. The ADHD symptoms of ED and ODD were particularly associated with borderline PD.

Regarding the neurobiological and neuropsychological underpinnings of ED, even though the executive or cognitive control of emotions, that is, deficient emotional self-regulation, has been prevalently considered (Barkley and Fischer, 2010; Faraone et al., 2019) more recently several studies suggested that youths with ED may present an altered sensory processing, with increased salience for emotional negative stimuli (i.e., impaired face-emotion labeling ability), with a perceptual bias toward threatening faces compared to healthy children (Benarous et al., 2020; Carlson et al., 2009; Rich et al., 2011; Stringaris et al., 2010).

In everyday practice, many clinical tools are available to evaluate impairments of emotion regulation competences (Marwaha et al., 2014). The most reliable and valid tools to assess ED in both adults and children are more deeply discussed in Supplementary Material 1. Given the multifaceted dimensional concept of ED, scales comprehensively assessing all components are currently lacking (Marwaha et al., 2014). However, a recently developed instrument to assess the different dimensions of ED in adults is the Reactivity, Intensity, Polarity and Stability (RIPoSt) scale (Hantouche, 2014).

This tool was originally drafted as a 60-item self-report questionnaire (RIPoSt-60) (available in its English, French and Italian versions),aimed at evaluating emotional Reactivity (items 1-15), affective Intensity (items 16-30), Polarity of emotional responses (items 31-45) and affective Stability (items 46-60). Answers are given in a six-point Likert-type scale ranging from 1 (never) to 6 (always). The only validation study available so far (Brancati et al., 2019) has been conducted on an Italian adult sample of 396 individuals from the general population and 174 patients affected with either ADHD or cyclothymia. The items selection and scale construction processes, carried out on the non-clinical sample, led to a 40-item version of the instrument (RIPoSt-40) encompassing the following four components: Affective Instability, Emotional Impulsivity, Negative Emotionality and Positive Emotionality. The first three factors may also be summed up to form a composite score, namely the Negative ED subscale, overall including thirty items.

Based on this newly developed measure of ED, we conducted an exploratory study on a small-sized clinical and non-clinical sample of youths using the 40-item version of the RIPoSt questionnaire to examine ED profiles in patients with ADHD and/or BSD (Masi et al., 2021). Our preliminary findings indicate that Affective Instability and Negative Emotionality are mostly related to BSD, both pure and with comorbid ADHD, and can reliably differentiate these conditions from pure ADHD. On the other hand, a more nuanced difference was shown for Emotional Impulsivity which was found to be similar in ADHD and BSD alone and higher in the comorbid condition. These three dimensions likely discriminate the dysregulated profile of ADHD youths compared to healthy controls, while Besides, we further confirmed that Positive Emotionality does not differentiate clinical and non-clinical groups. Gender-related differences also emerged, with females scoring higher than males in Affective Instability and Negative Emotionality dimensions, while Emotional Impulsivity was similar across gender. Based on this first clinical experience, we present here a validation study in youths, which includes both clinical and non-clinical samples. We proposed to delineate a factorial structure through a set of successive analyses by identifying the most convenient items for youths. This latter may not necessarily overlap the one found in adults while reflecting different dimensions of ED according to the clinical features characterizing psychopathology in youth.

2. Methods

2.1. Participants

Two samples were enrolled in the present study, both aged 13 to 19 years old. One sample from the general population was recruited between March and October 2020, and consisted of anonymous subjects

voluntarily enrolled from secondary schools (third year of lower secondary schools to fifth and last year of upper secondary schools) through an online survey on a digital platform. Inclusion criteria were as follows: age ranging from 13 to 19 years old and ability to autonomously fill out self-rated questionnaires. Parents of subjects who showed willingness to participate were emailed instructions to complete the online survey and provided informed written consent on the platform. They were initially asked about socio-demographical variables including birth date and gender of the offspring, currently attended school type and year, family unit type (i.e. either both biological parents or one, foster parents or home) and type of residence (i.e. urban, suburban or rural). Four-hundred-nine subjects (age range 11 – 20 years) completed the survey, of which 30 were excluded due to age exceeding the accepted range. Five additional respondents were excluded as multivariate outliers based on unusual or idiosyncratic patterns of response (see the Statistical Analysis paragraph). Thus, 374 adolescents were included in the non-clinical sample (mean age 15.74 ± 1.69 years old, age range 13 – 19 years, 25.40% boys). Among these, 72 subjects (19.25%) indicated their willingness to participate in a second run in February 2021, after 137.55 ± 2.05 days to assess test-retest reliability.

A second sample of referred adolescents was enrolled from April 2019 to October 2020 at our third-level Department of Child and Adolescent Psychiatry and Psychopharmacology. This sample included 78 inpatients and outpatients (age range 13 – 19 years) with a diagnosis of either BSD or ADHD with ED, defined as "severe irritability with temper outbursts, mood lability and instability, low tolerance to frustration and low reactivity threshold, inappropriate expression of emotions with excessive intensity, and slow affective normalization" (Faraone et al., 2019; Stringaris, 2011). Diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders-fifth edition (American Psychiatric Association, 2013), based on medical history, clinical observations and a semi-structured interview, the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997), administered by trained child psychiatrists to both patients and parents. Inclusion criteria overlapped those applied to the non-clinical sample, whereas exclusion criteria were as follows: a diagnosis of autism spectrum disorder or schizophrenia spectrum and other psychotic disorders and the presence of comorbid intellectual disability (either the Full-Scale Intelligence Quotient or the General Ability Index below 85 at the Wechsler Intelligence Scale for Children-fourth edition [Wechsler, 2004]). Parents of patients who showed willingness to participate provided informed written consent. Seventy-eight patients were included in the clinical sample (mean age 16.98 ± 1.62 years old, age range 13 – 19 years, 52.56% boys), of which 44 patients were diagnosed as BSD/ED (29.5% boys) and 34 as ADHD/ED (82.4% boys).

2.2. Measures

All participants were asked to fill in the Italian 60-item version of the RIPoSt scale which was initially used for the assessment of ED in adolescents. As described above, the original instrument included 60 items and answers were given in a 6-point Likert-type scale ranging through the following scores: 1 = never, 2 = rarely, 3 = sometimes, 4 = usually, 5 = mostly and 6 = always. Items of this version assessed Reactivity, Intensity, Polarity of emotional responses and affective Stability. Despite being validated in a 40-item version in the adult population (Brancati et al., 2019), we still decided to employ the original 60-item version with the aim to assess whether different domains of ED would emerge in our adolescent samples and a different scale would be constructed for youths (RIPoSt-Y).

Both samples were also asked to complete a measure of Cyclothymic and Hypersensitive Temperament (CHT). The 22-item CHT questionnaire (CHT-Q) (Pisano et al., 2020), a youth version derived from the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego questionnaire (TEMPS; Akiskal et al., 2005), has been assessed in a school-based sample of almost 3 thousands students aged 10-14 years and lead to a two-factor structure including a Moodiness/Hyper-Sensitiveness (MHS) domain – highly associated with internalizing symptoms – and an Impulsiveness/Emotional Dysregulation (IED) domain – strongly associated with externalizing symptoms. The measure showed adequate internal consistency, with Cronbach's alpha ranging from 0.809 to 0.863 and McDonald's omega ranging from 0.834 to 0.883, and good convergent and divergent validity, assessed with the Strength and Difficulties Questionnaire and the Inventory of Callous Unemotional traits, respectively.

Finally, the clinical sample was required to fill out the Youth Self Report for ages 11 to 18 years (YSR-11/18) (Achenbach and Rescorla, 2001), a widely used 113-item measure of emotional and behavioral problems based on self report. Moreover, parents or caregivers of recruited patients were asked to complete the Child Behavior Checklist for ages 6 to 18 years (CBCL-6/18) (Achenbach and Rescorla, 2001), a 118-item scale with eight different syndrome scales and three broad-band scores designated as Internalizing, Externalizing and Total Problems scores. In the current study, the DP index of the YSR-11/18 and the CBCL-6/18 questionnaires (YSR-DP and CBCL-DP) was computed as the sum of T-scores of the Anxious/Depressed, Attention Problems and Aggressive Behaviors subscales (Doelitzsch et al., 2016; Holtmann et al., 2011).

2.3. Items selection process

Data from the non-clinical sample were initially used to identify items to retain and to assess the validity of empirically derived subscales of the RIPoSt-Youth questionnaire (RIPoSt-Y). Items were initially excluded based on a selection process which is described in detail in Supplementary Material 1. Then, to determine the number of factors to be retained, a set of successive Principal Component Analyses (PCA) were performed and the final components of the RIPoSt-Y were extracted (see Supplementary Material 1). The corresponding subscales scores were finally computed as sums of the individual responses across the items loading highest on the same component.

2.4. Reliability and validity

Test-retest reliability was assessed by computing Spearman's correlation coefficients for each subscale individually. Internal consistency was evaluated by estimating Cronbach's alpha and McDonald's omega coefficients for each subscale and the whole scale; item-subscale Spearman's rank correlations coefficients were compared. Inter-subscale Spearman's rank correlations were also performed with a p-value corrected applying the Bonferroni method for multiple comparisons at the traditional significance level of 0.05.

Age and gender differences between samples were assessed using the Analysis of Variance (ANOVA) and χ^2 test, respectively. Construct validity was then assessed by comparing subscales scores across groups and genders. ANOVA were performed to compare the subscales scores between the two clinical subgroups and the non-clinical sample, while controlling for age and gender; as for age, participants were divided into two nearly equally distributed subgroups with age ranging from 13 to 15 and from 16 to 19 years, respectively. A Tukey post-hoc test was utilized whenever the ANOVA led to a statistically significant result in order to retrieve significant comparisons between variables (p-value < 0.05). Concurrent validity was assessed for each sample separately by performing Spearman's correlations between each subscale of the RIPoSt-Y and the two subscales of the CHT-Q. Convergent validity was finally evaluated in the clinical sample only, by performing Spearman's correlations between each subscale of the RIPoSt-Y and the CBCL and YSR-DP scores. Significance threshold was corrected applying the Bonferroni method for multiple comparisons at the traditional significance level of 0.05.

Finally, to differentiate clinical and non-clinical groups, cut-off

scores were also determined using the Youden's index which maximizes both the specificity and the sensitivity of discrimination, as recommended by Perkins and Schisterman (2006) (for further reference see Habibzadeh et al., 2016). Sensitivity and specificity were then calculated using the resulting cut-off scores for each subscale of the RIPoSt-Y.

3. Results

3.1. Scale development

The process of development of the scale is described in detail in Supplementary Material 1. Forty items out of the original sixty were ultimately retained in the final structure of the RIPoSt-Y scale. The four components were then carefully assessed (Table 1, Supplementary Table 1). The first component accounted for 22% of the variance and included 16 items which showed loadings greater than 0.495 on this component only (items 39, 43, 46, 47, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59 and 60). The majority of these items loaded on the Affective Instability factor of the RIPoSt-40 and on the Stability domain of the RIPoSt-60, except for two items (items 39 and 43) that belonged to the Negative Emotionality and Polarity subscales, respectively. A qualitative evaluation of the items loading on this first component confirmed that it is intended for assessing *Affective Instability*.

The second component accounted for 11% of the variance and included 9 items which showed loadings greater than 0.5 on this component only (items 18, 19, 27, 30, 32, 33, 36, 37 and 38); the two items showing negative association with most of the other items of the scale (32 and 37) were instead positively correlated with all the other items loading on this same component, and thus did not undergo reverse-coding. Almost all these items loaded on the Positive Emotionality factor of the RIPoSt-40, while being nearly equally distributed across the Polarity and the Intensity domains of the RIPoSt-60. A qualitative evaluation of the items loading on this second component confirmed that it is intended for assessing *Positive Emotionality*.

Seven items loaded more than 0.5 on the third component only, which accounted for 11% of the variance (items 1, 3, 5, 6, 14, 21 and 23). Nearly all these items loaded on the Emotional Impulsivity factor of the RIPoSt-40 and the majority of them on the Reactivity domain of the RIPoSt-60. A qualitative evaluation of the items loading on this third component confirmed that it is intended for assessing *Emotional Reactivity*.

Finally, eight items loaded more than 0.5 on the fourth component only, which accounted for 9% of the variance (items 2, 9, 10, 12, 13, 15, 25 and 26). Most of these items were not included in the RIPoSt-40 since

Table 1
Principal Component Analysis results of the Y–RIPoSt questionnaire.

Item	Question	Component 1	Component 2	Component 3	Component 4
55	From one day to the next I can be sociable, a 'ringleader' or isolated, alone, closed in on myself	**0.8395**	-0.0320	-0.0493	-0.0289
56	I have the impression that my emotions follow cycles with ups and downs	**0.8306**	0.0289	0.0097	-0.0287
57	My cycles of ups and downs tend to recur.	**0.8205**	-0.0041	0.0705	-0.0278
49	I often feel sad for a few days, then radiant and in a good mood	**0.7936**	0.1198	-0.0164	-0.0689
50	I tend to feel things in a very intense way or, otherwise, with great indifference	**0.7816**	0.1314	0.0244	-0.0165
51	My feelings are 'too high' or 'too low', rarely 'intermediate'.	**0.7422**	0.1670	0.0428	-0.0927
54	I can be sad and happy simultaneously	**0.7402**	0.0713	-0.2340	-0.0294
53	I have moments of pessimism in which I forget my moments of optimism and enthusiasm	**0.7303**	-0.0657	0.0102	0.0796
59	I can go to sleep in a good mood and wake up in a sad and gloomy one	**0.7178**	-0.1064	-0.0194	0.0599
47	My emotions are 'too high' or 'too low', rarely 'intermediate'.	**0.7088**	0.0494	0.1760	-0.1236
39	Moments when I feel really good are few and not common.	**0.6510**	-0.2029	0.0028	0.1070
46	I go through abrupt changes in mood and energy	**0.6224**	-0.0435	0.2889	-0.0395
52	I take great pleasure in being interested in other people, but then I feel completely indifferent to them.	**0.5841**	0.0956	-0.0312	-0.1019
60	I'm so unstable that I am unable to long-term projects	**0.5468**	-0.0722	0.1507	-0.0348
58	I often find myself giving up after moments of great ambition.	**0.5301**	-0.0393	-0.0699	0.2622
43	My emotions are closer to dissatisfaction or frustration than to joy.	**0.4888**	-0.3960	0.1729	0.1875
37	I often feel in a good mood, euphoric and full of energy	-0.1472	**0.8176**	-0.0722	-0.2653
36	When things go well, I feel as if I am on top of the world	-0.0099	**0.7141**	0.0268	0.0003
27	When I am happy, I feel full of energy	0.0549	**0.7121**	-0.0547	0.0246
32	My emotions tend to be more positive than those of most other people.	-0.0924	**0.6920**	-0.0308	-0.1419
38	When I feel full of energy, I am full of fun and high spirits	0.1184	**0.6749**	-0.0390	-0.0385
30	When I carry out a difficult task, I feel enthusiastic or exalted	0.1329	**0.6434**	0.0197	0.0118
33	When I solve a small personal problem, that makes me feel euphoric	0.0089	**0.6414**	-0.0760	0.0926
19	When something good happens to me, I usually rejoice more than others	0.0195	**0.6077**	0.2035	0.0648
18	When I'm happy, I always feel so much vibrancy	-0.0004	**0.5026**	0.2133	0.1263
06	I go through moments of severe nervousness during which I am liable to lose self-control	0.0538	-0.0881	**0.8787**	-0.1318
14	When I feel upset, I am likely to do silly things or say anything	-0.0397	0.0486	**0.8283**	-0.0179
01	I have quick, brutal, emotional reactions, almost impulsive ones	0.0528	-0.0127	**0.7440**	-0.0018
03	I tend to get nervous immediately, or quickly react when I'm frustrated	0.0313	0.0009	**0.7033**	0.0947
21	When I feel angry, it's hard for me to stay rational, without overreacting	0.0767	0.0878	**0.6696**	0.0075
05	When I get irritable, I have great difficulty in staying calm	0.2469	0.0322	**0.6310**	-0.0946
23	My friends sometimes say that I am tense or nervous.	0.3142	-0.0580	**0.4956**	-0.0098
09	I'm very sensitive to criticism	0.0282	-0.1379	-0.1637	**0.8927**
15	I have often been told that I am easily hurt.	-0.1437	0.0020	-0.0579	**0.8334**
10	I easily feel hurt or offended	0.0337	-0.1643	0.0437	**0.7984**
13	When I watch a film, I am often very emotional (so I cry, I get angry, I get scared).	-0.1715	0.1337	0.0865	**0.5868**
02	I often have emotional reactions to events that are not worth the trouble	0.0320	-0.0174	0.2088	**0.5583**
12	I can get deeply attached to someone I have just met.	-0.1522	0.1680	0.2209	**0.4826**
26	When I lie, I feel bad about it.	0.2494	0.2136	-0.2830	**0.4602**
25	When I feel guilty, that is a powerful emotion.	0.3290	0.1370	-0.1240	**0.3865**

	Affective Instability	Positive Emotionality	Emotional Reactivity	Interpersonal Sensitivity
Proportional Variance	0.22	0.11	0.11	0.09
Cumulative Variance	0.22	0.33	0.44	0.53
Explained Proportion	0.41	0.21	0.21	0.17
Cumulative Proportion	0.41	0.62	0.83	1.00

they were discarded in the items selection process, while only few items loaded on the Negative Emotionality and Emotional Impulsivity factors; on the other hand, the majority of them loaded on the Reactivity domain of the RIPoSt-60. A qualitative evaluation of the items loading on this third component suggested that they are specifically intended for assessing affective reactivity and sensitivity to interpersonal relationships; hence, the component was labeled *Interpersonal Sensitivity*.

3.2. Psychometric properties of the scale

In summary, items were unequally distributed across four factors, respectively interpreted as Affective Instability, Positive Emotionality, Emotional Reactivity and Interpersonal Sensitivity. As shown in Table 2, Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales scores were all significantly highly positively correlated with each other in the non-clinical sample with *r* coefficients ranging from 0.488 – for the correlation between Emotional Reactivity and Interpersonal Sensitivity – to 0.710 – for the correlation between Affective Instability and Emotional Reactivity. On the other hand, Positive Emotionality subscale was significantly positively correlated with Interpersonal Sensitivity subscale only, though weakly with a *r* coefficient of 0.358, whereas it was not significantly associated with the two other subscales.

As shown in Table 3, test-retest reliability was significant for each subscale ($p < 0.001$) with Spearman's *rho* coefficients ranging from 0.565 (for the Affective Instability subscale) to 0.712 (for the Emotional Reactivity subscale). Internal consistency was assessed in the non-clinical sample and related findings are reported in Table 3. Cronbach's alpha coefficients were excellent ($\alpha > 0.90$) for the Affective Instability subscale and the whole scale, while they were still good ($\alpha > 0.80$) for the other subscales. McDonald's omega coefficients showed a similar pattern. Item-subscale correlation coefficients were generally high ($r > 0.50$) for all subscales, except for the Affective Instability subscale for which they were still adequate ($r > 0.49$).

Validity of the RIPoSt-Y questionnaire was assessed both in the non-clinical sample and in the two clinical groups and related findings are reported in Tables 4-6. Demographic and clinical data for each sample, along with corresponding subscales scores, are described in Table 4. The three sample groups significantly differed in terms of mean age and gender distribution, with the ADHD/ED group showing significantly lower age and greater percent number of males (see Table 4); thus, differences in subscales scores between the three groups were controlled for age and gender. As shown in Table 5, the BSD group exhibited significantly greater scores in the Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales compared to the non-clinical sample, while the ADHD group scored significantly higher than the non-clinical sample in the Emotional Reactivity subscale only; the two clinical groups significantly differed in the Affective Instability and Interpersonal Sensitivity subscales. No significant differences were instead detected in the Positive Emotionality subscale. Significant gender effects were observed for the Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales, with females scoring higher than males. Finally, an age effect emerged only for the Affective Instability, with younger adolescents scoring significantly lower than the older peer.

As shown in Table 6, concurrent validity was assessed through correlations with the CHT-Q. Significant highly positive associations emerged in the non-clinical sample between the Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales of the RIPoSt-Y and the two subscales of the CHT-Q, as well as the total scale. Similarly, significant highly positive correlations were observed in the clinical sample between the Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales and the MHS subscale of the CHT-Q, as well as the total scale, and also between the Emotional Reactivity and the IED subscales. No significant association was instead detected for the Positive Emotionality subscale in both samples. As shown in Table 6, convergent validity was assessed through correlations with the DP index of the CBCL and the YSR questionnaires. Significant highly positive associations emerged between the Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales and the YSR-DP, while only the Emotional Reactivity subscale significantly positively correlated with the CBCL-DP.

For the reasons listed above, the Positive Emotionality component was removed from the scale and the final 31-item version of the RIPoSt-Y questionnaire ultimately included three factors: Affective Instability, Emotional Reactivity and Interpersonal Sensitivity. The English and Italian versions of the scale are available in Supplementary Table 2 and a scoring template is also provided in Supplementary Table 3; the Positive Emotionality subscale is still available in Supplementary Table 4 for research and clinical purposes.

3.3. Cut-off scores, specificity and sensitivity of the questionnaire

The cut-off scores were estimated using the Youden's index. For the Emotional Reactivity subscale, both clinical groups (BSD/ED and ADHD/ED) were used to differentiate clinical and non-clinical samples; on the other hand, for the Affective Instability and the Interpersonal Sensitivity subscales, only the BSD/ED group was used. Cut-off scores were not estimated for the Positive Emotionality subscale since the clinical and non-clinical samples did not differ significantly and the subscale was removed from the final version of the questionnaire.

The cut-off score for the Affective Instability subscale, estimated using the Youden's index, was 55; sensitivity of the discrimination between BSD patients and non-clinical participants was 62.50%, while specificity was 64.44%. As for the Emotional Reactivity subscale, the cut-off score, estimated using the Youden's index, was 22; sensitivity of the discrimination between clinical and non-clinical samples was 63.51%, whereas specificity was 69.52%. Finally, cut-off score for the Interpersonal Sensitivity subscale, estimated using the Youden's index, was 29; sensitivity of the discrimination between BSD patients and non-clinical participants was 52.5%, while specificity was 64.44%.

Table 2
Y–RIPoSt inter-subscale correlations.

Rho p–value	Affective Instability	Positive Emotionality	Emotional Reactivity	Interpersonal Sensitivity
Affective Instability	–	0.125	0.710	0.598
Positive Emotionality	0.032	–	0.141	0.358
Emotional Reactivity	0.000 ***	0.025	–	0.488
Interpersonal Sensitivity	0.000 ***	0.000 ***	0.000 ***	–

*** $p < 0.001$

4. Discussion

The need to identify and assess, both qualitatively and quantitatively, the presence of ED in adolescents is essential to provide an efficient clinical management and prevent negative outcomes. Indeed, as discussed above, ED represents a predisposing risk factor for both suicidality and non-suicidal self injury, substance abuse and bipolarity (Pisano et al., 2020; Sobanski et al., 2010; Stringaris et al., 2012) and a negative prognostic element for a greater impairment of global functioning and persistence of psychopathology in adult age (Rüfenacht et al., 2019; Uchida et al., 2018). Importantly, several psychopathological pictures in youths, such as borderline personality, bipolar spectrum, disruptive behavior disorders and ADHD, share a common substrate of severe irritability and aggressiveness, mood instability and outbursts which is still not fully outlined by current nosographic systems in developmental age, despite an extensive literature evidence (Masi

Table 3
Test-retest correlations and internal consistency of the Y–RIPoSt questionnaire.

rho (p–value)	Affective Instability	Positive Emotionality	Emotional Reactivity	Interpersonal Sensitivity	Total
Test-Retest Spearman's *r*	0.565 (0.000 ***)	0.605 (0.000 ***)	0.712 (0.000 ***)	0.636 (0.000 ***)	–
Cronbach's α	0.939 [0.928 – 0.947]	0.849 [0.822 – 0.872]	0.890 [0.868 – 0.907]	0.814 [0.780 – 0.838]	0.938 [0.928 – 0.946]
McDonald's ω	0.939 [0.930 – 0.948]	0.849 [0.826 – 0.874]	0.889 [0.870 – 0.909]	0.805 [0.772 – 0.837]	0.939 [0.930 – 0.949]
Item-Subscale *r*	0.496 – 0.828	0.580 – 0.747	0.727 – 0.774	0.588 – 0.717	–

*** $p < 0.001$

Table 4
Comparisons between non-clinical and clinical samples.

Tot = 452	Group 1non-clinical	Group 2BSD/ED	Group 3ADHD/ED	*p*–value
N	374	44	34	–
Gender, N males (%)	95 (25.4)	13 (29.5)	28 (82.4)	0.000 ***
Age, M ± SD	15.7 ± 1.7	15.2 ± 1.6	14.8 ± 1.7	0.001 **
Affective Instability	48.40 ± 18.32	58.35 ± 18.54	46.12 ± 15.14	0.003 **
Positive Emotionality	35.00 ± 8.31	32.18 ± 8.41	33.65 ± 8.63	0.108
Emotional Reactivity	19.10 ± 7.94	24.15 ± 7.87	24.09 ± 7.78	0.000 ***
Interpersonal Sensitivity	25.89 ± 8.36	28.03 ± 9.80	22.76 ± 6.60	0.027 *

* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Table 5
ANOVAs and Tukey post-hoc comparisons.

Affective Instability	F–value	*p*–value	Tukey post-hoc
Sample group	6.575	0.002 **	BSD > ADHD = NC
Gender	45.076	0.000 ***	F > M
Age	3.910	0.049 *	[16 – 19] > [13 – 15]
Residuals	297	–	–
Positive Emotionality	F–value	*p*–value	Tukey post-hoc
Sample group	2.231	0.109	–
Gender	1.186	0.277	–
Age	0.173	0.678	–
Residuals	69.70	–	–
Emotional Reactivity	F–value	*p*–value	Tukey post-hoc
Sample group	12.587	0.000 ***	BSD = ADHD > NC
Gender	8.381	0.004 **	F > M
Age	0.378	0.539	–
Residuals	61.8	–	–
Interpersonal Sensitivity	F–value	*p*–value	Tukey post-hoc
Sample group	4.124	0.017 *	BSD > ADHD = NC
Gender	62.062	0.000 ***	F > M
Age	0.591	0.442	–
Residuals	62	–	–

* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Table 6
Concurrent and convergent validity correlations.

Rho coefficients (p–value)	Affective Instability	Positive Emotionality	Emotional Reactivity	Interpersonal Sensitivity
CHT – IED subscale non-clinical sample	0.712 (0.000 ***)	0.124 (0.008)	0.781 (0.000 ***)	0.385 (0.000 ***)
CHT – MHS subscale non-clinical sample	0.661 (0.000 ***)	0.156 (0.009)	0.512 (0.000 ***)	0.487 (0.000 ***)
CHT – total scale non-clinical sample	0.742 (0.000 ***)	0.178 (0.014)	0.681 (0.000 ***)	0.564 (0.000 ***)
CHT – IED subscale clinical sample	0.299 (0.023)	0.201 (0.421)	0.702 (0.000 ***)	0.208 (0.113)
CHT – MHS subscale clinical sample	0.756 (0.000 ***)	0.082 (0.671)	0.403 (0.000 ***)	0.803 (0.000 ***)
CHT – total scale clinical sample	0.680 (0.000 ***)	0.112 (0.442)	0.627 (0.000 ***)	0.721 (0.000 ***)
CBCL – DP clinical sample	0.182 (0.103)	-0.002 (0.956)	0.526 (0.000 ***)	0.325 (0.010)
YSR – DP clinical sample	0.701 (0.000 ***)	-0.067 (0.785)	0.496 (0.000 ***)	0.528 (0.000 ***)

*** $p < 0.001$ (corrected *p*–values according to Bonferroni's method)

et al., 2015; Rüfenacht et al., 2019; Vannucchi et al., 2019). An early identification and assessment of ED in different psychopathological domains in youths, through validated clinical tools, may be crucial to ensure a better characterization and developmental outcome for at-risk individuals.

From this premise was born the idea to develop a novel clinical tool for the assessment of ED, the Youth-Reactivity, Intensity, Polarity and Stability scale (RIPoSt-Y), a self-report questionnaire to measure ED both in clinical and non-clinical samples, which is based on a previous version for adults (Hantouche, 2014), and is here re-conceptualized to better capture the complex characterization of ED in adolescents.

Starting from the originally proposed 60 items and the subsequently validated 40 items, our novel version consists of 31 items unequally distributed across three subscales, namely Affective Instability, Emotional Reactivity and Interpersonal Sensitivity. Compared to the adult version, a different internal factor structure has been identified, which led to the withdrawal of the Negative Emotionality subscale while preserving the Affective Instability and Emotional Reactivity subscales, though being composed of different sets of items. A new factor, instead, emerged from the analyses, which was purposefully labeled as Interpersonal Sensitivity, for its clear intent to catch cues of an undue and excessive awareness of behaviors and feelings of others. As for the Positive Emotionality component, this was ultimately removed from the initial scale, though nearly totally overlapping with the homologous subscale of the adult version, since it was weakly correlated with the other subscales, demonstrated inadequate concurrent and convergent

validity and did not differentiate clinical and non-clinical samples. On the contrary, the other three subscales were strongly correlated with each other, thus likely representing three dimensions of the same multifaceted construct.

The Affective Instability subscale, through its 16 items, explores the presence of a cyclic pattern of rapid mood swings of opposite polarities, which may compromise the social and performance functioning of the individual. This subscale demonstrated a moderate but still adequate test-retest reliability, an excellent internal consistency, and a significantly high concurrent and convergent validity. Our analyses also revealed higher scores in the BSD group, followed by ADHD and HC; such pattern confirmed the validity of this subscale, which seems to reflect an intrinsic core feature of bipolarity. Moreover, females and older adolescents scored higher than males and younger peers, respectively.

The Emotional Reactivity subscale, with its 7 items, is aimed to assess an excessive susceptibility to emotionally salient stimuli or, in other word, a disproportionate intensity of responsiveness with both negatively and positively charged emotions. Individuals with high scores on this subscale are, indeed, expected to react more rapidly and more intensely than peers. Such subscale showed a high test-retest reliability, a good internal consistency, a significantly high concurrent validity with the CHT-Q and a significantly convergent validity with both the YSR-DP and the CBCL-DP. We also found significantly higher scores in the BSD and ADHD groups than HC, with no significant difference between the two clinical samples. This result is consistent with previous findings (Perugi et al., 2015; Rüfenacht et al., 2019; Tenenbaum et al., 2019) showing emotional impulsivity and deficient inhibitory control over affective reactions in both ADHD and early onset BSD, while it is only partially overlapping with those reported by Brancati et al. (2019) who found a significant difference between ADHD and cyclothymic patients, with the former exhibiting higher scores in the corresponding subscale. It should be outlined, however, that the early age range of our patients may justify a higher prevalence of dysphoric and irritable symptoms with rage outbursts in both clinical groups, which might explain the overlapping scores of BSD and ADHD in terms of emotional and behavioral impulsivity.

Finally, the Interpersonal Sensitivity subscale, consisting of 8 items, reflects the presence of a marked or even exaggerated susceptibility to social judgement, criticism and rejection due to feelings of inadequacy and inferiority and poor self-esteem. These items clearly play a fundamental role in the definition of an ED profile in youths, being indeed a relevant feature in adolescent psychopathology (Guvenc and Aktas, 2006). This subscale exhibited a moderate though still adequate reliability, a good internal consistency, a significantly high concurrent and convergent validity. Significantly higher scores were also reported by the BSD group than HC and ADHD groups, with no significant difference between these two latter. We hypothesized this evidence reflecting a social inattention to interpersonal cues, and thus to judgement and criticism, in ADHD patients (Uekermann et al., 2010) and a hyper-sensitivity to social stimuli typically identified in BSD youths (Perugi et al., 2015).

As for concurrent validity of our measure, all the RIPoSt-Y subscales were significantly positively associated with both CHT-Q subscales in the HC sample, though correlation coefficients were higher between the Interpersonal Sensitivity and MHS subscales and between the Emotional Reactivity and IED subscales. Similarly, in the clinical sample significant correlations were confirmed only between the Affective Instability, Emotional Reactivity and Interpersonal Sensitivity subscales and the MHS subscale of the CHT-Q, as well as between the Emotional Reactivity and the IED subscales. These findings would likely reflect the externalizing conceptualization of the IED subscale, namely the reactivity/impulsivity facet of ED, and the internalizing one of the MHS subscale, which would further confirm the multidimensional nature of our scale.

Despite our effort to develop a valid and reliable scale, some methodological limitations should be outlined in our study. First, the use of a school-based survey to recruit the HC sample could have biased our results. Nonetheless, we supposed this latter to be representative of the general population and an exclusion criterium to prevent controls with intellectual disability or other severe neurodevelopmental disabilities to be recruited was indirectly applied by asking parents whether their offspring were autonomously able to fill in the questionnaires. A significantly different gender distribution between clinical and non-clinical samples represents a further limitation. As expected, women were more represented among the HC group, consistently with several studies conducted in larger community samples and similar surveys investigating the effect of gender-related differences in emotional engagement (Goldshmidt and Weller, 2000; Smith, 2008). Moreover, the ADHD group was largely composed of males, while the BSD group of females, in accordance with previous reports on neurodevelopmental and mood disorders (Akiskal et al., 2003; Nøvik et al., 2006).

To sum up, given the clinical and theoretical relevance of ED in youth, our novel questionnaire proved to be a valid and reliable tool able to effectively characterize this fundamental construct in its multidimensional facets. Indeed, our results support a good-to-excellent internal consistency and reliability of the scale, as well as its high concurrent and convergent validity, both in clinical and non-clinical samples. With its 31 items distributed across three subscales, it is also easy and rapid to be administered in clinical settings. Cut-off scores are also available to discriminate clinically significant values of ED.

Further studies are thus needed to overcome such limitations. Besides, additional studies assessing ED with respect to temperamental traits in youths, for instance, through the Junior Temperament and Character Inventory (Asch et al., 2009) or similar tools, will be also greatly recommended in order to provide further evidence of the complex relationship between these two dimensions. Finally, future studies conducted on larger clinical samples are welcome to compute cut-off scores aimed to discriminate between ADHD and BSD patients, or even to identify those ones, among ADHD patients with ED, who are at risk of further developing BSD or other major affective disorders.

Conflict of Interest

Dr. Masi has received research grants from Lundbeck and Humana, was in an advisory board for Angelini, and has been speaker for Angelini, FB Health, Janssen, Lundbeck, and Otsuka. All the other Authors do not have conflicts of interest to declare.

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Authors' contribution

GS and FD contributed to the recruitment of the non-clinical sample, the statistical analyses, the interpretation of data and the writing of the present article. SB and EV contributed to the recruitment of the non-clinical sample. FD, SB, NL, EV, CP, AM, FP and ARM contributed to the recruitment of the clinical sample. GM, AM and SP contributed to data interpretation and revision of the present article. All the authors have seen, revised and approved the final version of this manuscript.

Author agreement

All authors have seen and approved the final version of the manuscript being submitted, warrant that the article is the authors' original work, has not received prior publication and is not under consideration for publication elsewhere.

Supplementary material.docx

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Supplementary Table 1.docx

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Supplementary Table 2 Revised.docx

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Supplementary Table 3.xlsx

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Supplementary Table 4.docx

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.05.037.

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(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3798 del 08/05/2014, n. 778 del 05/02/2015, n. 5954 del 05/12/2016, N. 1077 del 02/02/2017 N. 1938 del 15/02/2019)
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