NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

BIBLIOGRAFIA ADHD APRILE 2022

Am J Intellect Dev Disabil. 2022 May;127:213-30.

ATTENTION/DEFICIT HYPERACTIVITY DISORDER IN ADOLESCENT AND YOUNG ADULT MALES WITH FRAGILE X SYNDROME.

Klusek J, O'Connor SL, Hickey A, et al.

This study characterized the rates of attention-deficit/hyperactivity disorder (ADHD) in adolescent and young adult males with fragile X syndrome (FXS) using a multi-method approach integrating a DSM-based parent interview (Children's Interview for Psychiatric Syndromes; P-ChIPS, Fristad et al., 1998) and a parent rating scale (Child Behavior Checklist; CBCL, Achenbach, 2001). Thirty-one males with FXS, aged 16-24 years, participated. Forty-two percent met DSM-5 criteria for ADHD and 35% exceeded the CBCL cut-offs. Agreement between the two classification methods was fair (Îº = 0.38). Autism symptom severity and nonverbal cognitive ability did not predict ADHD diagnoses/symptoms. Results show high rates of ADHD in males with FXS during late adolescence and young adulthood, which are not accounted for by impaired nonverbal cognitive skills or autism symptom severity. DSM-based ADHD-specific scales are recommended over broadband symptom scales to improve accurate identification

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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.

Arch Pediatr. 2022 May;29:277-80.

SLEEP, CHRONOTYPE, AND BEHAVIOR IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Martinez-Cayuelas E, Moreno-Vinues B, Pozo RL, et al.

Sleep problems are highly prevalent in patients with attention-deficit/hyperactivity disorder (ADHD). Although chronotype has been linked to behavioral problems, its specific contribution to ADHD symptoms remains unclear. We assessed the association between chronotype and sleep and behavioral problems in adolescents with ADHD between 12 and 18 years of age using questionnaires (Morningness-Eveningness Scale for Children [MESC], Strengths and Difficulties Questionnaire [SDQ], and Pediatric Sleep Questionnaire [PSQ]). Overall, 84 families (parents and adolescents) were enrolled. The intermediate chronotype was the most common in the study sample. No sex differences were detected in the proportion of morning, intermediate, and evening types. No correlation was found between MESC score and body mass index nor total PSQ score. Regarding SDQ, a significant negative correlation was found between the MESC score and hyperactivity/inattention score. We conclude that adolescents with ADHD tend to have an intermediate chronotype and eveningness is related to hyperactivity/inattention problems

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Asian J Psychiatr. 2022 Jun;72:103103.

EMERGENCY MENTAL HEALTH CARE FOR CHIÌ‡LDREN AND ADOLESCENTS OUTSIDE OF REGULAR WORKING HOURS: 7 YEARS OUTCOMES FROM A TERTIARY HOSPITAL.

Poyraz Findik OT, Poyraz Findik OT, et al.

OBJECTIVE: This study aims to define the clinical characteristics and management strategies of children and adolescents presenting with psychiatric crises to the emergency department (ED) of a tertiary health care facility outside of working hours, and to identify predictors of multiple ED visits among them.

METHODS: From January 2012 to December 2018, retrospective records of patients presenting with psychiatric symptoms to the ED and examined by a child psychiatrist after 5 p.m. on weekdays and for 24Â h on weekends and public holidays were analyzed.

RESULTS: Our sample consisted of 1576 visits and 1364 patient (Female:Male=1.8:1, mean age=14.86 ± 2.72). The most common reason for visits was self-injurious thought or behaviors (SITB), and the most common diagnosis was depression. While depression was statistically more common in girls, attention deficit hyperactivity disorder, autism and/or intellectual disability (ASD/ID), psychotic disorders, and bipolar disorder were more common in boys. The forensic evaluation was the most common reason for visits among children younger than 6 years old. Of visits, 23% transferred to hospitalization. A history of mental health contact was the lowest in depression (37.5%), psychosis (34.1%), and substance use disorders (33%). Of patients, 10.8% had multiple visits. A history of mental health contacts, conduct disorder, ASD/ID, bipolar disorder, psychotic disorder, and dissociative disorder were predictors of multiple visits to ED with psychiatric reasons.

CONCLUSION: Emergency mental health care outside of regular working hours can be a critical step in the diagnosis and treatment of serious psychiatric disorders in children and adolescents

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BMC Health Serv Res. 2022 Apr;22:472.

FIGHTING THE WAVES; COVID-19 FAMILY LIFE INTERFERENCE IN A NEURODEVELOPMENTAL DISORDER-CAREGIVER POPULATION.

Nylén-Eriksen M, Lara-Cabrera ML, Grov EK, et al.

INTRODUCTION: The current COVID-19 pandemic interferes with family lives across the world, particularly families of children with neurodevelopmental disorders (NDDs) are at a greater risk for being negatively impacted by the pandemic. Together with representatives from this caregiver population the aim was to explore the interference associated with normal family life caused by the COVID-19 pandemic.

METHOD: This is a descriptive study using a cross-sectional design. Following a strategic network sampling strategy, a user-developed national survey was completed by a larger sample (N=1,186) of parents and informal caregivers of children with NDDs. The survey utilized a combination of both closed and open-ended questions, and a logistic regression analysis was carried out to assess the association between family characteristics, characteristics of the child, and COVID-19 related family life interference. Before carrying out

the regression an inductive content analysis of the open-ended question on `How has the isolation affected the family was carried out to construct the outcome variable.
RESULTS: The initial analysis indicated that the COVID-19 pandemic induced a shift in everyday family life and a lack of guidance and support related to managing the challenges they were facing. Caregivers who reported that COVID-19 had significantly interfered with their family life, were more likely to report having anxious children, and to have experienced an increased number of conflicts at home. The logistic regression showed that both anxious children and increased conflicts considerably increased the risk for reporting family life interference compared to those that reported no increased conflicts or anxious children.
DISCUSSION: Considering how the COVID-19 related increased conflicts at home and anxious children threaten the family life of the NDD caregiver population, as an external source of family stress, which might lead to negative impact on their mental and physical well-being, the need for further research in collaboration with user representatives is apparent. Our study suggests that more information should be provided to healthcare providers, social professionals, peers, people with NDDs, and caregivers of people with NDDs about the potential threats that a stressful life event such as the current pandemic can pose to their mental and physical health and their family life

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BMC Med. 2022 Apr;20:153.

IMPACT OF PRENATAL TOBACCO SMOKING ON INFANT TELOMERE LENGTH TRAJECTORY AND ADHD SYMPTOMS AT 18 MONTHS: A LONGITUDINAL COHORT STUDY.

Howell MP, Jones CW, Herman CA, et al.

Background: Prenatal maternal tobacco smoking is a predictor of child attention-deficit/hyperactivity disorder (ADHD) and is associated with offspring telomere length (TL). In this study, we examine the relationship between maternal prenatal smoking, infant TL, and maternal report of early childhood symptoms of ADHD.
Methods: One-hundred and eighty-one mother-infant dyads were followed prospectively for the infant's first 18 months of life. Prenatal smoking was assessed from maternal report and medical records. TL was measured from infant buccal swab DNA obtained across the first 18 months of life. ADHD symptoms were obtained from maternal report on the Child Behavior Check List. Multiple regression models tested the relation between prenatal smoking and both ADHD symptoms and infant TL. Additional analyses tested whether the change in infant TL influenced the relation between prenatal smoking and ADHD symptoms.
Results: Sixteen percent of mothers reported prenatal smoking. Infant TL at 4, 12, and 18 months of age were correlated. Consistent with previous cross-sectional studies linking shorter offspring TL to maternal prenatal smoking, maternal prenatal smoking predicted greater telomere shortening from four to 18 months of infant age (β = - 5.797, 95% CI [-10.207, -1.386]; p = 0.010). Maternal depression was positively associated with both prenatal smoking (odds ratio (OR): 4.614, 95% CI [1.733, 12.282]; p = 0.002) and child ADHD symptoms (β = 4.713, 95% CI [2.073, 7.354]; p = 0.0006). To prevent confounding, analyses examined the relation between TL, ADHD symptoms, and prenatal smoking only in non-depressed mothers. In non-depressed mothers, infant TL attrition across the first 18 months moderated the relation between smoking and child ADHD.
Conclusions: The findings extend previous studies linking prenatal smoking to shorter infant TL by providing data demonstrating the effect on TL trajectory. The relation between prenatal smoking and early infant ADHD symptoms was moderated by the change in TL. The findings provide novel initial evidence suggesting that TL dynamics are one mechanistic pathway influencing the relation between maternal prenatal smoking and ADHD

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BMC Psychiatry. 2022 Apr;22:282.

ASD WITH ADHD VS. ASD AND ADHD ALONE: A STUDY OF THE QBTEST PERFORMANCE AND SINGLE-DOSE METHYLPHENIDATE RESPONDING IN CHILDREN AND ADOLESCENTS.

Stevanovic D, Wentz E, Nasic S, et al.

BACKGROUND: The continuous performance task (CPT) may help identify coexistent attention deficit hyperactivity disorder (ADHD) in autism spectrum disorder (ASD). The Quantified behavior Test (QbTest)

combines a CPT and motion-tracking data to assess ADHD symptoms. This study aimed to evaluate the QbTest performance of children and adolescents with ASD plus ADHD, including estimating the effects of single-dose methylphenidate (MPH). To achieve these aims, (1) the QbTest performances were evaluated in ASD alone, ASD plus ADHD, and ADHD alone, and (2) the effects on the QbTest performance of single-dose MPH before and after intake were estimated across the groups. It was assumed that the ASD plus ADHD performance, including the MPH response, would preferably resemble the performance in ADHD alone, rather than ASD alone.
METHODS: Retrospective data were analyzed for 482 children and adolescents: 69 with ASD alone, 142 with ASD plus ADHD (ASD/ADHD), and 271 with ADHD alone. For 343 subjects, the QbTest was performed before and up to four hours after a single-dose MPH intake. A summary index of the CPT and motion-capture data was provided for QbTest cardinal parameters.
RESULTS: Of 12 QbTest parameters assessed before given MPH, the ASD/ADHD group had scores in line with the ASD group regarding four parameters and the ADHD group regarding nine parameters. Significant differences between groups were seen with respect to QbInattention ($p>0.05$); the lowest scores in ASD and the highest in ADHD. Those with ASD/ADHD and ADHD had similar QbActivity and QbImpulsivity scores, but significantly higher than those with ASD. After MPH intake, scores for QbActivity decreased similarly in ASD/ADHD and ADHD, as well as scores for QbImpulsivity. QbImpulsivity increased in ASD. QbInattention scores decreased similarly in all groups after MPH intake.
CONCLUSIONS: Children and adolescents with ASD plus ADHD exhibited more atypical QbTest performances than those with ASD alone, while most of their performances were similar to those observed in ADHD alone. In addition, a single dose of MPH mitigated attention deficits and decreased hyperactivity while improved impulsivity in these children. Prospective studies should further clarify the role of the QbTest in the diagnostic and therapeutic interventions in ASD with ADHD

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BMC Psychiatry. 2022 May;22:325.

MORTALITY IN INDIVIDUALS WITH CHILDHOOD ADHD OR SUBTHRESHOLD SYMPTOMS - A PROSPECTIVE PERINATAL RISK COHORT STUDY OVER 40 YEARS.

Schiavone N, Virta Met al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is associated with negative life outcomes and recent studies have linked it to increased mortality. These studies have examined nationwide registers or clinic-referred samples and mostly included participants up until the age of 30. No studies have investigated mortality associated with subthreshold levels of ADHD symptoms. Our aim was to analyze mortality in a perinatal risk cohort of 46-year-old adults with childhood ADHD (cADHD) and milder childhood attention problems (including hyperactivity and inattention; cAP) compared with a group with similar birth risks but no or low levels of childhood ADHD symptoms (Non-cAP). Causes of death obtained from a national register were examined.
Methods: Mortality was analyzed with Cox proportional hazard models for all-cause mortality, cause-specific mortality (natural and unnatural causes), and age-specific mortality (under and over age 30). All models were adjusted with gender. The total n in the study was 839 (cADHD n = 115; cAP n = 216; Non-cAP n = 508).
Results: By the age of 46, 11 (9.6%) deaths occurred in the cADHD group, 7 (3.2%) in the cAP group, and 20 (3.9%) in the Non-cAP group. The cADHD group had the highest mortality risk (adjusted hazard ratio = 2.15; 95% CI 1.02, 4.54). Mortality was not elevated in the cAP group (adjusted hazard ratio = 0.72; 95% CI .30, 1.72). Mortality in the cADHD group was mainly attributed to unnatural causes of death (adjusted hazard ratio = 2.82; 95% CI 1.12, 7.12). The mortality risk in the cADHD group was sixfold before age 30 (adjusted hazard ratio = 6.20; 95% CI 1.78, 21.57).
Conclusions: Childhood ADHD was associated with a twofold risk of premature death by the age of 46 in this prospective longitudinal cohort study. Our results corroborate previous findings and the morbidity of ADHD. Subthreshold levels of childhood ADHD symptoms were not linked to increased mortality. Our results suggest that mortality risk is higher in young than middle adulthood. Future studies should examine mortality associated with ADHD in different ages in adulthood to identify those in greatest risk of premature death

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BMC Psychiatry. 2022 Apr;22:251.

IN TRANSITION WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): CHILDREN'S SERVICES CLINICIANS' PERSPECTIVES ON THE ROLE OF INFORMATION IN HEALTHCARE TRANSITIONS FOR YOUNG PEOPLE WITH ADHD.

Price A, Mitchell S, Janssens A, et al.

BACKGROUND: National clinical guidelines emphasise the need for good communication of information by clinicians to young people and their parent/carers about what to expect during transition into adult services. Recent research indicates that of young people in need of transition for attention deficit hyperactivity disorder (ADHD), only a minority experience continuity of care into adulthood, with additional concerns about quality of transition. This qualitative analysis explored the role that information plays in the transition from child to adult mental health services for young people with ADHD, from the perspectives of clinicians working in children's services.

METHODS: Participants were recruited from National Health Service (NHS) Trusts located across the United Kingdom (UK), with varying service configurations. Twenty-two qualitative interviews were conducted with 15 paediatricians and seven psychiatrists working in child services and supporting young people with ADHD. The Framework Method was used to complete a thematic analysis of data related to the role of information in transitional care.

RESULTS: Two themes were identified in relation to the role of information in supporting transition and promoting continuity of care. Information for clinicians; about adult mental health services, the young person and their ADHD, and exchanged between services. Sharing information with young people; about transition processes, self-management, to support service engagement, and tailored to be accessible to young people with ADHD. Clinicians in children's services reported variable access to information. Clear protocols and being able to communicate about ADHD as a long-term condition, were described as having a positive impact on the transition process.

CONCLUSIONS: These findings illustrate that clear information on the transition process, and communication of evidence based and up-to-date information on ADHD as a long-term condition are essential components for clinicians supporting transition into adult services. Information exchange can be supported through transition discussions with young people, and joint meetings between services Discussions should be accompanied by accessible resources for young people and parents/carers such as leaflets and websites. Further efforts should be focussed on enabling clinicians to provide timely and appropriate information to young people with ADHD to support transition

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BMC Psychiatry. 2022 Apr;22:263.

NETWORK ANALYSES OF OPPOSITIONAL DEFIANT DISORDER (ODD) SYMPTOMS IN CHILDREN.

Gomez R, Stavropoulos V, Gomez A, et al.

Based on parent and teacher ratings of their children, this study used regularized partial correlation network analysis (EBIC glasso) to examine the structure of DSM-5 Oppositional Defiant Disorder (ODD) symptoms. Parent and teachers (N = 934) from the general community in Malaysia completed questionnaires covering DSM-5 ODD symptoms. The most central ODD symptom for parent ratings was anger, followed by argue. For teacher ratings, it was anger, followed by defy. For both parent and teacher ratings, the networks revealed at least medium effect size connections for temper and argue, defy, and argue, blames others, and annoy, and spiteful and angry. Overall, the findings were highly comparable across parent and teacher ratings, and they showed a novel understanding of the structure of the ODD symptoms. The clinical implications of the findings for assessment and treatment of ODD are discussed

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BMJ Open. 2022 Apr;12:e049821.

CLINICAL PERSPECTIVES ON THE IDENTIFICATION OF NEURODEVELOPMENTAL CONDITIONS IN CHILDREN AND CHANGES IN REFERRAL PATHWAYS: QUALITATIVE INTERVIEWS.

Coughlan B, Woolgar M, Mann A, et al.

OBJECTIVE: Previous work has raised questions about the role of general practitioners (GPs) in the identification of neurodevelopmental conditions such as autism spectrum disorders (autism) and attention deficit hyperactivity disorders (ADHD). This study aimed to explore how GPs identify these conditions in

practice and their perspectives on recent changes to local referral pathways that mean referrals to the neurodevelopmental team come through educational professionals and health visitors, rather than GPs. This study also aimed to explore Child and Adolescent Mental Health Services (CAMHS) specialist's perspectives on the role of GPs.
SETTING: GP practices, local neurodevelopmental services and specialist CAMHS services in the UK.
PARTICIPANTS: semistructured interviews were conducted with GPs (n=8), specialists in local CAMHS (n=7), and professionals at national CAMHS services around the country (n=10). Interviews were conducted between January and May 2019. A framework approach informed by thematic analysis was used to analyse the data.
RESULTS: GPs drew on various forms of tacit and explicit information including behavioural markers, parental report, prior knowledge of the family, expert and lay resources. Opinions varied between GPs regarding changes to the referral pathway, with some accepting the changes and others describing it as a 'disaster'. CAMHS specialists tended to feel that GPs required more neurodevelopmental training and time to conduct consultations.
CONCLUSION: This study adds to the literature showing that GPs use an array of information sources when making referral decisions for autism and ADHD. Further work is urgently required to evaluate the impact of reconfiguring neurodevelopmental referral pathways such that GPs have a diminished role in identification

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Clin Epigenetics. 2022 Apr;14:53.

EPIGENOME-WIDE CONTRIBUTIONS TO INDIVIDUAL DIFFERENCES IN CHILDHOOD PHENOTYPES: A GREML APPROACH.

Neumann A, Pingault JB, Felix JF, et al.

Background: DNA methylation is an epigenetic mechanism involved in human development. Numerous epigenome-wide association studies (EWAS) have investigated the associations of DNA methylation at single CpG sites with childhood outcomes. However, the overall contribution of DNA methylation across the genome (R2Methylation) towards childhood phenotypes is unknown. An estimate of R2Methylation would provide context regarding the importance of DNA methylation explaining variance in health outcomes. We therefore estimated the variance explained by epigenome-wide cord blood methylation (R2Methylation) for five childhood phenotypes: gestational age, birth weight, and body mass index (BMI), IQ and ADHD symptoms at school age. We adapted a genome-based restricted maximum likelihood (GREML) approach with cross-validation (CV) to DNA methylation data and applied it in two population-based birth cohorts: ALSPAC (n = 775) and Generation R (n = 1382).
Results: Using information from > 470,000 autosomal probes we estimated that DNA methylation at birth explains 32% (SDCV = 0.06) of gestational age variance and 5% (SDCV = 0.02) of birth weight variance. The R2Methylation estimates for BMI, IQ and ADHD symptoms at school age estimates were near 0% across almost all cross-validation iterations.
Conclusions: The results suggest that cord blood methylation explains a moderate degree of variance in gestational age and birth weight, in line with the success of previous EWAS in identifying numerous CpG sites associated with these phenotypes. In contrast, we could not obtain a reliable estimate for school-age BMI, IQ and ADHD symptoms. This may reflect a null bias due to insufficient sample size to detect variance explained in more weakly associated phenotypes, although the true R2Methylation for these phenotypes is likely below that of gestational age and birth weight when using DNA methylation at birth

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Clin Rehabil. 2022 Jun;36:776-88.

EFFECTIVENESS OF COGNITIVE ORIENTATION TO OCCUPATIONAL PERFORMANCE INTERVENTION IN IMPROVING MOTOR SKILLS OF CHILDREN WITH DEVELOPMENTAL COORDINATION DISORDER: A RANDOMIZED WAITLIST-CONTROL TRIAL.

Izadi-Najafabadi S, Gunton C, Dureno Z, et al.

Objectives: To determine if Cognitive Orientation to Occupational Performance was effective in improving performance and transfer of motor learning in children with developmental coordination disorder (with/without

attention deficit hyperactivity disorder); and whether outcomes were maintained three months post-intervention.
Design: Randomized waitlist-control trial (ClinicalTrials.gov ID: NCT02597751).
Setting: BC Children's Hospital, Vancouver, Canada.
Subjects: Thirty-seven children with developmental coordination disorder and 41 children with co-occurring attention deficit hyperactivity disorder (all 8-12 years), randomized to treatment or waitlist groups.
Interventions: One-hour of intervention once weekly for 10 weeks.
Main measures: (1) Canadian Occupational Performance Measure to measure self-perceived performance of motor goals (10-point scale); (2) Performance Quality Rating Scale to measure therapist-observed movement quality (10-point scale); and (3) Bruininks-Oseretsky Test of Motor Proficiency - 2nd ed. to measure overall motor skill ability/transfer of motor learning (percentile).
Results: Both groups showed significant improvement ($p < 0.001$) in motor performance (developmental coordination disorder: pre: 2.7 ± 2.2, post: 7.0 ± 1.0; developmental coordination disorder with attention deficit hyperactivity disorder: pre: 2.3 ± 1.7, post: 7.0 ± 1.5) and movement quality (developmental coordination disorder: pre: 3.0 ± 1.5, post: 6.3 ± 1.7; developmental coordination disorder with attention deficit hyperactivity disorder: pre: 3.0 ± 1.9, post: 5.7 ± 2.3). Three months after treatment, children maintained their gains, but only children with developmental coordination disorder showed transfer of learning to overall motor skills (pre:12 ± 15, post:12 ± 12, follow-up:14 ± 20, $p < 0.001$).
Conclusion: Intervention was similarly effective for children with developmental coordination disorder with/without attention deficit hyperactivity disorder in achieving and maintaining functional motor goals, but only children with developmental coordination disorder showed transfer of learning to other motor skills

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Dev Cognitive Neurosci. 2022 Apr;54:1-11.
FRONTAL CORTICOSTRIATAL FUNCTIONAL CONNECTIVITY REVEALS TASK POSITIVE AND NEGATIVE NETWORK DYSREGULATION IN RELATION TO ADHD, SEX, AND INHIBITORY CONTROL.
Nikolaidis A, He X, Pekar J, et al.
Frontal corticostriatal circuits (FCSC) are involved in self-regulation of cognition, emotion, and motor function. While these circuits are implicated in attention-deficit/hyperactivity disorder (ADHD), the literature establishing FCSC associations with ADHD is inconsistent. This may be due to study variability in considerations of how fMRI motion regression was handled between groups, or study specific differences in age, sex, or the striatal subregions under investigation. Given the importance of these domains in ADHD it is crucial to consider the complex interactions of age, sex, striatal subregions and FCSC in ADHD presentation and diagnosis. In this large-scale study of 362 8–12 year-old children with ADHD (n = 165) and typically developing (TD; n = 197) children, we investigate associations between FCSC with ADHD diagnosis and symptoms, sex, and go/no-go (GNG) task performance. Results include: (1) increased striatal connectivity with age across striatal subregions with most of the frontal cortex, (2) increased frontal-limbic striatum connectivity among boys with ADHD only, mostly in default mode network (DMN) regions not associated with age, and (3) increased frontal-motor striatum connectivity to regions of the DMN were associated with greater parent-rated inattention problems, particularly among the ADHD group. Although diagnostic group differences were no longer significant when strictly controlling for head motion, with motion possibly reflecting the phenotypic variance of ADHD itself, the spatial distribution of all symptom, age, sex, and other ADHD group effects were nearly identical to the initial results. These results demonstrate differential associations of FCSC between striatal subregions with the DMN and FPN in relation to age, ADHD, sex, and inhibitory control

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Developmental Medicine & Child Neurology. 2022 Apr;64:488-94.
INFLUENCE OF SEX ON TIC SEVERITY AND PSYCHIATRIC COMORBIDITY PROFILE IN PATIENTS WITH PEDIATRIC TIC DISORDER.
Girgis J, Martino D, Pringsheim T.
Aim: To investigate sex-related differences in tic severity, tic-related impairments, and psychiatric comorbidities in childhood.

Method: In this cross-sectional study, tic severity/impairment and demographic factors were collected from 270 children and young people (aged 5–17y, mean 10y 6mo, SD 3y 4mo; 212 males and 58 females) with a tic disorder diagnosis at a specialty clinic. Psychiatric diagnoses and corresponding screening questionnaire scores were collected for attention-deficit/hyperactivity disorder (ADHD), obsessive–compulsive disorder (OCD), major depressive disorder, and anxiety disorders. Logistic regression was used to compare the effect of sex and age on psychiatric comorbid diagnoses. The Mann–Whitney U test and t-tests were used to assess differences in questionnaire score distribution between sexes.
Results: Females had more severe motor tics (12.55 vs 10.81, p=0.01) and higher global severity scores (38.79 vs 32.66, p=0.03) on the Yale Global Tic Severity Scale. Females were less likely to be diagnosed with ADHD (odds ratio=0.48, 95% confidence interval=0.26–0.89). No significant sex difference was observed in diagnosis rates or symptom severity scores for anxiety or OCD. Females had significantly higher scores than males on the Children's Depression Inventory, Second Edition.
Interpretation: The higher level of motor tic severity and global severity in females further supports the differential natural history of tic disorders in females. Females with tic disorders may be underdiagnosed for ADHD

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Environ Health. 2022 Apr;21:45.

POTENTIAL IMPACTS OF SYNTHETIC FOOD DYES ON ACTIVITY AND ATTENTION IN CHILDREN: A REVIEW OF THE HUMAN AND ANIMAL EVIDENCE.

Miller MD, Steinmaus C, Golub MS, et al.

Concern that synthetic food dyes may impact behavior in children prompted a review by the California Office of Environmental Health Hazard Assessment (OEHHA). OEHHA conducted a systematic review of the epidemiologic research on synthetic food dyes and neurobehavioral outcomes in children with or without identified behavioral disorders (particularly attention and activity). We also conducted a search of the animal toxicology literature to identify studies of neurobehavioral effects in laboratory animals exposed to synthetic food dyes. Finally, we conducted a hazard characterization of the potential neurobehavioral impacts of food dye consumption. We identified 27 clinical trials of children exposed to synthetic food dyes in this review, of which 25 were challenge studies. All studies used a cross-over design and most were double blinded and the cross-over design was randomized. Sixteen (64%) out of 25 challenge studies identified some evidence of a positive association, and in 13 (52%) the association was statistically significant. These studies support a relationship between food dye exposure and adverse behavioral outcomes in children. Animal toxicology literature provides additional support for effects on behavior. Together, the human clinical trials and animal toxicology literature support an association between synthetic food dyes and behavioral impacts in children. The current Food and Drug Administration (FDA) acceptable daily intakes are based on older studies that were not designed to assess the types of behavioral effects observed in children. For four dyes where adequate dose-response data from animal and human studies were available, comparisons of the effective doses in studies that measured behavioral or brain effects following exposure to synthetic food dyes indicate that the basis of the ADIs may not be adequate to protect neurobehavior in susceptible children. There is a need to re-evaluate exposure in children and for additional research to provide a more complete database for establishing ADIs protective of neurobehavioral effects

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Epidemiol Psychiatr Sci. 2022 Apr;31:e20.

ARE ALL CHILDREN TREATED EQUALLY? PSYCHIATRIC CARE AND TREATMENT RECEIPT AMONG MIGRANT, DESCENDANT AND MAJORITY SWEDISH CHILDREN: A REGISTER-BASED STUDY.

Gubi E, et al.

AIMS: Underutilisation of mental health services among migrant youth has been demonstrated repeatedly, but little is known about potential discrepancies in terms of treatment receipt for those who do reach services. This study examines the type and level of care received among migrant children and descendants of migrants, particularly investigating disparities in treatment receipt given a specific diagnosis.
METHODS: We used register data of the total population aged 6-17 years in Stockholm, followed from 2006 to 2015, comprising 444 196 individuals, categorised as refugees, non-refugee migrants, descendants of

migrants and Swedish-born. To identify recommended treatments for specific diagnoses we used official clinical guidelines. We report logistic regression estimated odds ratios (ORs) and 95% confidence intervals (CIs) of diagnosis receipt, treatment provision and level of care where a diagnosis was first registered.
RESULTS: Migrant children had a lower likelihood of receiving a wide range of psychiatric diagnoses, including mood disorder (OR 0.58; 95% CI 0.52-0.64), anxiety disorder (OR 0.62; 95% CI 0.57-69) and neurodevelopmental disorder (OR 0.59; 95% CI 0.55-0.63). Moreover, when these diagnoses were set, migrant children had a lower likelihood of receiving the recommended treatments for these conditions compared to the majority individuals with the same diagnosis (OR of receiving psychotherapy for anxiety disorder and depression: 0.71; 95% CI 0.62-0.95 and 0.50; 95% CI 0.33-0.75, respectively; OR for receiving ADHD-medication: 0.49; 95% CI 0.43-0.54).
CONCLUSIONS: Migrant children risk underdiagnosis of various mental health conditions, and, when reaching mental health services, risk not receiving the optimal care available

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Front Human Neurosci. 2022 Mar;16.

COGNITIVE CONTROL DEFICITS IN CHILDREN WITH SUBTHRESHOLD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chen C, Li Z, Liu X, et al.

Subthreshold Attention-Deficit/Hyperactivity Disorder (ADHD) is defined as a neurobiological condition with some core inattentive or hyperactive/impulsive symptoms of ADHD which do not meet the full diagnosis clinically. Although it has been well documented that deficits in cognitive control, a high-level cognitive construct closely related to attention, are frequently found among children with ADHD, whether subthreshold ADHD is also associated with similar deficits remains unclear. In this study, we examined the attention functions and the cognitive control capacity (CCC) in children with ADHD (n = 39), those with subthreshold ADHD (n = 34), and typically developing peers (TD, n = 36). The results showed that the ADHD and subthreshold ADHD groups exhibited similar patterns of the impaired executive function of attention (revealed as an augment in flanker conflict effect) and reduced cognitive control capacity, and no significant difference was found between the two groups. These findings suggest that although children with subthreshold ADHD have not met the full criteria of ADHD, they showed reduced efficiency in cognitive control and attention function, similar to children with ADHD

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Georgian Med News. 2022 Mar;92-101.

PRESENCE OF PRENATAL MATERNAL STRESS INCREASES THE RISK OF THE DEVELOPMENT OF ADHD SYMPTOMS IN YOUNG CHILDREN.

Kacharava T, Nemsadze K, Inasaridze K.

Aims - to identify association between maternal stress during pregnancy and the developemnt of the attention deficiency hyperactivity syndrom in young children We conducted a case-control study sequentially recruiting 200 children from the "Early detection of disease and screening" State Program, from them 100 children with ADHD diagnose, and 100 subjects, as a control group, without Disruptive Behavior Disorder (DBD), aged between 1 and 6 years. The children were diagnosed with ADHD according to the DSM-IV-R and a clinical interview of the parents that used the Diagnostic Interview Schedule for Children Version IV (DISC-IV). We investigated the effect of cumulative exposure separately for life events considered as dependent and independent.The mother's stress level was scored from 1 to 5 on the DSM-III and DSM-III-R axis IV scales, according to the highest level of stress experienced during the pregnancy. The presence of stress factor plays an important role in the development of ADHD syndrome, but does not play a statistically significant role in which type of syndrome develops: F90.0, F90.1, F90.2: p=.258. A statistically significant relationship between ADHD diagnosis and stress degree was not confirmed at p=.503. Our data revealed that moderate-grade stress is caused by dependent causes, severe stress by independent causes, this association is statistically significant(p=.001 Cramer's V=.750). A statistically significant negative association was also found between the presence of prenatal stress and the length and weight of the baby at birth. For our study population, the risk of developing the syndrome in children of stress-relieved mothers was 2 times higher than in children of non-stressed mothers RR = 2.042. These findings show that there is an association between maternal stress during pregnancy and ADHD symptoms in offspring and support the hypothesis

that prenatal stress causes offspring ADHD through a programming effect and future research should focus on exploring other prenatal factors that might be causally related to ADHD

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Indian J Ophthalmol. 2022 May;70:1664-68.

DOES METHYLPHENIDATE TREATMENT AFFECT FUNCTIONAL AND STRUCTURAL OCULAR PARAMETERS IN PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER? - A PROSPECTIVE, ONE YEAR FOLLOW-UP STUDY.

Bingöl-Kiziltunç P, et al.

PURPOSE: Methylphenidate hydrochloride, which blocks the reuptake mechanisms of dopamine and norepinephrine, is used in attention deficit hyperactivity disorder (ADHD) treatment. Methylphenidate has many general side effects including ocular findings. In this study, we investigated the long-term effects of methylphenidate treatment on functional and structural ocular parameters.

METHODS: In this prospective study, children with ADHD were evaluated. All patients underwent a detailed ophthalmic examination before methylphenidate treatment. All patients were examined in the 3(rd), 6(th), 9(th), 12(th) months of methylphenidate treatment. Visual acuities, color vision, pupil diameters, static, dynamic and cycloplegic retinoscopy, intraocular pressure (IOP), anterior chamber depth (ACD), axial length (AL) were evaluated and recorded.

RESULTS: A total of 22 children were included in this study. The best-corrected visual acuities (BCVA) of all patients for both eyes were 0.0 logMAR, and 90.9% of patients had blue-purple color weakness before the treatment. After 1 year of treatment, none of the patients had any change in BCVA and color vision. However, an increase in myopic values of static retinoscopy and a decrease in hyperopic values of cycloplegic retinoscopy were found. Additionally, accommodation capacities were found to be decreased and AL was found to be increased significantly for both eyes. Pupil diameter, IOP, and ACD values did not change significantly.

CONCLUSION: Our results suggest that patients with ADHD may have blue color vision deficiencies because of the decreased retinal dopamine levels. Additionally, structural and ocular parameters, especially accommodation capacity, may be affected by methylphenidate treatment

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Int J Environ Res Public Health. 2022 Apr;19.

COMPARING THE EFFECT OF METHYLPHENIDATE AND ANODAL TDCS ON INHIBITORY CONTROL AND WORKING-MEMORY IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A STUDY PROTOCOL FOR A RANDOMIZED, WITHIN-SUBJECT TRIAL.

D'Aiello B, Battisti A, Lazzaro G, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by inappropriate levels of attention, hyperactivity, and impulsivity that interfere with individual functioning. The international guidelines recommend targeting ADHD-related neurochemical brain abnormalities by intervening via drug treatment, such as methylphenidate (MPH), as first choice. Drug treatments are usually associated with a huge amount of cost for families and the healthcare system, suspension for low compliance, poor long-term efficacy, and side effects. Transcranial direct current stimulation (tDCS) has been suggested as a possible noninvasive means to safely manipulate brain activity and, in turn, improve behavior and cognition in developmental ages. Several studies have shown that tDCS has the potential to improve ADHD-related cognitive deficits, but the effect of tDCS compared with MPH has never been evaluated. The aim of the present within-subject, sham-controlled, randomized proof-of-concept study is to demonstrate the positive effect of one-session anodal tDCS analogous to the MPH drug on inhibitory control and working memory in children and adolescents with ADHD. We strongly believe that this study protocol will serve to accelerate research into low-cost, drug-free, feasible interventions for ADHD

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Int J Environ Res Public Health. 2022 Apr;19.

ASSOCIATIONS BETWEEN ALLERGIC AND AUTOIMMUNE DISEASES WITH AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITHIN FAMILIES: A POPULATION-BASED COHORT STUDY.

Li DJ, Tsai CS, Hsiao RC, et al.

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are commonly comorbid with allergic and autoimmune diseases in children. The aim of the current study was to investigate the association between children's and first-degree relatives' (i.e., mother, father, and full sibling) allergic and autoimmune diseases and children's ASD and ADHD. We enrolled participants from Taiwan's Maternal and Child Health Database. We used the Cox regression model to examine the associations of familial, siblings' and children's allergic and autoimmune diseases with children's ASD and/or ADHD. In total, we included 1,386,260 children in the current study. We found the significant association between familial allergic or autoimmune disease and development of ASD or ADHD among children. We also identified the predominant impact of familial aggregation on the above associations. The associations between some parental diagnoses of autoimmune or allergic diseases in children's ASD and/or ADHD were stronger in mothers than those in fathers. Early assessment of the possibility of ASD and ADHD is required for children who have a parent with an allergic or autoimmune disease

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Int J Environ Res Public Health. 2022 Mar;19.

DEVICE-BASED MOVEMENT BEHAVIORS, EXECUTIVE FUNCTION, AND ACADEMIC SKILLS AMONG AFRICAN AMERICAN CHILDREN WITH ADHD AND DISRUPTIVE BEHAVIOR DISORDERS.

Santiago-Rodriguez ME, Ramer JD, Marquez DX, et al.

BACKGROUND: Physical activity (PA) has been identified as a promising intervention to improve executive function (EF) and reduce ADHD symptoms in children. Few African American children with ADHD and Disruptive Behavior Disorders (DBDs) from families with low incomes are represented in this literature. The purpose of this study is to test the relationships between PA and sedentary time (ST), and EF and academic skills among African American children with ADHD and DBD from low-income families.

METHODS: Children (n = 23, 6-13 years old) wore an ActiGraph for one week to measure PA and ST. EF was measured through parent report and direct neuropsychological tests. Academic skills were measured with the Curriculum-Based Measurement System. Bivariate correlations tested relationships between PA, ST, EF, and academic skills.

RESULTS: A significant correlation was observed between vigorous PA time and parent reported EF (r = -0.46, p = 0.040). Light PA and moderate PA were not related to EF or academic skills, and neither was ST.

CONCLUSIONS: Vigorous PA may prove useful as an adjunct treatment to improve EF in African American children with ADHD and DBD in low-income neighborhoods. Research using experimental and longitudinal designs, and examining qualitative features of PA experiences, will be critical for understanding relationships between PA, academic skills, and EF in this population

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Int J Environ Res Public Health. 2022 Mar;19.

RELATIONSHIP BETWEEN INJURIES AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A POPULATION-BASED STUDY WITH LONG-TERM FOLLOW-UP IN TAIWAN.

Jin YT, Chwo MJ, Chen CM, et al.

OBJECTIVE: To investigate the association between various injuries and attention-deficit hyperactivity disorder (ADHD) and distinguish ADHD from non-ADHD with regards to risk of various injuries among children in Taiwan.

METHOD: Using the data from the National Health Insurance Research Database, we selected a total of 1802 subjects under the age of 18 who were diagnosed with ADHD as well as an additional 7208 subjects as a comparison group.

RESULTS: Compared with children who were not diagnosed with ADHD, children diagnosed with ADHD were more likely to intentionally injure themselves. During the school year, ADHD children were injured less frequently than were non-ADHD children on traffic-related incidents. The adjusted hazard ratio of injury for the ADHD children was 2.493 times higher than that of comparison subjects. The ADHD children had a

greater length of stay and medical cost when compared to those of the non-ADHD children. Age showed a significant inverse relationship with injury. Among the ADHD children, the injury rate was evidently higher for the low-income group than for the non-low-income group.
CONCLUSIONS: Age, cause of injuries, low-income household status, and school season all have a significant connection to the risk of injury for ADHD children

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Int J Environ Res Public Health. 2022 Apr;19.
INFLUENCE OF COMT (RS4680) AND DRD2 (RS1076560, RS1800497) GENE POLYMORPHISMS ON SAFETY AND EFFICACY OF METHYLPHENIDATE TREATMENT IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS.
Åšmiarowska M, Brzuchalski B, Grzywacz E, et al.
Fetal alcohol spectrum disorders (FASD) in a course of high prenatal alcohol exposure (hPAE) are among the most common causes of developmental disorders. The main reason for pharmacological treatment of FASD children is attention deficit hyperactivity disorder (ADHD), and methylphenidate (MPH) is the drug of choice. The aim of the study was to assess whether children born of hPAE with ADHD, with or without morphological FASD, differ in terms of catechol-O-methyltransferase (COMT) and dopamine receptor D2 (DRD2) gene polymorphisms, and if genetic predisposition affects response and safety of MPH treatment. The polymorphisms of COMT (rs4680) and DRD2 (rs1076560, rs1800497) were analyzed in DNA samples. A borderline significance was found for the correlation between MPH side effects and the G allele of COMT (rs4680) (p = 0.04994) in all ADHD children. No effect of COMT (rs4680) and DRD2 (rs1076560, rs1800497) polymorphisms and the treatment efficacy was observed. The analyzed DRD2 and COMT gene polymorphisms seem to play no role in MPH efficacy in ADHD children with hPAE, while low-activity COMT (Met158) variant carriers may be more intolerant to MPH. The MPH treatment is effective in ADHD independent of FASD, although the ADHD-FASD variant requires higher doses to be successful. These results may help in optimization and individualization in child psychiatry

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Int J Environ Res Public Health. 2022 Apr;19.
BODY-RELATED ATTITUDES, PERSONALITY, AND IDENTITY IN FEMALE ADOLESCENTS WITH ANOREXIA NERVOSA OR OTHER MENTAL DISORDERS.
Achermann M, et al.
The psychological integration of body-related attitudes (BodyRA) is a critical developmental task in adolescence. Adolescents must adapt to their changing body image and body satisfaction. For young people, BodyRA (body dissatisfaction, bulimia, and drive for thinness) are connected to insecurities, which can disturb identity integration and personality development. Our goal was to evaluate the importance of BodyRA also for other mental disorders other than anorexia nervosa (AN), and the association between BodyRA with temperament and personality traits and identity diffusion. Data for the period of 2012 to 2019 were retrospectively analyzed from a convenience sample of patients in a child and adolescent psychiatric hospital (n = 114). The patients were 13 to 17 years of age and had a BMI of 11.9-36.1 kg/m(2). As expected, BodyRA were found to be more pronounced in AN, as well as in borderline personality disorder (BPD), depression (DD), and attention deficit hyperactivity disorder (ADHD). BodyRA correlated significantly with internalizing problems in patients with DD (r = 0.428-0.565, p < 0.01) and BPD (r = 0.680, p < 0.01) as well as with BMI (r = 0.404, p < 0.01) in patients with DD. Moreover, we detected significant correlations with impaired identity development in patients with DD (r = 0.482-0.565, p < 0.01) and BPD (r = 0.681-0.703, p < 0.01). BodyRA also correlated significantly with the personality traits of harm avoidance (r = 0.377-0.541, p < 0.01) and self-directedness (r = -0.537--0.635, p < 0.01) in DD. These personality traits and bulimia were used as predictors for identity diffusion in the investigated disorders of this study. We conclude that BodyRA, harm avoidance and self-directedness are associated with identity development in adolescent females with mental disorders

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Int J Mol Sci. 2022 Apr;23.

SHORTENED INFANT TELOMERE LENGTH IS ASSOCIATED WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN CHILDREN AT AGE TWO YEARS: A BIRTH COHORT STUDY.

Pham C, Vryer R, O'Hely M, et al.

Environmental factors can accelerate telomere length (TL) attrition. Shortened TL is linked to attention deficit/hyperactivity disorder (ADHD) symptoms in school-aged children. The onset of ADHD occurs as early as preschool-age, but the TL-ADHD association in younger children is unknown. We investigated associations between infant TL and ADHD symptoms in children and assessed environmental factors as potential confounders and/or mediators of this association. Relative TL was measured by quantitative polymerase chain reaction in cord and 12-month blood in the birth cohort study, the Barwon Infant Study. Early life environmental factors collected antenatally to two years were used to measure confounding. ADHD symptoms at age two years were evaluated by the Child Behavior Checklist Attention Problems (AP) and the Attention Deficit/Hyperactivity Problems (ADHP). Associations between early life environmental factors on TL or ADHD symptoms were assessed using multivariable regression models adjusted for relevant factors. Telomere length at 12 months (TL12), but not at birth, was inversely associated with AP (Î² = -0.56; 95% CI (-1.13, 0.006); p = 0.05) and ADHP (Î² = -0.66; 95% CI (-1.11, -0.21); p = 0.004). Infant secondhand smoke exposure at one month was independently associated with shorter TL12 and also higher ADHD symptoms. Further work is needed to elucidate the mechanisms that influence TL attrition and early neurodevelopment

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Int J Pediatr Otorhinolaryngol. 2022 Jun;157:111138.

IMPROVEMENT OF INATTENTIVE AND HYPERACTIVE SYMPTOMS AFTER REAL-LIFE RHINITIS TREATMENT IN SCHOOL-AGED CHILDREN.

Thamrongsak C, Chirdkiatgumchai V, Jotikasthira W, et al.

OBJECTIVES: Rhinitis treatment may improve attention-deficit/hyperactivity symptoms in children. The current study evaluated changes in inattentive and hyperactive symptoms after treatment in children with chronic rhinitis.

METHODS: Children aged 5-18 years with chronic rhinitis were enrolled in a 3-month prospective study. The nasal provocation test for house dust mites (HDM) and evaluation of allergen sensitization, including the skin prick test and the Phadiatop test, were performed. The severity of rhinitis was assessed according to the ARIA guideline. The total nasal symptom score and the Vanderbilt ADHD Diagnostic Rating Scale (VADRS) score for assessing inattentive and hyperactive symptoms were recorded at baseline and at 1 and 3 months after rhinitis treatment. Children with rhinitis were classified into the following two groups: HDM-induced allergic rhinitis (AR group) and non-allergic rhinitis to HDM (NAR group) based on the NPT.

RESULTS: Overall, 83 children completed the 3-month prospective study, and they had a mean age of 9.12 ± 2.89 years and 44.6% were boys. After rhinitis treatment, VADRS scores assessed by the parents and teachers were significantly decreased compared with those at baseline (p = 0.005). In subgroup analysis, 61 (73.49%) children had AR, and 22 (26.5%) children had NAR. No significant difference in the baseline VADRS score was found between the AR and NAR groups. After treatment, VADRS scores assessed by the parents and teachers were significantly decreased only in the AR group (p < 0.001). Forty-five (54.2%) children had moderate persistent rhinitis, 29 (34.9%) had mild persistent rhinitis, and 9 (10.8%) had mild intermittent symptoms. There were no differences in baseline VADRS scores assessed by the parents and teachers among children with mild intermittent, mild persistent, or moderate persistent symptoms. The total nasal symptom score and VADRS score were significantly decreased after treatment for all severities of rhinitis compared with those at baseline. A greater baseline VADRS score was associated with substantial improvement of inattentive and hyperactive symptoms after treatment.

CONCLUSION: Early treatment for rhinitis may improve inattentive and hyperactive symptoms in school-aged children

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International Journal of Play Therapy. 2022 Mar.

A META-ANALYSIS OF SANDPLAY THERAPY TREATMENT OUTCOMES.

Wiersma JK, Freedle LR, McRoberts R, et al.

Sandplay therapy is a cross-cultural, psychodynamic, nondirective, multisensory psychotherapy method founded by Dora Kalff. Sandplay is used with children and adults with a range of mental health problems. Despite sandplay's growing popularity, its empirical evidence base is less developed than more well-known therapies. This international study provides a meta-analysis of the available quantitative outcome studies in order to summarize the growing evidence base of sandplay. The meta-analysis specifically examined emotional and behavioral outcome measures of treatment with sandplay therapy. The initial search identified 1,715 potential records from over 16 countries. After screening, 40 studies from eight countries representing 1,284 participants met the inclusion criteria. Mean effect sizes were calculated using a random effects model with the Comprehensive Meta-Analysis (CMA) program. The overall effect size was large (Hedges' g = 1.10). Large effect sizes were maintained for internalizing, externalizing, and attention-deficit/hyperactivity disorder (ADHD) symptoms. Improved effect sizes were associated with individual treatment over the group format. These results suggest that sandplay therapy is an effective treatment method for children and adults with a wide variety of mental health concerns. Limitations and suggestions for further research are discussed

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J Affect Disord. 2022 Jun;307:133-41.

AFFECTIVE-COGNITIVE-BEHAVIORAL HETEROGENEITY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): EMOTIONAL DYSREGULATION AS A SENTINEL SYMPTOM DIFFERENTIATING "ADHD-SIMPLEX" AND "ADHD-COMPLEX" SYNDROMES?

Yue X, Liu L, Chen W, et al.

BACKGROUND: Current DSM and ICD classifications of Attention-Deficit/Hyperactivity Disorder (ADHD) exclude emotional dysregulation (ED) in their diagnostic criteria, despite ED symptoms frequently co-occurring in ADHD and likely sharing common neurobiological substrates. In this study, we examined whether consideration of ED symptoms could delineate more informative "ADHD+ED" subphenotypes.

METHOD: 4106 children with ADHD were recruited. ED and inattentive (IA) and hyperactive/impulsive (HI) symptoms were profiled using latent class analyses (LCA). The derived latent class (LC) subphenotypes were evaluated and validated in relation to comorbidity patterns, executive functions, and functional impairments. RESULTS: Five LC subphenotypes with ED symptoms were identified: IA/HI + ED profile (LC1); HI + ED profile (LC2); IA + ED profile (LC3); IA/HI profile (LC4); and IA profile (LC5). Cross-validation of the LCA model using support vector machine analysis confirmed 83% accuracy. ED positive (ED+ve) subphenotypes were associated with higher rates of oppositional defiant disorder, mood disorders, anxiety disorders, as well as more severe autistic traits and sluggish cognitive tempo symptoms. Higher rates of ecological executive functioning impairments (BRIEF ratings) were found among ED+ve subphenotypes (though no differences were detected by laboratory-based measures). Functional impairments were also more severe among participants with ED+ve subphenotypes.

LIMITATIONS: The data for our LCA were cross-sectional and based primarily on parent ratings.

CONCLUSION: Our classification model has parcellated IA, HI, and ED symptoms into novel informative subphenotypes. These classifications provide preliminary evidence that ED symptoms could serve as sentinel features to identify a potential "ADHD-complex" syndrome, which demarcates a more pervasive condition of greater severity, complexity, and impairment

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J Child Adolesc Psychopharmacol. 2022 Apr;32:162-70.

LONG-TERM EFFECTS OF LITHIUM USE ON CHILDREN AND ADOLESCENTS: A RETROSPECTIVE STUDY FROM TURKEY.

Günes H, et al.

Background: The aim of this study was to evaluate the long-term effects of lithium treatment on white blood cell (WBC) count, serum creatinine, and thyroid-stimulating hormone (TSH) levels in children and adolescents with bipolar disorder (BD) and non-BD in a Turkish children and adolescent sample.

Methods: The study is based on retrospective chart review. Children and adolescent patients with BD and non-BD prescribed lithium in a mental health and neurological disorders hospital between 2012 and 2017 were included in the study. Data were collected from the electronic medical files. Laboratory values for WBC count, serum creatinine, and TSH levels at baseline within the week before the onset of lithium, and at 1st, 3rd, 6(th), and 12th month of treatment were recorded.
Results: A total of 143 patients (82 females, 61 males; 100 BD, 43 non-BD) aged 9-18 were included. Non-BD diagnoses were psychotic and schizoaffective disorders, unipolar depression, attention-deficit/hyperactivity disorder, conduct disorder, severe mood dysregulation syndrome, borderline personality disorder, and autism. Mean age of the participants were 15.90±1.16 years for the bipolar group and 14.88±1.79 years for the nonbipolar group. Patients with BD reported more adverse effects. There was a statistically significant increase in WBC counts and TSH levels at any time point. A statistically significant elevation in serum creatinine was found at 3rd and 12th month of treatment. During the course of lithium treatment, WBC counts exceeded 13,000 in 14 (9.8%) patients, and TSH levels exceeded 5.5mU/L in 41 patients (28.6%). Twenty-one (14.68%) patients were started on thyroxin replacement. Basal TSH levels and duration of the lithium treatment were higher in the participants with TSH levels exceeding 5.5mU/L. Lithium maximum dose, lithium blood level, basal TSH level, and duration of treatment were higher in the participants receiving thyroxin replacement. No patients had serum creatinine levels exceeding the normal reference values.
Conclusion: Our study suggests that lithium is a generally safe and tolerable agent for children and adolescents with BD and non-BD; however, close monitoring of thyroid functions particularly in patients with a higher basal TSH level and longer duration of lithium use is important

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J Clin Psychiatry. 2022 Apr;83.

IDENTIFYING PEDIATRIC MOOD DISORDERS FROM TRANSDIAGNOSTIC POLYGENIC RISK SCORES: A STUDY OF CHILDREN AND ADOLESCENTS.

Barnett EJ, Biederman J, Doyle AE, et al.

Objective: Mood disorders often co-occur with attention-deficit/hyperactive disorder (ADHD), disruptive behavior disorders (DBDs), and aggression. We aimed to determine if polygenic risk scores (PRSs) based on external genome-wide association studies (GWASs) of these disorders could improve genetic identification of mood disorders.
Methods: We combined 6 independent family studies that had genetic data and diagnoses for mood disorders that were made using different editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM). We identified mood disorders, either concurrently or in the future, in participants between 6 and 17 years of age using PRSs calculated using summary statistics of GWASs for ADHD, ADHD with DBD, major depressive disorder (MDD), bipolar disorder (BPD), and aggression to compute PRSs.
Results: In our sample of 485 youths, 356 (73%) developed a subthreshold or full mood disorder and 129 (27%) did not. The cross-validated mean areas under the receiver operating characteristic curve (AUCs) for the 7 models identifying participants with any mood disorder ranged from 0.552 in the base model of age and sex to 0.648 in the base model + all 5 PRSs. When included in the base model individually, the ADHD PRS (OR = 1.65, P < .001), Aggression PRS (OR = 1.27, P = .02), and MDD PRS (OR = 1.23, P = .047) were significantly associated with the development of any mood disorder.
Conclusions: Using PRSs for ADHD, MDD, BPD, DBDs, and aggression, we could modestly identify the presence of mood disorders. These findings extend evidence for transdiagnostic genetic components of psychiatric illness and demonstrate that PRSs calculated using traditional diagnostic boundaries can be useful within a transdiagnostic framework

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J Clin Psychopharmacol. 2022 May;42:238-46.

ACUTE HYPERKINETIC MOVEMENT DISORDERS AS A MULTIFACTORIAL PHARMACODYNAMIC DRUG INTERACTION BETWEEN METHYLPHENIDATE AND RISPERIDONE IN CHILDREN AND ADOLESCENTS.

Mohamoud M, Chen Q, Croteau D, et al.

PURPOSE/BACKGROUND: Acute hyperkinetic movement disorders have been reported with the concomitant use of attention-deficit/hyperactivity disorder (ADHD) stimulants and antipsychotics in children and adolescents. We analyzed postmarketing reports of suspected acute hyperkinetic movement disorder associated with concomitant use of ADHD stimulants and antipsychotics.

METHODS/PROCEDURES: We searched for postmarketing reports of acute hyperkinetic movement disorders associated with concomitant use of ADHD stimulants-antipsychotics in the US Food and Drug Administration Adverse Event Reporting System through December 6, 2019. PubMed and EMBASE were also searched for acute hyperkinetic movement reports with the concomitant use of ADHD stimulants-antipsychotics through January 13, 2020.

FINDINGS/RESULTS: We identified 36 cases resulting in acute hyperkinetic movement disorder associated with the concomitant use of ADHD stimulants-antipsychotics, 19 of which were also identified in the medical literature. From an ADHD stimulant perspective, methylphenidate products accounted for the largest number of cases (n = 23 [64%]), followed by amphetamine products (n = 9 [25%]) and atomoxetine (n = 4 [11%]). From an antipsychotic perspective, all 36 cases were reported with second-generation antipsychotics, particularly risperidone (n = 20 [56%]). Most of the cases were reported in boys (n = 31 [86%]) aged 6 to 12 years (n = 27 [75%]). Approximately 53% of the cases reported a time to onset within 24 hours of the drug change. Acute dystonic reactions (n = 27 [75%]) were the most frequently reported movement disorder.

IMPLICATIONS/CONCLUSIONS: As outlined in changes to the US prescribing information for all methylphenidate and risperidone products, health care professionals should be aware that changes to this combination may be associated with a pharmacodynamic drug-drug interaction resulting in acute hyperkinetic movement disorder

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J Healthc Eng. 2022;2022:5222136.

DEEP LEARNING ENABLED DIAGNOSIS OF CHILDREN'S ADHD BASED ON THE BIG DATA OF VIDEO SCREEN LONG-RANGE EEG.

Zhou D, Liao Z, Chen R.

Attention-deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in children. At the same time, ADHD is prone to coexist with other mental disorders, so the diagnosis of ADHD in children is very important. Electroencephalogram (EEG) is the sum of the electrical activity of local neurons recorded from the extracranial scalp or intracranial. At present, there are two main methods of long-range EEG monitoring commonly used in clinical practice: one is ambulatory EEG monitoring, and the other is long-range video EEG monitoring. The purpose of this study is to summarize the brain electrical activity and clinical characteristics of children with ADHD through the video long-range computer graphics data of children with ADHD and to explore the clinical significance of video long-range EEG in the diagnosis of children with ADHD. For a more effective analysis, this study further processed the video data of long-range computer graphics of children with ADHD and constructed several neural network algorithm models based on deep learning, mainly including fully connected neural network models and two-dimensional convolutional neural networks. Model and long- and short-term memory neural network model. By comparing the recognition effects of these several algorithms, find the appropriate recognition algorithm to improve the accuracy and then establish a recognition method for the diagnosis of children's ADHD based on deep learning long-range EEG big data. Finally, it is concluded that long-term video EEG can analyze the EEG relationship of children with ADHD and provide a diagnostic basis for the diagnosis of ADHD

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J Med Case Rep. 2022 Apr;16:152.

The partial μ-opioid agonist buprenorphine in autism spectrum disorder: a case report.

Skoglund C, Leknes S, Heilig M.

BACKGROUND: There are currently no approved medications for impaired social cognition and function, core symptoms of autism spectrum disorder. We describe marked improvement of these symptoms with long-term low-dose administration of the partial Âμ-opioid agonist buprenorphine. We discuss these observations in the context of a role for endogenous opioid systems in social attachment, and theories integrating those findings mechanistically with autism spectrum disorder.

CASE PRESENTATION: M, a 43-year-old Caucasian male, is medically healthy. Despite social difficulties since childhood, he completed high school with better-than-average grades, but failed university education. A psychiatric evaluation in his twenties diagnosed attention deficit hyperactivity disorder but also noted symptoms of coexisting autism spectrum disorder. M accidentally came across buprenorphine in his late twenties and experienced progressively improved social functioning on a low daily dosage (0.5-1.0Â mg/day), an effect maintained for 15 years. He lived independently and maintained a part-time occupation. After abrupt discontinuation of treatment, his autistic symptoms returned, and function deteriorated. Following evaluation by our team, buprenorphine was resumed, with gradual return to prior level of functioning. An attempt to formally evaluate M both on and off medication was agreed with him and approved by the Swedish Ethics Authority, but medication had to be resumed when the patient worsened following discontinuation.

CONCLUSIONS: According to the Âμ-opioid receptor balance model, both excessive and deficient Î¼-receptor activity may negatively influence social behavior, and accordingly both opioid agonist and opioid antagonist treatment may be able to improve social functioning, depending on an individual's opioid tone before treatment. Our case report is consistent with these hypotheses, and given the extensive unmet medical needs in individuals with autism spectrum disorders, randomized controlled trial appears warranted

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J Neurodev Disord. 2022 May;14:30.

THE ELECTRORETINOGRAM B-WAVE AMPLITUDE: A DIFFERENTIAL PHYSIOLOGICAL MEASURE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER.

Lee IO, Skuse DH, Constable PA, et al.

BACKGROUND: Attention Deficit Hyperactivity Disorder (ADHD) is the most prevalent childhood neurodevelopmental disorder. It shares some genetic risk with Autism Spectrum Disorder (ASD), and the conditions often occur together. Both are potentially associated with abnormal glutamate and GABA neurotransmission, which can be modelled by measuring the synaptic activity in the retina with an electroretinogram (ERG). Reduction of retinal responses in ASD has been reported, but little is known about retinal activity in ADHD. In this study, we compared the light-adapted ERGs of individuals with ADHD, ASD and controls to investigate whether retinal responses differ between these neurodevelopmental conditions.

METHODS: Full field light-adapted ERGs were recorded from 15 ADHD, 57 ASD (without ADHD) and 59 control participants, aged from 5.4 to 27.3 years old. A Troland protocol was used with a random series of nine flash strengths from -0.367 to 1.204 log photopic cd.s.m(-2). The time-to-peak and amplitude of the a- and b-waves and the parameters of the Photopic Negative Response (PhNR) were compared amongst the three groups of participants, using generalised estimating equations.

RESULTS: Statistically significant elevations of the ERG b-wave amplitudes, PhNR responses and faster timings of the b-wave time-to-peak were found in those with ADHD compared with both the control and ASD groups. The greatest elevation in the b-wave amplitudes associated with ADHD were observed at 1.204 log phot cd.s.m(-2) flash strength ($p < .0001$), at which the b-wave amplitude in ASD was significantly lower than that in the controls. Using this measure, ADHD could be distinguished from ASD with an area under the curve of 0.88.

CONCLUSIONS: The ERG b-wave amplitude appears to be a distinctive differential feature for both ADHD and ASD, which produced a reversed pattern of b-wave responses. These findings imply imbalances between glutamate and GABA neurotransmission which primarily regulate the b-wave formation. Abnormalities in the b-wave amplitude could provisionally serve as a biomarker for both neurodevelopmental conditions

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J Neuroimmunol. 2022 Jun;367:577848.

REGULATORY T CELLS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY.

Uçar HN, et al.

OBJECTIVE: The pathophysiology of attention deficit hyperactivity disorder (ADHD) are still not fully elucidated. Immune system dysregulation has emerged as a major etiological focus as a result of the high comorbidity of allergic disease, inflammatory biomarkers, and genetic research. The present study aimed to evaluate peripheral lymphocyte subpopulations and regulatory T cells (Tregs) in children with ADHD.

METHODS: This single-center cross-sectional case-control study assessed 49 children with ADHD and 35 age- and gender-matched healthy children aged 7-12 years (9.10± 2.37 and 9.45± 2.13, respectively). The participants were screened for psychopathology using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, while the severity of ADHD symptoms was measured by means of the distracted-Continuous Performance Test. Peripheral lymphocyte subpopulations and Tregs were analyzed with flow-cytometry.

RESULTS: There is no significant difference in peripheral blood lymphocyte subsets between ADHD and control groups The children diagnosed with ADHD exhibited significantly higher levels of CD3(+) CD4(+) CD25(+) Foxp3(+) (Tregs) than the healthy control subjects (8.23± 2.09 vs. 6.61± 2.89; z = 2.965, p = .004). The Tregs cell (Exp(B) = 1.334; p = .042; CI = 1.011-1.761) levels were determined to be statistically significant according to regression analysis and were associated with an increased probability of ADHD.

CONCLUSION: Elevated Treg levels were linked to an increased likelihood of ADHD. This study suggested that changes in immune regulatory cells represent an important part of research in treatment of ADHD

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J Psychiatr Pract. 2022 May;28:251-58.

ASSOCIATION BETWEEN MILD NEUROCOGNITIVE DISORDER DUE TO ALZHEIMER'S DISEASE AND POSSIBLE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CASE REPORT.

Carrillo P, Rey R, Padovan C, et al.

Recent literature concerning attention-deficit/hyperactivity disorder (ADHD) underlines the persistence of this neurodevelopmental illness in older patients. Comorbidity with a neurodegenerative disease is thus possible. However, few studies have investigated this topic. To our knowledge, this is the first case report of such a possible association, which raises important questions about clinical presentation, symptoms, diagnosis, and treatment. A 72-year-old man, without any psychiatric history, presented with depression, subjective memory loss, and attention deficit and anxious symptoms, and was diagnosed with mild neurocognitive disorder due to Alzheimer's disease. However, the patient's attentional symptoms appeared to have been present since childhood. A formalized diagnostic interview assessing for ADHD did not allow for a clear diagnosis, possibly due to recall bias. The patient's anxiety symptoms also did not respond well to cognitive behavioral therapy coupled with different antidepressants. We hypothesized the presence of ADHD, with the symptoms balanced until now by the patient's high cognitive capacities, and we postulated that the onset of a neurogenerative process may have disrupted this balance. In this case report, we discuss symptom dimensionality, the interplay between neurodegenerative and neurodevelopmental diseases, and various treatment options. Attentional deficits and anxiety symptoms are frequent in mild neurocognitive disorders due to neurodegenerative illnesses. It is important to explore the time of onset of such symptoms since neurodegenerative processes can worsen neurodevelopmental conditions. Moreover, identification of a pre-existing neurodevelopmental condition can lead to alternative care and treatment options. In addition, the unexplained worsening of ADHD symptoms should prompt clinicians to assess for a neurodegenerative process

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J Psychiatr Res. 2022 Jun;150:130-41.

EFFECTS OF CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION ON INHIBITORY AND ATTENTION CONTROL IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A PILOT RANDOMIZED SHAM-CONTROLLED CROSSOVER STUDY.

Klomjai W, Siripornpanich V, Aneksan B, et al.

The pathophysiological of attention-deficit hyperactivity disorder (ADHD) includes hypoactivation of the dorso-lateral prefrontal cortex (DLPFC). Most studies have used anodal (excitatory) transcranial direct current stimulation (tDCS) to improve ADHD symptoms, however, a meta-analysis showed limited effect on improving inhibition, and no evidence of attention improvement. We thus present a pilot protocol for investigating the effect of other montage i.e. cathodal (inhibitory) tDCS on neurophysiological and behavioral measures in ADHD. Eleven participants underwent active (1.5 mA, 20Â min) and sham cathodal tDCS over the left DLPFC for 5 consecutive days at a 1-month interval. Quantitative electroencephalography was recorded in a resting state with the eyes opened and closed during visual go/no-go and auditory continuous performance tasks at baseline, after five sessions, and at 1-week and 1-month follow-ups. Correct responses and omission errors were recorded. After five active sessions, alpha power increased in the right frontal area when the eyes were opened, and delta power in the left frontal area and omission errors decreased during go/no-go tasks, with no differences at follow-ups. The results revealed improvements in inhibitory control, but not for attention. No aftereffects were observed in either outcomes. However, the changes found in both hemispheres would probably support the hypothesis that cathodal stimulation over the left DLPFC may increase the activity of the right DLPFC via transcallosal inhibition. Results of this pilot trial would help to design and implement a full-scale randomized control trials for further ADHD research. This study was registered on ClinicalTrials.gov (NCT03955692)

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JAMA Netw Open. 2022 Apr;5:e228884.

ASSOCIATION OF PERINATAL AND CHILDHOOD ISCHEMIC STROKE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bolk J, Simatou E, SÃ¶derling J, et al.

IMPORTANCE: Early detection of attention-deficit/hyperactivity disorder (ADHD) plays a crucial role in reducing negative effects on everyday life, including academic failure and poor social functioning. Children who survive ischemic strokes risk major disabilities, but their risk of ADHD has not been studied in nationwide cohorts.

OBJECTIVE: To assess the risk of ADHD in children after pediatric ischemic stroke.

DESIGN, SETTING, AND PARTICIPANTS: Participants in this Swedish nationwide cohort study included 1320 children diagnosed with ischemic stroke recorded in linked Swedish national registers from January 1, 1969, to December 31, 2016, without prior ADHD diagnosis. Ten matched controls were identified for each index case, and first-degree relatives were identified for index individuals and controls. Analyses were stratified by perinatal and childhood strokes and presence of comorbid adverse motor outcomes and/or epilepsy. End of follow-up was the date of ADHD diagnosis, death, or December 31, 2016, whichever occurred first. Data analyses were performed August 1 to 28, 2021.

EXPOSURES: Pediatric ischemic stroke.

MAIN OUTCOMES AND MEASURES: Attention-deficit/hyperactivity disorder identified using codes from the International Classification of Diseases, Ninth Revision, and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, and/or prescribed ADHD medication recorded in the Medical Birth Register, National Patient Register, or Prescribed Drug Register after stroke. Cox proportional hazards regression was used to assess adjusted hazard ratios (aHRs) for ADHD after pediatric stroke, adjusting for parental age and ADHD in first-degree relatives.

RESULTS: Of 1320 children with stroke included in the analysis (701 boys [53.1%]), 75 (45 boys [60.0%]) were diagnosed with ADHD after stroke compared with 376 (252 boys [67.0%]) among the controls (aHR, 2.00 [95% CI, 1.54-2.60]). The risk was increased after both perinatal (aHR, 2.75 [95% CI ,1.65-4.60]) and childhood (aHR, 1.82 [95% CI, 1.34-2.48]) strokes and were similar if children born preterm or small for gestational age were excluded. Compared with controls, risks of ADHD were higher among children with perinatal stroke and adverse motor outcomes and/or epilepsy (aHR, 6.17 [95% CI, 2.80-13.62]) than among those without these comorbidities (aHR, 1.65 [95% CI, 0.80-3.42]). However, findings were similar in

childhood stroke for children with adverse motor outcomes and/or epilepsy (aHR, 1.80 [95% CI, 1.12-2.89]) and among those without these comorbidities (aHR, 1.92 [95% CI, 1.28-2.90]).
CONCLUSIONS AND RELEVANCE: This cohort study of 1320 children with pediatric ischemic stroke suggests that there is an increased risk of ADHD, particularly in children with adverse motor outcomes and/or epilepsy, compared with controls. The risk increases after childhood strokes regardless of comorbidities

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JAMA Netw Open. 2022 Apr;5:e227503.
ASSOCIATION OF MATERNAL AUTOIMMUNE DISEASES WITH RISK OF MENTAL DISORDERS IN OFFSPRING IN DENMARK.
He H, Yu Y, Liew Z, et al.
IMPORTANCE: Maternal immune activation during pregnancy is associated with increased risks of several mental disorders in offspring during childhood, but little is known about how maternal autoimmune diseases during pregnancy are associated with mental health in offspring during and after childhood.
OBJECTIVE: To investigate the association between maternal autoimmune diseases before childbirth and risk of mental disorders among offspring up to early adulthood.
DESIGN, SETTING, AND PARTICIPANTS: This population-based nationwide cohort study used data from Danish national registers on singletons born in Denmark from 1978 to 2015 with up to 38 years of follow-up. Data analyses were conducted from March 1, 2020, through September 30, 2021. EXPOSURES: Maternal autoimmune disease diagnosed before or during pregnancy according to the Danish National Patient Register.
MAIN OUTCOMES AND MEASURES: The main outcome was mental disorders, defined by hospital diagnoses, in offspring. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% CIs for mental disorders.
RESULTS: Of the 2 254 234 singleton infants included in the study (median age, 16.7 years [IQR, 10.5-21.7 years]; 51.28% male), 2.26% were born to mothers with autoimmune diseases before childbirth. Exposed participants had an increased risk of overall mental disorders compared with their unexposed counterparts (HR, 1.16; 95% CI, 1.13-1.19; incidence, 9.38 vs 7.91 per 1000 person-years). Increased risks of overall mental disorders in offspring were seen in different age groups for type 1 diabetes (1-5 years: HR, 1.35 [95% CI, 1.17-1.57]; 6-18 years: HR, 1.24 [95% CI, 1.15-1.33]; >18 years: HR, 1.19 [95% CI, 1.09-1.30]) and rheumatoid arthritis (1-5 years: HR, 1.42 [95% CI, 1.16-1.74]; 6-18 years: HR, 1.19 [95% CI, 1.05-1.36]; >18 years: HR, 1.28 [95% CI, 1.02-1.60]). Regarding specific mental disorders, increased risk after exposure to any maternal autoimmune disorder was observed for organic disorders (HR, 1.54; 95% CI, 1.21-1.94), schizophrenia (HR, 1.35; 95% CI, 1.21-1.51), obsessive-compulsive disorder (HR, 1.42; 95% CI, 1.24-1.63), mood disorders (HR, 1.12; 95% CI, 1.04-1.21), and a series of neurodevelopmental disorders (eg, childhood autism [HR, 1.21; 95% CI, 1.08-1.36] and attention-deficit/hyperactivity disorder [HR, 1.19; 95% CI, 1.12-1.26]).
CONCLUSIONS AND RELEVANCE: In this cohort study in Denmark, prenatal exposure to maternal autoimmune diseases was associated with increased risks of overall and type-specific mental disorders in offspring. Maternal type 1 diabetes and rheumatoid arthritis during pregnancy were associated with offspring's mental health up to early adulthood. Individuals prenatally exposed to autoimmune disease may benefit from long-term surveillance for mental disorders

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J Child Psychol Psychiatry. 2022 Apr;63:484-96.
ANNUAL RESEARCH REVIEW: ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN GIRLS AND WOMEN: UNDERREPRESENTATION, LONGITUDINAL PROCESSES, AND KEY DIRECTIONS.
Hinshaw SP, Nguyen PT, O'Grady SM, et al.
Attention-deficit/hyperactivity disorder (ADHD)—and its underlying behavioral dimensions of inattention and hyperactivity–impulsivity—have been understudied in females. We first cover the conceptual issues of prevalence, diagnostic practices, diversity, comorbidity, and causal factors, plus forces limiting awareness of ADHD in females. After a narrative review of cross-sectional and longitudinal findings, we conclude the following. (a) Girls meet diagnostic criteria for ADHD at just under half the rates of boys, a ratio that becomes

much closer to equal by adulthood. (b) Girls and women with ADHD show a predominance of inattention and associated internalizing problems; boys and men display greater levels of hyperactive–impulsive symptoms and associated externalizing problems. (c) Sex differences in ADHD symptoms and related outcomes depend heavily on the clinical versus nonreferred nature of the samples under investigation. (d) Females with ADHD experience, on average, serious impairments, with a particularly heightened risk for problems in close relationships and engagement in self-harm. (e) Clinicians may overlook symptoms and impairments in females because of less overt (but still impairing) symptom manifestations in girls and women and their frequent adoption of compensatory strategies. Our review of predictors and mediators of adult outcomes highlights (a) the potential for heterotypically continuous pathways in females with childhood ADHD and (b) developmental progressions to self-harm, intimate partner violence, unplanned pregnancy, and comorbid psychopathology. Focusing on ADHD in females is necessary to characterize causal and maintaining mechanisms with accuracy and to foster responsive interventions, as highlighted in our closing list of clinical implications and research priorities

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J Child Psychol Psychiatry. 2022 Apr;63:497-99.

ADHD IN GIRLS AND WOMEN: A CALL TO ACTION – REFLECTIONS ON HINSHAW ET AL (2021).

Chronis-Tuscano A.

Comments on an article by S. P. Hinshaw et al. (see record [rid]2021-67712-001[/rid]). This is a commentary on Hinshaw, Nguyen, O'Grady & Rosenthal's 'ADHD in Girls and Women: Underrepresentation, Longitudinal Processes, and Key Directions', which reviews the empirical literature on female-specific impairments, mechanisms and developmental pathways. Having conducted one of the most prominent and informative longitudinal investigations of girls with and without ADHD, Hinshaw et al. (2021) provide a compelling synthesis of their findings, highlighting research and clinical priorities. In this commentary, I highlight the pernicious effects of unrecognized and untreated ADHD in girls and women, challenges of making an accurate differential diagnosis and the need to raise awareness among health professionals, educators and parents about the clinical presentation of girls with ADHD in order to achieve earlier identification and intervention that can interrupt the developmental trajectory to widespread impairment, comorbidity and, in some cases, devastating outcomes

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J Child Psychol Psychiatry. 2022 Apr;63:421-43.

ANNUAL RESEARCH REVIEW: TRANSLATIONAL MACHINE LEARNING FOR CHILD AND ADOLESCENT PSYCHIATRY.

Dwyer D, Koutsouleris N.

Children and adolescents could benefit from the use of predictive tools that facilitate personalized diagnoses, prognoses, and treatment selection. Such tools have not yet been deployed using traditional statistical methods, potentially due to the limitations of the paradigm and the need to leverage large amounts of digital data. This review will suggest that a machine learning approach could address these challenges and is designed to introduce new readers to the background, methods, and results in the field. A rationale is first introduced followed by an outline of fundamental elements of machine learning approaches. To provide an overview of the use of the techniques in child and adolescent literature, a scoping review of broad trends is then presented. Selected studies are also highlighted in order to draw attention to research areas that are closest to translation and studies that exhibit a high degree of experimental innovation. Limitations to the research, and machine learning approaches generally, are outlined in the penultimate section highlighting issues related to sample sizes, validation, clinical utility, and ethical challenges. Finally, future directions are discussed that could enhance the possibility of clinical implementation and address specific questions relevant to the child and adolescent psychiatry. The review gives a broad overview of the machine learning paradigm in order to highlight the benefits of a shift in perspective towards practically oriented statistical solutions that aim to improve clinical care of children and adolescents

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J Neural Transm. 2022 Apr;129:431-39.

MEF2C GENE VARIATIONS ARE ASSOCIATED WITH ADHD IN THE CHINESE HAN POPULATION: A CASE–CONTROL STUDY.

Fu X, Yao T, Chen X, et al.

Myocyte enhancer factor 2C (MEF2C) is associated with hyperactivity and might be a novel risk gene for susceptibility to attention deficit hyperactivity disorder (ADHD). Therefore, this study aimed to explore the association between MEF2C genetic variants and ADHD in the Chinese Han population. A total of 215 patients with ADHD and 233 controls were recruited for this study. The Swanson, Nolan, and Pelham version IV questionnaire was used to evaluate the clinical features of ADHD. In silico analysis was used to annotate the biological functions of the promising single nucleotide polymorphisms. Our findings indicated that MEF2C rs587490 was significantly associated with ADHD in the multiplicative model (OR = 0.640, p = 0.002). Participants with the rs587490 TT allele exhibited less hyperactivity/impulsivity than those with the rs587490 CC allele. Furthermore, the expression quantitative trait loci analysis suggested that rs587490 could regulate the gene expression of MEF2C in the hippocampus, putamen, thalamus, and frontal white matter. Our study concluded that the MEF2C rs587490 T allele is significantly associated with a reduced risk of ADHD in the Chinese Han population, which provides new insight into the genetic etiology of ADHD

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Neuropsychology. 2022 Apr.

VISUOSPATIAL WORKING MEMORY IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: CHARACTERIZING PATH LENGTH AND PATH CROSSINGS AS MECHANISMS OF IMPAIRMENT.

Arrington EF, Alderson RM, Tarle SJ, et al.

Objective: A growing body of research provides reliable evidence of moderate to large magnitude deficits in the visuospatial (VS) working memory (WM) of children with attention-deficit/hyperactivity disorder (ADHD), relative to typically developing (TD) children. Studies of ADHD-related Visuo-spatial Working Memory (VS-WM) functioning most often present sequential presentations of VS stimuli and examine general performance characteristics. Only a few studies have examined the effects of varying VS-WM task parameters on performance in children with ADHD, despite evidence from basic-cognitive research that indicates methodological heterogeneity in VS-WM task parameters yields significant performance variability that is associated with underlying mechanistic processes. This study is the first to examine the effect of the task parameters path characteristics and path crossings on performance in children with ADHD and TD children.
Method: School-aged children with ADHD (n = 50) and TD children (n = 59) completed a VS-WM task that varied by path lengths and path crossings.
Results: Multilevel analyses indicated a negative effect of relatively long paths on VS-WM performance of both TD children and children with ADHD, and a negative effect of increasing path crossings that appears to be unique to TD children and dependent on path length.
Conclusions: Overall, findings appear to suggest that school-aged children engage in dynamic rehearsal of VS information (i.e., mental rehearsal of path sequences), rather than static rehearsal (i.e., rehearsal of a gestalt). Moreover, ADHD-related VS-WM deficits are most likely to yield real-world impairments when information is presented with relatively long path lengths. (PsycInfo Database Record (c) 2022 APA, all rights reserved)
Question: Is the WM of children with and without ADHD affected by varying the representational format of VS information? Findings: Compared to TD children, WM performance of children with ADHD was differentially affected by more complex visual representations. Importance: The findings suggest that children with ADHD may rehearse VS information differently than their neurotypical peers. Next Steps: Further investigate the potential ADHD-specific variation in VS WM using additional proxy measures of rehearsal processes (e.g., eye-tracking, directly asking participants

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Pharmacol Biochem Behav. 2022 May;216:173378.

RODENT MODELS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: AN UPDATED FRAMEWORK FOR MODEL VALIDATION AND THERAPEUTIC DRUG DISCOVERY.

Kantak KM.

There are over twenty rodent models of Attention-Deficit Hyperactivity Disorder (ADHD), with most reflecting a recognized ADHD subtype. Of these, only five rat models (Neonatal 6-Hydroxydopamine, Spontaneously Hypertensive Rat, Prenatal Alcohol Exposure, Prenatal Nicotine Exposure, and Lphn3 Knockout) and three mouse models (Dopamine Transporter Knockout, Neurokinin-1 Receptor Knockout, and Prenatal Nicotine Exposure) have a sufficient number of publications to explore their suitability for modelling ADHD with respect to core features, executive dysfunction, and medication effects. An updated view is advanced specifying that an informative model encompasses elevated drug use risk as a means to assess ADHD/Substance Use Disorder (SUD) comorbidity, a common co-occurrence among patients. Based on the full range of symptoms and medication effects, it is concluded that the Spontaneously Hypertensive Rat (specifically the Charles River Laboratories substrain) has the most translational support at this stage to model ADHD/SUD comorbidity. The Lphn3 knockout rat model and the prenatal nicotine exposure mouse model are strong contenders if additional validation work is performed, as they have a high degree of construct validity pertaining to genetic and environmental etiologies of ADHD. Research using validated rodent models of ADHD is warranted because their study can provide insights for drug discovery geared toward the development of safer ADHD therapeutics, particularly for adolescent patients

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Psychiatr Danub. 2022;34:96-99.

SOCIAL COMMUNICATION DISORDER IN AN ADOLESCENT WITH ADHD AND TOURETTE'S DISORDER TREATED WITH ARIPIPRAZOLE.

Tsai LH, Lin JW, Lee MC.

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Psychiatr Danub. 2022;34:51-56.

SERUM TUMOR NECROSIS FACTOR-LIKE WEAK INDUCER OF APOPTOSIS (TWEAK) LEVELS ARE DECREASED IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Isik Ü, et al.

INTRODUCTION: There has been no study in the literature evaluating serum tumor necrosis factor-like weak inducer of apoptosis (TWEAK) levels in attention-deficit/hyperactivity disorder (ADHD). Therefore, we performed the present study to specifically measure serum TWEAK levels to see whether or not its eventual alterations might have an etiopathogenetic significance in children with ADHD.

SUBJECTS AND METHODS: A total of 49 treatment-naive children with ADHD and 39 healthy controls were included in the present study. The severities of ADHD and conduct disorder symptoms were assessed via parent- and teacher-rated questionnaires. Venous blood samples were collected, and serum TWEAK levels were measured.

RESULTS: Serum TWEAK levels of the ADHD group were significantly lower than the control group.

CONCLUSIONS: This study shows that ADHD patients have decreased serum TWEAK levels, suggesting a possible involvement of TWEAK in the etiopathogenesis of ADHD

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Res Dev Disabil. 2022 Jun;125:104220.

THE FACTOR STRUCTURE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN SCHOOLCHILDREN.

Arildskov TW, Virring A, Lambek R, et al.

BACKGROUND: Most studies support a bifactor model of childhood ADHD with two specific factors. However, several studies have not compared this model with a bifactor model with three specific factors, few have tested the actual strength of the factors, and none have examined whether "talks excessively" should be treated as a hyperactivity versus impulsivity symptom in children with ADHD. AIMS: To examine the factor structure of ADHD symptoms and evaluate the relative strength of potential factors.

METHODS: Parent-reports on the ADHD-Rating Scale (ADHD-RS-IV) were collected for 2044 schoolchildren from the general population and 147 children with ADHD from a clinical sample. Single-, two- and three-(correlated and bi-)factor models were tested using confirmatory factor analysis.
RESULTS: Most models had a satisfactory fit. However, a correlated three-factor model where "talks excessively" was included as an indicator of impulsivity, and especially a bifactor model with one strong, well-defined general and two/three (ICD-10 defined) weak specific factors fit the data slightly better than the remaining models.
CONCLUSIONS: The factor structure is best characterized by a bifactor model with a strong general factor and two/three weaker specific factors. Therefore, we suggest emphasizing the ADHD-RS-IV total score rather than the subscale scores in clinical practice

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Research on Child and Adolescent Psychopathology. 2022 Apr;50:417-30.
EVIDENCE-BASED TREATMENTS IN COMMUNITY MENTAL HEALTH SETTINGS: USE AND CONGRUENCE WITH CHILDREN'S PRIMARY DIAGNOSIS AND COMORBIDITY.
Lee P, Lang JM, Vanderploeg JJ, et al.
Many evidence-based treatments (EBTs) have been identified for specific child mental health disorders, but there is limited research on the use of EBTs in community-based settings. This study used administrative data from a statewide system of care to examine 1) the extent to which EBTs were provided congruent with the child's primary diagnosis, 2) whether there were differences in effectiveness of EBTs that were congruent or incongruent with the child's primary diagnosis, and 3) whether comorbidity moderated the effectiveness of EBTs for children based on congruence with their primary diagnosis. The sample consisted of 23,895 children ages 3–17 with at least one of the most common diagnoses (attention-deficit/hyperactivity disorder, conduct problems, depressive disorders, anxiety disorders, and post-traumatic stress disorder) who received outpatient psychotherapy. Data were collected as part of routine care, including child demographic characteristics, diagnosis, treatment type, and problem severity. Forty-two percent of children received an EBT congruent with their diagnosis, and these children showed greater improvement than the 35% of children who received no EBT (ES = 0.14–0.16) or the 23% who received an EBT incongruent with their diagnosis (ES = 0.06–0.15). For children with comorbid diagnoses, the use of EBTs congruent with the primary diagnosis was also associated with the greatest improvement, especially when compared to no EBT (ES = 0.22–0.24). Results of the current study support the use of EBTs in community-based settings, and suggest that clinicians should select EBTs that match the child's primary diagnosis to optimize treatment outcomes, especially for children with comorbidity

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Research on Child and Adolescent Psychopathology. 2022 Apr;50:463-75.
FEATURE BINDING AND WORKING MEMORY IN CHILDREN WITH ADHD: EVIDENCE OF EPISODIC BUFFER IMPAIRMENT.
Alderson RM, Tarle SJ, Roberts DK, et al.
Previous examinations of working memory impairments in children with attention-deficit/hyperactivity disorder (ADHD) have predominantly focused on discreet visuospatial and phonological subsystem processes, as well as the domain-general central executive. The episodic buffer component of working memory, a neurocognitive process that allows for temporary storage and maintenance of bound episodes/features of information, is understudied in ADHD and initial findings have been equivocal. Heterogeneity in previous findings may reflect between-study methodological variability, floor effects unrelated to episodic buffer processes (i.e., excessive central executive demands), and limitations associated with previous investigations' use of novel paradigms. This study examined ADHD-related episodic buffer processing via an established paradigm (Allen et al., 2006) in well-defined groups of children with attention-deficit/hyperactivity disorder (ADHD) and typically developing peers (TD). Seventy-one children (ADHD n = 34, TD n = 37) aged 8–12 years (M = 9.81, SD = 1.50; 32% female) completed two conditions of a computerized working memory task that presented single feature stimuli (color and shape), and a third condition that presented dual-feature stimuli (color/shape binding). Overall, the ADHD group exhibited a large-magnitude deficit during the color/shape binding condition (d = .77), and both groups evinced worse performance accuracy in the color/shape binding condition compared to the single feature color and shape

conditions. Collectively, these findings appear to provide evidence that children with ADHD exhibit large magnitude episodic buffer deficits that are not attributable to visuospatial subsystem or domain-general central executive processes

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Research on Child and Adolescent Psychopathology. 2022 Apr;50:447-62.

SLOW CORTICAL POTENTIAL VERSUS LIVE Z-SCORE NEUROFEEDBACK IN CHILDREN AND ADOLESCENTS WITH ADHD: A MULTI-ARM PRAGMATIC RANDOMIZED CONTROLLED TRIAL WITH ACTIVE AND PASSIVE COMPARATORS.

Hasslinger J, Bölte S, Jonsson U.

Neurofeedback (NF) as a treatment for Attention Deficit Hyperactivity Disorder (ADHD) has been evaluated in several trials, but the specificity and generalizability of effects remain unclear. This four-arm randomized controlled trial evaluated the efficacy of Slow Cortical Potential (SCP; standard NF protocol) and Live Z-score (LZS; non-standard NF protocol) delivered in high-frequency format (five sessions per week during five weeks), compared to Working-memory training (WMT; active comparator) and Treatment-as-usual (TAU; passive comparator). N = 202 children/adolescents aged 9 to 17 years with ADHD participated. The primary outcome measure was multi-report (self-, teacher-, and parent-report) ADHD core symptoms on the Conners-3, assessed at baseline, posttreatment, and 6-months follow-up. Data were analyzed using a linear mixed model. Between-group differences were scarce and did not show a distinct pattern. Superiority of LZS over TAU at endpoint were observed for teacher-rated measures only, while significant differences between SCP and TAU were restricted to posttreatment measurements. Contrary to our expectations, LZS outperformed SCP at endpoint for teacher-rated hyperactivity (-5.37; 95% CI: -10.14 to -0.60; p = .028; d = -.36) and overall ADHD symptoms (-2.20; -4.18 to -0.22; p = .030; d = -.41). There was no indication that either form of NF was superior to WMT. No severe adverse events were reported during the trial, whereas transient stress-related problems were quite frequent. Overall, the results from this pragmatic trial do not provide convincing support for broad implementation of NF in child and adolescent psychiatric services. Future research should try to clarify for whom and under what circumstances NF might be a viable treatment option

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Sci Rep. 2022 May;12:7295.

SPARSE REPRESENTATIONS OF HIGH DIMENSIONAL NEURAL DATA.

Mody SK, Rangarajan G.

Conventional Vector Autoregressive (VAR) modelling methods applied to high dimensional neural time series data result in noisy solutions that are dense or have a large number of spurious coefficients. This reduces the speed and accuracy of auxiliary computations downstream and inflates the time required to compute functional connectivity networks by a factor that is at least inversely proportional to the true network density. As these noisy solutions have distorted coefficients, thresholding them as per some criterion, statistical or otherwise, does not alleviate the problem. Thus obtaining a sparse representation of such data is important since it provides an efficient representation of the data and facilitates its further analysis. We propose a fast Sparse Vector Autoregressive Greedy Search (SVARGS) method that works well for high dimensional data, even when the number of time points is relatively low, by incorporating only statistically significant coefficients. In numerical experiments, our methods show high accuracy in recovering the true sparse model. The relative absence of spurious coefficients permits accurate, stable and fast evaluation of derived quantities such as power spectrum, coherence and Granger causality. Consequently, sparse functional connectivity networks can be computed, in a reasonable time, from data comprising tens of thousands of channels/voxels. This enables a much higher resolution analysis of functional connectivity patterns and community structures in such large networks than is possible using existing time series methods. We apply our method to EEG data where computed network measures and community structures are used to distinguish emotional states as well as to ADHD fMRI data where it is used to distinguish children with ADHD from typically developing children

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Sci Rep. 2022 Apr;12:6072.

BEHAVIOURAL AND NEURAL INDICES OF PERCEPTUAL DECISION-MAKING IN AUTISTIC CHILDREN DURING VISUAL MOTION TASKS.

Manning C, Hassall CD, Hunt LT, et al.

Many studies report atypical responses to sensory information in autistic individuals, yet it is not clear which stages of processing are affected, with little consideration given to decision-making processes. We combined diffusion modelling with high-density EEG to identify which processing stages differ between 50 autistic and 50 typically developing children aged 6-14 years during two visual motion tasks. Our pre-registered hypotheses were that autistic children would show task-dependent differences in sensory evidence accumulation, alongside a more cautious decision-making style and longer non-decision time across tasks. We tested these hypotheses using hierarchical Bayesian diffusion models with a rigorous blind modelling approach, finding no conclusive evidence for our hypotheses. Using a data-driven method, we identified a response-locked centro-parietal component previously linked to the decision-making process. The build-up in this component did not consistently relate to evidence accumulation in autistic children. This suggests that the relationship between the EEG measure and diffusion-modelling is not straightforward in autistic children. Compared to a related study of children with dyslexia, motion processing differences appear less pronounced in autistic children. Exploratory analyses also suggest weak evidence that ADHD symptoms moderate perceptual decision-making in autistic children

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Sci Rep. 2022 Apr;12:6932.

A NATIONWIDE COHORT STUDY ON THE RISK OF ADHD IN CHILDREN WITH AMBLYOPIA MEDIATED BY FINE MOTOR SKILL IMPAIRMENT IN EAST ASIA.

Kim M, Lee S, Lee JE, et al.

This national administrative investigation of Republic of Korea compared the risk of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders(ASD) in preschool amblyopic children and identified factors that possibly mediate this association. After propensity score (PS) matching, 7762 amblyopic children and 31,030 non-amblyopic children were included. Amblyopia was associated with ADHD (aOR:1.687; 95% CI 1.444, 1.970) but not with ASD (aOR: 0.591; 95% CI 0.341, 1.026). Fine motor skill impairment was a mediating factor in association of amblyopia with ADHD, accounting for 4.2% (95% CI 1.7, 8.0). In conclusion, amblyopic children have a greater risk of ADHD, and deficits in fine motor skills mediate this association. We suggest increased attention given to fine motor skill underdevelopment in amblyopic children to prevent the development of ADHD

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The Clinical Neuropsychologist. 2022 Apr;36:664-98.

SPONTANEOUS AGE-RELATED CHANGES OF ATTENTION IN UNMEDICATED BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Erdogan Bakar E, Karakas S.

Objective: Neuropsychological, neuroanatomical, and electrophysiological studies have reported a steady increase in the different attention types until the age of 10 years. Moreover, differences between healthy control (HC) boys and those with attention deficit hyperactivity disorder (ADHD) become nonsignificant in late childhood. This cross-sectional study aimed to perform a comparative analysis of attentional processing in boys with ADHD and HC in the 6:00-10:11 years age range.

Methods: Age-related changes in attentional processing were compared between Caucasian Turkic boys (72-131 months of age) with ADHD (n = 144) and HC (n = 112). Selective, focused, and inhibitory attention were measured using the Stroop Test (5 scores); sustained attention was measured using the Cancellation Test (3 scores); and attention span was measured using the Visual Aural Digit Span Test-Revised (6 scores).

Results: At the age of 6 years, the ADHD group had a significantly lower performance for all attention types. By the age of 10 years, there were no significant between-group differences. However, the component structure of the neuropsychological test scores in the ADHD group differed from that in the HC group and previous studies.

Conclusions: Attentional processing in boys with ADHD changes within the age-range of 6:00-10:00 years where it finally becomes similar to that in HC boys. This delayed maturation is consistent with the maturational lag model of ADHD. However, there was a between-group difference in the component structure of attentional processing, which is consistent with the maturational deviance model of ADHD

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Transl Psychiatry. 2022 Apr;12:165.

TRANSCUTANEOUS ELECTRICAL ACUPOINT STIMULATION FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CLINICAL TRIAL.

Zhuo L, Zhao X, Zhai Y, et al.

Little is known about the effects of transcutaneous electrical acupoint stimulation (TEAS) for children with attention-deficit/hyperactivity disorder (ADHD). Here, we carried out a 4 week randomized clinical trial in which patients aged 6-12 years old with an ADHD diagnosis received TEAS or sham TEAS. The primary outcome measure was the investigator-rated Clinical Global Impression-Improvement (CGI-I) score at week 4. Secondary outcomes included changes from baseline to week 4 in the investigator-rated Clinical Global Impression-Severity of Illness (CGI-S) score, the Conners' Parent/Teacher Rating Scales-Revised: Short Form (CPRS-R: S/CTRS-R: S) score, go/no-go task performance, and functional near-infrared spectroscopy (fNIRS)-based oxygenated hemoglobin level within the prefrontal cortex. At week 4, the CGI-I score indicated improvement in 33.3% of the TEAS group compared with 7.7% of the sham group (P = 0.005). The TEAS group had a greater decrease in the mean CGI-S score (-0.87) than the sham TEAS group (-0.28) (P = 0.003). A greater enhancement in the mean cerebral oxygenated hemoglobin within the prefrontal cortex was found in the TEAS group (0.099 mM mm) compared with the sham TEAS group (0.005 mM mm) (P < 0.001). CPRS-R: S score, CTRS-R: S score, and go/no-go performance exhibited no significant improvement after TEAS treatment. The manipulation-associated adverse events were uncommon in both groups, and events were very mild. Our results show that noninvasive TEAS significantly improved general symptoms and increased prefrontal cortex blood flow within 4 weeks for children with ADHD. Further clinical trials are required to understand the long-term efficacy in a larger clinical sample. This trial was registered on ClinicalTrials.gov (NCT03917953)

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Trials. 2022 Apr;23:291.

THE IMPACT OF SESSION-INTRODUCING MINDFULNESS AND RELAXATION INTERVENTIONS IN INDIVIDUAL PSYCHOTHERAPY FOR CHILDREN AND ADOLESCENTS: A RANDOMIZED CONTROLLED TRIAL (MARS-CA).

Kalmar J, Baumann I, Gruber E, et al.

BACKGROUND: The investigation of mindfulness-based interventions (MBIs) in cognitive-behavioral therapy has greatly increased over the past years. However, most MBI research with youth focuses on structured, manualized group programs, conducted in school settings. Knowledge about the implementation and effects of MBIs in individual psychotherapy with children and adolescents is scarce. To fill this research gap, the "Mindfulness and Relaxation Study - Children and Adolescents" (MARS-CA) is designed. It aims to assess the effects of short session-introducing interventions with mindfulness elements on juvenile patients' symptomatic outcome and therapeutic alliance in individual child and adolescent psychotherapy.

METHODS: MARS-CA is conducted at a university outpatient training center for cognitive-behavior therapy. Short session-introducing interventions with mindfulness elements will be compared to short session-introducing relaxation interventions and no session-introducing intervention to explore their effects on symptomatic outcome and therapeutic alliance. The session-introducing interventions will take place at the beginning of 24 subsequent therapy sessions. We hypothesize that patients' symptomatic outcome and therapeutic alliance improve more strongly in the mindfulness condition than in the other two conditions and that the mindfulness condition moderates the relationship between therapeutic alliance and symptomatic outcome. Patients and their trainee therapists will be randomized to one of the three treatment arms. Participants aged between 11 and 19years and having a primary diagnosis of either a depressive disorder, an anxiety disorder, or a hyperkinetic disorder will be included. Therapeutic alliance will be assessed after every therapy session (therapy session 1 to therapy session 24), symptomatic outcome will be assessed before the start of treatment (pre), after the 3rd, the 10th, and the 17th therapy sessions, at the end of

treatment (24th therapy session, post), and at a 6-month follow-up. Additionally, mindfulness and mindfulness-related measures as well as demographic data, adherence, allegiance, and therapeutic techniques will be assessed. It is our aim to assess a sample of 135 patients. We will conduct multilevel modeling to address the nested data structure.
DISCUSSION: The study can provide information about how add-on MBIs, conducted by trainee therapists, influence therapeutic alliance and symptomatic outcome in individual psychotherapy in children and adolescents.
TRIAL REGISTRATION: ClinicalTrials.gov NCT04034576. Registered on July 17, 2019

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Zh Nevrol Psikhiatr Im S S Korsakova. 2022;122:75-86.
RESULTS OF A MULTICENTRE DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED CLINICAL TRIAL EVALUATING THE EFFICACY AND SAFETY OF MEXIDOL IN THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN (MEGA).
Zavadenko NN, Suvorinova NY, Batysheva TT, et al.
OBJECTIVES: To evaluate the efficacy and safety of two dosing regimens of Mexidol film-coated tablets, 125 mg (Â«RPC «PHARMASOFT» LLC Russia), compared with placebo in children with attention deficit hyperactivity disorder (ADHD) aged 6 to 12 years.
MATERIAL AND METHODS: A multicenter randomized, double-blind, placebo-controlled study in 3 parallel groups was conducted in 14 clinical centres of the Russian Federation to assess efficacy and safety of Mexidol film-coated tablets, 125 mg («RPC «PHARMASOFT» LLC Russia) in the treatment of attention deficit hyperactivity disorder (ADHD) in children 6-12 years old with different dosing regimens. The study involved 333 boys and girls aged 6 to 12 years with a confirmed diagnosis of ADHD established in accordance with ICD-10 and DSM-5 criteria. After screening (up to 14 days) the patients were randomised into 3 treatment groups in a 1:1:1: Mexidol 125 mg 2 times daily, Mexidol 125 mg daily+placebo and the placebo group. The duration of treatment in all groups was 42 days. 332 children completed the study. ADHD and comorbid disorders assessment scales were used.
RESULTS: There were statistically significant changes in the sum of the total scores on the SNAP-IV inattention and hyperactivity/impulsivity subscales after 6 weeks of therapy in all three study groups ($p<0.05$). There were statistically significant differences between the Mexidol 125 mg and placebo groups and between the Mexidol 125 mg 2 times daily and placebo groups (for the PP population: $p=0.000308$ and $p=0.000024$, respectively; for the FAS population: $p=0.000198$ and $p=0.000024$, respectively), indicating that Mexidol therapy is superior to placebo. Statistically significant differences ($p<0.05$) were also obtained for most of the secondary efficacy criteria (average change in SNAP-IV inattention subscale score, average change in SNAP-IV hyperactivity/impulsivity subscale score, average change in SNAP-IV subscale score - Conners index, average change in ADHD-RS-IV score, change in CGI-ADHD-S scores, change in CGI-I score - the Clinical Global Impressions Scale - Improvement) when comparing Mexidol therapy with placebo. The results of statistical analysis of the incidence of adverse events, laboratory values, physical examination show no significant differences between the compared groups in the main safety parameters.
CONCLUSIONS: The regimen of Mexidol, 125 mg film-coated tablets twice daily has been shown to be superior to the regimen of Mexidol, 125 mg film-coated tablets once daily and placebo. The safety profiles of the studied dosing regimens of Mexidol and placebo were comparable

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International Journal of
Environmental Research and Public Health

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Study Protocol

Comparing the Effect of Methylphenidate and Anodal tDCS on Inhibitory Control and Working-Memory in Children and Adolescents with Attention Deficit/Hyperactivity Disorder: A Study Protocol for a Randomized, within-Subject Trial

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Abstract: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by inappropriate levels of attention, hyperactivity, and impulsivity that interfere with individual functioning. The international guidelines recommend targeting ADHD-related neurochemical brain abnormalities by intervening via drug treatment, such as methylphenidate (MPH), as first choice. Drug treatments are usually associated with a huge amount of cost for families and the healthcare system, suspension for low compliance, poor long-term efficacy, and side effects. Transcranial direct current stimulation (tDCS) has been suggested as a possible noninvasive means to safely manipulate brain activity and, in turn, improve behavior and cognition in developmental ages. Several studies have shown that tDCS has the potential to improve ADHD-related cognitive deficits, but the effect of tDCS compared with MPH has never been evaluated. The aim of the present within-subject, sham-controlled, randomized proof-of-concept study is to demonstrate the positive effect of one-session anodal tDCS analogous to the MPH drug on inhibitory control and working memory in children and adolescents with ADHD. We strongly believe that this study protocol will serve to accelerate research into low-cost, drug-free, feasible interventions for ADHD.

Keywords: MPH; drug treatments; transcranial direct current stimulation; executive functions; evidence-based medicine

Citation: D'Aiello, B.; Battisti, A.; Lazzaro, G.; Pani, P.; De Rossi, P.; Di Vara, S.; Pretelli, I.; Costanzo, F.; Vicari, S.; Menghini, D. Comparing the Effect of Methylphenidate and Anodal tDCS on Inhibitory Control and Working-Memory in Children and Adolescents with Attention Deficit/Hyperactivity Disorder: A Study Protocol for a Randomized, within-Subject Trial. *Int. J. Environ. Res. Public Health* **2022**, *19*, 4575. https://doi.org/10.3390/ijerph19084575

Academic Editors: Regina Lee, Michael Brown, Wai Tong Chien and Sally Chan

Received: 8 February 2022
Accepted: 6 April 2022
Published: 11 April 2022

1. Introduction

Emerging during childhood, attention deficit/hyperactivity disorder (ADHD) is one of the most common lifelong brain-based disorders characterized by a mixture of inappropriate levels of inattention and/or hyperactivity/impulsivity [1]. With a prevalence of ~2–7% worldwide, it significantly interferes with or reduces the quality of academic, social, or occupational functioning. Patients with ADHD frequently suffer from psychiatric comorbid conditions such as rule-breaking behaviors, substance use disorders, and mood and anxiety disorders that become more and more of a problem during adolescence and even more so in adulthood. The clinical phenotype of ADHD is also commonly associated with a range of neurocognitive dysfunctions involving atypical responses to reward/punishment contingencies, pronounced aversion to the experience of delay, attentional fluctuation, and sluggish cognitive processing speed [2].

Several studies have attributed the symptoms of ADHD primarily to a deficit in executive functions, especially working memory (WM), response inhibition, and set shifting [3–8]. Executive dysfunctions are critically dependent on the prefrontal cortex and can result from dysregulated catecholaminergic neurotransmission in the basal ganglia-thalamocortical circuit [9–15]. Pharmacological interventions that modulate the dysregulated catecholaminergic neurotransmission are recommended by the international guidelines (ESCAP European Guidelines), and psychostimulants, first, methylphenidate (MPH), are indicated as first-line treatment for ADHD. More than 150 randomized placebo-controlled clinical trials promote MPH as one of the most effective treatments for alleviating behavioral and cognitive symptoms, as well as for improving life outcomes in school-aged children with ADHD. Nevertheless, about 30% of patients with ADHD do not respond well to medications, show side effects, no long-term effects [16,17], and, in adolescence, adhere to treatment poorly [18]. In addition, the critical attitude of parents to pharmacotherapy pushes them to consider other treatment options, such as cognitive behavioral therapy, which however produces modest effects [19]. Last, the cost of pharmacological interventions has a huge impact on the healthcare system.

Transcranial direct current stimulation (tDCS) has been suggested as a promising technique to scaffold the key dysfunctional brain regions associated with ADHD, with the potential to alleviate the symptoms and the related cognitive deficits [20–24]. By placing electrodes on the scalp, tDCS generates subthreshold polarity-dependent shifts in resting membrane potentials in underlying brain regions, inducing neuroplastic aftereffects lasting for over an hour [25,26]. When combined with a stimulus or a task, tDCS can improve synaptic transmission and empower the synaptic strength effect of the neural networks activated by concomitant activities [27]. Results documented that even one anodal-tDCS session over left DLPFC causes positive effects on inhibitory control and WM compared to placebo conditions [28,29].

Considering safety, several studies have demonstrated that tDCS induces minimal side effects, which are summarized as mild tingling and itching sensations under the electrodes, predominantly in the first few seconds of the stimulation session [21,27]. A recent systematic review [30] confirmed no serious adverse effects after 747 sessions of tDCS in patients with ADHD, supporting the safety and feasibility of this technique.

With these premises, tDCS could be promoted as a valid alternative approach to drug-based treatment that may improve cognition, as well as prompt greater adherence and reduce side effects compared to pharmacological interventions [31]. To date, only 14 studies have investigated the use of tDCS on patients with ADHD [22].

To the best of our knowledge, studies that directly compare the effect of brain-based intervention (i.e., tDCS) and treatment as usual (i.e., MPH) on executive functions—especially inhibitory control and WM—are still missing in children and adolescents with ADHD. A detailed reporting of study protocols and procedures would be useful to accelerate the reproducibility of the results and to ensure the soundness of the methods.

Research Objectives

This is a proof-of-concept study that aims at demonstrating the effectiveness of tDCS and MPH in improving executive functions in children and adolescents with ADHD. In particular, the project aims at:

1. Investigating whether one session of anodal tDCS over left DLPFC will improve inhibitory control compared to placebo condition (sham tDCS) and to MPH;
2. Exploring whether one session of anodal tDCS over left DLPFC will enhance WM compared to placebo condition (sham tDCS) and to MPH.

2. Materials and Methods

2.1. Ethical Committee

Ethical approval for the study was granted by the local research ethics committee (process number 2185_OPBG_2020) and was registered at ClinicalTrials.gov (ID: NCT04964427)

on the 13 July 2021. This study will be performed following the Declaration of Helsinki. The protocol adheres to the SPIRIT guidelines (Standard Protocol Items: Recommendations for Interventional Trials).

2.2. Participants

Children and adolescents will be recruited at the Child and Adolescent Neuropsychiatry Unit of the Bambino Gesù Children's Hospital in Rome. All participants and their parents will be fully informed of the procedures and the purpose of the experiment, and the principal investigator will obtain written consent from both parents and the adolescent over the age of 12 before entering the study. Participation will be on a purely voluntary basis. Only patients for whom a clinical indication has already been given for the introduction of drug therapy with MPH and who come to the hospital for the administration of the first test dose will be recruited.

The inclusion criteria will be the following: (1) participants of both genders, diagnosed with severe ADHD (combined presentation) accordingly to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition—DSM-5 [1]; (2) an intelligence quotient (IQ) higher or equal to 85 (IQ $\geq$ 85); (3) age ranging from 8 years to 13 years and 11 months included; (4) having a normal or corrected-to-normal vision; (5) having carried out at least 6 months of psychosocial and psycho-behavioral interventions; and (6) drug naïve and needing drug treatment for the severity of the ADHD symptoms.

The exclusion criteria will include: (1) the presence of neurodevelopmental disorders (i.e., autism spectrum disorders) or specific psychiatric disorders (i.e., bipolar disorders, schizophrenia spectrum disorders, or adjustment disorder) as comorbid conditions; (2) having a history of neurological or medical or genetic conditions; and (3) having a basal medical condition (i.e., heart, kidney, or liver diseases) that may exclude the possibility to administer MPH.

2.3. Study Design

A sham-controlled within-subjects design will be conducted. Clinical eligibility screening (Day 0) will be completed at baseline (see Figure 1). All participants will undergo an extensive neuropsychiatric evaluation in which developmental neuropsychiatrists and psychologists will investigate the cognitive and the adaptive level, the severity of ADHD symptoms, and the presence of comorbid psychiatric disorders. The following design does not involve pharmacological placebo administration as it does not aim to evaluate the effectiveness of pharmacological therapy with MPH in ADHD, which has already been established in numerous studies used for the registration of the drug on the market.

After completing baseline assessment (Day 0), participants will be exposed to three conditions with an intersession-interval of 24 h (Day 1, Day 2, Day 3, see Figure 1): (A) a single shot of active tDCS session; (B) a single shot of sham tDCS session; and (C) a single dose of MPH (Ritalin®) administered according to the National Institute for Clinical Excellence (NICE) guidelines for ADHD (NICE, 2000). The order of the conditions will be counterbalanced across participants. After recruitment, they will be assigned to one of the six possible combinations of the conditions (ABC, ACB, BAC, BCA, CBA, or CAB). We will use the stratified random sampling, based on the participants' characteristics (e.g., age, IQ, and ADHD severity) by means of the minimal sufficient balancing method to prevent imbalances in baseline. The assignment to one of the six possible combinations will be according to a randomization order generated by a computer. The randomization information will be maintained by an independent researcher until the completion of data collection. An emergency code break envelope will be provided to the principal investigator and will only be opened in the case of an emergency, such as a serious adverse event that requires the knowledge of the interventions being taken to manage the participant's condition.

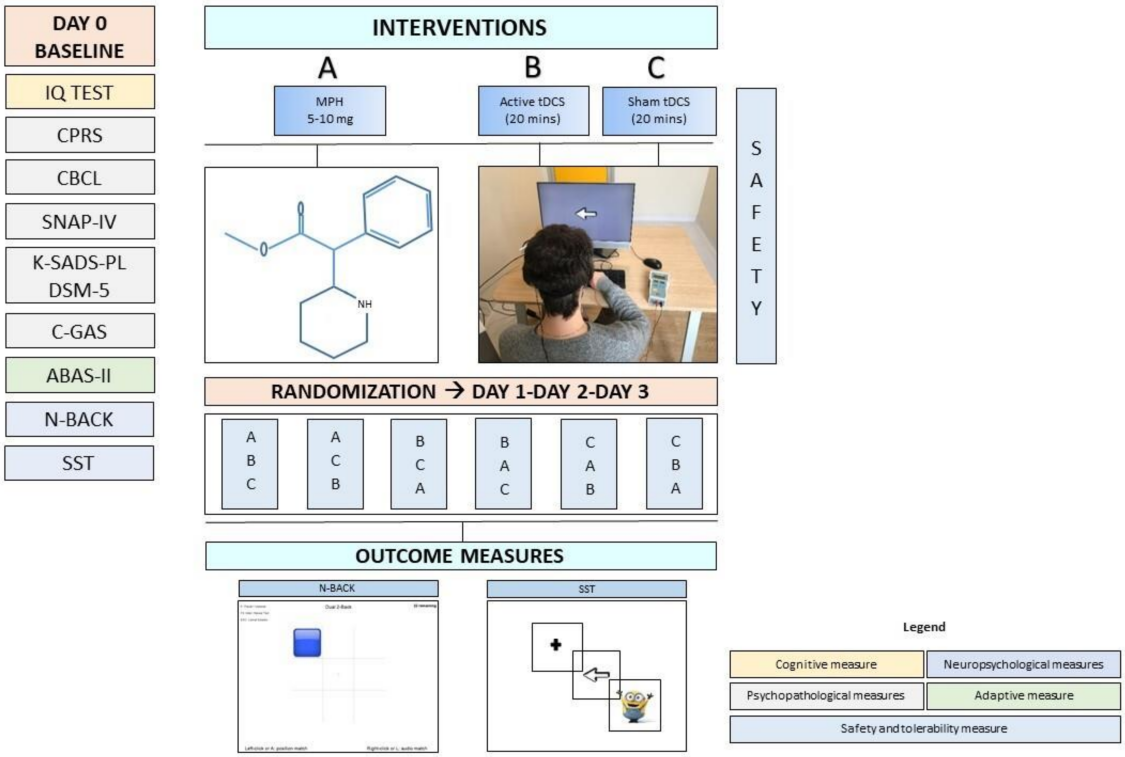

Figure 1. Overview of the study design. DAY 0, Baseline; DAY 1, DAY 2, DAY 3, Day of conditions administration; (**A**) single shot of active tDCS session; (**B**) single shot of sham tDCS session; (**C**) single dose of MPH (Ritalin®); CBCL, Child Behavior Checklist; CPRS, Conners' Rating Scales; SNAP-IV; K-SADS-PL DSM-5, Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version for DSM-5; C-GAS, Children Global Assessment Scale (questionnaire from the K-SADS-PL DSM-5); ABAS-II, Adaptive Behavior Assessment System; N-Back; SST, Stop Signal Task; Safety and Tolerability Questionnaire.

The outcomes will be recorded at Day 0, Day 1, Day 2, and Day 3 to compare the effects of the three conditions. Specifically, at Day 0 and during the maximum peak of the tDCS effects (10 min after the start of stimulation) or MPH effects (90 min after dose administration), participants will undergo the Stop Signal Task (SST)—a measure of inhibitory control—and the N-Back task—a measure of WM. To verify that carry-over effects will not occur, the SST and the N-Back task will be performed before each session and results will be compared with those obtained at Day 0. The tDCS conditions will last approximately 40 min, including 20 min of tDCS session duration (active or sham) and 30 min of outcome measures administration, which will begin after the first 10 min of the tDCS session. The MPH condition will last approximately 2 h, including a 90 min wait time after dose administration and 30 min of outcome measures administration.

2.4. Interventions

2.4.1. Transcranial Direct Current Stimulation

Direct current will be delivered by a battery-driven direct current stimulator (BrainStim stimulation by E.M.S S.R.L—Bologna, Italy) via a pair of identical square (25 cm^2) saline-soaked sponge electrodes kept firm by elastic bands. Anodal electrodes will be positioned over the left DLPFC, according to the International 10–20 System, on the sites corresponding F3, whereas the cathodal electrode will be placed above the contralateral supraorbital area (orbitofrontal cortex; OFC), corresponding to Fp2 (see Figure 2). In the active tDCS condition, the current will increase slowly during the first 30 s to 1 mA (ramp-up) and, at the end of the stimulation, the current will decrease slowly to 0 mA during the last 30 s (ramp-down). Between the ramp-up and ramp-down, constant current will be delivered

for 20 min, with a density of 0.04 mA/cm^2. In the sham tDCS condition, the stimulation will be delivered by using the same active tDCS montage, respectively left-anodal DLPFC and right-reference electrode over Fp2. Stimulation intensity will be set at 1 mA, but the current will be applied for 30 s and will be ramped down without the participants' awareness. This placebo condition provides sensations (i.e., tingling) associated with tDCS and, therefore, it is indistinguishable by the participants from the active condition [32]. The study will be conducted in single blind: all children and their parents will be blinded to their stimulation condition.

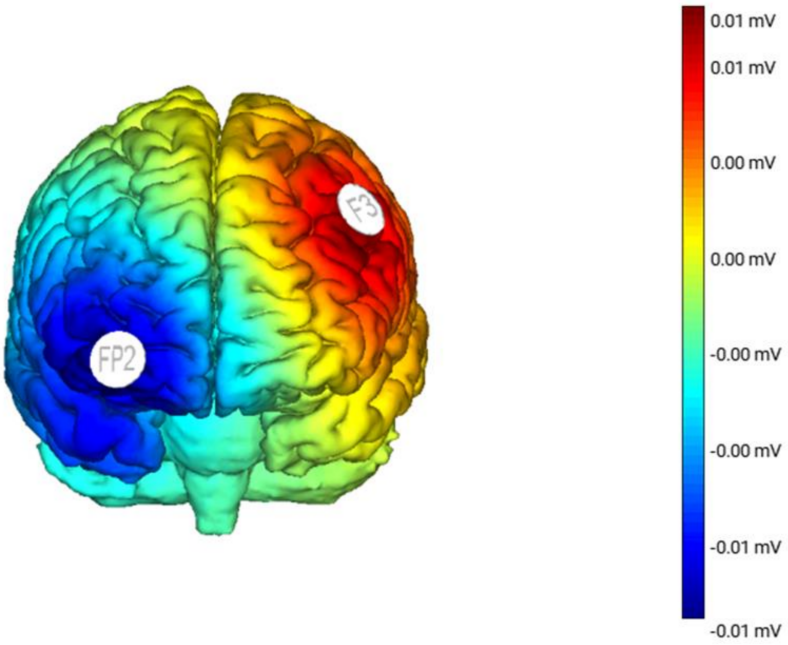

Figure 2. Map of electric field magnitudes in a male brain model from the frontal. The stimulating electrode will be placed over the left DLPFC, whereas the reference (cathodal electrode) will be placed above the contralateral supraorbital area with a current amplitude of 1 mA. The actual stimulation will last for 20 min, whereas the sham stimulation will consist of a current ramping up and down within 30 s.

2.4.2. Methylphenidate

Depending on the age and weight of the child, a single dose of 5–10 mg of immediate-release MPH (Ritalin®) will be administered by the psychiatrist in accordance with NICE and AIFA (Agenzia Italiana del Farmaco) guidelines for the treatment of ADHD.

The indication for the prescription of the drug will be clinical and not part of an experimental study model with randomization to placebo. For this reason, the dose will not be predetermined by an algorithm involving the hospital pharmacy and the pharmaceutical company, as is the case of randomized clinical trials for drugs.

2.5. Clinical Eligibility Assessment

The child psychiatric examination and assessment will be conducted by experienced developmental psychiatrists and neuropsychologists. Psychiatric diagnosis will be based on developmental history, extensive clinical examination, and the semi-structured interview K-SADS-PL DSM-5 [33]. The level of severity of ADHD will be determined by clinicians according to DSM-5 criteria and classified as:

- Mild, when few symptoms beyond the required number for diagnosis are present, and symptoms result in minor impairment in social, school, or work settings;
- Moderate, when symptoms or functional impairment between "mild" and "severe" are present;

- Severe, when many symptoms are present beyond the number needed to make a diagnosis, and result in marked impairment in social, school, or work settings.

2.5.1. K-SADS- PL DSM-5: The Semi-Structured Interview

Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version (K-SADS-PL) for DSM-5 (K-SADS-PL DSM-5) [33] will be submitted by trained psychiatrists and neuropsychologists. Through a comprehensive checklist of the patient's clinical history, the clinician will ask questions of the patients and their parents separately to investigate the possible presence of current and past episodes of psychopathology, according to DSM-5 criteria [1].

Psychopathological disorders assessed by K-SADS-PL DSM-5 include the following: depressive and bipolar-related disorders; schizophrenia spectrum and other psychosis disorders; anxiety, obsessive-compulsive, and trauma-related disorders; neurodevelopmental disorders (ADHD/autism spectrum disorder); disruptive and conduct disorders; feeding and eating disorders; substance-related disorders; and elimination disorders.

2.5.2. Children Global Assessment Scale

Global functioning will be assessed with the Children's Global Assessment Scale (C-GAS) [34]. The C-GAS estimates the overall severity of disturbance (range: 0–100). Scores over 90 indicate superior functioning, whereas scores under 70 suggest impaired global functioning.

2.5.3. SNAP-IV

The SNAP-IV [35] is a parent-report rating scale usually administered to evaluate comorbidity with Oppositional Defiant Disorder. It consists of 26 items that are rated on a 4-point scale (0 = no symptoms to 3 = severe symptoms). The items are divided into three subscales: inattention, hyperactivity/impulsivity, and oppositional behaviors. Subscale scores are calculated by creating an average. Higher scores represent more problem symptoms. T-scores will be used for statistical analyses.

2.5.4. Child Behavior Checklist

The Child Behavior Checklist (CBCL) parent questionnaire [36] is a well-known tool for detecting behavioral and emotional problems in children and adolescents. Parents are required to evaluate the child's behaviors and emotions during the preceding 6 months on a 3-point Likert scale for each item (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true). The hierarchic structure of the CBCL encompasses several scales, as follows: (1) syndrome scales (anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior); (2) broad band scales (internalizing problems, which incorporates anxious/depressed, withdrawn/depressed, somatic complaints; externalizing problems, which incorporates rule-breaking behavior, and aggressive behavior; total problems); (3) DSM-oriented scales (affective problems, anxiety problems, somatic problems, ADHD problems, oppositional defiant problems, and conduct problems); and (4) 2007 scales (sluggish cognitive tempo, obsessive-compulsive problems, and post-traumatic stress problems). The scoring software of the CBCL (Achenbach System of Empirically Based Assessment, University of Vermont: Burlington, VT, USA) generated t-scores based on the Italian standardization of the CBCL. According to the cut-off thresholds of Achenbach and Rescorla (2001), t-scores > 69 were classified as clinically relevant, t-scores between 65 and 69 were classified as borderline, and t-scores < 65 indicated non-clinical symptoms. For the internalizing problems, externalizing problems, and total problems scales, t-scores > 63 were classified as clinically relevant, t-scores between 60 and 63 were classified as borderline, and t-scores < 63 indicated non-clinical symptoms. T-scores will be used for statistical analyses.

The CBCL-Dysregulation Profile (CBCL-DP), characterized by simultaneous high values (t-scores > 70) in three syndrome scales (anxious/depressed, attention problems, and

aggressive behavior), will be also calculated using the sum of t-scores of the three syndrome scales. Scores $\geq$ 210 are considered clinical, between 180 and 209 are in the borderline range, and $\leq$179 are not-clinical scores.

2.5.5. Conners' Rating Scales—Italian Adaptation

Conners' Parent Rating Scales-Long Version Revised (CPRS) [37] are informant-report rating scales commonly used to assess behaviors related to ADHD in children. They contain 80 items that are rated on a 3-point Likert scale (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true). The t-score cut-off for relevance is >70 (very elevated). T-scores from 60 to 70 are considered high average or elevated. T-scores will be used for statistical analyses.

2.5.6. Adaptive Behavior Assessment System

Adaptive Behavior Assessment System—Second Edition (ABAS-II) [38] evaluates adaptive behavior defined as an individual's ability to engage in skills of daily living autonomously. The ABAS-II comprises four composite scores that are made up of different domain areas: Global Adaptive Composite (GAC), Conceptual Adaptive Composite (CAC), Social Adaptive Composite (SAC), and Practical Adaptive Composite (PAC). Parents will be required to complete 232 items that are rated on a 4-point Likert scale (0 = is not able; 1 = never or rarely; 2 = sometimes when needed; and 3 = always or almost always). According to normative data, raw scores will be converted into composite scores (M $\pm$ SD: 100 $\pm$ 15). Composite scores will be used for statistical analyses.

2.5.7. Non-Verbal Intelligence Quotient

The Perceptual Reasoning Index of the Wechsler Intelligence Scale for Children Fourth Edition [39] or Colored Progressive Matrices or Standard Progressive [40] will be considered as non-verbal intelligence quotient.

2.6. Outcome Measures

As already described, the outcome measures will be proposed to each participant individually at Day 0, before and during each condition. Specifically, to detect the maximum effects of both interventions, the outcome measures will be collected at 10 min after the start of stimulation (maximum peak for tDCS effects) [41] and 90 min after MPH dose administration (maximum peak for MPH effects as mentioned in Ritalin® label).

2.6.1. Stop Signal Task

The primary outcome of the study will be the inhibition of response (Stop Signal Reaction Time—SSRT, see Figure 3) measured with the SST [42] that consist of randomly intermixed go and stop trials (75% and 25%, respectively). The task will be performed on PsychoPy® software (Open Science Tools Ltd., Nottingham, UK), and it is structured in line with the consensus guide of SST [43]. All participants will be familiarized with the tasks before the experimental session starts. They will be performed about 10 trials of the go and no-stop task, and about 25 trials of the go no-go and the stop task. All participants will have then a clear idea of the task demand before the collection of the data starts.

All trials will begin with the presentation of a cross in the center of a computer screen. After 1500 ms, a stimulus target (go signal) will replace the cross. On go trials, children will be instructed to press the space bar as fast as possible after the go signal's appearance. In stop trials, after a variable delay (Stop-Signal Delay, SSD), a stop signal stimulus target will appear after the go signal. Children will be instructed to refrain from responding. The SSD duration will be controlled by a simple staircase procedure (50 ms step) to keep the probability of inhibition around 50% of trials. SSD will be increased or decreased by a single step after successful or unsuccessful stopping. The stop-signal reaction time (SSRT) will be estimated (in ms) by subtracting a mean estimate of SSDs from the observed mean of the reaction times (RTs) in no-stop trials. The go no-go task will evaluate the ability to

suppress a dominant response. It will consist of randomly intermixed go (75%) and no-go (25%) trials.

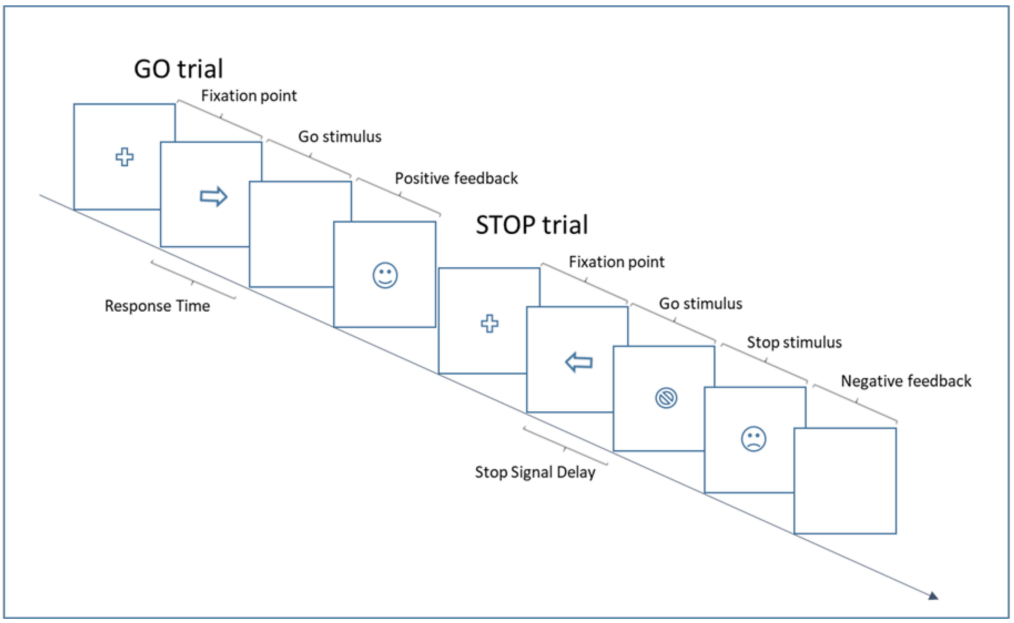

Figure 3. Depiction of the sequence of events in a stop-signal task.

The output of the SST will be the following measures: SSRT, go accuracy, go RTs, SSD, and variability of reaction times (VRTs). The mean duration of the task will be 14 min.

In Figure 3, participants respond to the direction of arrows (by pressing the corresponding arrow key) in the go task. On one of the trials, the arrow is replaced by a stop symbol after a variable SSD. Positive or negative feedback follows each response.

2.6.2. Visual-Spatial N-Back Task

The N-Back task is one of the most widely used culture-free tools applied to evaluate working memory. The visual-spatial condition consists of presenting a series of visual stimuli (blue boxes) in a certain location on the screen. After a training phase, participants are required to indicate whether the location of each box presented is the same as the location of the box presented n trials before. For example, in a 2-Back task participants have to decide whether the current location is the same as the location in trial $n - 2$. When the accuracy will be more than 80%, the difficulty of the N-Back task will increase (for example, passing from 1-Back to 2-Back). The N-Back score will be determined based on the last achieved span (where the accuracy percentage $\geq$80%) and the corrected percentage of the next unachieved span (where the accuracy percentage <80%). For example, when the participant achieves the 1-Back span (accuracy percentage $\geq$80%) and achieves only 30% accuracy in the 2-Back span, the score would be 1.3.

2.7. Safety Procedures

Several safety procedures will be adopted to monitor the study progress.

2.7.1. Safety and Tolerability of tDCS

Symptoms and side effects will be assessed using a standard questionnaire [44] that will be completed by participants after each tDCS session. The questionnaire will list adverse effects, such as headache, neck pain, scalp pain, tingling, itching, burning sensation, skin redness, sleepiness, trouble concentrating, and acute mood change. Participants will quantify the intensity of the symptoms or side effects that will be related to tDCS (1—absent; 2—mild; 3—moderate; 4—severe).

2.7.2. Safety and Tolerability of MPH

Prevention of errors and adverse effects to patients associated with MPH will be reduced to the minimum by the medical protocol for subjects under treatment with psychostimulant in line with NICE guidelines [45]. Among the most common adverse effects of MPH were reported: headache, decreased appetite, weight loss, abdominal pain, nausea and vomiting, insomnia, aggression, anxiety, depression, and hypertension. Less common are: suicidal ideation, diplopia, blurred vision, sedation and dyspnoea, and misperception. Rare, although documented, are: cardiac arrest, myocardial infarction, cerebral vasculitis, leukopenia, and thrombocytopenia. In medical emergencies, the investigator should use medical judgment and remove the subject from the immediate hazard.

2.7.3. Informed Consent and Data Treatments

Before carrying out any procedure of the study, the parents or a legally authorized representative (LAR) of the subject must sign the informed consent (AIFA) and documentation of the assent (if necessary) must certify that the subject is aware of the nature of the study and the established procedures and limitations, following the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) and applicable regulations.

2.7.4. Protection of Risks

To minimize risks associated with tDCS, participants will be monitored throughout stimulation sessions and asked to report any discomfort. If the scalp sensation is uncomfortable, stimulation will be stopped. In the event of a headache, stimulation will be stopped. All tDCS sessions will be administered and continually supervised by a trained experimenter. tDCS side effects are minimal in children and adults, typically involving transient itching and reddening site of stimulation of the scalp on some participants [46]. However, to avoid any chance of seizure, prior history of neurological disorders is an exclusionary criterion for our study and no participants will have to have a history of seizure.

MPH. Neuropsychiatric preventive and naturalistic assessment (anamnestic history, the mental state examination, and the neurological examination) according to the AIFA guidelines for ADHD will be conducted by a developmental psychiatrist before recruitment. At that time, cardiovascular risk factors associated with MPH assumption (i.e., Brugada syndrome) will be excluded by clinicians. After this first evaluation, the participants will undergo medical examinations. Specifically, an electrocardiogram and the correction of the QT segment will be preventively evaluated by a cardiologist. Moreover, blood exams will be carried out by developmental nurses to exclude any other medical condition associated with ADHD and that may mime this disorder's symptoms (i.e., thyroiditis). All the assessment included in this section will be at Day 0.

2.7.5. Missed Sessions and Early Termination of Participation

The experimenters will register each participant's suspension or interruption of the study. Participants will be promptly withdrawn from the study in the case of any unpredictable adverse effects. If the suspension happens during the testing session, data will be excluded from the analyses. Clinical care will not be affected.

2.7.6. Study Monitoring and Data Management

The principal investigator (or the ethics committee) will identify a study monitor assigned to follow this study following this clinical trial protocol [European guidelines for Good Clinical Practice (CPMP/ICH/135/1995) and Decree-Law Italian Minister of Health, 15 July 1997]. The investigator agrees to provide reliable data and all information requested by the protocol accurately and legibly according to the instructions provided and to ensure direct access to source documents to the ethics committee representatives. If any particular circuits have to be defined, particular attention should be paid to the confidentiality of the participant's data to be transferred.

In this case, the investigator may appoint such other individuals as he/she may deem appropriate as sub-investigators to assist in the conduct of the clinical trial following the clinical trial protocol. All sub-investigators shall be timely appointed and listed. The sub-investigators will be supervised by and under the responsibility of the investigator. The investigator will provide them with a clinical trial protocol and all necessary information.

The participant's data will be anonymous and coded. The hard files will be placed in a closed drawer. The database will be protected by a password. The investigator will allow the monitoring with an appropriate frequency. The original documents will be available at any moment to be verified by the clinical monitor and the regulatory authority.

2.8. Power and Sample Size Considerations

The sample size is calculated by a priori analysis in G*Power, version 3.1.9.7 (The G*Power Team, Düsseldorf, Germany).

The estimated result will be obtained on the assumption that participants, receiving a single dose of MPH or a single session of active tDCS, will decrease the SSRT compared to the baseline, whereas participants receiving a single session of sham tDCS will not significantly change their SSRT compared to the baseline.

Because the design of this project has never been employed in children and adolescents with ADHD, we will refer to studies in which patients with ADHD completed the SST before (baseline) and after interventions (a single dose of MPH or a single session of tDCS). Regarding MPH, Rosch and collaborators' study [47] on SSRT found a Cohen's d effect size of 0.68 and an f effect size of 0.34. Regarding tDCS, Allenby and collaborators' study [23] showed a Cohen's d effect size of 0.34 and an f effect size of 0.17.

Based on these observations, we estimate an f effect size of 0.25.

With an estimated f = 0.25, α value = 0.05 (i.e., probability of false positives of 5%), and β = 0.80 (i.e., at least 80% power), the sample size is 24 as calculated using a Repeated-measures analysis of variance (RM-ANOVA) model with four within factors (baseline, active tDCS, sham tDCS, and MPH).

3. Data Analyses and Expected Results

The Shapiro–Wilk test will be used to test the normality of the data and Levene's test for the homogeneity of variances. When data is normally distributed and the assumption of homogeneity will not be violated, parametric analyses will be computed. When one assumption will not be met, non-parametric tests will be conducted or a log-transformation of the distribution will be applied, if appropriate. When appropriate, sphericity will be verified by Mauchly's sphericity test. When sphericity will not be met, Greenhouse–Geisser correction will be applied.

Categorical data will be represented as count and proportion, while continuous data as mean and standard deviation or median and range. Chi-Square analyses will be used to compare the groups on demographic and safety measures (categorical variables).

A preliminary analysis to test the effect of the four repetitions of the tasks (Day 0, Day 1, Day 2, and Day 3) for WM and SSRT will be conducted.

RM-ANOVA will be used to compare SST measures (SSRT, go accuracy, go RTs, SSD, and VRTs) and visual N-Back index, separately, with conditions (Day 0, A, B, C) as a within-subjects factor.

Post hoc comparisons will be assessed using Tukey's honest significance test. Partial eta squares (η_p^2) will be used as measures of effect sizes.

We hypothesize that tDCS will improve inhibitory control and WM, as well as MPH. Specifically, we assume that a single session of anodal tDCS can induce a similar improvement from baseline as a single dose of MPH does. The sham condition should discriminate possible task learning effects.

4. Discussion

We have described the rationale and design of a trial conceived to compare the efficacy of a drug-based treatment (i.e., MPH) and of a brain-directed intervention (i.e., tDCS) in producing clinically meaningful impact on cognitive function in patients with ADHD.

This study will represent the first attempt to test whether a single session of anodal tDCS is as effective as a single dose of MPH, or even more so. The results will represent a significant step toward implementing large-scale multi-sessions clinical trials in the field.

The choice to compare tDCS and MPH is based on the observation that they have similar mechanisms of action at the neural level since they both modulate dopaminergic neurotransmission system in the basal ganglia-thalamocortical circuit. Specifically, MPH intervenes on dopamine active transporter DAT-1 [48,49], the primary protein responsible for clearing dopamine from the synaptic space [50], via inhibiting catecholamine reuptake inhibitor and, in turn, increasing levels of extracellular dopamine in the striatum [51,52], as well as in frontal, thalamic, and temporal brain regions [53]. Doing so, MPH would increase and stabilize catecholaminergic neurotransmission in prefrontal cortices [16], increasing activity in frontostriatal and frontoparietal networks of patients with ADHD [12]. Similarly, a recent preclinical study [54] observed a decrement of DAT-1 activity after anodal tDCS over DLPFC and MPH administration with increasing dopamine at synaptic level, especially in the hippocampus and prefrontal cortex. In line with this result, a neuroimaging study [55] in adults demonstrated that anodal tDCS over DLPFC induces extracellular dopamine release in the subcortical regions, such as the striatum and left putamen. Moreover, another neuroimaging study [56] in adults showed that one session of anodal tDCS over DLPFC increased dopamine in the right ventral striatum and that such dopamine release was significantly associated with attention enhancement. Overall, these findings suggest that anodal tDCS over DLPFC may induce a positive effect on the dopaminergic system because of the lower density of DAT-1 and may improve prefrontal-related cognitive functions usually impaired in ADHD [6].

Concerning electrode placement, the methodological decision of placing anode over DLPFC was based on the aforementioned evidence. The left lateralization of the excitatory electrode over DLPFC was supported by neuroimaging studies demonstrating the involvement of left DLPFC in response stopping [57,58], as well as in other inhibition-related phenomena [21]. The hypoactivity of these regions in ADHD is assumed to be associated with attentional, inhibitory control, and executive dysfunctions [6]. Accordingly, we selected the anodal tDCS because of its well-known excitatory potential and because of a recent meta-analysis [30] showing that anodal but not cathodal DLPFC significantly improves inhibitory control and WM in patients with ADHD. In addition, the left DLPFC (anode electrode)-right OFC (reference electrode) montage proved to be the most effective electrodes placement. In fact, the four experiments that used this montage reported better performance than the others showing that the target area of the reference electrode has an impact on the effects of tDCS on inhibitory control.

Concerning tDCS parameters, such as intensity, the selection was based on previous studies using tDCS in children with ADHD [24]. The application of 1 mA showed to be well-tolerated in children without adverse effects in previous studies [24]. Furthermore, the decision to apply 1 mA was based on the pediatric population having certain characteristics, such as smaller head size, thinner scalp, and less cerebrospinal fluid that would influence current distribution and density at the site of stimulation [59–61].

We choose to administer online tDCS instead of offline tDCS [62]. Indeed, it has been demonstrated that tDCS during concomitant activities enhanced synaptic strength in neural networks already activated by cognitive tasks [63]. Accordingly, a systematic review and meta-analysis [64] comparing the effects of tDCS over the DLPFC in healthy and neuropsychiatric groups showed that accuracy in online tasks was superior to offline tasks.

Concerning neuropsychological measures, we selected inhibitory control [43] and WM to have sensible and objective measure [65] of MPH [66] and tDCS [24] effect.

In the current within-subject study, the participants will be exposed in a random order to a single shot of anodal tDCS session, a single shot of sham tDCS session, and a single dose of immediate-release MPH (Ritalin®) with an interval session of 24 h, according to previous studies from our lab [67]. The potential carry-over effects have been considered. However, physiological studies demonstrated that a single tDCS session of 10–20 min results in transitory effects that last for an hour and a half at most and return to baseline after 2 h [22,68,69]. Similarly, as indicated by AIFA, even a single administration of MPH has effects, although transient. The maximum plasma concentrations of the main unesterified metabolite are reached about 2 h after administration. MPH is eliminated from plasma with an average half-life of 2 h and after oral administration, 78–97% of the dose is excreted with urine and 1–3% with feces in the form of metabolites within 48–96 h.

To ascertain the absence of carry-over effects, a preliminary analysis will be conducted by evaluating the effect of the order of the four condition repetitions.

The possibility to demonstrate the non-inferiority of tDCS to improve ADHD symptoms compared to MPH would promote its investigation as reliable and evidence-based intervention for children with ADHD. This clinical study could lay the foundation for future research perspectives on interventions for children with ADHD, speeding up the process of the understanding of this technique in pediatric rehabilitation.

Further studies are needed to compare MPH and tDCS effects in multisession double-blind treatment studies and in larger group of patients with ADHD. In addition, functional neuroimaging studies should be designed to verify that dopamine release caused by tDCS has a brain effect comparable to that of MPH.

5. Conclusions

We firmly believe that detailed reporting of clinical trial protocols would reduce the publication bias of future research, by prompting the reproducibility and the reliability of experimental designs.

Author Contributions: Conceptualization, B.D., D.M. and S.V.; methodology, B.D., D.M., G.L., P.P. and S.V.; supervision, S.V. and D.M.; writing original draft, B.D., A.B. and G.L.; writing review and editing, B.D., D.M., G.L., A.B., P.D.R., S.D.V., I.P., F.C. and S.V. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Institutional Review Board Statement: All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of the Bambino Gesù Children Hospital (2185_OPBG_2020).

Informed Consent Statement: Informed consent will be obtained from all subjects involved in the study.

Acknowledgments: We would like to thank in advance all of the children and adolescents who will take part in the study and their parents.

Conflicts of Interest: The authors declare no conflict of interest.

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Pubblicata la Linea Guida sulla gestione dei disturbi specifici dell'apprendimento

Superata la valutazione con AGREE II (il processo di valutazione previsto all'art. 5 comma 3 della Legge n° 24/2017 e dall'art. 4 comma 2 del DM 27 febbraio 2018), il 20 gennaio 2022 è stata ufficialmente pubblicata sul sito dedicato dell'Istituto Superiore di Sanità (ISS) la Linea Guida sulla gestione dei Disturbi Specifici dell'Apprendimento (DSA). Il testo finale, presentato a giugno 2021 e rivisto definitivamente a dicembre 2021, è scaricabile dal seguente link: *https://snlg.iss.it/wp-content/uploads/2022/01/LG-389-AIPO_DSA.pdf*.

La linea guida, frutto di un lavoro multidisciplinare e multiprofessionale lungo, accurato, impegnativo e rigoroso in ogni suo passaggio, in linea con le direttive del Sistema Nazionale Linee Guida dell'Istituto Superiore di Sanità (SNLG ISS), analizza diverse questioni inerenti ai DSA, "aggiornando il quesito sui trattamenti, proponendo degli indici predittivi, integrando con nuove indicazioni sulle diagnosi esistenti e introducendo altre indicazioni diagnostiche completamente nuove".

I DSA sono, "per definizione, disturbi circoscritti a domini cognitivi specifici, che non interessano il funzionamento cognitivo più generale, ma le loro conseguenze possono comunque essere pervasive e interessare molti ambiti del funzionamento cognitivo, come anche dell'adattamento personale e sociale". Si caratterizzano per il carattere evolutivo; per la diversa espressività del disturbo nelle differenti fasi evolutive dell'abilità in questione; per la quasi costante associazione con altri disturbi, cui conseguono una marcata eterogeneità dei profili funzionali e di espressività clinica e ricadute sulla fase diagnostica - la frequente comorbidità con altri disturbi del neurosviluppo ha portato negli ultimi anni a riconsiderare lo status della caratteristica peculiare della "specificità" di questi disturbi e del criterio della "discrepanza" dal QI, aspetto già segnalato anche nella *Consensus Conference* a opera dell'Istituto Superiore di Sanità[1]; per il carattere neurobiologico delle anomalie che caratterizzano i disturbi, con una interazione attiva di fattori ambientali nella determinazione della loro comparsa.

Il documento rammenta che "non sono però disponibili a oggi *marker* biologici affidabili per l'identificazione di questi fattori e conseguentemente per la diagnosi, che di fatto continua a basarsi prevalentemente sulla osservazione comportamentale e sulla misurazione testistica delle abilità di lettura, scrittura e calcolo".

Le precedenti raccomandazioni cliniche sui DSA, emerse dai documenti delle due *Consensus Conference*[1,2] e del *panel* di Aggiornamento e Revisione della CC DSA 2007[3], hanno certamente contribuito a migliorare le conoscenze circa la diagnosi dei DSA e a sistematizzare una quantità di aspetti controversi per la migliore prassi clinica, ma hanno anche lasciato zone d'ombra e incertezze. Hanno anche animato il dibattito culturale e scientifico sui diversi aspetti del disturbo, ulteriormente stimolato dalle novità introdotte dal DSM-5.

Con tale consapevolezza, dopo avere valutato la possibilità di un aggiornamento delle linee guida sui disturbi specifici dell'apprendimento e dopo un percorso esplorativo di esame della utilità e fattibilità da parte di un gruppo di lavoro "preliminare", si è confermata l'utilità di aggiornare le raccomandazioni cliniche precedentemente prodotte e di rispondere a questioni non ancora esaminate e presenti nella vita quotidiana con un alto interesse clinico e sociale.

Il consiglio direttivo dell'Associazione Italiana Dislessia (AID) ha quindi successivamente deliberato l'avvio del processo che ha portato alla costituzione del Gruppo di Sviluppo delle linee guida che, seguendo tutte le indicazioni del SNLG, ha lavorato alla produzione di raccomandazioni cliniche.

In continuità col precedente documento di consenso (CC-ISS[1]), attraverso revisioni sistematiche della letteratura in merito alle evidenze attualmente disponibili, la Linea Guida si propone sia di aggiornare raccomandazioni cliniche per le quali vi è stato nell'ultimo decennio uno sviluppo apprezzabile delle conoscenze scientifiche, sia di formulare indicazioni per aspetti non presi in considerazione in precedenza. L'obiettivo generale è quello di fornire in questo modo raccomandazioni utili a migliorare e uniformare i protocolli diagnostici e riabilitativi.

La formulazione dei quesiti clinici ha guidato tutto il processo di revisione sistematica, dalla definizione dei criteri di inclusione ed esclusione degli studi al processo di ricerca e loro selezione. Sono stati individuati nove quesiti clinici. Quattro di essi sono stati esaminati secondo la metodologia GRADE: quali sono gli indici predittivi per l'identificazione precoce di bambini a rischio di disturbo specifico dell'apprendimento? - in bambini/ragazzi in età scolare, quali sono i criteri e le procedure diagnostiche per accertare il disturbo di comprensione del testo? - quali sono i criteri e le procedure per l'identificazione di DSA in bambini bilingui in età scolare? - quali sono le prove disponibili sull'efficacia di interventi per il trattamento di DSA in età evolutiva?

I seguenti sono i quesiti in cui non è stata condotta una valutazione GRADE ma, sulla base dei risultati della valutazione della qualità metodologica, è stato formulato un giudizio globale di qualità "buona", "media" o "scarsa": il riconoscimento di quantità simboliche e non-simboliche e le funzioni esecutive sono deficitarie in bambini e ragazzi in età scolare con disturbo specifico del calcolo? - quali competenze matematiche e quali processi cognitivi devono risultare deficitari per porre diagnosi e per descrivere il profilo funzionale in bambini e ragazzi in età scolare con disturbo specifico del calcolo? - quali criteri/parametri sono necessari per porre diagnosi di disgrafia e quali strumenti sono più sensibili per rilevare la sua presenza? - in bambini in età scolare con diagnosi di DSA, quali sono le funzioni/abilità compromesse?

Il testo del documento riporta i criteri di inclusione per ogni quesito clinico e l'accurata descrizione delle strategie di valutazione per ciascuno di essi.

Quale l'interesse della Linea Guida per la Pediatria (partecipante all'elaborazione del documento e nella sua revisione finale) e in particolare per la Pediatria delle Cure primarie?

Anzitutto la disponibilità di un documento che è anche una opportunità di aggiornamento affidabile, garantito da un processo rigoroso, metodologicamente trasparente e ben determinato. È un percorso dove la valutazione delle evidenze è stata affiancata dalla considerazione di aspetti e valori portati dai diversi soggetti (inclusi nei gruppi di lavoro) intorno al bambino e all'adulto con DSA: fattibilità, accettabilità di azioni e interventi messi a confronto, utilizzo delle risorse, equità[4].

Sono aspetti che investono anche l'ambito della Pediatra delle Cure primarie dove è frequente una situazione/problema in cui ci sono l'osservazione dell'insegnante e/o la valutazione dell'esperto; l'interpretazione del genitore e le sue preoccupazioni circa la gravità delle comunicazioni ricevute; l'urgenza di risolvere un problema che diventa sempre più impellente; la difficoltà a capirne l'origine; la frustrazione causata dagli insuccessi di tentate soluzioni talvolta messe in atto dalla famiglia in autonomia; i dubbi circa le proprie responsabilità/capacità genitoriali.

Ci dice il SNLG che "la Linea Guida ha superato la valutazione con AGREE II; se ne raccomanda l'utilizzo": un'indicazione anche per il pediatra che vuole evitare valutazioni sommarie, rassicurazioni generiche, risposte di senso comune, e anche gestire correttamente l'invio al livello specialistico, facilitare la comprensione del problema e degli obiettivi a medio e lungo termine delle proposte di intervento, supportare l'attivazione della rete di cura.

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Screening della celiachia e la diagnosi al Bar Sport

Al Bar Sport, Pompilio spiega all'amico Vladimiro che gli hanno trovato la puffalina alta. Sembra, spiega Pompilio, che sia un segno di rischio per la *stranosi*, una malattia cronica poco simpatica… Vladimiro cerca di rincuorare l'amico, e gli chiede: cos'è sta malattia? Mai sentita dire… ce l'hanno in tanti? Pompilio si è informato su internet: sembra che colpisca una persona su mille… A questo punto Vladimiro sembra avere gioco facile: valà, gli dice, non l'avrai mica proprio te la stranosi… Ma Pompilio non si tranquillizza, il dottore, dice, vuole fare degli approfondimenti, speriamo bene… Il medico di Pompilio è prudente, doverosamente, farà altri accertamenti… ma Vladimiro era stato così superficiale? Se abbiamo di fronte un paziente con la puffalina alta, test con altissima sensibilità e specificità per la stranosi, entrambe al 99%, che probabilità abbiamo che sia affetto da questa malattia con prevalenza di 1 su 1000? Il valore predittivo per il test positivo, VPP, sarà pari al 9%. Cioè invece che un caso su mille, fra i positivi alla puffalina la probabilità sale a quasi 1 su 10. Però 9 su 10 sono sani. Vladimiro ci aveva preso, il suo amico molto probabilmente, 9 volte su 10, è sano.

Per lo screening di massa della celiachia abbiamo questi numeri: poniamo che l'anti-tTG abbia il 99% di sensibilità e di specificità. Per una prevalenza di 3 su 100 abbiamo che su 10.000 sottoposti a screening, 300 sono malati e 9700 sono sani. Sensibilità del 99% significa che dei 300 malati 297 sono positivi e 3 negativi al test (falsi negativi), mentre specificità del 99% significa che su 9700 sani, 9603 sono negativi e 97 sono positivi al test (falsi positivi). Il confronto fra positivi al test in quanto malati e totale dei positivi (VPP) è pari a 297 su 394 (297 + 97 falsi positivi) ovvero pari al 75,38%; per una prevalenza di 1 su 100, con uguale sensibilità e specificità del test, avremo 99 malati positivi su 100 malati, e 99 falsi positivi su 9900 sani. Il VPP è uguale 99 su 198, pari al 50%.

Dunque con specificità e sensibilità dell'anti-TG al 99% (ammesso e non concesso che siano così alte) e prevalenza di 3 su 100, il VPP è del 75%. Con prevalenza dell'1% il VPP è del 50%. 1 su 4, nel primo caso e 1 su 2 nel secondo caso, sono bambini sani, falsi positivi al test.

Quindi sottoponendo a screening la popolazione generale con anti-TG faremo la biopsia duodenale in un caso su quattro, fino a un caso su due, a bambini sani. Siamo consapevoli di questo? L'impegno che questo comporta, l'ansia generata ecc., in una buona parte dei casi inutilmente, sono state considerate? E un asintomatico che rimanesse o meno tale per tutta la vita, non ha diritto a rimanere nell'ignoranza? Anni fa Duccio Peratoner, primario della Pediatria di Pordenone, al convegno di Tabiano invitò i pediatri di famiglia a proteggere i bambini "dall'accanimento diagnostico" dei colleghi ospedalieri. Maria Merlo (*Medico e Bambino* 2021;40 (9):601-6. doi: 10.53126/MEB40601) scrive che è "difficile il dialogo fra medici di base e medici specialisti che, con casistiche molto differenti, hanno disponibilità mentale di casi molto differenti" nell'approccio a un paziente. I pediatri ospedalieri sono consapevoli della loro "deformazione professionale" dovuta al fatto che la popolazione che curano è inevitabilmente una popolazione selezionata?

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Caro Alberto,
grazie della tua lettera un po' ondivaga tra il voler divertirci col tuo spirito e il voler farci la morale sull'accanimento terapeutico.

Non ho molto da ribattere se non che, per mia personale natura, soffro di idiosincrasia per l'enfasi delle dichiarazioni morali-moralistiche ("lasciamo in pace i bambini, non accaniamoci..."): perché più spesso ostacolano, piut-

tosto che favorire, l'analisi della realtà reale e perché mettono a priori chi le enuncia dalla parte della ragione assoluta. Nei fatti, per tutta l'esperienza accumulata negli ultimi trent'anni, il contesto della celiachia mi sembra obiettivamente poco invasivo, molto ragionato e, ormai, anche molto validato. Ragionando senza enfasi emotiva e moraleggiante, anche gli stessi numeri che ricavi dai tuoi calcoli sui falsi positivi e sui richiami impropri che uno screening di massa comporterebbe mi sembrano accettabili (anche perché molte biopsie inutili possono essere risparmiate adottando degli adeguati cut-off degli anti-tTG). Oltretutto (anzi, soprattutto) andrebbe messo in conto anche il peso di tutti i guai di salute che lo screening preverrebbe nei bambini correttamente individuati (anche il loro punto di vista merita un po' di morale-moraleggiante... o no?). Per adesso comunque, al di là di ogni considerazione, siamo nel concreto d'accordo: non è ancora tempo di screening di massa per la celiachia. Soprattutto perché, nonostante qualche recente esperienza riportata anche sulla Pagina gialla sembri dare qualche indicazione in questo senso (Sandstrom O, et al. Five-year follow-up of new cases after a coeliac disease mass screening. Arch Dis Child 2021. doi: 10.1136/archdischild-2021-322755), non possiamo ancora stabilire con la dovuta certezza l'età in cui lo screening ha effettivamente un valore predittivo negativo sufficientemente adeguato: non sappiamo cioè qual è l'età alla quale un test negativo rimarrà negativo per sempre. Sono poi sicuro che anche tu, come me, sia invece sempre convinto dell'opportunità di continuare nell'azione di case-finding: avendo ben presenti tutti i segni/sintomi, anche generici, che possono sottendere una celiachia e dosando sempre gli anti tTG in tutti i bambini che li presentassero. Operatività questa della cui resa ed efficacia abbiamo ormai ampia evidenza e che costituisce senz'altro un indicatore della qualità del nostro agire professionale.

Alessandro Ventura

La Pediatria di famiglia

Dopo tanto decantare la figura del medico di famiglia e dopo aver tanto apprezzato la sua *mission* sul territorio, ora la si vuole ridimensionare e portare alla dipendenza. Credo che il valore enorme della Pediatria di famiglia sta nel rapporto di fiducia-collaborazione con l'utente, tutto ciò per prevenire e curare al meglio le varie patologie, evitare le ripetizioni di esami ed evitare tanto stress all'utente; tutto ciò legato sempre a una Medicina che diventa sempre più intelligenza artificiale senza cuore. Credo che occora innovare per crescere, ma conservando l'umanesimo delle cure. Perché non bisogna sostituire le persone con i numeri, dimenticando che ogni persona è unica per genetica, ambiente e storia. Quindi va bene il Pronto Soccorso bene attrezzato e dislocato in maniera diffusa sul territorio, ma è importante validare al tempo stesso le competenze acquisite negli anni dal pediatra per affrontare misure e programmi di aggiornamento, affrontando ad esempio le notevoli difficoltà dei bambini spesso soli, o degli adolescenti in balia di mode violente con l'uso o l'abuso di sostanze, anche perché il bambino e l'adolescente hanno diritto a spazi fisici e comunitari, ad affetto e non a semplici giornate dedicate all'infanzia.

Il mio vuole essere un invito a pensare alla nuova Pediatria, ma sempre come una disciplina umanistica con notevoli competenze scientifiche e relazionali.

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I bambini della felicità

Ci sono cose e azioni che si rinnovano come la natura a primavera. Saltare sul lettone, il lettone di mamma e papà, riportare quei movimenti nel pensiero ancestrale, un rimando preciso, attento, un punto della situazione, un'epifania…
Se tutto intorno si muove, e le braccia e le mani sono protese ad accogliere quelle del "cucciolo d'uomo", in quell'istante bisogna annientare l'accumulo che gli adulti hanno posto nel granaio del loro percorso.
In pochi istanti è necessario avere la capacità di gettare via le menzogne, gli egoismi, le grandi paratie inutili costruite per illudersi di difendersi. Da cosa? Ancora non lo sappiamo! Dalla semplicità del vivere? Dalle paure dell'altro?

È in quel momento, in quei pochi secondi, che bisogna gettarsi, iniziare a saltare e chiedere a quei "cieli sopra Dio", che sono i bambini: Sei felice? Sei felice? Sei felice?

Fu in quella mattina di primavera che Eleonora, nel salto più alto, rispose:
"*Sono una bambina della Felicità, sono felice perché sono una bambina. I bambini creano felicità e sono il senso della Vita sulla Terra, amorosa, universale, che ci ospita. Per essere felici, sempre, bisogna essere bambini, per voi grandi, distratti, noiosi, egoisti, egocentrici, spaesati, abbiamo un'idea da regalarvi: chiudete gli occhi, fate un lungo respiro, e diventate bambini. È facile! Solo diventando bambini potrete assaporare nuovamente la Felicità…*"

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Accogliere: un'azione attiva

Siamo un gruppo di 70 pediatri di famiglia della provincia di Bergamo. Vorremmo condividere con le Società scientifiche e con con le riviste di interesse pediatrico, tra cui la vostra, un progetto volto alla presa in carico dei bambini rifugiati.

Nella nostra provincia, come da linee guida di Regione Lombardia, sono stati predisposti tre *hub* (uno per ogni Azienda Socio Sanitaria Territoriale - ASST) per la prima visita, l'anamnesi patologica e vaccinale, il tampone per SARS-CoV-2 e il rilascio della tessera sanitaria.

Abbiamo proposto alla nostra Azienta Territoriale Sanitaria (ATS) (e il progetto è stato accettato e condiviso anche con le tre ASST del nostro territorio) la rete dei nostri ambulatori in modo da consentire l'esecuzione del tampone associata alla raccolta anamnestica e alla prima visita in un ambiente che, per struttura e personale, è da sempre rivolto al bambino. La capillarità dell'offerta di questi ambulatori di pediatri volontari consente inoltre di rispondere al modello di accoglienza diffusa attuata in provincia. In sintesi il percorso è il seguente:

- chi si occupa del bambino profugo (liberi cittadini, Associazioni, Enti pubblici) si rivolge all'ambulatorio pediatrico più vicino (l'elenco è pubblicato sul sito di ATS-Bergamo ed è inoltre disponibile un numero unico) per la visita pediatrica, il tampone e l'anamnesi, in particolare quella relativa a patologie croniche e quella vaccinale;
- la registrazione avviene tramite *form* condiviso con ATS/ASST (a breve sarà sostituito dalla piattaforma regionale);
- se la copertura vaccinale risulta completa (secondo criteri condivisi con il Dipartimento di Prevenzione, il pediatra rilascia da subito un certificato per l'idoneità alla frequenza scolastica);
- una volta ricevuta la tessera sanitaria provvisoria il bambino rientra nel normale percorso assistenziale.

Una casella *mail* autogestita dal gruppo è dedicata alla segnalazione di situazioni particolari (gruppi in arrivo, bambini con bisogni speciali) che richiedano una risposta snella come ad esempio il reclutamento di più pediatri in una struttura.

Il numero unico, gestito da volontari del CSV di Bergamo, raccoglie eventuali chiamate e le indirizza al pediatra di riferimento e fornisce indicazioni in merito a come ottenere la tessera sanitaria.

Abbiamo inoltre previsto una bacheca *Padlet* per i pediatri dove caricare tutti i documenti necessari.

Restiamo a disposizione dei colleghi di altri territori che ritenessero di interesse il modello da noi proposto.

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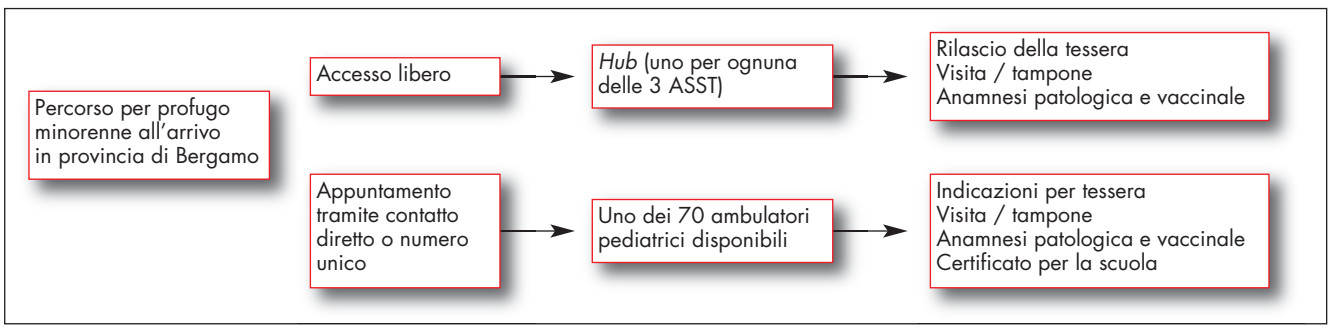

Uno sguardo al neurosviluppo raggiunto ai 2 anni d'età

Giulia Segre[1], Ilaria Costantino[2], Francesca Scarpellini[1], Valeria Tessarollo[2], Antonio Clavenna[1], Maurizio Bonati[1]

ABSTRACT

A look at neurodevelopmental status at 2 years of age

When a child develops a psychological disorder, even a mild one, early diagnosis is essential to provide a timely and appropriate intervention that can improve, both, the child's symptoms and development. Early identification can prevent consequences of differing levels, in the short and long term, and in the individual, in his or her family, and in society as a whole. Hence the importance of paediatrician's point of view and clinical know-how in identifying potential disorders early, but also the parents' views. It is therefore important to actively involve parents upon initial diagnosis.

In this regard, within the NASCITA Project, a study branch aimed at building a shared, active approach between parents, paediatricians and neuropsychiatrists/psychologists was activated for the age 2-year health assessments (well-child visits) phase. Three tests were used: the M-CHAT-R (Modified Checklist for Autism in Toddlers, Revised) to evaluate language, social skills, behaviour, sensory areas; the PSI-SF (Parenting Stress Index – Short Form) to verify the degree of discrepancy perceived by the parent between the child's requests and his or her ability to deal with them adequately; the DERS (Difficulties in Emotion Regulation Scale) to highlight the difficulties of each parent in recognising, interpreting, and managing their emotions. The tests were given to 380 parents (142 couples, 215 mothers and 23 fathers) by 45 family paediatricians during the well-child visit held at two years of age. In all, 33 children (9%) resulted at risk, with a score of ≥3, 1 of whom was found to be at high risk. For 64 children (16.8%) at least one of the parents tested positive for PSI-SF and for 19 (5%) children at least one parent tested positive with the DERS. After combining the results obtained from the three tests and the clinical evaluation, and assessing the child's condition with respect to those results, the pediatrician can provide the parents with a concise description of what emerged and provide a summarised report for the specialist. Such an effort leads to timely, shared communication within the parent-paediatrician-neuropsychiatrist triad that includes specificity of intervention and that can contribute to the effectiveness of the response.

▶ **Key words.** *Child development | screening | infant mental health | child advocacy | primary care.*

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RIASSUNTO

Alla comparsa di un disturbo psicologico nel bambino, anche lieve, una diagnosi precoce è fondamentale per dar seguito ad un intervento tempestivo e appropriato finalizzato ad un miglioramento sia del quadro sintomatologico che dello sviluppo del bambino. Un'identificazione precoce consente di prevenire le conseguenze di varia entità, a breve e lungo termine, sia sull'individuo che sulla famiglia e sull'intera società. Da qui l'importanza dell'"occhio" e della pratica clinica del pediatra nell'individuare precocemente potenziali disturbi, ma anche quello dei genitori. È quindi importante coinvolgere attivamente i genitori sin dalla fase della diagnosi. A tale proposito, nell'ambito dell'albero-progetto NASCITA è stato attivato un ramo mirato a costruire un approccio condiviso e attivo tra genitori, pediatri e neuropsichiatri/psicologi in occasione dei bilanci di salute dei due anni d'età. Sono stati utilizzati tre test: l'M-CHAT-R (Modified Checklist for Autism in Toddlers, Revised) per valutare il linguaggio, le competenze sociali, il comportamento, l'area sensoriale; il PSI-SF (Parenting Stress Index – Short Form) per verificare il grado di discrepanza percepita dal genitore tra le richieste del figlio e le proprie capacità di farvi fronte adeguatamente; la DERS (Difficulties in Emotion Regulation Scale) per evidenziare difficoltà di ciascun genitore nel riconoscere, interpretare e regolare le proprie emozioni. I test sono stati sottoposti a 380 genitori (142 coppie, 215 madri e 23 padri) da parte di 45 pediatri di famiglia in occasione della visita per il bilancio di salute ai due anni d'età. 33 bambini (9%) sono risultati a rischio riportando un punteggio ≥3 e 1 di questi è risultato essere ad elevato rischio. Per 64 bambini (16,8%) almeno uno dei genitori è risultato positivo al PSI-SF e per 19 (5%) bambini per quanto concerne i risultati positivi della compilazione della DERS. Combinando i risultati ottenuti dai tre test e dalla valutazione clinica, accertatosi delle condizioni del bambino rispetto ai risultati emersi, il pediatra può restituire ai genitori una sintetica descrizione di quanto emerso e sintetizzare una relazione strutturata per lo specialista. Una comunicazione condivisa all'interno della triade genitore-pediatra-neuropsichiatra in termini di tempestività e specificità di intervento che può contribuire anche all'efficacia della risposta.

▶ **Parole chiave.** Sviluppo del bambino | screening | salute mentale in età evolutiva | difesa dei bambini | cure primarie.

Sviluppo mentale: viene definito da capitale umano e da benessere mentale.

Lo sviluppo mentale può essere definito in termini di capitale mentale e benessere mentale. Il capitale mentale rappresenta risorse cognitive ed emotive (processi di acquisizione di conoscenze, flessibilità ed efficienza dell'apprendimento, capacità di comprendere e gestire le proprie emozioni, abilità sociali). Il benessere mentale è la capacità di un individuo di sviluppare il proprio potenziale, di lavorare in modo produttivo, di costruire relazioni forti e positive con gli altri e di contribuire alla comunità. Sono quindi molteplici le esposizioni relazionali, culturali e ambientali che nel corso della vita contribuiscono al capitale e al benessere mentale sin dalla nascita[1].

Il piano genetico che guida lo sviluppo cerebrale si basa in modo significativo sulle prime esperienze per stimolare l'organizzazione delle interconnessioni neurali. Lo sviluppo del cervello è di natura cumulativa e avviene in modalità multimodale, con "finestre di opportunità" nei primi periodi sensibili e critici della vita quando la recettività alle esperienze è elevata[2].

Se queste "opportunità" non vengono adeguatamente colte sono probabili deficit nel funzionamento psicologico. Alla comparsa di un disturbo anche lieve una diagnosi precoce è fondamentale se a questa fa seguito un intervento tempestivo e appropriato finalizzato ad un miglioramento sia del quadro sintomatologico che dello sviluppo del bambino[3-5]. Un'identificazione precoce a cui consegue un'immediata presa in carico e trattamento è fondamentale in quanto consente di prevenire le conseguenze di varia entità, a breve e lungo termine, sia sull'individuo che sulla famiglia e sull'intera società.

Un disturbo lieve va indagato e diagnosticato precocemente perché possa seguire un intervento tempestivo ed efficace.

L'attenzione ai fattori di rischio e l'attivazione dei fattori protettivi consentono di mettere in atto interventi di promozione della salute (anche) mentale non solo curativi, ma anche preventivi per tutti i livelli, atti e fasi della prevenzione. Alcuni fattori di rischio sono maggiormente associati a specifici disturbi, per esempio quelli relativi allo spettro autistico sono: l'età paterna, il basso peso alla nascita, l'ipossia fetale e lo stress respiratorio. Mentre il basso peso alla nascita, l'età gestazionale e il reddito famigliare sono invece maggiormente correlati al disturbo dell'attenzione e dell'iperattività[6]. La grande plasticità del sistema nervoso nei primi anni di vita può essere regolata sia da fattori positivi che negativi e l'attivazione di programmi di screening basati su tali associazioni può ridurre la gravità dell'espressione sintomatologica e delle ricadute funzionali dei disturbi[7-10].

Da qui l'importanza dell'"occhio" e della pratica clinica del pediatra, in particolare quello di famiglia, nell'individuare precocemente potenziali disturbi.

Il ruolo dei genitori nell'identificazione dei primi sintomi è cruciale e anche i genitori devono essere coinvolti nella valutazione. Sono i genitori che si accorgono del ritardo nell'acquisizione di alcune tappe evolutive fondamentali o delle caratteristiche comportamentali atipiche nella risposta del proprio bambino agli stimoli, ai richiami o in generale nella comunicazione e nella relazione con gli altri. È quindi importante coinvolgere attivamente i genitori sin dalla fase della diagnosi.

In ambito di neuropsichiatria infantile e salute mentale del bambino la prevenzione è ancora e sempre più importante.

In tutta la medicina e anche nell'ambito della neuropsichiatria infantile l'attenzione è sempre più rivolta alla prevenzione. È infatti ampiamente dimostrato che nella psicopatologia infantile la prevenzione consente di ridurre l'incidenza di patologie psichiatriche gravi non solo nel corso della crescita, ma anche nell'età adulta. Preservare la salute mentale del bambino è essenziale per prevenire l'insorgenza dei disturbi mentali in tutto il corso della vita e questa azione dovrebbe essere una delle priorità anche a livello politico e istituzionale[9]. Purtroppo la disattenzione istituzionale è cronica e l'organizzazione dei servizi di cura e riabilitazione neuropsichiatrica per l'età evolutiva sconta ritardi nell'allocazione di risorse e nell'uso appropriato e qualitativo di queste ultime[11]. In tale contesto diventa ancora più rilevante il ruolo delle figure e delle professionalità che accompagnano il bambino per l'acquisizione del miglior benessere: i genitori osservatori privilegiati; il pediatra di famiglia come referente dei genitori, primo punto di riferimento e responsabile dell'*advocacy* a sostegno dello star bene del bambino; il neuropsichiatra/psicologo in quanto specialista. Col crescere saranno anche l'educatore e l'insegnante a dover essere coinvolti affinché l'efficacia di un intervento con il bambino ne benefici. Purtroppo nella pratica sia la condivisione di informazioni che la raccolta/osservazione necessitano di sistematizzazione, di criteri basati su

prove di evidenza e di fattibilità. A tale proposito, nell'ambito dell'albero-progetto NASCITA[12] è stato attivato un ramo mirato a costruire un approccio condiviso e attivo tra genitori, pediatri e neuropsichiatri/psicologi in occasione dei bilanci di salute dei due anni d'età. La possibilità di avviare programmi di screening è connessa alla difficoltà di individuare uno strumento specifico e sensibile per identificare i soggetti maggiormente a rischio[13]. Sono stati scelti tre test che fossero semplici da utilizzare da parte del pediatra e dei genitori, validati per il contesto italiano e che fossero sensibili in termini di precisione e accuratezza nel fornire informazioni, quindi utili nell'individuare precocemente un potenziale bisogno così da attivare l'accompagnamento del bambino e della famiglia ad un approfondimento (vedi Appendice).

Tre test per identificare i soggetti maggiormente a rischio, semplici da utilizzare sia per il pediatra sia per i genitori.

LE COMPETENZE E LE ATTITUDINI DEL BAMBINO

Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R)

L'M-CHAT-R è uno strumento di screening per l'autismo. I destinatari dello strumento sono i genitori e il suo obiettivo è valutare il rischio del bambino di soddisfare i criteri per un disturbo dello spettro autistico. Tuttavia con il test si vogliono indagare quattro aree (il linguaggio, le competenze sociali, il comportamento, l'area sensoriale) oggetto di valutazione di tutti i bambini da parte del pediatra.

Ricevere una diagnosi tempestiva dovrebbe consentire l'attivazione al bisogno di interventi volti a migliore il livello verbale, di apprendimento e relazionale[13]. Sebbene nell'ultimo decennio la diagnosi precoce dei disturbi dello spettro sia migliorata vi è un ulteriore margine di miglioramento e il contributo del pediatra di famiglia è determinante[14].

La M-CHAT-R è uno strumento di screening da sottoporre ai genitori costituito da 20 item a risposta dicotomica (sì/no) volti a indagare i comportamenti usuali del bambino[15]. La maggior parte delle domande che portano a una risposta negativa indica un potenziale rischio di disturbo. Se il punteggio è minore di 3, il bambino risulta essere a basso rischio, con punteggio tra 3 e 7 a medio rischio, infine se il punteggio è maggiore di 8, il bambino risulta essere a rischio elevato. In questo caso si suggerisce un intervento immediato di approfondimento diagnostico da parte di un neuropsichiatra/psicologo.

Nel caso di un punteggio 3-7 si può procedere ad un approfondimento ulteriore da parte del pediatra di famiglia utilizzando l'intervista di follow-up. L'intervista consente di migliorare il valore predittivo positivo del test raccogliendo informazioni aggiuntive ed esempi specifici dei comportamenti risultati "a rischio" nella checklist iniziale. Qualora all'intervista di follow-up si dovesse avere un numero di risposte positive ≥ 2 viene suggerito un approfondimento diagnostico da parte di uno specialista. Per il progetto NASCITA l'intervista di follow-up non è stata utilizzata perché per l'approfondimento da parte del pediatra è stata utilizzata una apposita lista di domande a cui rispondere acquisendo informazioni nel corso della visita (tra queste la batteria prevista dai CDC ai due anni d'età)[16].

L'utilizzo della M-CHAT-R da parte del pediatra consente una valutazione più accurata e condivisa con l'osservazione dei genitori delle quattro aree dello sviluppo così da meglio gestire i potenziali bisogni (tabella I).

M-CHAT-R: consente una valutazione accurata e condivisa con i genitori.

L'M-CHAT-R è un'importante risorsa anche per i genitori in quanto permette loro di osservare i comportamenti «usuali» del bambino, potendo confrontare ciò che il proprio figlio è in grado di fare rispetto ai comportamenti normotipici di quella fascia evolutiva, acquisendo maggiori consapevolezza e capacità di osservazione dei comportamenti del bambino (*empowerment* genitoriale).

IL DISTRESS GENITORIALE

Parenting Stress Index – Short Form (PSI-SF)

Il distress genitoriale è stato descritto come il grado di discrepanza percepita dal genitore tra le richieste del figlio e le proprie capacità di farvi fronte adeguatamente[17]. È influenzato dalle caratteristiche del bambino, del geni-

Tabella I. Informazioni che il pediatra e il genitore possono acquisire con i risultati dei 3 test.

Per il pediatra	Per il genitore
M-CHAT-R	**M-CHAT-R**
• Intercettare i segni di allarme relativi al bambino, soprattutto in coloro che sono considerati a maggior rischio evolutivo. • Mobilitare in anticipo la rete territoriale, «accompagnando» ai servizi/professionisti in modo appropriato. • Apprendere nuove tecniche tramite utilizzo di strumenti/test standardizzati e utilizzati nella pratica clinica. • Verificare se vi è una concordanza tra i comportamenti osservati durante la visita e quelli evidenziati come deficitari dai genitori nel questionario.	• I genitori diventano osservatori dei comportamenti «usuali» del bambino, potendo confrontare ciò che il proprio figlio è in grado di fare rispetto ai comportamenti «tipici» di quella fascia evolutiva. • Maggiore consapevolezza dei comportamenti tipici e atipici. • Viene rafforzato il ruolo del pediatra come figura di riferimento al quale potersi affidare nel momento del bisogno/dubbio. • Confrontarsi con gli altri genitori rispetto alle proprie preoccupazioni sullo sviluppo del figlio.
PSI-SF	**PSI-SF**
• Ottenere una misura «oggettiva» del malessere del genitore, a supporto dell'invio ai servizi e professionisti appropriati. • Instaurare una buona alleanza con i genitori, conoscere le loro preoccupazioni, percezioni, vissuti negativi o positivi, con il fine di supportarli.	• Concedersi uno spazio di riflessione sui propri vissuti e percezioni di sé come genitore, dell'influenza che la genitorialità ha sul proprio benessere generale. • Notare come questi aspetti interagiscono con le caratteristiche del bambino. • Ricevere rispecchiamento e validazione delle proprie fatiche e un feedback oggettivo sul proprio stato psicologico. • Vedere riconosciuta la possibilità di chiedere aiuto. • Il pediatra diventa una figura di riferimento al quale potersi affidare nel momento del bisogno/dubbio, non solo rispetto alle esigenze del bambino, ma anche alle proprie.
DERS	**DERS**
• Intercettare i segni di allarme relativi a ciascun genitore. • Tranquillizzare il genitore ansioso. • Modulare la propria comunicazione in base all'emotività del genitore. • Individuare fattori di rischio nel genitore. • Rafforzare le risorse del genitore. • Prevenire interazioni disfunzionali genitore-bambino. • Supportare il genitore nelle proprie difficoltà emotive.	• Concedersi uno spazio per riflettere sul proprio funzionamento emotivo. • Acquisire maggiore consapevolezza delle proprie risorse e limiti. • Prendere contatto con le proprie emozioni. • Imparare a modulare le reazioni emotive. • Riflettere sulle strategie messe in atto. • Sostituire strategie poco efficaci. • Confrontarsi con il proprio partner.

tore, e del contesto di appartenenza. Diventare genitori rappresenta di per sé un fattore potenzialmente stressante e il distress genitoriale aumenta in presenza di bambini difficili, con sviluppo atipico, eventi stressanti e ridotto supporto sociale[18].

Per valutarlo è stato utilizzato il *Parenting Stress Index – Short Form* (PSI-SF), un questionario autosomministrato validato in italiano nel 2008[19]. Il PSI-SF è composto di 36 item a cui il genitore deve attribuire un punteggio su una scala Likert a 5 punti in base al grado d'accordo. Gli item appartengono a 3 scale:

- la scala del **Distress genitoriale** descrive la percezione dell'impatto che la genitorialità ha avuto sulla propria vita, in termini di sacrificio, responsabilità e conflitto con il partner, oltre che più generali sentimenti di insoddisfazione, inefficacia personale e solitudine;
- la scala dell'**Interazione disfunzionale genitore-figlio** mira ad individuare i sentimenti negativi connessi alla delusione delle aspettative di rinforzo positivo che il genitore ripone nei confronti dell'interazione con il figlio;
- la scala del **Bambino difficile** indica la percezione che il genitore ha delle richieste e delle caratteristiche di temperamento difficile del bambino, come l'emotività negativa, l'irritabilità, i comportamenti provocatori e disobbedienti.

Sommando i tre punteggi si ottiene un totale quale indicatore generale del distress del genitore. I valori ≥ 85 (per i genitori di bambini di età < di 3 anni) sono considerati come indicativi di livelli elevati di distress.

Il test comprende anche una scala di Risposta difensiva (non inclusa nel punteggio totale), la quale valuta il grado con cui il soggetto risponde al questionario con la tendenza a dare un'immagine di sé più favorevole.

Punteggi elevati di distress genitoriale valutato nell'infanzia e nell'età prescolare del figlio sono stati associati a sintomi internalizzanti ed esternalizzanti e a ridotte competenze sociali del bambino in età prescolare[18,20], così come a esiti psicopatologici nello sviluppo successivo[21,22].

Esiste, confermata dalle evidenze, una forte associazione tra distress genitoriale e benessere psicologico del bambino.

Esistono evidenze che il distress genitorale influenzi il benessere psicologico del bambino[18,21]. Questo avviene perché il bambino subisce lo stress, l'irritabilità del genitore e la negatività del clima familiare che ne deriva, anche quando i comportamenti del genitore non sono rivolti al figlio stesso. Inoltre, fattori che causano distress nel genitore, come avversità famigliari, eventi stressanti, fattori genetici e temperamentali, possono quindi spiegare anche problematiche emotive e comportamentali del bambino. Tuttavia nella forza dell'associazione tra distress genitoriale e stato psicologico del figlio anche altri fattori possono agire quali il *parenting* (le competenze genitoriali, il modo in cui i genitori assolvono alle funzioni genitoriali, la genitorialità) e la relazione d'attaccamento[23,24]. Un genitore stressato è propenso a interpretare negativamente i comportamenti del bambino e rispondere con minore sensibilità e responsività ai suoi bisogni, mostra meno coinvolgimento e vicinanza affettiva nella relazione con il figlio e assume uno stile educativo maggiormente autoritario. Risultano pertanto più frequenti i conflitti nella diade ed è più alto il rischio di maltrattamento.

Poiché i punteggi ottenuti dalla somministrazione del PSI-SF costituiscono validi indicatori non solo delle difficoltà psicologiche del genitore, ma anche

delle interazioni genitore-bambino stressanti e di difficoltà psicologiche del bambino, il test può essere considerato un ottimo strumento per identificare precocemente le situazioni a rischio psicopatologico, con il fine di compiere valutazioni specialistiche più approfondite e avviare tempestivamente interventi con il genitore, con il bambino o con la diade.

Con i risultati del PSI-SF il pediatra dispone di una misura «oggettiva» del malessere del genitore in termini di preoccupazioni, percezioni, vissuti negativi o positivi così da poter meglio contribuire, anche indirizzando/accompagnando ai servizi appropriati, a contenere o ridurre il distress genitoriale (tabella I). Il pediatra diviene inoltre una figura di riferimento alla quale potersi affidare nel momento del bisogno, non solo per le esigenze del bambino, ma anche per le proprie.

Compilare il PSI-SF da parte del genitore lo costringe a riflettere sui propri vissuti, sulle percezioni di sé come genitore e sull'influenza che questi hanno non solo sul proprio benessere generale, ma anche su quello del figlio. Anche in questo caso un'azione volta all'*empowerment* genitoriale.

LA DISREGOLAZIONE EMOTIVA

Difficulties in Emotion Regulation Scale (DERS)

La disregolazione emotiva corrisponde con la difficoltà di riconoscimento, interpretazione e regolamentazione delle proprie emozioni.

Per disregolazione emotiva si intende la difficoltà della persona nel riconoscere, interpretare e regolare le proprie emozioni, rendendole adattive in base al contesto in cui si trova[25,26]. Non significa quanto la persona sia capace di controllare o reprimere le emozioni, specialmente quelle spiacevoli, ma quanto lo sia di sperimentarle tutte (gioia, paura, tristezza, rabbia, sorpresa, disgusto), modularne l'intensità e l'espressività. La disregolazione emotiva gioca un ruolo importante nello sviluppo emotivo del bambino e più tardi nello sviluppo sociale dell'adolescente, costituendo uno dei fattori di rischio per lo sviluppo dei disturbi del neurosviluppo come l'ADHD, i disturbi del comportamento, l'uso di sostanze e il rischio suicidario[27-29].

Dove si apprende? Come si tramanda? La traiettoria intergenerazionale della disregolazione emotiva viene tramandata di genitore in figlio influenzandone lo sviluppo emotivo e più tardi lo sviluppo sociale[25,26,28]. Diversi sono i meccanismi attraverso i quali il bambino impara a regolare le emozioni. La prima è quella dell'osservazione e imitazione dei modelli genitoriali. Ma anche il clima emotivo famigliare che può essere allarmante, imprevedibile oppure distanziante, repressivo e punitivo può determinare la regolazione delle emozioni. La modalità in cui vengono percepite le emozioni da parte dei genitori è importante: se sono accolte positivamente oppure punite; se sia lecito esprimerle apertamente oppure siano fonte di vergogna; quali credenze sono associate ad esse; se il bambino viene reputato debole, lamentoso; se provocano senso di colpa nel genitore per non essere in grado di far fronte allo stato d'animo del proprio figlio. I genitori insegnano ai propri figli (anche inconsapevolmente o in modo passivo) strategie per far fronte alle emozioni, se esternarle (es. pianto, grida) oppure reprimerle e tenerle per sé per non mostrarsi deboli davanti agli altri, imparare a calmarsi attraverso il respiro, oppure evitarle e nasconderle. La regolazione emotiva non può essere scissa dalla relazione di attaccamento che si instaura tra il bambino e il *caregiver*, come il genitore accoglie e risponde ai bisogni

del figlio, costituisce una base sicura per quest'ultimo alla quale rivolgersi quando è in difficoltà per poi tornare ad esplorare l'ambiente e costruirsi la propria autonomia e indipendenza.

I fattori che contribuiscono alla disregolazione emotiva possono essere individuali, famigliari, socio-culturali, economici. Le caratteristiche temperamentali proprie del genitore e del bambino sono mediatori nella regolazione delle emozioni, oltre al livello di stress percepito. Maggiore è lo stress percepito e minore è la capacità di regolare le emozioni aumentando l'esito negativo nello sviluppo emotivo, cognitivo e sociale del bambino già dai primi anni di vita.

La disregolazione emotiva può dipendere da fattori individuali, famigliari, socio-culturali ed economici.

La scala DERS è un questionario autosomministrato sviluppato nel 2004 e tradotto in diverse lingue, tra cui l'italiano[30,31]. Formata da 36 item con risposta su scala Likert a 5 punti (da "quasi mai" a "quasi sempre") la DERS è composta da 6 scale dimensionali che misurano: il grado di attenzione prestata al proprio stato emotivo (*awareness*), la chiarezza nel comprendere distintamente quale emozione si sta provando (*clarity*), la difficoltà nel mantenere il controllo del proprio comportamento quando si provano emozioni negative (*impulsivity*), la difficoltà nel distrarsi dall'emozione negativa che si sta provando e quindi portare a termine ciò che si sta svolgendo (*goals*), la scarsa accettazione rispetto le proprie emozioni (*non acceptance*) e il livello di fiducia nelle proprie capacità e strategie di regolazione emotiva (*strategies*).

Maggiore è il punteggio totale ottenuto, maggiori saranno le difficoltà emotive riscontrate (la disregolazione emotiva di chi compila). Caratteristiche dei genitori "disregolati" sono: la tendenza a provare emozioni negative secondarie, ossia in risposta al proprio stato d'animo come vergogna, disagio e frustrazione; la tendenza a reprimere e minimizzare il vissuto emotivo, arrivando a "far finta di niente"; la difficoltà nel portare a termine un compito perché sopraffatti dal rimuginio; il senso di inadeguatezza che rende difficile distrarsi da ciò che si sta provando in quel momento; l'impulsività e lo scarso controllo emotivo che può essere esternalizzato (es. aggressività, urla, scoppi d'ira, pianto) oppure internalizzato (es. ansia, depressione, sintomi psicosomatici)[32-34]. Altri aspetti della mancata regolazione emotiva sono la scarsa fiducia nelle proprie capacità, come il sentirsi inadeguati, sopraffatti e disperati o la mancanza di mentalizzazione, ossia di prestare adeguata attenzione al proprio vissuto, riconoscere l'emozione che si sta sperimentando sentendosi quindi confusi, spaventati e paralizzati.

La scala DERS permette al pediatra di intercettare sintomi di interazioni disfunzionali genitore-bambino.

Disporre dei risultati di questa scala permette al pediatra di intercettare sintomi di interazioni disfunzionali genitore-bambino relativi a ciascun genitore così da poter indirizzare/consigliare il genitore ad un approfondimento presso uno specialista nell'interesse reciproco, del genitore e del figlio, e anche poter sostenere il genitore nelle proprie difficoltà emotive, individuandone le risorse e aiutandolo a prestare maggiore attenzione a sé, ad ascoltarsi e a riflettere sul proprio vissuto (tabella I). Compilare il questionario DERS comporta per il genitore il concedersi uno spazio in cui riflettere sul proprio vissuto emotivo e farne una valutazione. Se lo fa anche il partner e ci si confronta dopo la compilazione può rappresentare un'occasione di condivisione e partecipazione dei propri limiti e delle capacità di

modulare le proprie reazioni oppure esternarle rinforzando il rapporto di genitorialità e l'individuazione di bisogni.

DATI PRELIMINARI DELLO STUDIO NASCITA

3 test, 380 genitori, 45 pediatri di famiglia, nell'ambito della visita del bilancio di salute ai due anni di età.

L'analisi preliminare fa riferimento ai risultati dei test sottoposti a 380 genitori (142 coppie, 215 madri e 23 padri) e dalle informazioni raccolte da 45 pediatri di famiglia durante la visita del bilancio di salute ai due anni d'età.

▶ **M-CHAT-R.** 33 bambini (9%) sono risultati a rischio riportando un punteggio ≥3 e 1 di questi è risultato essere ad elevato rischio. Questi tassi sono in accordo con quanto riportato in letteratura con ampia variabilità (4-14%) utilizzando lo stesso strumento[35-38]. Nel corso delle analisi è emersa una correlazione significativa tra i comportamenti descritti dai genitori come deficitari nell'M-CHAT-R e tre specifici item valutati dal pediatra e contemplati dalla *Milestone Checklist*[38] utilizzata nel corso dei vari bilanci di salute. Gli item risultati significativi di approfondimento sono:

1. usa il dito indice per indicare (richiedere o mostrare);
2. tiene una matita o un bastoncino e scarabocchia sulla carta o per terra/sul pavimento;
3. sa dire alcune frasi con un numero di parole compreso tra 2 e 4.

▶ **PSI-SF.** Per 64 bambini (16,8%) il test è risultato positivo di distress dei genitori e in particolare nel 13,2% dei questionari compilati dalle madri, nel 13,9% di quelli compilati dai padri e nel 4,2% di quelli da entrambi. Possiamo ipotizzare che in queste famiglie, dove entrambi i genitori esprimono distress riconducibile alla genitorialità, i bambini siano esposti a maggiore rischio di sviluppare problematiche psicologiche e l'intervento debba essere tempestivo. Inoltre non sono trascurabili i risultati relativi alle risposte difensive che rappresentano il 25,6% dei risultati positivi nelle madri, il 29,3% nei padri e il 41,5% nelle coppie genitoriali – almeno un genitore con risultato positivo. È ipotizzabile dunque che diversi genitori abbiano voluto offrire un'immagine di sé e della propria esperienza genitoriale più positiva. Questi dati evidenziano l'importanza per il pediatra di costruire un rapporto di fiducia e alleanza con i genitori affinché si sentano maggiormente disponibili a condividere le proprie difficoltà e ricevere aiuto.

Considerando le sottoscale del PSI-SF la maggiore prevalenza di positività si osserva nelle risposte della scala Bambino difficile (26,1% nelle madri, 26,3% nei padri, 37,3% nella coppia genitoriale), mentre risultano inferiori i punteggi delle scale Distress genitoriale e Interazione disfunzionale genitore-figlio. L'andamento si inverte nei casi risultati negativi. Quindi il PSI-SF è efficace nell'identificare bambini che posseggono tratti temperamentali difficili con maggiore rischio psicopatologico e che i genitori di questi bambini siano soggetti a sperimentare maggiori livelli di stress.

▶ **DERS.** Sono 19 i bambini (5%) con almeno un genitore positivo al test. Il 2,8% delle madri e il 6,1% dei padri riportano punteggi clinicamente significativi. Le prevalenze sono risultate simili nei test effettuati da entrambi i genitori, suggerendo quindi una tendenza dei papà a esprimere una maggiore disregolazione emotiva e una minore sicurezza riguardo le proprie capacità genitoriali.

▶ **M-CHAT-R, PSI-SF, DERS.** Analizzando i risultati ottenuti con i tre test il pediatra è nella condizione di valutare potenziali disturbi del bambino, ma anche l'associazione con la genitorialità nel manifestarsi della sintomatologia così da accompagnare adeguatamente la diade dallo specialista (neuropsichiatra/psicologo) a cui verrà riferito il caso.

La maggior parte dei genitori (287/380) non riporta alcun campanello d'allarme rispetto al proprio bambino, nessun segnale di stress genitoriale e una buona regolazione emotiva (tabella II). Nessun campanello d'allarme viene rilevato da 60/380 genitori dei quali: 42 si ritengono stressati pur mantenendo una buona regolazione emotiva, 7 non segnalano livelli elevati di stress a fronte di una eccessiva disregolazione emotiva, e 11 sono eccessivamente allarmati e disregolati. Aspetti problematici nel bambino emergono per 33/380 genitori: 21 non mostrano segnali di stress né di mancata regolazione emotiva, 11 riferiscono un elevato livello di stress con buone capacità di regolazione emotiva e un solo genitore ha difficoltà a regolarsi senza tuttavia percepire il livello di stress. Lo scenario peggiore, in cui tutti i test risultano positivi, non si profila per nessuno. Combinando i risultati ottenuti dai tre test e dalla valutazione clinica, accertatosi delle condizioni del bambino rispetto ai risultati emersi, il pediatra può restituire ai genitori una sintetica descrizione di quanto emerso e sintetizzare una relazione strutturata per lo specialista (ultima colonna tabella II). In generale sembrano emergere due tendenze opposte, la minimizzazione e l'esagerazione del potenziale disturbo. Quindi compito del pediatra è anche quello di verificare che quanto riportato dai genitori corrisponda alla reale condizione del bambino. Sarà poi lo specialista, se necessario, a meglio definire la presenza del disturbo e la sua entità.

Due le tendenze opposte che emergono: minimizzare o esagerare il potenziale disturbo da parte dei genitori; compito del pediatra è anche verificare la reale condizione del bambino.

I risultati discordanti tra M-CHAT-R e PSI-SF potrebbero indicare scenari a rischio psicopatologico elevato, dove il genitore non coglie e non si prende cura in modo adeguato dei bisogni del bambino.

LA COMUNICAZIONE ATTESA PER PROCEDERE

L'utilizzo nella pratica della pediatria di famiglia di strumenti standardizzati come quelli qui presentati può consentire di individuare precocemente e in modo oggettivo elementi indicativi di un problema potenziale o in essere, consentendo una valutazione specialistica più tempestiva.

Pensiamo per esempio a quelle situazioni nelle quali il genitore segnala problematiche che il pediatra non ha modo di osservare direttamente, ma che deve valutare per poi agire. Oppure, al contrario, quando il pediatra coglie elementi disfunzionali che invece il genitore non vuole o non è in grado di vedere: situazione che dilata i tempi e limita le modalità di intervento.

Il genitore arriva dal neuropsichiatra infantile con uno stato d'animo che varia da una vaga diffidenza, a uno stato d'ansia e di paura, fino ad arrivare ad atteggiamenti di resistenza e ostilità. C'è paura del giudizio, del "verdetto diagnostico", che venga messa in dubbio la stessa potestà genitoriale. Tutto questo condiziona l'atteggiamento iniziale del genitore nella relazione con il neuropsichiatra: spesso di tipo normalizzante o al contrario eccessivamente allarmato, oppure negante. Questa condizione fa sì che molte informazioni utili alla comprensione del problema vengano perse o emergano molto avanti

nella valutazione. Si tratta di informazioni relative a tutti quei fattori che intervengono nell'eziopatogenesi della psicopatologia dell'età evolutiva, non solo inerenti direttamente il bambino, ma anche la storia dei genitori e delle famiglie di origine, lo stile educativo e il tipo di attaccamento. Queste informazioni sono importanti per lo specialista per orientare la diagnosi, per ipotizzare una traiettoria evolutiva del disturbo e per impostare un'appropriata terapia, potendo scegliere il tipo di trattamento funzionale non solo alla cura del sintomo manifestato, ma anche a prevenire l'aggravamento. È compito del neuropsichiatra vincere le resistenze del genitore e instaurare una relazione di fiducia affinché queste informazioni possano emergere. In tale contesto il ruolo del pediatra di famiglia può essere facilitante perché conosce sia il bambino fin dalla nascita che il nucleo famigliare e ha osservato e valutato le potenziali disfunzionalità.

Una comunicazione condivisa all'interno della triade genitore-pediatra-neuropsichiatra in termini di tempestività e specificità di intervento potrebbe quindi contribuire anche all'efficacia della risposta. Con l'esercizio fatto creando un ramo pilota del progetto NASCITA, si è dimostrata la fattibilità di attivare un processo di comunicazione utilizzando un linguaggio comune

Tabella II. Dati preliminari studio NASCITA per M-CHAT-R, PSI-SF, DERS e potenziali indicazioni del pediatra per lo specialista.

M-CHAT-R	PSI-SF	DERS	Totale	Relazione pediatra
–	–	–	287	Non emergono difficoltà: nella norma.
+	–	–	21	Verificare i segni di allarme relativi al bambino; se presenti: **a.** il genitore minimizza questi campanelli d'allarme? **b.** il genitore riesce a far fronte allo stress e alla regolazione emotiva in modo adeguato?
–	+	–	42	In quali dimensioni il genitore risulta stressato? Percepisce se stesso / il bambino / l'interazione come difficile? Esagera le difficoltà?
–	–	+	7	La disregolazione è data da altri fattori (individuali / coppia / lavoro / salute…).
+	+	–	11	Verificare segni di allarme relativi al bambino; se presenti: **a.** in quali dimensioni il genitore risulta stressato? **b.** percepisce se stesso / il bambino / l'interazione come difficile? **c.** riconosce lo stress, ma riesce a far fronte alla regolazione emotiva in modo adeguato.
+	–	+	1	Verificare i segni di allarme relativi al bambino; se presenti: **a.** il genitore minimizza questi campanelli d'allarme? **b.** riesce a far fronte allo stress, ma ha difficoltà a regolare le proprie emozioni. Non comprende perché si sente così? **c.** la disregolazione è data da altri fattori (individuali / coppia / lavoro / salute…)?
–	+	+	11	In quali dimensioni il genitore risulta stressato? Percepisce se stesso / il bambino / l'interazione come difficile? Esagera le difficoltà? Non riesce a far fronte alla regolazione emotiva in modo adeguato (ansia, panico).
+	+	+	0	Verificare i segni di allarme relativi al bambino. Nucleo ad elevato rischio.

Cut off: M-CHAT-R ≥ 3; PSI-SF ≥ 85; DERS ≥ 98
–, risultati sotto il valore soglia; +, risultati clinicamente significativi, sopra il valore soglia.

rappresentato anche da strumenti standardizzati quali quelli qui presentati. Si pensi per esempio all'M-CHAT come segnalatore precoce di comportamenti suggestivi dei disturbi dello spettro autistico, in base al quale il neuropsichiatra inizierà a svolgere subito approfondimenti in quella direzione. Così come la DERS come indicatore di alta espressività emotiva genitoriale in grado di orientare, fin dall'inizio della fase valutativa, verso una problematica nelle dinamiche di attaccamento. Ovviamente la comunicazione pediatra-neuropsichiatra dovrebbe essere a doppio senso e prevedere una restituzione di informazioni da parte del neuropsichiatra concernenti la diagnosi, la presa in carico, il trattamento.

Una comunicazione diretta oltre a garantire la collaborazione fra le parti consentirebbe di evitare errori dovuti all'intermediario-genitore che non sempre è in grado di comprendere o di riferire correttamente. Nei casi più lievi, nei quali si decide di assumere una condotta d'attesa e di rivedere il paziente dopo un tempo prefissato, il coinvolgimento attivo del pediatra di famiglia può contribuire a prevenire i casi di *drop out* avendo l'occasione di vedere il bambino o il genitore nel periodo di attesa; trasformando un tempo d'attesa in vigile osservazione. Come ha avuto modo di mettere in luce aspetti disfunzionali per i quali ha dato indicazione documentata per una prima valutazione specialistica, allo stesso modo il pediatra di famiglia è "alleato" attivo monitorando il percorso di cura condiviso con il neuropsichiatra. Un percorso che vede la partecipazione attiva del pediatra di famiglia nel triage d'accesso ai servizi di neuropsichiatria infantile. Un percorso a tutt'oggi accidentato per pazienti e famiglie che ne hanno diritto. **R&P**

Il presente articolo esce in contemporanea anche sull'edizione di *Medico e Bambino* del mese di maggio e sul numero 3 di *Quaderni acp*.

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M-CHAT-R

Per favore risponda a queste domande tenendo presente qual è il comportamento usuale del suo bambino/a. Se ha visto un certo comportamento alcune volte, ma normalmente il suo bambino/a non si comporta in quel modo, per favore risponda "No".
Sbarri la casella vicino al "Sì" o al "No" a fianco ad ogni domanda. Grazie molte.

1.	Se Lei indica qualcosa che si trova dall'altra parte della stanza, il suo bambino/a guarda da quella parte? (*per esempio*, se Lei indica un giocattolo o un animale, Suo figlio/a guarda verso il giocattolo o l'animale?)	Sì ☐	No ☐
2.	Si è mai domandato/a se il suo bambino/a possa essere sordo/a?	Sì ☐	No ☐
3.	Il suo bambino/a gioca a "far finta che" (gioco di finzione)? (*per esempio*, fa finta di bere da una tazza vuota, o fa finta di parlare al telefono, o fa finta di dar da mangiare ad una bambola o a un peluche?)	Sì ☐	No ☐
4.	Al suo bambino/a piace arrampicarsi sulle cose? (*per esempio*, sui mobili o sugli attrezzi al parcogiochi, o sulle scale?)	Sì ☐	No ☐
5.	Il suo bambino/a fa dei movimenti insoliti con le dita davanti agli occhi? (*per esempio*, muove le dita avanti e indietro vicino agli occhi?)	Sì ☐	No ☐
6.	Il suo bambino/a indica con un dito per chiedere qualcosa o per chiedere aiuto? (*per esempio*, indica una merendina o un gioco fuori portata?)	Sì ☐	No ☐
7.	Il suo bambino/a indica con un dito per farle vedere qualcosa di interessante? (*per esempio*, indica un aereoplano in cielo o un grosso camion per strada?)	Sì ☐	No ☐
8.	Il suo bambino/a mostra interesse per gli altri bambini? (*per esempio*, guarda altri bambini, sorride a loro, o va verso di loro?)	Sì ☐	No ☐
9.	Il suo bambino/a Le mostra delle cose portandogliele o tenendole in alto per fargliele vedere? Non per chiedere aiuto, ma soltanto per condividere? (*per esempio*,, le mostra un fiore, un peluche, o un camion giocattolo?)	Sì ☐	No ☐
10.	Il suo bambino/a reagisce quando Lei lo/a chiama per nome? (*per esempio*, quando Lei lo chiama per nome, il suo bambino/a guarda verso di Lei, parla o fa delle sequenze di suoni (come "ba-ba", "la-la"…) o smette di fare quello che sta facendo?)	Sì ☐	No ☐
11.	Quando Lei sorride al suo bambino/a, lui/lei sorride a sua volta verso di Lei?	Sì ☐	No ☐
12.	Il suo bambino/a è agitato da rumori comuni? (*per esempio*, grida o piange per il rumore di un aspirapolvere o per una musica ad alto volume?)	Sì ☐	No ☐
13.	Il suo bambino/a cammina?	Sì ☐	No ☐
14.	Il suo bambino/a La guarda negli occhi quando Lei gli/le sta parlando, sta giocando con lui/lei, o lo/a sta vestendo?	Sì ☐	No ☐
15.	Il suo bambino/a cerca di copiare ciò che Lei fa? (*per esempio*, La copia quando Lei fa ciao con la mano, batte le mani o fa un rumore buffo?)	Sì ☐	No ☐
16.	Se Lei gira la testa per guardare qualcosa, il suo bambino/a si guarda intorno per vedere che cosa Lei sta guardando?	Sì ☐	No ☐
17.	Il suo bambino/a cerca di farsi guardare da Lei? (*per esempio*, il suo bambino La guarda per farsi fare un complimento, o dice "Guarda" o "Guardami"?)	Sì ☐	No ☐
18.	Il suo bambino/a capisce quando Lei gli/le dice di fare qualcosa? (*per esempio*, il suo bambino capisce "Metti il libro sulla sedia", o "Portami la copertina" anche se Lei non indica queste cose?)	Sì ☐	No ☐
19.	Se capita qualcosa di insolito, il suo bambino/a La guarda in faccia per capire come Lei si sente in quel momento? (*per esempio*, se sente un rumore strano o buffo, o se vede un giocattolo nuovo, il suo bambino/a La guarda in faccia?)	Sì ☐	No ☐
20.	Al suo bambino/a piace fare giochi di movimento? (*per esempio*, gli/le piace che lo si faccia dondolare o che lo si faccia rimbalzare sulle ginocchia?)	Sì ☐	No ☐

PARENTING STRESS INDEX – PSI – SF

Compilata da ☐ Mamma ☐ Papà

Informazioni sul bambino

Data di nascita |__|__| |__|__| |__|__|__|__| ☐ Maschio ☐ Femmina

giorno mese anno

Indichi con una X la risposta che meglio interpreta esattamente i suoi sentimenti. Indichi la risposta che descrive meglio o che più si avvicina a ciò che Lei prova.

LA PRIMA REAZIONE A CIASCUNA DOMANDA DOVREBBE ESSERE LA SUA RISPOSTA.

Indichi una sola risposta per ogni domanda e risponda a tutte le domande.
Grazie per la collaborazione!

		Fortemente d'accordo	D'accordo	Non è sicuro	In disaccordo	Fortemente in disaccordo
1.	Spesso ho la sensazione di non riuscire a far fronte molto bene alle situazioni.	1	2	3	4	5
2.	Per venire in contro al bisogno di mio/a figlio/a mi accorgo di sacrificare la mia vita più di quanto mi aspettassi.	1	2	3	4	5
3.	Mi sento intrappolata/o dalle mie responsabilità di genitore.	1	2	3	4	5
4.	Da quando ho avuto questo/a figlio/a non riesco a fare cose nuove e diverse.	1	2	3	4	5
5.	Da quando ho avuto questo/a figlio/a, mi rendo conto che quasi mai riesco a fare le cose che mi piacciono.	1	2	3	4	5
6.	Non sono soddisfatto/a dell'ultimo acquisto di abbigliamento che ho fatto per me.	1	2	3	4	5
7.	Ci sono un bel po' di cose della mia vita che mi disturbano.	1	2	3	4	5
8.	Aver avuto un figlio/a ha causato, nel rapporto con mio/a marito/moglie (o col partner), più problemi di quanto mi aspettassi.	1	2	3	4	5
9.	Mi sento sola/o e senza amici.	1	2	3	4	5
10.	Quando vado ad una festa di solito mi aspetto di non divertirmi.	1	2	3	4	5
11.	Non sono così interessato/a alla gente come lo ero una volta.	1	2	3	4	5
12.	Non mi diverto più come una volta.	1	2	3	4	5
13.	Mio/a figlio/a raramente fa per me cose che mi gratificano.	1	2	3	4	5
14.	A volte mi sento di non piacere a mio/a figlio/a e che lui/lei non vuole stare vicino a me.	1	2	3	4	5
15.	Mio/a figlio/a mi sorride molto meno di quanto mi aspettassi.	1	2	3	4	5
16.	Quando faccio le cose per mio/a figlio/a ho la sensazione che i miei sforzi non siano molto apprezzati.	1	2	3	4	5
17.	Quando mio/a figlio/a gioca non ride né mostra di divertirsi spesso.	1	2	3	4	5
18.	Mio/a figlio/a non sembra imparare così velocemente come la maggioranza dei bambini.	1	2	3	4	5
19.	Mio/a figlio/a non sorride tanto quanto la maggioranza dei bambini.	1	2	3	4	5
20.	Mio/a figlio/a non riesce a fare tanto quanto mio aspettavo.	1	2	3	4	5
21.	Ci vuole molto tempo ed è molto difficile per mio/a figlio/a abituarsi alle novità.	1	2	3	4	5

→

	Fortemente d'accordo	D'accordo	Non è sicuro	In disaccordo	Fortemente in disaccordo
22. In relazione alla prossima affermazione scelga **una sola risposta** tra le alternative qui di seguito indicate: Sento di essere: ☐ Non molto bravo come genitore ☐ Una persona che ha qualche problema ad essere genitore ☐ Un genitore medio ☐ Un genitore al di sopra della media ☐ Un genitore molto bravo					
23. Mi aspettavo di provare per mio/a figlio/a sentimenti di maggior calore e vicinanza di quelli che provo e questo mi dispiace.	1	2	3	4	5
24. Talvolta mio/a figlio/a fa cose che mi disturbano, solo per farmi dispetto.	1	2	3	4	5
25. Mio/a figlio/a sembra che pianga o si agiti molto più della maggioranza dei/lle bambini/e.	1	2	3	4	5
26. Mio figlio/a di solito si sveglia di cattivo umore.	1	2	3	4	5
27. Ritengo che mio/a figlio/a sia facilmente irritabile e di umore variabile (lunatico).	1	2	3	4	5
28. Mio/a figlio/a fa alcune cose che mi infastidiscono molto.	1	2	3	4	5
29. Mio/a figlio/a reagisce duramente quando succede qualcosa che non gli piace.	1	2	3	4	5
30. Mio/a figlio/a rimane facilmente male per le più piccole cose.	1	2	3	4	5
31. I ritmi del sonno e dell'alimentazione di mio/a figlio/a sono stati molto più difficili da regolare di quanto mi aspettassi.	1	2	3	4	5
32. In relazione alla prossima affermazione scelga **una sola risposta** tra le alternative qui di seguito indicate: Mi sono resa/o conto che convincere mio/a figlio/a a fare qualcosa o a smettere di fare qualcosa è: ☐ Molto più difficile di quanto mi aspettassi ☐ Un po' più difficile di quanto mi aspettassi ☐ All'incirca difficile come mi aspettavo ☐ Un po' più facile di quanto mi aspettassi ☐ Molto più facile di quanto mi aspettassi					
33. In relazione alla prossima affermazione, scelga la sua risposta tra le alternative da "+10" a "1-3": Pensi con attenzione e conti il numero di cose che suo/a figlio/a fa e che la infastidiscono (p.es., perde tempo, si rifiuta di ascoltare, è troppo attivo, piange, interrompe, fa le lotte, fa a pugni, piagnucola, ecc): ☐ +10 ☐ 8-9 ☐ 6-7 ☐ 4-5 ☐ 1-3					
34. Alcune cose che fa mio/a figlio/a mi infastidiscono veramente molto.	1	2	3	4	5
35. Mio/a figlio/a si è dimostrato un problema più grande di quanto mi aspettassi.	1	2	3	4	5
36. Mio/a figlio/a mi chiede di più della maggior parte dei/lle bambini/e.	1	2	3	4	5

DIFFICULTIES IN EMOTION REGULATION SCALE – DERS

Indichi con una X la risposta che meglio interpreta esattamente i suoi sentimenti.
Indichi la risposta che descrive meglio o che più si avvicina a ciò che Lei prova.

LA PRIMA REAZIONE A CIASCUNA DOMANDA DOVREBBE ESSERE LA SUA RISPOSTA.

Indichi una sola risposta per ogni domanda e risponda a tutte le domande.
Grazie per la collaborazione!

		Quasi mai	A volte	Circa la metà delle volte	Molte volte	Quasi sempre
1.	Sono sereno riguardo a ciò che provo.	1	2	3	4	5
2.	Presto attenzione a come mi sento.	1	2	3	4	5
3.	Vivo le mie emozioni come travolgenti e fuori dal controllo.	1	2	3	4	5
4.	Non ho idea di come mi sento.	1	2	3	4	5
5.	Ho difficoltà a dare un senso a ciò che provo.	1	2	3	4	5
6.	Presto attenzione alle mie emozioni.	1	2	3	4	5
7.	So esattamente come mi sento.	1	2	3	4	5
8.	Mi interessa come mi sento.	1	2	3	4	5
9.	Sono confuso riguardo a ciò che provo.	1	2	3	4	5
10.	Quando sono turbato, riconosco le mie emozioni.	1	2	3	4	5
11.	Quando sono turbato, mi arrabbio con me stesso perché mi sento in quel modo.	1	2	3	4	5
12.	Quando sono turbato, mi imbarazza sentirmi in quel modo.	1	2	3	4	5
13.	Quando sono turbato, ho delle difficoltà a completare il mio lavoro.	1	2	3	4	5
14.	Quando sono turbato, perdo il controllo.	1	2	3	4	5
15.	Quando sono turbato, credo che rimarrò in quello stato per molto tempo.	1	2	3	4	5
16.	Quando sono turbato, credo che finirò per sentirmi depresso.	1	2	3	4	5
17.	Quando sono turbato, credo che i miei sentimenti siano validi e importanti.	1	2	3	4	5
18.	Quando sono turbato, faccio fatica a focalizzarmi su altre cose.	1	2	3	4	5
19.	Quando sono turbato, mi sento senza controllo.	1	2	3	4	5
20.	Quando sono turbato, posso comunque finire le cose che devo fare.	1	2	3	4	5
21.	Quando sono turbato, mi vergogno con me stesso perché mi sento in quel modo.	1	2	3	4	5
22.	Quando sono turbato, so che alla fine posso trovare un modo per sentirmi meglio.	1	2	3	4	5
23.	Quando sono turbato, mi sento debole.	1	2	3	4	5

	Quasi mai	A volte	Circa la metà delle volte	Molte volte	Quasi sempre
24. Quando sono turbato, sento di potere avere ancora il controllo dei miei comportamenti.	1	2	3	4	5
25. Quando sono turbato, mi sento in colpa perché mi sento in quel modo.	1	2	3	4	5
26. Quando sono turbato, ho delle difficoltà a concentrarmi.	1	2	3	4	5
27. Quando sono turbato, ho delle difficoltà nel controllare i miei comportamenti.	1	2	3	4	5
28. Quando sono turbato, credo che non ci sia niente che io possa fare per sentirmi meglio.	1	2	3	4	5
29. Quando sono turbato, mi irrito con me stesso perché mi sento in quel modo.	1	2	3	4	5
30. Quando sono turbato, inizio a sentirmi molto male con me stesso.	1	2	3	4	5
31. Quando sono turbato, credo che crogiolarmi in questa emozione sia l'unica cosa che io possa fare.	1	2	3	4	5
32. Quando sono turbato, perdo il controllo sui miei comportamenti.	1	2	3	4	5
33. Quando sono turbato, faccio fatica a pensare a qualcosa di diverso.	1	2	3	4	5
34. Quando sono turbato, mi prendo del tempo per riflettere su quello che sto provando veramente.	1	2	3	4	5
35. Quando sono turbato, mi ci vuole molto tempo per sentirmi meglio.	1	2	3	4	5
36. Quando sono turbato, le mie emozioni sono travolgenti.	1	2	3	4	5

Gratz, 2004. Adattamento italiano a cura di Sighinolfi, Norcini Pala, Chiri, Marchetti e Sica, 2010.

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Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3798 del 08/05/2014, n. 778 del 05/02/2015,
n. 5954 del 05/12/2016, n. 1077 del 02/02/2017,
n. 1938 del 15/02/2019, n. 3885 del 30/03/2020)
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"
"*Percorsi diagnostico-terapeutici per l'ADHD*".

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