NEWSLETTER

INDICE:

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NEURODEVELOPMENTAL PROBLEMS IN CHILDREN WITH FEBRILE SEIZURES FOLLOWED TO YOUNG SCHOOL AGE: A PROSPECTIVE LONGITUDINAL COMMUNITY-BASED STUDY IN SWEDEN.

Nilsson G, et al.

Aim: To estimate the accumulated prevalence of neurodevelopmental problems from preschool to school age in children with a history of febrile seizures (FS).

Methods: In a community-based cohort of children with previous FS, 25/73 clinically assessed children met diagnostic criteria for neurodevelopmental disorders or had major indications of such problems at the age of 4–5 years. Parents of 54 of the 73 children accepted to take part in an interview according to the Autism-Tics, ADHD and other Comorbidities (A-TAC) inventory, when the children were 9–10 years.

Results: There was a trend for ADHD symptom scores to be higher in the FS group. Non-participants at age 9–10 years had had much higher rates of neurodevelopmental problems at 4–5 years, and the total number of such problems at either 4–5 or age 9–10 was 41% (30/73).

Conclusion: High rates of neurodevelopmental problems (41%) were found at either age 4–5 or 9–10 years or both in this group of 73 children with FS. Non-participants at 9–10 years had had much higher rates of neurodevelopmental problems at 4–5 years. Further follow-up of this cohort is needed before definite conclusions can be drawn about whether FS should be considered a marker for more complex neurodevelopmental problems.

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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.

Ann Neurol. 2021;90:S75.

PAIN, COGNITION, AND ATTENTION IN CHILDREN AND ADULTS WITH CEREBRAL PALSY: A STUDY OF RETROSPECTIVE CLINICAL PAIN RATINGS.

Chin E, Hoon A, Ye X, et al.

Objective: Previous studies identify that the prevalence of chronic pain in individuals with CP 1) increases with age and 2) is reported less frequently in individuals with greater cognitive or communicative disability. Based on separate preliminary findings, we query whether superimposed attention deficits represent an additional risk factor for chronic pain.

Methods: Retrospective medical records of individuals with a diagnosis of CP with at least one documented numeric 0-10 clinical visit pain rating at Johns Hopkins campuses between 1/1/2003 and 6/30/2019 were reviewed. Abstracted data included clinical visit-associated pain scores, age, and ICD 9/10 codes for CP, intellectual disability, and ADHD. Medication and surgical history were not available.For cross-sectional analysis, each individual's most recent clinical pain rating was collected. We tested the hypothesis that coexisting attention deficit/hyperactivity disorder (ADHD) impacts clinical pain while including age and intellectual disability (ID) in a linear fixed-effects model. ADHD diagnoses were uncommon (<5%) in adults over age 45; we restricted analysis to individuals aged 5-45.

Results: 3,041 individuals were included in this analysis (Table). As previously reported, main effects of age and ID diagnosis were associated with pain scores (+0.52 points/decade and -0.32, respectively). A diagnosis of ADHD was associated with elevated pain scores (+0.42; 95% CI 0.01-0.84 points; p=0.043). Interaction with ID diagnosis was not significant.

Conclusions: Attention deficits may represent an additional risk factor for pain in individuals with CP. Caution is needed in interpreting findings from bulk clinical pain ratings without standardized assessment protocols or detailed information on covariates

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Ann Neurol. 2021;90:S117.

QUALITY OF LIFE FOR CAREGIVERS OF CHILDREN WITH ADHD AND/OR ASD DECREASED AS A RESULT OF THE COVID-19 PANDEMIC, IRRESPECTIVE OF ETHNICITY OR INSURANCE STATUS.

Barbayannis G, Garcia D, Pecor K, et al.

Objective: While they are a potentially vulnerable population, few studies have examined the impact of the COVID-19 pandemic on the quality of life of African American and/or Hispanic caregivers of children with ADHD and/or ASD. This study aimed to test for an association between ethnicity and/or insurance status and caregiver quality of life during the current pandemic.

Methods: Subjects were female caregivers of children with ADHD and/or ASD who reported being members of one of two ethnic groupings (Caucasian, African American and/or Hispanic). In addition to ethnicity, we also considered insurance status (public insurance, private insurance). Total, Parent Health-Related Quality of Life, Family Functioning, Physical Functioning, Emotional Functioning, Social Functioning, Cognitive Functioning, and Worry Summary Scores from the Family Impact Module of the Pediatric Quality of Life InventoryTM were contrasted between ethnic and insurance groups both before and during the COVID-19 pandemic.

Results: During COVID-19, all scores were significantly lower than pre-COVID-19 (all p<0.001). There were no differences between ethnic groupings or insurance providers during COVID-19 (all p>0.05); interactions between ethnicity and insurance status were found for the Parental Health-Related Quality of Life scores (p=0.03) and the Cognitive Functioning scores (p=0.01).

Conclusions: While not true for all measures, in general, caregivers of children with ADHD and/or ASD reported lower quality of life during the COVID-19 pandemic compared to before the pandemic, irrespective of ethnicity or insurance status

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Arch Dis Child. 2021;106:A496-A497.

15Q11.2 MICRO-DELETION ASSOCIATED WITH ADHD: TWO CASE REPORTS AND LITERATURE REVIEW.

Ayyash H, Abulail JA, Dobreva-Chaban H, et al.

Background Due to an increased awareness of the significance of genetics in neurodevelopmental disorders (NDD) such as Attention Deficit/Hyperactivity Disorder (ADHD) and autism Spectrum Disorder (ASD), there is an ever-increasing discovery of rare genetic mutations in these patients that are associated risk factors for these NDDs. 15q11.2 micro-deletion is a very rare genetic variant where affected patients are likely to require support with learning, have an element of speech delay and/or neuropsychiatric disorders such as ASD and ADHD. It is often due to a de novo mutation but it can also be inherited unknowingly due to variable expressivity. Genetic chromosomal microarray testing has become increasingly requested for patients with 'unexplained developmental delay/intellectual disability, autism spectrum disorders or multiple congenital anomalies.

Objectives We aimed to describe the clinical, behavioural and learning profile of two patients with 15q11.2 micro-deletion among the cohort of children and young people (CYP) diagnosed with ADHD in a large Teaching Hospital in the South East of England.

Methods We conducted a search in our hospital electronic database for ADHD patients to identify the occurrence of any associated genetic Copy Number Variants (CNV), specifically looking at the presence of the 15q11.2 micro-deletion. We also carried out a literature review of the latest research on the association between ADHD and 15q11.2 micro-deletion using several databases including the OVID, EMBASE, CINHAL and Cochrane's Databases.

Results We identified two ADHD patients with 15q11.2 BP1- BP2 micro-deletion, also known as Burnside-Bulter Syndrome. Both of our patients also had learning difficulties with unremarkable neonatal backgrounds. Patient A has additional neuro-developmental features and is currently under assessment for possible ASD. He also presents with mild facial dysmorphic features, which has been reported in 92 out of 200 individuals. Patient B was a looked-after child due to neglect in infancy. The published literature regarding 15q11.2 micro-deletion showed wide variation in the reported signs and symptoms among the affected individuals. Most of the papers reported small case series and the article with the highest number of reported cases included 200 individuals. There are a number of individuals that do not have any apparent signs or symptoms. The most commonly reported features include neurological dysfunction, developmental delay (especially with speech and language and motor delay) and neuropsychiatric disorders such as Autism spectrum disorder and Attention deficit hyperactivity disorder. De novo mutations are reported to account for approximately 5% to 22% of all 15q11.2 micro-deletions. There is also a phenotypic overlap with both Prader-Willi and Angelman syndromes.

Conclusions 15q11.2 micro-deletion is proving to be one of the 'most common cytogenetic abnormalities' in patients with neurodevelopmental disorders and intellectual impairment. More data would be required to investigate its true significance and value in microarray analysis for all patients referred for ADHD and/or ASD assessment. Clinicians should consider routine assessment for CNVs in CYP with ADHD, especially if they have other multiple comorbid neurodevelopmental disorders and or dysmorphism

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Arch Dis Child. 2021;106:A54-A55.

ADHD MONITORING: AUDIT OF NICE GUIDELINES.

Power AL, Abbas E.

Background ADHD is a complex, diverse and common neurodevelopmental disorder, associated with many comorbidities. NICE guidelines set out the monitoring requirements for children being treated for ADHD. Wigan has more than 1000 children on its database with ADHD on medication, mostly on stimulant medication. Monitoring of the effectiveness of medication and adverse effects is crucial. Adverse effects on growth, heart rate, blood pressure changes and worsening behaviour may significantly impact the child if left unmonitored.

Objectives To review children who are on ADHD medication and to ensure parameters are monitored as per the NICE & Regional GM guidelines in order to improve our patient care.

Methods 47 patients who attended clinic in November 2018 and completed a symptom rating scale at this clinic visit were reviewed. The notes for these patients were reviewed for every clinic visit for these patients in the period January 2018 - July 2019. Results In total we reviewed 118 clinic visits in 47 patients. 28% were

age under 10 and 72% over 10. Of these 30% of under 10 were seen the minimum of 3 times a year, whereas for the over tens 44% were seen the minimum of twice a year. Core ADHD symptoms were recorded in 30%.The effectiveness of the medication was discussed in 56% and the side effects in 9%. The ongoing need for medication was only discussed once. Height and weight were well documented in 97% of cases, yet only 11% recorded the growth centile. 21/118 (18%) clinic visits showed a loss in weight compared with previous visit, 33% of those had a plan to address the problem. Cardiovascular side effects monitoring was poor, with heart rate measured in 65% and blood pressure in 78%. Heart rate was found to be greater than 120 in one case but no action was taken. Blood pressure was only plotted on the centile chart in 1 case. Symptoms like tics were discussed in 7%, seizures 0% and Sleep 59%. Worsening behaviour was discussed in 70% cases.

Conclusions NICE guidelines recommend that children age under 10 should be reviewed at least 3 times per year and over 10 should be seen twice a year. In our audit only 30% of under 10s were seen three times. Monitoring of patients on medication for ADHD was not good. Height and weight should be checked in all children but this is poorly plotted on the correct growth chart. Blood pressure and heart rate are not always being checked. The audit highlighted gaps in monitoring of our ADHD patients. Following this audit, a side effect questionnaire was introduced for use at all clinic visits. Rating scale questionnaires were also introduced to assess the effectiveness of the medication. Also we appointed a clinical pharmacist, who completed his prescribing course. Our ADHD specialist nurse also completed the prescribing course to help the paediatricians review medication as per NICE recommendation

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Arch Dis Child. 2021;106:A148-A149.

EFFECT OF COVID-19 PANDEMIC ON THE BLOOD PRESSURE OF CHILDREN AND ADOLESCENTS WITH ADHD: IMPLICATIONS FOR CLINICAL PRACTICE.

Ogundele M, Ani C.

Background ADHD is one of the commonest reasons for prescribing psychotropic medications for children and young people (CYP), and the efficacy is up to 70%. Three of the four medications licensed for ADHD in the UK (Methylphenidate, Dexamfetamine/Lisdexamfetamine, and Atomoxetine) are sympathomimetic amines that exert their beneficial effect by increasing levels of dopamine and or noradrenaline in the prefrontal cortex. These sympathomimetic amines also stimulate adrenergic receptors in the heart and blood vessels; hence are associated with small but statistically significant increases in Blood Pressure (BP). Thus, while medications for ADHD are effective and generally well tolerated and safe, patients need to be monitored for cardiovascular and other side effects. Clinical guidelines recommend that if children and young people (CYP) taking medication for ADHD experience raised BP above cut-off for hypertension, dose reduction and cardiology referral should be made. However, guidelines do not specify the need to consider contextual factors.

Objectives We aimed to test the hypothesis that the most plausible explanation for elevated BP among CYP with ADHD during the Covid-19 lockdown was related to Covid-linked stress and the additional anxiety about coming to the clinic during the pandemic.

Methods We carried out a prospective cardiovascular assessment of a cohort of 41 CYP (88% males) attending routine medical reviews for ADHD treatment in the Borough district of Halton in North West England within the first 6 weeks of the UK-wide Covid-19 lockdown in March-May 2020. Mean age was 12 years (range 5-18 years), and 92.5% were on psycho- stimulants while 7.5% were on non-stimulants. All the medications were within the lower range of normally approved doses. Their Blood Pressures were measured with regularly calibrated electronic sphygmomanometers based on standard clinical procedures and compared to BP recorded within the previous one year. Definition of Hypertension (HT) or Pre- HT was based on the British reference charts for CYP. The CYP were followed up with non-clinic-based BP monitoring at home or by GP.

Results We identified 32 CYP seen within the first 6 weeks of the UK-wide Covid-19 lockdown who had BP above cut-off for prehypertension (44%) or hypertension (37%) (figure 1), all of whom previously had their BP in the normal range. Their medication types and doses had not changed. Their medical histories and anthropometric centiles were stable. By August 2020 when the lockdown had eased, their BP were back in the normal range without any further investigations or interventions.

Conclusions This audit highlights the point that clinical evaluation of changes in BP among CYP taking medications for ADHD should take the socio-ecological context into account and not automatically translate into making major clinical changes to treatment such as dose reduction or referral for cardiology review. A conservative approach of non-clinic-based monitoring may be in the best interest of such young people, who, otherwise, may lose treatment efficacy following dose reduction. This conservative approach could also prevent the affected CYP being exposed to the inconvenience and risks associated with unnecessary medical investigations. There could also be additional efficacy gains for the wider health economy

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Arch Dis Child. 2021;106:A243-A244.

AN EVIDENCE-BASED CLINICAL GUIDANCE DESIGNED FOR MANAGING CHILDREN AND ADOLESCENTS WITH SLEEP PROBLEMS AND ASSOCIATED NEURODEVELOPMENTAL DISORDERS.

Ogundele M, Yemula C, Ayyash HF.

Background There is a paucity of national evidence-based guidelines that emphasises holistic care of children and adolescents with neurodevelopmental disorders, who are highly vulnerable to significant sleep disorders. In addition, clinical practice varies widely about melatonin use with enormous financial implications. There is an urgent need for implementation of safe and effective cost-saving measures to ensure sustainable provision of essential NHS services to the entire UK population. Sleep problems are common in children and adolescents, especially among those who have recognizable neurodevelopmental, emotional, behavioural or intellectual disorders (NDEBID). 50% to 80% of children and adolescents with NDEBID experience various types of insomnias. There is a complex relationship between sleep disorders and childhood neurodevelopmental disorders. Chronic sleep deprivation is known to significantly aggravate externalising and internalising bhaviour disorders, including depression, suicide and self-harm behaviors, impaired cognitive development and learning abilities. It can also cause disorders of the cardiovascular, immune and metabolic systems, including growth disorders. It negatively impacts on the child's academic performance, personal and wider family emotional and social wellbeing.

Objectives To review the most recent published research literature and develop a practical guidance on managing sleep disorders in children and adolescents with NDEBID along with a flowchart.

Methods We carried out a literature review of the latest research on the use of cognitive-behavioural strategies and pharmacotherapy in the management of sleep problems among children with neurodevelopmental disorders such as ADHD, ASD, Epilepsy and Learning disorders using several databases including the OVID, EMBASE, CINHAL and Cochrane's Databases.

Results Treatment options for paediatric sleep insomnias include parent psychoeducation/training, sleep hygiene (modifiable daytime, bedtime, and night-time practices), behavioural strategies and pharmacological treatment for selected cases. Cognitive behavioural therapy (CBT) is also effective for adolescents. We provide an outline of evidence-based clinical guideline for clinicians managing CYP with diverse NDEBIDs in 4 sections, including overview of sleep disorders, special circumstances, transition to adult care, shared care and appendix of definitions, online resources and easy-to-use flowchart. Every CYP with sleep difficulties should have detailed medical and sleep history, including any possible underlying sleep apnoea, other physical explanations for insomnia including obesity, emotional problems or sources of discomfort, complemented by use of screening questionnaires, sleep diary and actigraphy (if available). This should lead to identification of specific sleep disorder type, consideration of differential diagnosis and formulation of a sleep plan with the parents or carers. Stepwise introduction of behavioural and pharmacological treatment options are outlined, including mandatory follow-up for effectiveness, side-effects and trial of discontinuation.

Conclusions This clinical guideline and the accompanying flowchart is expected to help clinicians provide a more uniform holistic evidence-based management for every child presenting with co-morbid sleep problems associated with complex emotional behavioural and neurodevelopmental disorders. It will likely lead to less risks of patient/ parent dissatisfaction with individual clinicians and help the individual NHS Trusts to identify potential areas of cost saving involved in melatonin prescriptions, as well as identifying an integrated commissioning of further services such as Behavioural/parent training interventions. We plan to pilot the guidelines among a small number of CCH clinics

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Arch Dis Child. 2021;106:A497-A498.

AN AUDIT OF OUR ADHD SERVICE TO REVIEW ASSESSMENTS BEFORE AND AFTER STARTING ADHD MEDICATION AND TO CHECK COMPLIANCE WITH NICE GUIDELINES.

Yemula C, Cope K.

Background Attention Deficit and Hyperactivity Disorder (ADHD) is a common neurodevelopmental condition seen in 5% of school age children. Children who are commenced on ADHD medication require regular assessments to ensure safety and continuation of medication and to check progress of their condition.
Objectives We would like to ascertain whether: baseline cardiovascular assessment and measurements (height, weight, blood pressure and heart rate) have been carried out on children and young people prior to starting ADHD medication. the initial assessment and subsequent follow ups met the criteria outlined within NICE guidance (2019). there are any safeguarding concerns and if present, escalated appropriately
Methods The sample of children and young people was obtained randomly via SystmOne (electronic record) using the read code 'Attention deficit hyperactivity disorder' to identify them between January to December 2019. They were all started on one of the following medications: Medikinet, Medikinet XL, Matoride XL, Concerta XL, Equasym XL and Elvanse. They were assessed and reviewed by an array of different clinicians. The audit was reviewed against NICE guidance: Attention Deficit Hyperactivity Disorder: Diagnosis and Management (2019).
Results 20 children and young people were included in the audit. All (100%) had a baseline height, weight, blood pressure and heart rate (H, W, BP and HR) taken and recorded at their initial assessment. 95% of the children had the baseline readings of their H, W, BP and HR documented on their clinic letter, and 75% had their BP and HR percentiles recorded. As per NICE guidance, children on ADHD medication require a repeat blood BP and HR after each dose change and every six months. 25% of the children in this audit had a repeat BP and HR within six months, associated with a medication change or dose adjustment. Similarly, NICE advises that children should have a follow up height every 6 months and a follow up weight every 3 months for children under the age of years and every 6 months for children over the age of 10 years. 20% of children in this audit had a repeat height and weight within these specified timeframes, and this was also associated with a medication change or dose adjustment. NICE guidance states that all children should have a cardiovascular assessment prior to starting ADHD medication; this audit found that 85% of children had documentation pertaining to 'normal heart sounds/heart murmur', and the ADHD pre-drug checklist was completed in 80% of cases. Safeguarding was also included in this audit, however only 15% had current or recent safeguarding needs and none of these required any further escalation.
Conclusions Undoubtedly some of the results of this audit may have been impacted by the COVID 19 pandemic, which commenced in March 2019 and naturally had a significant impact on service delivery and provision during the months that followed. With regards to this audit, this is likely to be particularly relevant to the children's blood pressure and heart rate measurements and follow up appointments. To overcome this, Saturday Blood Pressure clinics were established locally and measurements were recorded along with centiles. Any children and young people who were due/overdue these checks were invited to attend to ensure ongoing holistic care. Escalation process is implemented to alert the child's paediatrician in case of concerns and for timely action

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Arch Dis Child. 2021;106:A30-A31.

QUALITY OF LIFE IN CHILDREN WITH ADHD-A LOCAL REVIEW.

McGrath N, Bhide S, Abeyweera N.

Background Quality of life (QoL) is an important consideration for children with long-term neurodevelopmental conditions. The WHO define QoL as 'the individual's perception of their position in life, in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns'. In attention-deficit hyperactivity disorder (ADHD), there may be some difficulties in self-reporting outcomes due to the children's concentration difficulties. However, the impressions of parents can also be used to reflect changes in a child's quality of life over time. QoL outcomes are not routinely measured, but one could argue that such subjective results can be used to demonstrate the effectiveness of our medical interventions better than an observational assessment of symptomatology.

Objectives To review the quality of life for patients prescribed medication for the management of attention deficit hyperactivity disorder (ADHD) initiated by the community paediatric team, using the PaedsQL Γäó Paediatric Quality of Life inventory 'core scales'.
Methods Suitable patients were selected by treating clinicians over a 6 month period from May 2019. Children with a diagnosis of ADHD who were started on stimulant medications were identified by each prescribing clinician and approached for inclusion in the study. Parents were asked to complete an age-appropriate PaedsQ ó questionnaire during the appointment when the child was first prescribed stimulant medications. The questionnaire was repeated after 6 weeks of continued medical therapy. The PaedsQ ó ratings were compared for each child before and after medical treatment.
Results A total of 19 parents completed questionnaires over the 6 month study period. Of these 1 questionnaire was excluded as less than half of the questions were completed. For one questionnaire less than 50% of questions in the physical functioning section were completed, so this section was excluded. Scores were stratified in accordance with PaedsQ ó guidance, with a maximum of 100. Scores were divided into four QoL subgroups: physical functioning; emotional functioning; social functioning and school functioning. The total QoL score improved by an average of 4.44 points after starting medical treatment for ADHD. An improvement was seen across all subgroups, with the greatest increase seen in the social subgroup (+11.11).
Conclusions Our study found there was an improvement in QoL scores for children diagnosed with ADHD following initiation of medical management. The greatest improvement was seen for social functioning. Unfortunately there was no statistically significant difference in these results, due to the small number of cases included. Further follow-up of these children would be useful to assess if the QoL improvements are maintained over time

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Arch Dis Child. 2021;106:A493.

'DOES DIET INFLUENCE THE BEHAVIOUR OF THE CHILD WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)?' RECOMMENDATIONS FOR PRACTICE AS A SPECIALIST ADHD NURSE.

Middleditch G.

Background Introduction This poster presents research pertaining to diet and effect on ADHD children, to inform nursing practice. It will develop recommendations for future service pathway, while further embedding research into practice. Background Kent has the highest cost for prescribing ADHD medication (Henry 2017). Thus healthy eating discussions could be useful in nurse review clinic (NICE 2020).
Aims and Objectives. Literature review, deriving key themes: Diet and ADHD. Ascertain parental belief systems and coping mechanisms. Recommend for future practice, how the nurse can integrate findings.
Methods Methodology Literature inclusion criteria: Participants below 18 years, papers from various countries and English written, research from 2005 onwards. Exclusion criteria: - Adults, conditions linked with ADHD. Papers were selected: some countries had comparable healthcare systems, while others had limited resources; this gave overview of variable diets. Allowing for holistic review regards diet and ADHD. Key search terms: ADHD child and diet included: Child (ren), ADHD, Diet, Feeding, Problems in Child. Key Search terms, Parent's viewpoints: ADHD, Dietary in children, Parent experience, Healthy, Habits and Neurodevelopment.Databases: Google scholar, MEDLINE, APA PsychInfo, CINAHL, Science- Direct, British Library EtHOS, Child Development and Adolescent Studies.
Results and Findings Ten papers were reviewed: Six papers used quantitative research, which included: Randomised control trialled research and meta-analysis studies. One paper qualitative and three papers mixed method. Literature on parental viewpoints was low. The key areas are listed below: 1. Poor Nutrition and Behaviour: - Poor nutrition, increases risk of ADHD and poor weight gain 2. Artificial Food Colourings (AFCs) and Supplements - AFCs increase hyperactivity. - Improved behaviour using free fatty acid supplementation. - Minerals: calcium, selenium, zinc and phosphorous protective against ADHD. 3. Decreased Nutritional value diets and Parental experiences. - Diet of fruit and vegetables reduce risk of ADHD. - Western diet attributes to ADHD. 4. Restricted elimination diet. - Requires persistence, maintenance from parents.ecreased nutritional value diets and Parental experienc - Three studies included parental viewpoints/coping mechanisms, allowing for recommendations for future service delivery, supporting families in practice. Developing practice Poor Nutrition and Behaviour. Mealtime management through virtual observations, regular review of growth and Mid Upper Arm Circumference (MUAC). Nurse to discuss safety

using supplements. Parents keep food diaries, reviewed regularly by professionals. . Parental belief systems impact interventions chosen. Nurse to promote healthy eating. . Diet high in refined grains, sugar, saturated fat, low in diary, calcium and vitamin B2 linked to ADHD. Parents may use food as reward. Nurse to guide behavioural management.
Conclusions Discussion A healthy diet discussion should take place by the nurse, to enable for a holistic assessment and build a therapeutic relationship. The nurse must not exclude, from the assessment process parent's nor child's beliefs systems, this will allow for understanding of how best to support the child's ongoing needs and how to formulate the conversation of healthy diet into practice. It highlights, parental views and education of what constitutes a healthy diet, could be led by the nurse; this maybe be facilitated through integrated 'patient involvement groups' and further reviewed in nurse led clinics, obtaining essential feedback. Conclusion The research reviewed derived key themes, which gives evidence, that diet can affect a child with ADHD behaviours; healthy diets can be used as a compliment to ADHD medication. Parental involvement in dietary management is essential in supporting the child to follow a healthy diet. Equally, the nurse's holistic assessment will allow incorporation of strategies; that take in to account parental belief systems and coping mechanisms, in order to achieve the best outcomes for the child's needs. The literature reviewed has also allowed for recommendations for future practice

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Arch Neurocienc. 2021;26:10-16.

PREVALENCE OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN MEXICAN UNIVERSITY STUDENTS.

Yanez Tellez MG, Villase+¦or Valadez VD, Prieto Corona B, et al.

Introduction: Attention-Deficit/Hyperactivity Disorder (ADHD) in adulthood causes relevant deterioration in daily functioning. Specifically, in educational scenarios, complications including an elevated rate of failed courses and desertion have been found. The reported prevalence of ADHD in adults varies widely, therefore studying specific populations becomes important.
Objective: To determine the prevalence of ADHD in students at a public university using screening tools to determine the presence of current and retrospective symptomatology during childhood and to describe their sociodemographic characteristics.
Method: The study was conducted with a probabilistic sample of undergraduate students (N = 1837), to whom the Adult Self Report Scale for ADHD (ASRS-6) and the Wender Utha Rating Scale (WURS) were administered to determine current and childhood ADHD symptoms.
Results: The prevalence of ADHD in the studied population was 16.2%, with a significantly higher frequency in males (22.14%) than in females (13%). ADHD was most prevalent in Biology students (23.7%) and least in Nursery students (9.9%).
Discussion and conclusion: Results indicate a higher frequency of ADHD in Mexican undergraduate students than that reported in adult populations of other countries, but consistent with previous reports of Mexican undergraduate students and children. The association of ADHD and difficulties in academic, work, and social achievement in the studied population should be further investigated

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Bahrain Med Bull. 2021;43:597-600.

PHYSICAL INJURY AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: SITUATIONS AND MEDICAL CARE NEEDS.

Janahi AI, Janahi MI, Al-Ansari AMS.

Background: Young individuals with attention deficit hyperactivity disorder (ADHD) are renowned for their impulsivity and recklessness, which can lead to serious accidents and even death. Compared to their typically developed peers, children and adolescents with ADHD are at greater risk of sustaining injury in normal life situations (e.g., during sports, in school, and in traffic). These injuries were less prevalent among individuals with ADHD who were compliant with their medication.
Methods: A cross-sectional study with a one-to-one comparative group design was employed. The ADHD group consisted of 50 children who were previously diagnosed with ADHD. The comparative group included 50 typically developed participants from the same age group (7-19 years). A questionnaire was developed

for this study to assess the risk and magnitude of injury in different daily life situations by assessing the frequency of each participant's need to visit a doctor.
Results: Members of the ADHD group exhibited a significantly higher rate of injury associated with fights, traffic, and sports participation, and they sustained injuries significantly more often at school and at home. The severity of the injuries was greater in the ADHD group than in the comparative group in three out of the six situations analyzed.
Conclusion: In comparison to their usually developing counterparts, this study stresses the risk and extent of damage in children and adolescents with ADHD. The nature of ADHD in this age range, which is characterized by impulsivity, carelessness, and inattention, is thought to be the reason for the increased risk among children and adolescents with ADHD

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Biomedizinische Technik. 2021;66:S182.

A DEEP LEARNING BASED CLINICAL DECISION SUPPORT SYSTEM FOR THE CLASSIFICATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Makaram N, Karuvee MSR.

Introduction Attention Deficit Hyperactivity Disorder (ADHD) is a neurological disorder which results in hyepractivity and impulsive behavior. Conventional clinical invesitgations using questionaires and general examination are influenced by subjective bias. In this work, an attempt is made to quatitatively assess the changes in brain function with ADHD using electroencephelography (EEG) and deep learning techniques.
Methods This study considers EEG signals obtained from a publicly available database ' EEG data for ADHD / Control children'. The signals are recorded from 60 normal and 61 ADHD subjects during a visual attention task. These signals are preprocesed with a 0.5 to 48 Hz bandpass filter and along with a dynamic line frequency filter. The segments with artefacts are removed based on statestical and frequency based methods. Channels removed by the preprocessing is interpolated with the neighbouring electrode data. Independent component analysis is used to remove noise from sources such as muscle, eye and line frequency. This preprocecssed signals are divided into 5 second epochs with 2.5 s overlap. These signals are classifed using a custom eight layer Convolutional Neural Network (CNN) based architecture. A 5 fold cross validation is used to analyse the performance The EEGLAB toolbox is used for the EEG processing and the CNN is developed with pytorch.
Results The results indicate that the ADHD subjects require more time to complete the visual attention task. Further, the signals in normal and ADHD exhibit unique spectral and amplitude characteristics. The CNN based method is able to characterize the two conditions and results in a classification accuracy of greater than 85%.
Conclusion The quatitative assessment of ADHD can ensure to provide better healthcare deivery. The findings of this study indicates that this pipeline of analysis appears to be reliable to support clinical diagnosis of ADHD condition

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BMC Pediatr. 2021;21.

HOW EFFECTIVE IS FINE MOTOR TRAINING IN CHILDREN WITH ADHD? A SCOPING REVIEW.

Lelong M, Zysset A, Nievergelt M, et al.

Background: Motor deficiencies are observed in a large number of children with ADHD. Especially fine motor impairments can lead to academic underachievement, low self-esteem and frustration in affected children. Despite these far-reaching consequences, fine motor deficiencies have remained widely undertreated in the ADHD population. The aim of this review was to systematically map the evidence on existing training programs for remediating fine motor impairments in children with ADHD and to assess their effectiveness.
Methods: The scoping review followed the PRISMA-ScR guidelines. In March 2020, PsycINFO, MEDLINE (PubMed), Web of Science, Google Scholar and The Cochrane Database of Systematic Reviews were searched for evidence. The eligibility criteria and the data charting process followed the PICO framework, complemented by study design. The investigated population included children with a formal ADHD diagnosis (either subtype) or elevated ADHD symptoms aged between 4 and 12 years, both on and off medication. All

training interventions aiming at improving fine motor skills, having a fine motor component or fine motor improvements as a secondary outcome were assessed for eligibility; no comparators were specified.
Results: Twelve articles were included in the final report, comprising observational and experimental studies as well as a review. Both offline and online or virtual training interventions were reported, often accompanied by physical activity and supplemented by training sessions at home. The training programs varied in length and intensity, but generally comprised several weeks and single or multiple training sessions per week. All interventions including more than one session were effective in the treatment of fine motor deficiencies in children with ADHD and had a wide range of additional positive outcomes. The effects could be maintained at follow-up.
Conclusions: Fine motor training in children with ADHD can be very effective and multiple approaches including specific fine motor and cognitive training components, some kind of physical activity, feedback mechanisms, or multimodal treatments can be successful. Training programs need to be tailored to the specific characteristics of the ADHD population. A mHealth approach using serious games could be promising in this context due to its strong motivational components

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BMC Psychiatry. 2021;21.

TIME OF ONSET AND/OR DIAGNOSIS OF ADHD IN EUROPEAN CHILDREN: A SYSTEMATIC REVIEW.

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

Background: Attention-Deficit/ Hyperactivity Disorder (ADHD) is one of the most common childhood neurobehavioral conditions. Symptoms related to this disorder cause a significant impairment in school tasks and in the activities of children's daily lives; an early diagnosis and appropriate treatment could almost certainly help improve their outcomes. The current study, part of the Models Of Child Health Appraised (MOCHA) project, aims to explore the age at which children experience the onset or diagnosis of ADHD in European countries.
Methods: A systematic review was done examining the studies reporting the age of onset/diagnosis (AO/AD) of ADHD in European countries (28 European Member States plus 2 European Economic Area countries), published between January 1, 2010 and December 31, 2019. Of the 2276 identified studies, 44 met all the predefined criteria and were included in the review.
Results: The lowest mean AO in the children diagnosed with ADHD alone was 2.25 years and the highest was 7.5 years. It was 15.3 years in the children with ADHD and disruptive behaviour disorder. The mean AD ranges between 6.2 and 18.1 years.
Conclusions: Our findings indicate that there is a wide variability in both the AO and AD of ADHD, and a too large distance between AO and AD. Since studies in the literature suggest that an early identification of ADHD symptoms may facilitate early referral and treatment, it would be important to understand the underlying reasons behind the wide variability found.
Trial registration: PROSPERO registration: CRD42017070631

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Brain Behav. 2021.

FRONTAL INTERHEMISPHERIC STRUCTURAL CONNECTIVITY, ATTENTION, AND EXECUTIVE FUNCTION IN CHILDREN WITH PERINATAL STROKE.

Larsen N, Craig BT, Hilderley AJ, et al.

Perinatal stroke affects ~1 in 1000 births and concomitant cognitive impairments are common but poorly understood. Rates of Attention Deficit/Hyperactivity Disorder (ADHD) are increased 5–10× and executive dysfunction can be disabling. We used diffusion imaging to investigate whether stroke-related differences in frontal white matter (WM) relate to cognitive impairments. Anterior forceps were isolated using tractography and sampled along the tract. Resulting metrics quantified frontal WM microstructure. Associations between WM metrics and parent ratings of ADHD symptoms (ADHD-5 rating scale) and executive functioning (Behavior Rating Inventory of Executive Function (BRIEF)) were explored. Eighty-three children were recruited (arterial ischemic stroke [AIS] n = 26; periventricular venous infarction [PVI] n = 26; controls n = 31). WM metrics were altered for stroke groups compared to controls. Along-tract analyses showed differences in WM metrics in areas approximating the lesion as well as more remote differences at midline

and in the nonlesioned hemisphere. WM metrics correlated with parental ratings of ADHD and executive function such that higher diffusivity values were associated with poorer function. These findings suggest that underlying microstructure of frontal white matter quantified via tractography may provide a relevant biomarker associated with cognition and behavior in children with perinatal stroke.

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Brain Sciences. 2021;11.

ABNORMAL FUNCTIONAL NETWORK TOPOLOGY AND ITS DYNAMICS DURING SUSTAINED ATTENTION PROCESSING SIGNIFICANTLY IMPLICATE POST-TBI ATTENTION DEFICITS IN CHILDREN.

Cao M, Halperin JM, Li X.

Traumatic brain injury (TBI) is highly prevalent in children. Attention deficits are among the most common and persistent post-TBI cognitive and behavioral sequalae that can contribute to adverse outcomes. This study investigated the topological properties of the functional brain network for sustained attention processing and their dynamics in 42 children with severe post-TBI attention deficits (TBI-A) and 47 matched healthy controls. Functional MRI data during a block-designed sustained attention task was collected for each subject, with each full task block further divided into the pre-, early, late-, and post-stimulation stages. The task-related functional brain network was constructed using the graph theoretic technique. Then, the sliding-window-based method was utilized to assess the dynamics of the topological properties in each stimulation stage. Relative to the controls, the TBI-A group had significantly reduced nodal efficiency and/or degree of left postcentral, inferior parietal, inferior temporal, and fusiform gyri and their decreased stability during the early and late-stimulation stages. The left postcentral inferior parietal network anomalies were found to be significantly associated with elevated inattentive symptoms in children with TBI-A. These results suggest that abnormal functional network characteristics and their dynamics associated with the left parietal lobe may significantly link to the onset of the severe post-TBI attention deficits in children

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Brain Sciences. 2021;11.

BIOLOGICAL BASES OF EMPATHY AND SOCIAL COGNITION IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A FOCUS ON TREATMENT WITH PSYCHOSTIMULANTS.

Fantozzi P, Sesso G, Muratori P, et al.

In recent years, there has been growing interest in investigating the effect of specific pharmacological treatments for ADHD not only on its core symptoms, but also on social skills in youths. This stands especially true for ADHD patients displaying impulsive aggressiveness and antisocial behaviors, being the comorbidity with Disruptive Behavior Disorders, one of the most frequently observed in clinical settings. This systematic review aimed to synthesize research findings on this topic following PRISMA guidelines and to identify gaps in current knowledge, future directions, and treatment implications. Search strategies included the following terms: ADHD; methylphenidate and other ADHD drugs; empathy, theory of mind and emotion recognition. Fulltext articles were retrieved and data from individual studies were collected. Thirteen studies were finally included in our systematic review. Ten studies assessing changes in empathy and/or theory of mind in patients with ADHD treated after pharmacological interventions were identified. Similarly, seven partially overlapping studies assessing changes in emotion recognition were retrieved. Despite a great heterogeneity in the methodological characteristics of the included studies, most of them reported an improvement in emphatic and theory of mind abilities in youths with ADHD treated with psychostimulants and nonstimulant drugs, as well as positive but less consistent results about emotion recognition performances

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Brain Sciences. 2021;11.

SLEEP INSTABILITY CORRELATES WITH ATTENTIONAL IMPAIRMENT IN BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Gagnon K, Labrosse M, Gingras MA, et al.

Theoretical models of sleep and attention deficit hyperactivity disorder (ADHD) suggest that symptoms of ADHD are associated with daytime sleepiness, but it has received little support. The present study aimed at testing an alternative model involving the association of attentional instability with sleep instability, i.e., sleep stage transitions and arousals. Twelve ADHD and 15 healthy control (HC) boys aged between 8 and 12 years old underwent polysomnography recording and attentional testing. The microarousal index, the number of awakenings, and the number of stage shifts between stages 1, 2, 3, 4 and REM sleep throughout the night were computed as sleep stability parameters. Attentional functioning was assessed using the Continuous Performance Test II. We found significantly higher sleep instability in ADHD compared to HC. Sleep arousals and stage transitions (micro arousal index, stage 4/3 and 2/4 transitions) in ADHD significantly correlated with lower attentional scores. No association whatsoever was found between sleep instability and attentional functioning in HC. The results show that sleep instability is associated with lower attentional performance in boys with ADHD, but not in HC. This could be compatible with a model according to which attention and sleep stability share a common neural substrate in ADHD

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Brain Topogr. 2021.

EXECUTIVE FUNCTION BRAIN NETWORK ACTIVATION PREDICTS DRIVING HAZARD DETECTION IN ADHD.

Bednarz HM, Stavrinos D, Svancara AM, et al.

Drivers with neurodevelopmental disorders (NDDs), such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are at increased risk of experiencing driving difficulties. An important aspect of driving safety and skill involves hazard detection. This functional magnetic resonance imaging study examined the neural responses associated with driving hazard detection in drivers with ASD, ADHD, and typically developing (TD) drivers. Forty participants (12 ASD, 15 ADHD, 13 TD) ages 16ΓÇô30-áyears completed a driving simulator task in which they encountered social and nonsocial hazards; reaction time (RT) for responding to hazards was measured. Participants then completed a similar hazard detection task in the MRI scanner so that neural response to hazards could be measured. Activation of regions of interest considered part of the executive function (EF) and theory of mind (ToM) networks were examined and related to driving simulator behavior. Results showed that stronger activation of the EF network during social hazard processing, including the bilateral dorsolateral prefrontal cortex and posterior parietal cortex, was associated with faster RT to social hazards among drivers with ADHD, but not among drivers with ASD. This provides the first evidence of a relationship between EF network brain activation and driving skills in ADHD and suggests that alterations in this network may underlie driving behavior. In comparison, the current study did not observe a relationship between ToM network activation and RT to social hazards in any group. This study lays the groundwork for relating neural activation to driving behavior among individuals with NDDs

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Child Neuropsychol. 2021.

THE RELATIONSHIP BETWEEN COGNITION AND MATHEMATICS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.

Kanevski M, Booth JN, Oldridge J, et al.

Cognitive processes play an imperative role in childrenΓÇÖs mathematics learning. Difficulties in cognitive functioning are a core feature of Attention Deficit Hyperactivity Disorder (ADHD) in children, who also tend to show lower levels of mathematics attainment than their typically developing peers. This review (registration number: CRD42020169708) sought to aggregate findings from studies assessing the relationship between cognition and mathematics in children with a clinical ADHD diagnosis aged 4ΓÇô12-áyears. A total of 11,799 studies published between 1992 and August 2020 were screened for eligibility using various database (PsycINFO, PubMed, SCOPUS, EMBASE, ERIC, Web of Science, and additional sources), from which four studies met inclusion criteria. A narrative synthesis was conducted on the correlations between mathematics and cognitive domains, including an evaluation of the risk of bias within the studies. Across four studies

meeting inclusion criteria, memory, inhibitory control, and processing speed were assessed. The results showed a positive association between cognition and mathematics performance in this population. The strength of associations across these studies varied as a function of the cognitive domain in question, means by which mathematics performance was assessed, as well as whether confounding factors such as age and IQ were controlled for. Collectively, this review demonstrates a lack of research in this area and points to various methodological considerations for identifying the association between cognition and mathematics performance in ADHD

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Child Neuropsychol. 2021.

IS THERE AN EFFECTIVE DOSE OF AEROBIC EXERCISE ASSOCIATED WITH BETTER EXECUTIVE FUNCTION IN YOUTH WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER?

Khodaverdi Z, Moreau D, Garber CE.

Attention-deficit/hyperactivity disorder (ADHD) is the most prevalent neurodevelopmental disorder in children, and it's linked to a higher risk of academic failure, interpersonal issues, mental illness, and criminality. Despite several of the comparative and detailed reviews on the effects of ADHD interventions on core symptoms, there is no data summarizing the effects of aerobic exercise (AE) on executive functions (EFs). Therefore, this study aimed to systematically review and determine the relationship between AE (acute and chronic) dosage and EFs (attention, inhibition, set-shifting, and working memory) in youth with ADHD. The consideration of how AE dosage impacts aspects of EFs has not been investigated in detail previously. The study adhered to PRISMA guideline. Sixdatabases were searched without any date restrictions, up to February 2021, for articles relating to AE interventions to influence EFs in youth with ADHD (Formula presented.) 18 years old. Quality assessment of the reviewed papers was addressed. Thirteen studies met the inclusion criteria. Improvements in all aspects of EFs were reported after children with ADHD engaged in acute AE lasting 20-30-áminutes with at least moderate intensity (65% 80% HRmax).Furthermore, chronic exercise that lasts at least 45-áminutes and in the range of moderate tohigh intensity (i.e., 60% 75% HRmax), 3-ádays/week for 6-12, elicits additional benefits in inhibition and set-shifting.Different dosage of AE might differently influence aspects of EFs; however, this finding rests on preliminary evidence at this stage and thus should be treated with caution.It is necessary to establish suitable interventions with regard to the dosage of AE types to improve EFs in young people with ADHD

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Clin Psychopharmacol Neurosci. 2021;19:705-11.

COMBINED MEDICATION WITH STIMULANTS AND NON-STIMULANTS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bahn GH, Seo K.

Objective: To study the efficiency and indication of combined medication with a stimulant and non-stimulant for attention- deficiency/hyperactivity disorder (ADHD), herein, the authors examined children and adult patients with ADHD.

Methods: Subjects included patients diagnosed with ADHD who paid two or more visits to the outpatient clinic of the Kyung Hee University hospital from January 2009 to December 2019. The authors examined the age, sex, drugs, treatment adherence, and reason for combined medication. The subjects were classified into four groups: Treatment with a non-stimulant (atomoxetine) only (Group ATX), treatment with a stimulant (methylphenidate immediate-release, extended-release, or osmotic-release oral system) only (Group MPH), exposed to both but separately used (Group SEP), and exposed to both with combined use (Group COM). The patient was considered adherent to treatment (1) on visiting the hospital ten or more times or consecutively for six months, and (2) medication possession ratio ΓëÑ 0.8.

Results: Of 929 patients, 229 (24.7%) were female. Group ATX comprised 146 (15.7%) patients, Group MPH comprised 627 (67.5%) patients, Group SEP comprised 106 (11.4%) patients, and Group COM comprised 50 (5.4%) patients. Longer-term adherence was seen with combined medication and in females than with monopharmacy and in males. The main indication for combination was dose-limiting untoward effects.

Conclusion: These results suggest that combined medication would facilitate treatment adherence for ADHD. Further research is essential for the replication of these results in a large sample and the investigation of the indications for administering combined medication in children and adults with ADHD

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Clin Psychopharmacol Neurosci. 2021;19:712-20.

EFFECTS OF IRON SUPPLEMENTATION ON ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN TREATED WITH METHYLPHENIDATE.

Tohidi S, Bidabadi E, Khosousi MJ, et al.

Objective: To evaluate the effect of iron on the attention deficit hyperactivity disorder, treated with methylphenidate.

Methods: This double-blind, randomized placebo-controlled clinical trial was performed on 50 children with attention deficit hyperactivity disorder under the treatment of methylphenidate, with ferritin levels below 30 ng/ml and absence of anemia. They were randomly assigned into two groups of ferrous sulfate and placebo, for 12 weeks. Conners' Parent Rating Scale (CPRS) was used to assess the outcome in the first, sixth, and twelfth weeks.

Results: Almost all CPRS subscales improved in the ferrous sulfate group from the baseline to the endpoint, although only the changes in conduct subscale scores were significant ($p = 0.003$). There was no significant difference in score changes between two groups in intergroup comparison. Also, the score of learning problems ($p = 0.007$) in the first six weeks, and conduct ($p = 0.023$) and psychosomatic ($p = 0.018$) subscales in the second six weeks were improved in the ferrous sulfate group compared with the placebo group.

Conclusion: Our study showed promising effects of iron supplementation in the improvement of subscales of the CPRS

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Clin Psychopharmacol Neurosci. 2021;19:739-50.

COMPARISON OF QUANTITATIVE ELECTROENCEPHALOGRAPHY BETWEEN TIC DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN.

Lee I, Lee J, Lim MH, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) and tic disorder (TD) are among the most common comorbid psychopathologies and have a shared genetic basis. The psychopathological and neurophysiological aspects of the mechanism underlying the comorbidity of both disorders have been investigated, but the pathophysiological aspects remain unclear. Therefore, this study aimed to compare the neurophysiological characteristics of ADHD with those of TD using resting-state electroencephalography and exact low-resolution brain electromagnetic tomography (eLORETA) analysis.

Methods: We performed eLORETA analysis based on the resting-state scalp-recorded electrical potential distribution in 34 children with ADHD and 21 age-matched children with TD. Between-group differences in electroencephalography (EEG) current source density in delta, theta, alpha, beta, and gamma bands were investigated in each cortical region.

Results: Compared with the TD group, the ADHD group showed significantly increased theta activity in the frontal region (superior frontal gyrus, $t = 3.37$, $p < 0.05$; medial frontal gyrus, $t = 3.35$, $p < 0.05$). In contrast, children with TD showed decreased posterior alpha activity than those with ADHD (precuneus, $t = -3.40$, $p < 0.05$; posterior cingulate gyrus, $t = -3.38$, $p < 0.05$). These findings were only significant when the eyes were closed.

Conclusion: Increased theta activity in the frontal region is a neurophysiological marker that can distinguish ADHD from TD. Also, reduced posterior alpha activity might represent aberrant inhibitory control. Further research needs to confirm these characteristics by simultaneously measuring EEG-functional magnetic resonance imaging

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Cortex. 2022;146:50-65.

OSCILLATORY NEURAL NETWORK ALTERATIONS IN YOUNG PEOPLE WITH TUBEROUS SCLEROSIS COMPLEX AND ASSOCIATIONS WITH CO-OCCURRING SYMPTOMS OF AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Shephard E, McEwen FS, Earnest T, et al.

Tuberous sclerosis complex (TSC) is a genetic disorder caused by mutations on the TSC1/TSC2 genes, which result in alterations in molecular signalling pathways involved in neurogenesis and hamartomas in the brain and other organs. TSC carries a high risk for autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), although the reasons for this are unclear. One proposal is that TSC-related alterations in molecular signalling during neurogenesis lead to atypical development of neural networks, which are involved in the occurrence of ASD and ADHD in TSC. We investigated this proposal in young people with TSC who have been studied longitudinally since their diagnosis in childhood. Electroencephalography (EEG) was used to examine oscillatory connectivity in functional neural networks and local and global network organisation during three tasks (resting-state, attentional and inhibitory control Go/Nogo task, upright and inverted face processing task) in participants with TSC (n = 48) compared to an age- and sex-matched group of typically developing Controls (n = 20). Compared to Controls, the TSC group showed hypoconnected neural networks in the alpha frequency during the resting-state and in the theta and alpha frequencies during the Go/Nogo task (P Γëñ .008), as well as reduced local network organisation in the theta and alpha frequencies during the Go/Nogo task (F = 3.95, P = .010). There were no significant group differences in network metrics during the face processing task. Increased connectivity in the hypoconnected alpha-range resting-state network was associated with greater ASD and inattentive ADHD symptoms (rhoΓëÑ.40, P Γëñ .036). Reduced local network organisation in the theta-range during the Go/Nogo task was significantly associated with higher hyperactive/impulsive ADHD symptoms (rho = .43, P = .041). These findings suggest that TSC is associated with widespread hypoconnectivity in neural networks and support the proposal that altered network function may be involved in the co-occurrence of ASD and ADHD in TSC

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Crescent Journal of Medical and Biological Sciences. 2021;8:179-84.

THE RELATIONSHIP BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND FUNCTIONAL CONSTIPATION IN PATIENTS REFERRED TO PEDIATRIC GASTROINTESTINAL CLINIC OF THE HOSPITALS OF KHORRAMABAD CITY, IRAN.

Zafari Z, Shokri S, Hasanvand A, et al.

Objectives: Both Functional constipation and attention deficit hyperactivity disorder (ADHD) have a high prevalence among children. The aim of this study was to determine the relationship between functional constipation and ADHD.

Materials and Methods: In this case-control study, 4-12-year-old children who were diagnosed with functional constipation were included in the case group and children with no functional constipation were included in the control group. Diagnosis of functional constipation was performed according to ROME III criteria. All participants were interviewed for ADHD using the Persian version of Conners' Parent Rating Scale (short form). Statistical analysis was performed by Chi-square test for investigating the relationship between functional constipation and ADHD.

Results: A total of 100 children with functional constipation and 147 children without constipation were selected. Among the functional constipation group, 27 (27%) had a high score for ADHD and among the group without functional constipation, 16 (10.0%) had a high score for ADHD. The odds ratio was 3.028 (95% confidence interval = 1.532-5.986; P value = 0.001). There was no statistically significant relationship between constipation and ADHD considering the age and gender.

Conclusions: Functional constipation has a relationship with ADHD. The chance of having ADHD is 3 times higher in children with functional constipation. Further studies, particularly cohort studies, are recommended to assess the incidence of ADHD symptoms in infants with functional constipation in the future. Further studies on the possible pathophysiology of the digestive system and bacterial intestinal flora, especially in early childhood and infancy, are suggested for investigating the development of behavioral disorders and ADHD

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Dev Med Child Neurol. 2021;63:13-14.

AUTISM AND ADHD ARE MAIN ASSOCIATED IMPAIRMENTS IN CHILDREN WITH CEREBRAL PALSY.

Pahlman M, Himmelmann K.

Background and Objective(s): For children with cerebral palsy (CP), associated impairments can be more limiting than the motor disorder. Early identification of impairments is important for adequate understanding and support. Autism and attention-deficit/hyperactivity disorder (ADHD) are more prevalent in children with CP according to several reports, but study populations and methods differ. The aim of this project was to establish accurate prevalence rates of autism and ADHD in children with CP, and to describe the associations with sex, gestational age, CP type, motor function, intellectual disability (ID) and other associated impairments.

Study Design: Prevalence study Cohort study, both retrospective and prospective Consecutive sample. Study Participants & Setting: A well-defined population-based group of 264 children, born 1999 to 2006, from the CP register of western Sweden, was assessed at school age (median 14y, range 7-17y). After systematic and active evaluation 200 children (76%, 109 males and 91 females) remained and comprised the study group.

Materials/Methods: First, all available medical records were retrieved regarding identified diagnoses of autism, ADHD and other associated impairments. Then, all parents were asked to complete a comprehensive questionnaire primarily aiming to identify signs of autism and ADHD. Further, children without full concordance between clinical diagnoses and screening results were assessed. Results were merged with existing information about the already assessed children where diagnoses and screening were concordant.

Results: Ninety of the 200 children (45%) were diagnosed with autism and/or ADHD. Fifty-nine children had autism and 60 had ADHD. Fifteen percent had autism only, 15% had ADHD only and 15% had both diagnoses. ID was present in 51% and epilepsy in 38%. Fifteen percent had visual impairment, 7% hearing impairment and 27% speech impairment. Autism and ADHD prevalence rates were not associated with degree of gross motor function impairment, in contrast to other known associated impairments in children with cerebral palsy. Multiple regression analyses revealed that both autism and ADHD were predicted mainly by intellectual disability (OR=4.1 and OR=2.3) and by each other (OR=3.2 and OR=3.0 respectively). Autism, ADHD and ID were often co-existing; two thirds of the 200 children had one, two or all three of these impairments.

Conclusions/Significance: Autism and/or ADHD were nearly as common as ID in this population-based study, and more common than epilepsy and other associated impairments. Due to the high prevalence rates, assessment for autism and ADHD is warranted as part of the evaluation of children with CP before school start age. The children will benefit from early diagnosis and adapted support for all their impairments, hopefully leading to a better function and participation in life

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Environ Int. 2022;158.

PHASING OUT DEHP FROM PLASTIC INDWELLING MEDICAL DEVICES USED FOR INTENSIVE CARE: DOES IT REDUCE THE LONG-TERM ATTENTION DEFICIT OF CRITICALLY ILL CHILDREN?

Vanhorebeek I, Malarvannan G, G++iza F, et al.

Background: Children who have been critically ill face long-term developmental impairments. Iatrogenic exposure to di(2-ethylhexyl)phthalate (DEHP), a plasticizer leaching from plastic indwelling medical devices used in the pediatric intensive care unit (PICU), has been associated with the pronounced attention deficit observed in children 4 years after critical illness. As concerns about DEHP toxicity increased, governmental authorities urged the phase out of DEHP in indwelling medical devices and replacement with alternative plasticizers. We hypothesized that exposure to DEHP decreased over the years, attenuating the pronounced long-term attention deficit of these vulnerable children.

Methods: We compared plasma concentrations of 3 oxidative DEHP metabolites (5cx-MEPP, 5OH-MEHP, 5oxo-MEHP) on the last PICU day in 216 patients who participated in the Tight Glucose Control study (2004-2007) and 334 patients who participated in the PEPaNIC study (2012-2015) and survived PICU stay. Corresponding minimal exposures to these metabolites (plasma concentration multiplied with number of days in PICU) were also evaluated. In patients with 4-year follow-up data, we compared measures of attention

(standardized reaction times and consistency). Comparisons were performed with univariable analyses and multivariable linear regression analyses adjusted for baseline risk factors.
Results: In the PEPaNIC patients, last PICU day plasma concentrations of 5cx-MEPP, 5OH-MEHP, 5oxo-MEHP and their sum, and corresponding minimal exposures, were reduced to 17-69% of those in the Tight Glucose Control study ($p < 0.0001$). Differences remained significant after multivariable adjustment (p 0.001). PEPaNIC patients did not show better attention than patients in the Tight Glucose Control study, also not after multivariable adjustment for risk factors.
Conclusion: Exposure of critically ill children to DEHP in the PICU decreased over the years, but the lower exposure did not translate into improved attention 4 years later. Whether the residual exposure may still be toxic or whether the plasticizers replacing DEHP may not be safe for neurodevelopment needs further investigation

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Environ Int. 2022;158.
ENVIRONMENTAL NOISE EXPOSURE AND EMOTIONAL, AGGRESSIVE, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-RELATED SYMPTOMS IN CHILDREN FROM TWO EUROPEAN BIRTH COHORTS.
Essers E, et al.
Background: Environmental noise exposure is increasing but limited research has been done on the association with emotional, aggressive, and attention-deficit/hyperactivity disorder (ADHD)-related symptoms in children.
Objective: To analyze the association between prenatal and childhood environmental noise exposure and emotional, aggressive, and ADHD-related symptoms in children from two European birth cohorts.
Methods: We included 534 children from the Spanish INMA-Sabadell Project and 7424 from the Dutch Generation R Study. Average 24 h noise exposure at the participants home address during pregnancy and childhood periods were estimated using EU maps from road traffic noise and total noise (road, aircraft, railway, and industry). Symptom outcomes were assessed using validated questionnaires: Strengths and Difficulties Questionnaire, Child Behavioral Checklist, ADHD Criteria of Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition List, and Conner's Parent Rating Scale-Revised at 4, 7 and 9 years (INMA-Sabadell cohort) and 18 months, 3, 5, and 9 years (Generation R Study). Adjusted linear mixed models of prenatal and repeated childhood noise exposure with repeated symptom outcomes were run separately by cohort and overall estimates were combined with random-effects meta-analysis.
Results: Average prenatal and childhood road traffic noise exposure levels were 61.3 (SD 6.1) and 61.7 (SD 5.8) for INMA-Sabadell and 54.6 (SD 7.9) and 51.6 (SD 7.1) for Generation R, respectively. Prenatal and childhood road traffic noise exposure were not associated with emotional, aggressive, or ADHD-related symptoms. No heterogeneity was observed between cohorts and results were comparable for total noise exposure.
Conclusions: No association was observed between prenatal or childhood road traffic or total noise exposure and symptom outcomes in children. Future studies should include a more comprehensive noise exposure assessment considering noise sensitivity and noise exposure at different settings such as work for pregnant women and school for children

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Epilepsy and Paroxysmal Conditions. 2021;13:254-63.
REGULATORY RESTRICTIONS ON THE USE OF VALPROATE IN GIRLS AND WOMEN OF CHILDBEARING POTENTIAL: STATUS UPDATE.
Blinov DV, Akarachkova ES, Tsibizova EI, et al.
In 2019, some restrictions for use of valproic acid in women with reproductive potential by regulatory authorities and the original drug manufacturer based on the results of studies in real clinical practice were introduced. During 2019ΓÇô2021, there were a further clinical data accumulation and labeling changes. The review presents a critical analysis of the changes in prescribing information and product label. There is a long lead time from the moment when safety data become known to the moment when changes are made to the medicinal product label and patient brochures. Some of the changes, including the need for high doses of folic acid to prevent neural tube defects, are debatable. Repealing the provision for mandatory archiving

of informed consent forms for valproic acid use in girls and women raises legal risks. Improvements in pregnancy prevention programs and further research on the safety of valproic acid in real-world clinical settings are needed

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Eur J Neurosci. 2021;53:3447-62.

CAUDATE AND CEREBELLAR INVOLVEMENT IN ALTERED P2 AND P3 COMPONENTS OF GO/NOGO EVOKED POTENTIALS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Zarka D, Cebolla AM, Cevallos C, et al.

Previous studies showed reduced activity of the anterior cingulate cortex (ACC) and supplementary motor area during inhibition in children with attention-deficit/hyperactivity disorder (ADHD). This study aimed to investigate deep brain generators underlying alterations of evoked potential components triggered by visual GO/NoGO tasks in children with ADHD compared with typically developing children (TDC). Standardized weighted low-resolution electromagnetic tomography (swLORETA) source analysis showed that lower GO-P3 component in children with ADHD was explained not only by a reduced contribution of the frontal areas but also by a stronger contribution of the anterior part of the caudate nucleus in these children compared with TDC. While the reduction of the NoGO-P3 component in children with ADHD was essentially explained by a reduced contribution of the dorsal ACC, the higher NoGO-P2 amplitude in these children was concomitant to the reduced contribution of the dorsolateral prefrontal cortex, the insula, and the cerebellum. These data corroborate previous findings showed by fMRI studies and offered insight relative to the precise time-related contribution of the caudate nucleus and the cerebellum during the automatic feature of inhibition processes in children with ADHD. These results were discussed regarding the involvement of the fronto-basal ganglia and fronto-cerebellum networks in inhibition and attention alterations in ADHD

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Eur J Psychiatry. 2021.

THE ASSOCIATION BETWEEN CONGENITAL HEART DISEASE AND THE RISK OF AUTISM SPECTRUM DISORDERS OR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG CHILDREN: A META-ANALYSIS.

Jenabi E, Bashirian S, Fariba F, et al.

Background and objective: To our knowledge, this is the first meta-analysis conducted about the association between congenital heart disease (CHD) and the risk of attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorders (ASD) based on observational studies.

Methods: PubMed, Web of Science, and Scopus were systematically searched from the earliest possible year to December 2020. Heterogeneity was conducted using the chi-square test and its quantity was measured using the I2 statistic. The publication bias was assessed using Egger's and Begg's line regression tests. The results were reported using the odds ratio (OR) estimated with its 95% confidence interval (CI) using a random-effects model.

Results: In total, 812 citations were included in the search initial until December 2020 with 467,164 children. Based on the random effect model, the estimated OR of the risk of ASD associated with CHD was OR=1.35 (95% CI: 1.17, 1.52; 6 studies; I2=0.0%) and the risk of ADHD associated with CHD was OR=3.04 (95% CI: 1.58, 4.49; 15 studies; I2=88.1%).

Conclusions: Our findings suggested that CHD is a risk factor for ASD and ADHD. Therefore, Screening for ASD and ADHD should be considered among young children with CHD

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Evidence-Based Practice in Child and Adolescent Mental Health. 2021.

TELEHEALTH DELIVERY OF THE RELAX INTERVENTION FOR FAMILIES OF ADOLESCENTS DIAGNOSED WITH ADHD: PRELIMINARY TREATMENT OUTCOMES AND EVIDENCE OF ACCEPTABILITY AND FEASIBILITY.

Breaux R, Shroff DM, Cash AR, et al.

Regulating Emotions Like An eXpert (RELAX) is a group-based intervention that targets emotion dysregulation (ED) and interpersonal conflict among adolescents diagnosed with attention-deficit/hyperactivity disorder (ADHD). This study is a preliminary evaluation of the feasibility, acceptability, and efficacy of RELAX across in-person and telehealth groups, examining differences in treatment outcomes

and feedback based on format. Participants included 32 families (18 in-person, 14 telehealth) with adolescents diagnosed with ADHD, ages 11ΓÇô16. Caregiver-, clinician- and adolescent-report of adolescent ED, adolescent communication, and caregiver-adolescent/family conflict, as well as caregiver self-report of ED and emotion socialization were collected pre- and post-RELAX; caregivers and adolescents completed a feedback survey post-RELAX. Attendance was higher for telehealth (95% vs. 87%), but homework completion was higher for in-person (85% vs. 70%). Caregiver and adolescent feedback indicated very high rates of satisfaction with RELAX, with no significant differences in caregiver satisfaction and minimal differences in adolescent satisfaction between the in-person and telehealth groups. Large improvements were found for caregiver and clinician ratings of adolescent ED (+À2=.18 .48) and family conflict (+À2=.26 and.43), moderate decreases in non-supportive emotion socialization were found (+À2=.11), and small improvements were found for caregiver ED (+À2=.03). Treatment outcomes were similar for in-person and telehealth groups, with some evidence for larger improvement of adolescent ED for telehealth, whereas larger improvement in family conflict emerged for in-person. RELAX was successfully adapted to be administered via telehealth with similar feasibility, acceptability, and efficacy to the in-person intervention. Efforts to continue disseminating and evaluating ED-focused interventions are warranted and imperative

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Front Neural Circuits. 2021;15.

STATE-DEPENDENT EFFECTIVE CONNECTIVITY IN RESTING-STATE FMRI.

Park HJ, Eo J, Pae C, et al.

The human brain at rest exhibits intrinsic dynamics transitioning among the multiple metastable states of the inter-regional functional connectivity. Accordingly, the demand for exploring the state-specific functional connectivity increases for a deeper understanding of mental diseases. Functional connectivity, however, lacks information about the directed causal influences among the brain regions, called effective connectivity. This study presents the dynamic causal modeling (DCM) framework to explore the state-dependent effective connectivity using spectral DCM for the resting-state functional MRI (rsfMRI). We established the sequence of brain states using the hidden Markov model with the multivariate autoregressive coefficients of rsfMRI, summarizing the functional connectivity. We decomposed the state-dependent effective connectivity using a parametric empirical Bayes scheme that models the effective connectivity of consecutive windows with the time course of the discrete states as regressors. We showed the plausibility of the state-dependent effective connectivity analysis in a simulation setting. To test the clinical applicability, we applied the proposed method to characterize the state- and subtype-dependent effective connectivity of the default mode network in children with combined-type attention deficit hyperactivity disorder (ADHD-C) compared with age-matched, typically developed children (TDC). All 88 children were subtyped according to the occupation times (i.e., dwell times) of the three dominant functional connectivity states, independently of clinical diagnosis. The state-dependent effective connectivity differences between ADHD-C and TDC according to the subtypes and those between the subtypes of ADHD-C were expressed mainly in self-inhibition, magnifying the importance of excitation inhibition balance in the subtyping. These findings provide a clear motivation for decomposing the state-dependent dynamic effective connectivity and state-dependent analysis of the directed coupling in exploring mental diseases

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Frontiers in Neuroscience. 2021;15.

AUTISTIC TRAITS AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER SYMPTOMS ASSOCIATED WITH GREATER PAIN INTERFERENCE AND DEPRESSION, AND REDUCED HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH CHRONIC PAIN.

Wiwe Lipsker C, Hirvikoski T, Balter LJT, et al.

Previous research indicates elevated levels of clinically significant traits and symptoms of autism spectrum disorder and attention-deficit hyperactivity disorder (ADHD) in children with chronic pain, but associations with functioning and depression are yet unclear. The current study examined the relationships of autistic traits and ADHD symptoms with pain interference, depression, and health-related quality of life, as well as the mediating roles of insomnia and psychological inflexibility, in children with chronic pain (n = 146, 8ΓÇô17

years, 102 girls) presenting at a tertiary pain clinic. Children completed measures of pain intensity, depression, pain interference, health-related quality of life, insomnia, and psychological inflexibility. Parents (n = 146, 111 mothers) completed measures to assess autistic traits and ADHD symptoms in their children. Children with clinically significant autistic traits and ADHD symptoms presented with significantly higher levels of depressive symptoms and pain interference, and significantly lower health-related quality of life, than did the other children. Autistic traits and ADHD symptoms contributed significantly to the prediction of pain interference and depressive symptoms, as well as health-related quality of life. Psychological inflexibility mediated the relationships between ADHD symptoms and autistic traits on the one hand and depression, pain interference, and health-related quality of life on the other, while insomnia mediated the relationships between ADHD symptoms and depression, pain interference, and health-related quality of life. All analyses were adjusted for demographics and pain intensity. Results suggest the utility of screening for neurodevelopmental disorders in children with chronic pain. Furthermore, the findings may indicate insomnia and skills related to psychological flexibility as potential treatment targets in interventions aiming at improving functioning and health-related quality of life in children with chronic pain and co-occurring symptoms of neurodevelopmental disorders

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Frontiers in Neuroscience. 2021;15.

BRAIN VOLUMETRIC MEASUREMENTS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A COMPARATIVE STUDY BETWEEN SYNTHETIC AND CONVENTIONAL MAGNETIC RESONANCE IMAGING.

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

Objective: To investigate the profiles of brain volumetric measurements in children with attention deficit hyperactivity disorder (ADHD), and the consistency of these brain volumetric measurements derived from the synthetic and conventional T1 weighted MRI (SyMRI and cT1w MRI).

Methods: Brain SyMRI and cT1w images were prospectively collected for 38 pediatric patients with ADHD and 38 healthy children (HC) with an age range of 6-14 years. The gray matter volume (GMV), white matter volume (WMV), cerebrospinal fluid (CSF), non-WM/GM/CSF (NoN), myelin, myelin fraction (MYF), brain parenchyma volume (BPV), and intracranial volume (ICV) were automatically estimated from SyMRI data, and the four matching measurements (GMV, WMV, BPV, ICV) were extracted from cT1w images. The group differences of brain volumetric measurements were performed, respectively, using analysis of covariance. Pearson correlation analysis and interclass correlation coefficient (ICC) were applied to evaluate the association between synthetic and cT1w MRI-derived measurements.

Results: As for the brain volumetric measurements extracted from SyMRI, significantly decreased GMV, WMV, BPV, and increased NON volume ($p < 0.05$) were found in the ADHD group compared with HC; No group differences were found in ICV, CSF, myelin volume and MYF ($p > 0.05$). With regard to GMV, WMV, BPV, and ICV estimated from cT1w images, the group differences between ADHD and HC were consistent with the results estimated from SyMRI. And these four measurements showed noticeable correlation between the two approaches ($r = 0.692, 0.643, 0.898, 0.789$, respectively, $p < 0.001$; ICC values are 0.809, 0.782, 0.946, 0.873, respectively).

Conclusion: Our study demonstrated a global brain development disability, but normal whole-brain myelination in children with ADHD. Moreover, our results demonstrated the high consistency of brain volumetric indices between synthetic and cT1w MRI in children, which indicates the high reliability of SyMRI in the child-brain volumetric analysis

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Front Psychiatry. 2018;9.

THE PRESENCE OF COMORBID ADHD AND ANXIETY SYMPTOMS IN AUTISM SPECTRUM DISORDER: CLINICAL PRESENTATION AND PREDICTORS.

Avni E, Ben-Itzchak E, Zachor DA.

High rates of attention deficit/hyperactivity disorder (ADHD) and anxiety symptoms have been documented in autism spectrum disorder (ASD), and have been associated with social and adaptive impairments. The study examined the frequency of clinically elevated ADHD and anxiety symptoms in an ASD group in comparison to a non-clinical group, compared the clinical presentation in the ASD group with and without

ADHD and anxiety, assessed which child and familial variables add to the severity of Inattention, Hyperactivity/Impulsivity (HI), and anxiety symptoms, and evaluated whether having clinically elevated ADHD and/or anxiety symptoms adds to the prediction of adaptive functioning in ASD. The study included 260 participants diagnosed with ASD (mean age: 7.5 -¦ 1.1), using standardized tests. The rate of clinically elevated ADHD and anxiety symptoms in ASD was 62.7 and 44.6%, respectively, and symptom severity was significantly greater than the non-clinical sample. The entire population was divided into four subgroups: ASD alone, ASD+ADHD, ASD+anxiety, ASD+ADHD+anxiety, based on the parental behavioral questionnaire. The ASD alone group showed less severe autism symptoms in comparison to the other groups. Having ASD+ADHD symptoms was associated with greater impairments in socialization adaptive skills. Only the group with ASD+ADHD+anxiety was associated with poorer daily living adaptive skills. Regression analyses for prediction of ADHD and anxiety symptoms revealed that being a female and having lower adaptive skills scores predicted higher Inattention severity; being older, having better cognition, and more severe Restrictive Repetitive Behavior symptoms predicted more severe HI symptoms; being older and having more severe social impairments predicted higher anxiety scores. A regression analysis for the prediction of adaptive skills revealed that in addition to cognition and autism severity, the severity of Inattention symptoms added to the prediction of overall adaptive skills. In light of these findings, clinicians should diagnose these comorbidities in ASD early on, and provide effective interventions to reduce their negative impact on functioning, thereby improving outcome

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Front Psychiatry. 2018;9.

INFERIOR FRONTAL GYRUS VOLUME LOSS DISTINGUISHES BETWEEN AUTISM AND (COMORBID) ATTENTION-DEFICIT/HYPERACTIVITY DISORDERΓÇöA FREESURFER ANALYSIS IN CHILDREN.

Nickel K, Tebartz van Elst L, Manko J, et al.

Objective: Autism spectrum (ASD) and attention-deficit/hyperactivity disorder (ADHD) are neurodevelopmental disorders with a high rate of comorbidity. To date, diagnosis is based on clinical presentation and distinct reliable biomarkers have been identified neither for ASD nor ADHD. Most previous neuroimaging studies investigated ASD and ADHD separately.

Method: To address the question of structural brain differences between ASD and ADHD, we performed FreeSurfer analysis in a sample of children with ADHD (n = 30), with high-functioning ASD (n = 14), with comorbid high-functioning ASD and ADHD (n = 15), and of typically developed controls (TD; n = 36). With FreeSurfer, an automated brain imaging processing and analyzing suite, we reconstructed the cerebral cortex and calculated gray matter volumes as well as cortical surface parameters in terms of cortical thickness and mean curvature.

Results: A significant main effect of the factor ADHD was detected for the left inferior frontal gyrus (Pars orbitalis) volume, with the ADHD group exhibiting smaller Pars orbitalis volumes. Dimensional measures of autism (SRS total raw score) and ADHD (DISYPS-II FBB-ADHD score) had no significant influence on the left Pars orbitalis volume. Both, ASD and ADHD tended to have an effect on cortical thickness or mean curvature, which did not survive correction for multiple comparisons.

Conclusion: Our results underline that ADHD rather than ASD is associated with volume loss in the left inferior frontal gyrus (Pars orbitalis). This area might play a relevant role in modulating symptoms of inattention and/or impulsivity in ADHD. The effect of comorbid ADHD in ASD samples and vice versa, on cortical thickness and mean curvature, requires further investigation in larger samples

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Front Psychiatry. 2018;9.

SCREENING FOR ADHD-RELATED SYMPTOMS IN PRESCHOOLERS SHOULD BE CONSIDEREDΓÇöRESULTS FROM A REPRESENTATIVE SAMPLE OF 5-YEAR-OLDS FROM A GERMAN METROPOLITAN REGION.

Mechler K, Kr+Âmer T, Landauer M, et al.

Background: Early assessment and intervention are crucial to alleviate symptoms and prevent long-term negative outcomes in children suffering from Attention-deficit/hyperactivity disorder (ADHD). In Germany, at present, no standardized screening for ADHD is routinely administered. This study aims to evaluate a

potential screening measure in a study population that is representative for a primary school entrance exam population in a German metropolitan region.
Methods: Based on various socio-demographic variables, a sample of n = 500 5-year-old children (58% boys, 42% girls), representative of a primary school entrance exam population from a German metropolitan region, was selected. Their parents completed a written survey consisting of the CBCL and a brief screening tool for ADHD symptomatology based on the DISYPS-II questionnaire. Demographic data were also collected.
Results: The subscale Attention problems of the CBCL/4-18 showed results in the clinical range for n = 10 (2%) participants. The ADHD screening identified n = 23 (4.6%) participants as suspect of having ADHD with a statistically significant gender difference (n = 17 boys vs. n = 6 girls, p = 0.03). In n = 5 (1%) participants, all boys, both CBCL/4-18 and the ADHD screening were indicative of ADHD.
Conclusions: Results indicate that screening for ADHD in this population may be both feasible and reasonable given the high prevalence and chronic nature of this disorder and the benefit of an early initiation of treatment. Results match previously reported figures for prevalence of ADHD-related symptoms and gender differences in preschool and older pediatric populations and thus do not support the hypothesis that the prevalence of ADHD in a metropolitan region is significantly higher than in other regions

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Front Psychiatry. 2018;9.
NEURAL CORRELATES OF DURATION DISCRIMINATION IN YOUNG ADULTS WITH AUTISM SPECTRUM DISORDER, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND THEIR COMORBID PRESENTATION.
Lukito SD, O'Daly OG, Lythgoe DJ, et al.
Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) often co-occur and share neurocognitive deficits. One such shared impairment is in duration discrimination. However, no studies using functional magnetic resonance imaging (fMRI) have investigated whether these duration discrimination deficits are underpinned by the same or different underlying neurofunctional processes. In this study, we used fMRI to compare the neurofunctional correlates of duration discrimination between young adult males with ASD (n = 23), ADHD (n = 25), the comorbid condition of ASD+ADHD (n = 24), and typical development (TD, n = 26) using both region of interest (ROI) and whole brain analyses. Both the ROI and the whole-brain analyses showed that the comorbid ASD+ADHD group compared to controls, and for the ROI analysis relative to the other patient groups, had significant under-activation in right inferior frontal cortex (IFG) a key region for duration discrimination that is typically under-activated in boys with ADHD. The findings show that in young adult males with pure ASD, pure ADHD and comorbid ASD+ADHD with no intellectual disability, only the comorbid group demonstrates neurofunctional deficits in a typical duration discrimination region

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Front Psychiatry. 2021;12.
UNIQUE TRANS-FATTY ACID PROFILE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.
Armon-Omer A, Amir E, Neuman H, et al.
Background: Attention deficit hyperactivity disorder (ADHD) is the most common developmental disorder in children. Studies suggest an association between fatty acids composition and ADHD pathogenesis. We aimed to investigate whether children diagnosed with ADHD present unique fatty acid profiles in red blood cells (RBC), as compared to children without ADHD.
Method: We examined 60 children aged 6ΓÇô14 years, out of which 32 were diagnosed with ADHD, and 28 were not. Blood was collected from all children to quantify an array of 26 fatty acids from RBC membranes. Fatty acid methyl esters were generated by acid transesterification and analyzed by gas chromatography.
Results: We found that children with ADHD presented unique fatty acid profiles on RBC membranes with significantly higher levels of most of the trans-fatty acids (Total trans-fatty acids 0.64 -¦ 0.21 vs. 0.49 -¦ 0.18 p = 0.003) and lower levels of docosahexaenoic acid (DHA), as compared to controls (4.06 -¦ 0.79 vs. 4.68 -¦ 1.37 p = 0.040). Additionally, total trans-fatty acids were higher in children with extremely severe clinical ADHD condition score, as compared to milder ADHD scores and to control children (0.72 -¦ 0.18, 0.64 -¦ 0.20, 0.61 -¦ 0.22, 0.49 -¦ 0.18, p = 0.010, accordingly).

Conclusion: Children with ADHD have higher levels of trans-fatty acids in RBCs, compared to children without ADHD. This study points to a possible link between trans-fatty acids and ADHD. Understanding these findings and the clinical meaning will potentially contribute to a more targeted dietary intervention

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Front Psychiatry. 2021;12.

CASE REPORT: TREATMENT OF A COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OBSESSIVE-COMPULSIVE DISORDER WITH PSYCHOSTIMULANTS.

Dogan-Sander E, Strau+ſM.

Introduction: Attention deficit hyperactivity disorder (ADHD) is a common disease in childhood and adolescence. In about 60% of pediatric patients, the symptoms persist into adulthood. Treatment guidelines for adult ADHD patients suggest multimodal therapy consisting of psychostimulants and psychotherapy. Many adult ADHD patients also suffer from psychiatric comorbidities, among others obsessive-compulsive disorder (OCD). The treatment of the comorbidity of ADHD and OCD remains challenging as the literature is sparse. Moreover, the impact of psychostimulants on obsessive-compulsive symptoms is still unclear.

Case Presentation: Here, we report on a 33-year-old patient with an OCD who was unable to achieve sufficient remission under long-term guideline-based treatment for OCD. The re-examination of the psychological symptoms revealed the presence of adult ADHD as a comorbid disorder. The patient has already been treated with paroxetine and quetiapine for the OCD. Due to the newly established diagnosis of ADHD, extended-release methylphenidate (ER MPH) was administered in addition to a serotonin reuptake inhibitor. After a dose of 30 mg ER MPH, the patient reported an improvement in both the ADHD and the obsessive-compulsive symptoms. After discharge, the patient reduced ER MPH without consultation with a physician due to subjectively described side effects. The discontinuation of medication led to a renewed increase in ADHD and obsessive compulsive symptoms. The readjustment to ER MPH in combination with sertraline and quetiapine thereafter led to a significant improvement in the compulsive symptoms again.

Conclusion: The present case shows that in ADHD and comorbid obsessive-compulsive disorder, treatment with psychostimulants can improve the obsessiveΓÇôcompulsive symptoms in addition to the ADHD-specific symptoms. To our knowledge, this is only the second case report describing a treatment with ER MPH for an adult patient with OCD and ADHD comorbidity in the literature. Further research, especially randomized controlled trials, is needed to standardize treatment options

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Front Psychiatry. 2021;12.

DECLINING TRAJECTORIES OF CO-OCCURRING PSYCHOPATHOLOGY SYMPTOMS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER: A 10-YEAR LONGITUDINAL STUDY .

Orm S, et al.

Objective: Our objective was to examine developmental trajectories of co-occurring psychopathology symptoms from childhood to young adulthood in individuals with Attention-Deficit/Hyperactivity Disorder (ADHD), individuals with Autism Spectrum Disorder (ASD), and typically developing (TD) individuals.

Method: We assessed co-occurring psychopathology symptoms in 61 individuals with ADHD, 26 with ASD, and 40 TD individuals at baseline (T1; Mage = 11.72, 64% boys), 2-year follow up (T2; Mage = 13.77), and 10-year follow up (T3; Mage = 21.35). We analyzed trajectories of internalizing behaviors, externalizing behaviors, and total problems with linear mixed models.

Results: From T1 to T3, the ADHD group displayed a small decline in internalizing behaviors (d = 0.49) and large declines in externalizing behaviors (d = 0.78) and total problems (d = 0.71). The ASD group displayed large declines in internalizing behaviors (d = 0.79), externalizing behaviors (d = ΓêÆ0.80), and total problems (d = 0.89). From T1 to T2, the decline in externalizing behaviors and total problems were significantly smaller in the ADHD group compared with the ASD group. The ADHD and the ASD group displayed more co-occurring symptoms compared with the TD group at T3.

Conclusion: Individuals with ADHD and ASD, respectively, displayed declines in co-occurring symptoms from childhood to young adulthood. Individuals with ASD displayed an earlier decline compared with individuals with ADHD. Compared with TD individuals, individuals with ADHD and ASD, respectively, continued to display elevated levels of co-occurring symptoms in young adulthood

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Front Psychiatry. 2021;12.

REWARD-RELATED DYSFUNCTIONS IN CHILDREN DEVELOPING ATTENTION DEFICIT HYPERACTIVITY DISORDER-ROLES OF OPPOSITIONAL AND CALLOUS-UNEMOTIONAL SYMPTOMS.

Schlos S, Derz F, Schurek P, et al.

Objectives: Neurocognitive functions might indicate specific pathways in developing attention deficit hyperactivity disorder (ADHD). We focus on reward-related dysfunctions and analyze whether reward-related inhibitory control (RRIC), approach motivation, and autonomic reactivity to reward-related stimuli are linked to developing ADHD, while accounting for comorbid symptoms of oppositional defiant disorder (ODD), and callous-unemotional (CU) traits.

Methods: A sample of 198 preschool children (115 boys; age: m = 58, s = 6 months) was re-assessed at age 8 years (m = 101.4, s = 3.6 months). ADHD diagnosis was made by clinical interviews. We measured ODD symptoms and CU traits using a multi-informant approach, RRIC (Snack-Delay task, Gift-Bag task) and approach tendency using neuropsychological tasks, and autonomic reactivity via indices of electrodermal activity (EDA).

Results: Low RRIC and low autonomic reactivity were uniquely associated with ADHD, while longitudinal and cross-sectional links between approach motivation and ADHD were completely explained by comorbid ODD and CU symptoms.

Conclusion: High approach motivation indicated developing ADHD with ODD and CU problems, while low RRIC and low reward-related autonomic reactivity were linked to developing pure ADHD. The results are in line with models on neurocognitive subtypes in externalizing disorders

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Front Psychiatry. 2021;12.

BRAIN AROUSAL AS MEASURED BY EEG-ASSESSMENT DIFFERS BETWEEN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND DEPRESSION.

Berger C, et al.

Objective: Disturbed regulation of vigilance in the wake state seems to play a key role in the development of mental disorders. It is assumed that hyperactivity in adult ADHD is an attempt to increase a general low vigilance level via external stimulation in order to avoid drowsiness. For depression, the avoidance of stimulation is interpreted as a reaction to a tonic increased vigilance state. Although ADHD is assumed to start during childhood, this vigilance model has been barely tested with children diagnosed for ADHD so far.

Methods: Resting-state EEG (8 min) measures from two groups of children diagnosed with either ADHD [N = 76 (16 female, 60 male), age: (mean/SD) 118/33 months] or depression [N = 94 (73 female, 21 male), age: 184/23 months] were analyzed. Using the VIGALL toolbox, EEG patterns of vigilance level, and regulation were derived and compared between both groups. In correlation analysis, the relations between vigilance measures, attentional test performance (alertness and inhibition), and mental health symptoms were analyzed.

Results: Children with ADHD differed from children with most prominent depressive symptoms in brain arousal regulation and level, but EEG vigilance was not related to behavior problems and not related to the attentional test performance. Brain arousal was dependent on the age of the participant in the whole sample; younger children showed lower vigilance stages than teenagers; this effect was not present when analyzed separately for each diagnostic group. EEG assessment time and received medication had no effect on the EEG vigilance.

Discussion: Although based on a small sample, this explorative research revealed that EEG vigilance level is different between children with ADHD and with depression. Moreover, even the standard procedure of the clinical routine EEG (resting state) can be used to differentiate brain arousal states between participants with ADHD and depression. Because routine EEG is not specialized to vigilance assessment, it may not be

sufficiently sensitive to find vigilance-symptomatology associations. Further research should address developmental changes in EEG measurements in children and use bigger samples of participants within the same age range

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Front Psychiatry. 2021;12.

DISINHIBITION OF PRIMITIVE REFLEXES IN ATTENTION DEFICIT AND HYPERACTIVITY DISORDER: INSIGHT INTO SPECIFIC MECHANISMS IN GIRLS AND BOYS.

Bob P, Konicarova J, Raboch J.

Objective: Cognitive and motor disintegration and other functional disturbances in various neuropsychiatric disorders may be related to inhibitory deficits that may manifest as a persistence or re-expression of primitive reflexes and few recent data suggest that these deficits may occur in Attention Deficit and Hyperactivity Disorder (ADHD).

Methods: We have tested a hypothesis to which extent ADHD symptoms and balance deficits are related to persisting primitive reflexes, such as Asymmetric Tonic Neck Reflex (ATNR) and Symmetric Tonic Neck Reflex (STNR) in 80 medication-naïve children with ADHD (40 boys and 40 girls) in the school age (8-11 years) and compared these data with a control group of 60 children (30 boys and 30 girls).

Results: These data show new finding that ADHD symptoms and balance deficits are strongly and specifically associated with persistent ATNR in girls and STNR in boys.

Conclusions: These results provide first evidence in medical literature that ADHD in girls and boys is specifically related to distinguished neurological developmental mechanisms related to disinhibition of primitive reflexes

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Front Psychiatry. 2021;12.

EFFECTIVENESS OF PHYSICAL ACTIVITY INTERVENTION ON ADHD SYMPTOMS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Xie Y, Gao X, Song Y, et al.

Objective: To assess the effectiveness of physical activity (PA) intervention on attention-deficit/hyperactivity disorder (ADHD)-related symptoms.

Method: Studies that investigated PA intervention for ADHD-related symptoms were identified through searching PubMed, Web of Science, Cochrane Library, and Embase databases from inception through June 2021. Standardized mean difference (SMD) with 95% confidence interval (CI) was used to assess the effectiveness of PA intervention on improving ADHD-related symptoms. The meta-analyses were conducted using fixed-effect or random-effect models according to the heterogeneity of the studies.

Results: Nine before after studies (232 participants) and 14 two-group control studies (162 participants/141 controls) were included in this meta-analysis. Combined results for before after studies indicated significant improvements on all studied ADHD-related symptoms (inattention: SMD = 0.604, 95% CI: 0.374ΓÇô0.834, p < 0.001; hyperactivity/impulsivity: SMD = 0.676, 95% CI: 0.401-0.950, p < 0.001; emotional problems: SMD = 0.416, 95% CI: 0.283 0.549, p < 0.001; behavioral problems: SMD = 0.347, 95% CI: 0.202 0.492, p < 0.001). Meta-analyses for two-group control studies further confirmed that PA intervention significantly improved the inattentive symptom (SMD = 0.715, 95% CI: 0.105, 1.325, p = 0.022). Subgroup analyses suggested significant beneficial effect on inattention symptoms in children. Moreover, closed motor skills were beneficial for hyperactive/impulsive problems (SMD = 0.671, p < 0.001), while open motor skills were beneficial for attention problems (SMD = 0.455, p = 0.049). When excluding studies with combined medication, the studies in unmedicated participants in before after studies still showed significant results in all studied ADHD-related symptoms as in the overall analysis. Given the limited sample size, the best frequency and intensity of PA intervention need further investigation.

Conclusion: Our results suggested that PA intervention could possibly improve ADHD-related symptoms, especially inattention symptoms. Closed-skill and open-skill activities could be beneficial for hyperactivity/impulsivity and inattention symptoms, respectively. Further high-quality randomized clinical trials with large sample size are needed

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Front Psychiatry. 2021;12.

INTEGRATED CARE FOR PREGNANT WOMEN AND PARENTS WITH METHAMPHETAMINE-RELATED MENTAL DISORDERS.

Petzold J, Spreer M, Kr++ger M, et al.

Background: Methamphetamine use is a rapidly increasing cause of morbidity and mortality. Pregnant women and new parents who consume methamphetamine are at high risk since they seldom seek health services despite having multiple needs. We addressed this care gap by implementing an easily accessible program that pools resources from psychiatric, obstetric, and pediatric departments as well as community and government agencies.

Method: This real-life observational study evaluated an integrated care program in 27 expecting parents and 57 parents of minors. The outcome criteria were treatment retention, psychosocial functioning, and abstinence. We compared participant demographics according to outcome and applied ordinal logistic regression to predict treatment success.

Results: Patients received integrated care for almost 7 months on average. Nearly half achieved stable abstinence and functional recovery. Only one pregnant woman dropped out before a care plan could be implemented, and all women who gave birth during treatment completed it successfully. Three-fourths of patients had psychiatric comorbidities. Patients with depressive disorders were almost 5 times less likely to succeed with treatment. Attention-deficit hyperactivity disorder (ADHD) was diagnosed in nearly 30% of patients who dropped out of a care plan, which was about 4 times more often than in the successful outcome group.

Conclusion: Our program engaged pregnant women and parents in treatment and helped them recover from methamphetamine-related mental disorders. Management of comorbid ADHD and depression should be an integral part of care initiatives to counter the methamphetamine crisis that affects parents and children across the globe

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Graefe's Archive for Clinical and Experimental Ophthalmology. 2021.

ASSOCIATION OF MENTAL DISORDERS AND STRABISMUS AMONG SOUTH KOREAN CHILDREN AND ADOLESCENTS: A NATIONWIDE POPULATION-BASED STUDY.

Choi DD, Park KA, Yang M, et al.

Purpose: The aim of this study is to determine the association between mental disorders and strabismus in South Korean children and adolescents.

Methods: Using data from the Korean National Health Claims Database from 2011 to 2017, the prevalence rates of mental illnesses and odds ratio were calculated. Children and adolescents (1-19-áyears) with strabismus and their randomly selected nonstrabismic age- and sex-matched controls (1:1) were enrolled. The odds ratios were adjusted for preterm birth, cerebral palsy, and mental retardation. Subgroup analysis was performed according to sex and the type of strabismus.

Results: A total of 327,076 subjects (male, 158,597; female, 168,479) identified as strabismus patients were enrolled. After adjusting for preterm birth, cerebral palsy, and mental retardation, the corrected odds ratio of overall mental illness was 1.10 (95% CI, 1.08-1.12) for the strabismus group compared to the controls: 1.7 (95% CI, 1.62-1.78) for developmental disorder, 1.36 (95% CI, 1.27-1.45) for pervasive developmental disorder (autism), 1.14 (95% CI, 1.10ΓÇô1.17) for attention-deficit hyperactivity disorder (ADHD), 1.15 (95% CI, 1.05-1.27) for obsessive-compulsive disorder (OCD), 1.08 (95% CI, 1.05-1.11) for pediatric behavioral and emotional disorders, 0.93 (95% CI, 0.88-0.99) for post-traumatic stress disorder (PTSD), and 0.85 (95% CI, 0.82-0.89) for tic disorder.

Conclusion: South Korean children and adolescents with strabismus had a higher relative risk for various types of mental disorders such as a developmental disorder, autism, ADHD, and OCD than the controls, whereas they had a relatively lower risk of tic disorder

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Hum Brain Mapp. 2021.

ALTERED SINGLE-SUBJECT GRAY MATTER STRUCTURAL NETWORKS IN DRUG-NA+»VE ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN.

Chen Y, Lei D, Cao H, et al.

Altered topological organization of brain structural covariance networks has been observed in attention deficit hyperactivity disorder (ADHD). However, results have been inconsistent, potentially related to confounding medication effects. In addition, since structural networks are traditionally constructed at the group level, variabilities in individual structural features remain to be well characterized. Structural brain imaging with MRI was performed on 84 drug-na+»ve children with ADHD and 83 age-matched healthy controls. Single-subject gray matter (GM) networks were obtained based on areal similarities of GM, and network topological properties were analyzed using graph theory. Group differences in each topological metric were compared using nonparametric permutation testing. Compared with healthy subjects, GM networks in ADHD patients demonstrated significantly altered topological characteristics, including higher global and local efficiency and clustering coefficient, and shorter path length. In addition, ADHD patients exhibited abnormal centrality in corticostriatal circuitry including the superior frontal gyrus, orbitofrontal gyrus, medial superior frontal gyrus, precentral gyrus, middle temporal gyrus, and pallidum (all p-á<.05, false discovery rate [FDR] corrected). Altered global and nodal topological efficiencies were associated with the severity of hyperactivity symptoms and the performance on the Stroop and Wisconsin Card Sorting Test tests (all p-á<.05, FDR corrected). ADHD combined and inattention subtypes were differentiated by nodal attributes of amygdala (p-á<.05, FDR corrected). Alterations in GM network topologies were observed in drug-na+»ve ADHD patients, in particular in frontostriatal loops and amygdala. These alterations may contribute to impaired cognitive functioning and impulsive behavior in ADHD

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Infant Behav Dev. 2022;66.

RELATIONSHIP OF WITHDRAWN, ANXIOUS/DEPRESSED AND ATTENTION PROBLEMS TO COGNITIVE PERFORMANCE IN PRETERM CHILDREN AT 18 MONTHS AND 36 MONTHS OF AGE.

Ross GS, Perlman JM.

Objective: A positive significant association has been found between behavior problems and lower cognition in very low birthweight (VLBW) preterm children at school age, but there is relatively little information about whether such an association exists in toddlers and on the continuity of this association. The aim of this study was to assess if there is a relationship between behavior problems and cognitive performance in VLBW preterm children at 18 months post conception and 3 years old, independent of socioeconomic status and sex.

Method: Parents of 124 preterm children completed a behavior rating questionnaire (Child Behavior Checklist 1.5ΓÇô5) to measure behavior problems characteristic of preterm children (Withdrawn, Anxious/Depressed, and Attention Problems). Children completed the Cognitive Scale of the Bayley Scales of Infant Development-III at 18 months and the Wechsler Preschool and Primary Scale (III or IV) at 36 months old. Socioeconomic status (SES), sex, and diagnoses of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) at 3 years were recorded for each child.

Results: Withdrawn problems at 18 months were associated with lower cognitive scores at 18 months and both Withdrawn problems at 18 months and 36 months were associated with lower cognitive scores at 36 months. Increases in Attention Problems scores from 18 to 36 months were associated with decreases in cognitive scores over that period. Lower SES was associated with lower cognitive scores at 36 months and decreases in cognitive scores between 18 and 36 months. Sex was not related to behavior problems or cognition. Diagnoses of ASD and ADHD were significantly associated with increased Withdrawn behavior and Attention Problems, respectively.

Conclusions: The early association of Withdrawn behaviors with less favorable cognitive performance at 18 months and 36 months and the relationship between increases in Attention Problems with decreases in cognitive scores between the toddler and preschool period indicate the need for early assessment of and intervention for behavior problems, as well as concurrent cognitive delays, in VLBW preterm children

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Int J Environ Res Public Health. 2016;13.

SUGAR-SWEETENED BEVERAGE CONSUMPTION IS ADVERSELY ASSOCIATED WITH CHILDHOOD ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Yu CJ, Du JC, Chiou HC, et al.

Attention deficit/hyperactivity disorder (ADHD) is one of the most common childhood neurobehavioral conditions. Evidence of the negative effects of sugar-sweetened beverages (SSBs) on mental health has not been convincing, although a few studies have found an association between high SSB levels and attention problems in children. This study aimed to test the hypothesis that SSB consumption is associated with ADHD among children. Doctor-diagnosed ADHD cases (n = 173) and non-ADHD controls (n = 159) between age 4 to 15 were recruited. SSB consumption, socio-demographic and lifestyle characteristics of the children, as well as of their mothersΓÇÖ characteristics during pregnancy, were collected using a questionnaire. Blood lead levels and polymorphisms of two commonly verified dopaminergic-related genes (the D4 dopamine receptor gene DRD4 and the dopamine transporter gene DAT1) were also analyzed. There was a dose-response relationship between SSB consumption and ADHD. After covariates were adjusted, children who consumed SSBs at moderate levels and high levels had 1.36 and 3.69 odds, respectively, of having ADHD, compared with those who did not consume SSBs (p for trend < 0.05). Similar results were obtained when females were excluded. Our findings highlighted the adverse correlation between SSB consumption and ADHD and indicated a dose-response effect even after covariates were adjusted

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Int J Environ Res Public Health. 2021;18.

SLEEP DISORDERS IN EARLY CHILDHOOD AND THE DEVELOPMENT OF MENTAL HEALTH PROBLEMS IN ADOLESCENTS: A SYSTEMATIC REVIEW OF LONGITUDINAL AND PROSPECTIVE STUDIES.

Lam LT, Lam MK.

The association between sleep problems, particularly sleep disorders, and mental health has long been studied and recognized. However, the causal relationship between sleep disorders, particularly during early childhood, on mental health problems in adolescence are yet to be established. From a preventive perspective, it is important to understand the causality of mental health problems in adolescents so that intervention measures can be derived and implemented as early as possible for maximum effectiveness. To provide more precise information on the effect of early childhood sleep disorders on mental health problems during adolescence, a systematic review was conducted on longitudinal and prospective studies reported in the literature. Following the PRISMA guidelines with an extensive search of the literature 26 studies were identified. Seven of these identified studies satisfied all selection criteria with sufficient data on the effect of early childhood sleep disorders and mental health problems in adolescence. Information was extracted and analyzed systematically from each study and tabulated. The overall results obtained from these studies indicate a significant and possible causal relationship between early childhood sleep disorders and the development of mental health problems, such as anxiety, depression, and ADHD in adolescence. These results are discussed with regards to the theoretical and practical implications as well as preventive strategies

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Int J Neuropsychopharmacol. 2021;24:776-86.

EXPLORING THE EFFECTS OF PHARMACOLOGICAL, PSYCHOSOCIAL, AND ALTERNATIVE/COMPLEMENTARY INTERVENTIONS IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: META-REGRESSION APPROACH.

Yang KH, Lane HY, Chang YC, et al.

Background: There have been various therapies for attention-deficit/hyperactivity disorder (ADHD), but the previous meta-analysis of ADHD efficacy remains unclear. This study aims to systemically meta-regress the effect sizes (ES) of psychostimulant pharmacotherapy (methylphenidate and lisdexamfetamine), non-stimulant pharmacotherapy (atomoxetine and alpha-2 agonists), psychosocial therapy (parental behavioral therapy [PBT]), combination therapy (psychostimulant plus PBT), and alternative/complementary interventions to determine the right treatment for ADHD.

Methods: We searched various ADHD interventions from the MEDLINE and PubMed databases (National Center for Biotechnology Information) between January 1, 1980, and July 30, 2018. Following the meta-

analysis of random effects, the meta-regression analyses were used to explore factors potentially influencing treatment efficacy. The confounding variables included type of treatment, type of study, age, type of symptom scale used, and year of publication.
Results: A total of 107 trials (n = 9883 participants) were included. After adjustment, compared with the psychostimulant therapy (28 trial, 2134 participants), non-stimulant pharmacotherapy (28 trials, 4991 participants) and alternative/complement intervention (25 trials, 1195 participants) were less effective by the ES of -0.384 (P =. 004) and -0.419 (P =. 028), respectively. However, compared with psychostimulant, PBT (19 trials, 1122 participants; ES = -0.308, P =. 095) and the combination of psychostimulant and PBT (7 trials, 441participants; ES = -0.196, P =. 209) did not differ significantly.
Conclusions: Psychostimulant therapy surpassed non-stimulant pharmacotherapy and alternative/complement intervention. Psychostimulant therapy, PBT, and the combination of psychostimulant therapy and PBT appear to be similar in efficacy according to this meta-regression

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Int J Psychiatry Med. 2021;56:422-32.

RISK FACTORS FOR ADHD AND COMORBID PSYCHIATRIC, ACADEMIC AND BEHAVIOR PROBLEMS AMONG PRIMARY SCHOOL STUDENTS IN JEDDAH, SAUDI ARABIA.

Al Zaben F, Sehlo M, Alghamdi W, et al.

Risk factors for attention deficit hyperactivity disorder (ADHD), psychiatric, and classroom academic/behavioral problems were examined in 929 students grades 1ΓÇô6 in Jeddah, Saudi Arabia. Teachers identified ADHD by completing the Vanderbilt ADHD scale. Compared to controls without ADHD, students with ADHD were more likely to have early parental loss, head trauma, motor/language delay, family psychiatric problems, and high family stress. Among those with ADHD, risk factors for psychiatric comorbidity were older age, family psychiatric history, and motor/language delay. Risk factors for impaired academic/behavioral performance were high family stress, family psychiatric problems, and chronic illness. Identifying risk factors for ADHD and common comorbidities associated with this disorder may help parents, teachers and clinicians detect this condition, increasing effective management

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Iran J Psychiatr Behav Sci. 2021;15.

A COMPARISON OF METHYLPHENIDATE (MPH) AND COMBINED METHYLPHENIDATE WITH CROCUS SATIVUS (SAFFRON) IN THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ADHD: A RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, CLINICAL TRIAL.

Khaksarian M, Ahangari N, Masjedi-Arani A, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is characterized by behavioral and neurodevelopmental problems. It is estimated that 3 - 7% of children and adolescents suffer from this problem. Apart from synthetic drugs, other effective types of medication like herbal medicines are of great importance.
Objectives: This study aimed to evaluate the effectiveness of methylphenidate (MPH) and its combination with Crocus sativus (saffron) in the treatment of children suffering from ADHD.
Methods: The sample included 70 children aged between 6 and 16 years who had been diagnosed with ADHD. The patients were randomly assigned into two equal groups (n = 35 in each group). While both groups received 20 or 30 mg/d of MPH (20 and 30 mg/d for < 30 and > 30, respectively), one of them also received 20 or 30 mg/d of saffron in a capsule based on BMI (20 and 30 mg/d for < 30 and > 30, respectively). To collect data, parents and teachers completed Attention-Deficit/Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV). Also, for analyzing the data, the repeated measures analysis of variance (RMANOVA) was used.
Results: The results of general linear model (GLM) repeated measures indicated that in both groups, the patients had less symptoms after eight weeks of treatment. However, after four weeks, the average score assigned by the parents and teachers in the MPH with saffron group was lower than the average total score in the MPH group (P < 0.05).

Conclusions: Using MPH combined with saffron proved to be more effective in the treatment of patients suffering from ADHD compared to separate treatments. It seems that the duration of therapy can be reduced and the effectiveness be improved by prescribing proposed combined treatment

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J Affective Disord. 2022;298:322-28.

THE ASSESSMENT OF CYCLOTHYMIC-HYPERSENSITIVE TEMPERAMENT IN YOUTH WITH MOOD DISORDERS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Pisano S, Sesso G, Senese VP, et al.

Background: Cyclothymic-hypersensitive temperament (CHT) has been related to both depression and bipolarity, as well as to suicidality. Recently, a psychometrically sound way of assessment has been validated in youth (Cyclothymic-Hypersensitive Temperament Questionnaire, CHTQ), but data on clinical populations are still scant. Aim of our study is to further explore the structure and other psychometric properties of the revised version of CHTQ and its clinical implications in clinical samples.

Methods: The study is based on a dataset of patients with unipolar depression, bipolar disorder and attention deficit and hyperactivity disorder (ADHD) (243 patients, 135 males, mean age 14.22 -¦ 2.16 years, age range 9-18 years), compared to a community sample of adolescents (398 subjects, 95 boys, mean age 15.47 -¦ 1.96 years, age range 10ΓÇô18 years)

Results: The two-correlated factor structure of CHT has been confirmed, with a moodiness/hypersensitiveness factor, correlated with internalizing symptoms, and an impulsiveness/emotional dysregulation factor, correlated with externalizing symptoms. All CHTQ scores correlate with global functioning. CHTQ total scores discriminate patients from healthy controls. Only CHTQ impulsiveness/emotional dysregulation subscale score is higher in bipolar patients, compared to unipolar depression and ADHD, whereas neither CHTQ moodiness/hypersensitiveness subscale score nor CHTQ total score discriminate between clinical groups.

Limitation: Data on current mood states are unavailable. Patients were recruited in a third level clinic. The unipolar depression group is relatively small.

Conclusion: CHT may be a rapid and reliable screening and diagnostic tool in the clinical practice with youth, exploring the cyclothymic dimension in different psychiatric disorders

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J Autism Dev Disord. 2021.

HEART RATE VARIABILITY IN CHILDREN AND ADOLESCENTS WITH AUTISM, ADHD AND CO-OCCURRING AUTISM AND ADHD, DURING PASSIVE AND ACTIVE EXPERIMENTAL CONDITIONS.

Bellato A, Arora I, Kochhar P, et al.

Despite overlaps in clinical symptomatology, autism and ADHD may be associated with opposite autonomic arousal profiles which might partly explain altered cognitive and global functioning. We investigated autonomic arousal in 106 children/adolescents with autism, ADHD, co-occurring autism/ADHD, and neurotypical controls. Heart rate variability was recorded during resting-state, a passive auditory oddball task and an active response conflict task. Autistic children showed hyper-arousal during the active task, while those with ADHD showed hypo-arousal during resting-state and the passive task. Irrespective of diagnosis, children characterised by hyper-arousal showed more severe autistic symptomatology, increased anxiety and reduced global functioning than those displaying hypo-arousal, suggesting the importance of considering individual autonomic arousal profiles for differential diagnosis of autism/ADHD and when developing personalised interventions

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Journal of Clinical Neuroscience. 2021;94:237-43.

OMEGA-3 SUPPLEMENTATION IN CHILDREN WITH ADHD AND INTRACTABLE EPILEPSY.

Elsadek AE, Maksoud YHA, Suliman HA, et al.

Background: Omega-3 may have a role in the treatment of drug- resistant epilepsy.

Objectives: To evaluate omega-3 supplementation in seizure control in children with attention deficit hyperactivity disorder (ADHD) and intractable epilepsy.

Patients and Methods: Sixty children with ADHD and intractable epilepsy were enrolled. They were randomly assigned in a double-blind fashion in a 1:1 ratio into the omega-3 supplementation group or the placebo group in addition to risperidone and antiepileptic drugs. All patients were assessed for the frequency and severity of the epileptic attacks at baseline, monthly, and at 6 months from the beginning of the study; 30 children received omega-3 and the other 30 children received placebo.
Results: At baseline, the median number of seizures per month was 5 in both groups. After one month, this median decreased to 3 and became 2 after two months of supplementation with omega-3 in the supplementation group while it remained 5 in the control group. After 3 months and till the end of the study, this median decreased to 0 while it remained 5 in the control group throughout the study period. Children who were supplemented with omega-3 showed a significant decrease in the monthly frequency of seizure attacks after six months of supplementation compared to the baseline before supplementation ($P < 0.05$) There was no significant decrease in the severity of the seizures attacks among our patients with omega-3 supplementation ($P > 0.05$).
Conclusion: Omega 3 may help in achieving good seizure control in children with ADHD and intractable epilepsy

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Journal of Healthcare Engineering. 2021;2021.

META-ANALYSIS STUDY ON TREATMENT OF CHILDREN'S ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY.

Xue J, Hao Y, Li X, et al.

With the development of society and the economy, the prevalence of attention deficit hyperactivity disorder (ADHD) has been increasing. Due to its high comorbidity and high harm, it has received increasing attention. It causes damage to functions in multiple areas, and this damage may continue into adulthood. ADHD is a common developmental disorder characterized by persistent attention deficit and hyperactivity/impulsivity. ADHD often merges with other diseases, such as oppositional defiant disorder, conduct disorder, personality disorder, anxiety disorder, mood disorder, and substance dependence. The disease tends to cause children with learning difficulties, poor grades, strained relationships with family members and children of the same age, lack of self-esteem, and children with low occupation, low income, substance abuse, and antisocial personality characteristics when they grow up to adults. Many countries have formulated ADHD treatment guidelines for this purpose, but there is still a lack of consensus. This article uses literature research and the meta method: RevMan 5.3 software is used for data analysis. The analysis results show that traditional Chinese medicine has characteristics and advantages in the clinical total effective rate and hyperactivity index score in the treatment of ADHD. The overall clinical syndrome differentiation of the treatment can be summarized as liver and kidney yin deficiency and liver yang partial prosperity. The overall medication is based on the methods of nourishing yin and clearing heat, calming the liver and nourishing kidney, and nourishing yin and suppressing yang. The efficacy and safety evaluation of traditional Chinese medicine in the treatment of ADHD need to be further verified by large-sample clinical trials with strict design and standardized outcome index reporting

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J Intellect Disabil Res. 2021.

WORKING MEMORY TRAINING IN CHILDREN WITH BORDERLINE INTELLECTUAL FUNCTIONING AND NEUROPSYCHIATRIC DISORDERS: A TRIPLE-BLIND RANDOMISED CONTROLLED TRIAL.

Roording-Ragetlie S, Spaltman M, de Groot E, et al.

Background: Poor working memory, lower IQ and maladaptive behaviour form a triple disability known to have negative effects on the academic and social development of children with borderline intellectual functioning (BIF; IQ: 70<IQ<85) and neuropsychiatric disorders [attention-deficit hyperactivity disorder (ADHD) and/or autism spectrum disorder (ASD)]. Treatment possibilities for these children are scarce and hardly evidence based. This study primarily investigated whether adaptive computerised working memory training (WMT) may lead to significantly more improvement on a non-trained visuospatial WM task compared with a non-adaptive control WMT (placebo) in children with BIF and neuropsychiatric disorders. As secondary outcome measures, we used the scores on several non-trained neuropsychological near-transfer and far-transfer tasks as well as behavioural measures.

Method: We conducted a triple-blind placebo-controlled randomised clinical trial in 72 children (aged 10;0-13;11-áyears, 53 boys, 19 girls) with BIF and comorbid neuropsychiatric disorders (ADHD=37, ASD=21, both=14) that were referred to child and adolescent psychiatry care, between May 2012 and March 2019. Children completed the Dutch version of Cogmed WMT, either the adaptive training version or the non-adaptive placebo version, 25 sessions (30ΓÇô45 min a day), for 5 weeks. The primary outcome measure was the score on a non-trained visuospatial working memory task. The primary outcome was measured before and directly after 5 weeks of WMT and again 6 months after training.
Results: A total of 375 children were screened for eligibility and 72 were randomised. No significantly higher levels of improvement over time were found on our primary outcome measure in the experimental WMT group compared with the placebo control WMT, nor in the secondary (near-transfer and far-transfer tasks) or tertiary (behavioural measures) outcome measures. However, this study did show changes over time for these measurements for both the experimental and placebo conditions.
Conclusions: This study was unable to document superior training effects over time of an adaptive WMT in children with BIF and neuropsychiatric disorders, compared with a placebo (non-adaptive) WMT. The objectively documented changes over time in the non-adaptive WMT arm suggest that these children with persistent impairments in WM may benefit from a structured learning environment that is associated with improvement of neurocognitive functioning and coping strategies. Further research is needed to examine which elements of cognitive training may be useful for which specific patients and to study long-term effects of training

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Journal of Medical Investigation. 2021;68:53-58.
J Pediatr. 2021.

PREDICTORS OF CHANGES IN HEIGHT, WEIGHT, AND BODY MASS INDEX AFTER INITIATION OF CENTRAL NERVOUS SYSTEM STIMULANTS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Waxmonsky JG, Pelham WE, Baweja R, et al.

Objective: To identify predictors of changes in height, weight, and body mass index (BMI) in children with attention deficit hyperactivity disorder (ADHD) starting central nervous system (CNS) stimulants.
Study design: There were 230 medication-naïve children aged 5-12 years with ADHD who participated in a randomized trial evaluating the impact of CNS stimulants on growth over 30 months. This observational analysis focused on the 141 participants using study medication for 65 or more days in the first 6-months after starting medication. Biometric variables, ADHD, and oppositional defiant disorder symptom scores at medication initiation, and medication use over the study were examined as predictors of changes in standardized (z) height, weight, and BMI.
Results: Mean changes in z-BMI, z-weight. and z-height were negative throughout the study. The most consistent predictors of change in z-BMI, z-weight, and z-height were percent days medicated and total medication exposure. Children with lower z-height and z-weight at medication initiation experienced greater z-BMI and z-weight decreases over the first 6 months on medication. Greater appetite suppression during dose optimization predicted greater decreases in z-weight over the entire study and a greater decrease in z-height over the first 6 months on medication. z-weight change correlated with z-height change. Behavioral symptoms did not predict changes in z-BMI, z-weight, or z-height.
Conclusions: How much and how often CNS stimulants are used predicts changes in z-BMI, z-weight, and z-height in children. Even smaller and lighter children may be at risk for decreases in z-weight and z-BMI. Parent ratings of appetite during dose titration may serve as feasible indicators of future weight and height change in children using CNS stimulants. Trial registration: Clinicialtrials.gov: NCT01109849

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J Psychiatr Res. 2021.

PILOT STUDY OF A MOBILE APPLICATION-BASED INTERVENTION TO INDUCE CHANGES IN NEURAL ACTIVITY IN THE FRONTAL REGION AND BEHAVIORS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND/OR INTELLECTUAL DISABILITY.

Ha S, Han JH, Ahn J, et al.

Children with neurodevelopmental disorders, such as attention deficit hyperactivity disorder (ADHD) and intellectual disability (ID), need early intervention and continuous treatment. We aimed to investigate the feasibility and acceptability of mobile application-based interventions in children with ADHD and ID in supporting attention and cognitive function. Twenty-six children with ADHD and/or ID with attention and cognition difficulties were recruited. Participants completed a 12-week mobile application-based intervention. To assess whether digital intervention improved attention and cognitive function, we used the Comprehensive Attention Test (CAT), Cambridge Neuropsychological Tests Automated Battery (CANTAB), and electroencephalography (EEG) to examine direct changes in children's behavior and neural activity. Clinicians and parents assessed changes using the Behavior Rating Inventory of Executive Function, Second Edition (BRIEF-2), Korean version of the ADHD Rating Scale (K-ARS), Clinical Global Impression-Improvement Scale, and parental questionnaires. The intervention induced changes in neural activities on EEG and behavior but there were no significant changes in CAT and CANTAB results. Relative theta and alpha power were significantly lower post-intervention in the eyes-open (EO) condition of EEG recording and these changes were mainly observed in the frontal regions of the brain. Parental reports using the BRIEF-2 and K-ARS noted significant improvements in executive function, attention, and hyperactivity-impulsivity. In addition, the clinical impression improved in 60% of participants. These results provide evidence that a mobile application-based intervention has the benefit of supporting children with ADHD and/or ID. Digital intervention could change neural activity and improve children's attention and cognitive function. Given our findings, we suggested that mobile application-based digital therapeutics may have great potential for helping children with neurodevelopmental disorders who need continuous treatment

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J Psychiatr Res. 2021.

CAFFEINE-RELATED GENES INFLUENCE ANXIETY DISORDERS IN CHILDREN AND ADULTS WITH ADHD.

Fraporti TT, Bandeira CE, Tovo-Rodrigues L, et al .

Attention-deficit/hyperactivity disorder (ADHD) and anxiety disorders (AD) frequently co-occur, increasing morbidity and challenging treatment. Caffeine is a central nervous system stimulant and acts in the brain through adenosine receptors, influencing attention, alertness, and anxiety. In the present study, we performed a gene-set analysis to verify if genes related to caffeine response are associated with anxiety disorders in 240 children and 406 adults with ADHD. We demonstrated an association between the gene-set with AD in children (P = 0.0054) and with the number of anxiety disorders in adults (P = 0.0197). In order to test if this effect is a result of anxiety in general or is related to AD comorbid with ADHD, we evaluated the association between caffeine gene-set with AD in an adult control sample. The gene-set was neither associated with the AD presence (P = 0.3008) nor with the number of AD (P = 0.5594) in this control sample. We also test this gene set with ADHD (n = 55,374) and AD (n = 18,186) GWAS summary statistics, and we did not observe significant results with ADHD (P = 0.5587) or AD (P = 0.3930). These findings suggest the caffeine-related genes play a role in the etiology of an anxiety disorder phenotype present in children and adults with ADHD

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J Psychopathol Behav Assess. 2021.

AN EXAMINATION OF THE PARENT-RATED ADOLESCENT ACADEMIC PROBLEMS CHECKLIST: WHAT DO PARENTS REALLY KNOW?

Benson K, Evans SW, Sibley MH, et al.

Adolescents with attention-deficit/hyperactivity disorder (ADHD) experience academic difficulties, but there are limitations to current methods of measuring these problems. The parent-rated Adolescent Academic Problems Checklist (AAPC) is a particularly promising measure, as the items were derived from concerns of parents and teachers of adolescents with ADHD and the scale demonstrates good concurrent validity and

treatment sensitivity (Sibley et al. in School Psychology Quarterly, 29(4), 422, 2014; Sibley et al. Journal of Consulting and Clinical Psychology, 84(8), 699, 2016b). Because parents do not observe some academic behaviors queried on the AAPC, they may provide inaccurate responses to some items, leading to measurement error. In the current study, we sought to (1) determine the extent to which parents of adolescents with ADHD possess knowledge of the academic behaviors assessed on the AAPC, (2) determine if the scale maintains the two-factor structure (academic skills and disruptive behavior) and continues to relate to indicators of academic functioning after removing items associated with low parent knowledge, and (3) validate findings with the revised scale in a separate sample of adolescents with ADHD. Results identified five items for which the majority of parents reported little to no knowledge. When removing items with low parental knowledge, the AAPCs model fit was maintained and the two-factor model remained a better fit than the one-factor model. The relationships between the revised subscales and measures of academic functioning remained significant and largely equivalent to the original version. The revised model demonstrated similar fit in the second sample and was also related to indicators of academic functioning. Implications for clinical practice are discussed

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J Shanghai Jiaotong Univ Med Sci. 2021;41:1366-70.

PROGRESS OF TRANSCRANIAL DIRECT CURRENT STIMULATION IN THE TREATMENT OF CHILDREN AND ADOLESCENTS PSYCHIATRIC DISORDERS.

Qian NS, Hong W, Li CB.

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique. It can modulate brain current activities and treat psychiatric disorder through affecting neural excitability and synaptic plasticity. At present, there are substantial application researches of tDCS, and it is effective on the treatment of adult depressive disorder, bipolar depressive disorder, schizophrenia and other mental diseases. Preliminary researches have showed that children and adolescents have certain tolerance to tDCS, however, there are only few randomized controlled clinical studies about tDCS applying to the children and adolescents with psychiatric disorders, and reliable conclusions couldn't be drawn due to limitations of small sample size and open label trials. This paper reviews the utilization of tDCS among children and adolescents with schizophrenia, attention deficit/hyperactivity disorder, autism spectrum disorder and dyslexia. Details including parameters, efficacy, side effects and limitations are discussed, and different sessions, duration, current, intensity, stimulation sites and effect are compared. Information discussed may provide reference for development of neuromodulation techniques and clinical applications of tDCS to the treatment of children and adolescents with psychiatric disorders

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Journal of the Academy of Consultation-Liaison Psychiatry. 2021.

ASSOCIATIONS BETWEEN SLEEP-DISORDERED BREATHING AND BEHAVIORAL AND COGNITIVE FUNCTIONS IN CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kim KM, Lim MH, Ha M, et al.

Background: Sleep-related problems are highly prevalent comorbidities in Attention-Deficit/Hyperactivity Disorder (ADHD).

Objective: This study aimed to investigate the associations between sleep-disordered breathing (SDB) and behavioral and cognitive functions in children with and without ADHD.

Methods: A total of 341 children were included (ADHD group: 155, control group: 186; age: 6-10 years). The participants' sleep-related symptoms were assessed using a parent-rated questionnaire, and they were categorized into low- and high-risk SDB groups based on their scores. Behavioral symptoms were assessed using the Behavioral Assessment System for Children, Second Edition (BASC-2), and cognitive sustained attention and inhibitory control were assessed using a computer-based continuous performance test.

Results: In the ADHD group, the high-risk SDB children showed significantly higher scores than the low-risk SDB group in externalizing problems ($F = 4.22$; $P = 0.042$), including hyperactivity ($F = 4.65$; $P = 0.033$) and attention problems ($F = 8.19$; $P = 0.005$), but not internalizing problems. Meanwhile, in the control group, the high-risk SDB children showed significantly higher scores than the low-risk SDB group in internalizing problems ($F = 9.89$; $P = 0.002$), depression ($F = 9.45$; $P = 0.002$), and somatization ($F = 7.83$; $P = 0.006$), as

well as in externalizing problems (F = 7.72; P = 0.006), including hyperactivity (F = 6.23; P = 0.013), aggression (F = 5.00; P = 0.027), and conduct problems (F = 6.79; P = 0.010). Contrary to the behavioral outcomes, none of the attention performance subscale scores showed significant differences between the high- and low-risk SDB groups in either the ADHD or control group.
Conclusions: The present findings suggest that SDB is associated with behavioral problems in children with ADHD and controls, with stronger associations in control children. On the contrary, SDB has no association with cognitive attention performance. This study extends our understanding of the associations of SDB with behavioral symptoms and cognitive functions in children

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J Am Acad Child Adolesc Psychiatry. 2021.
EDITORIAL: EVIDENCE CONCERNING DOSE-DEPENDENT EFFECTS OF STIMULANTS ON NEUROCOGNITIVE FUNCTION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Rhodes SM.

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J Am Acad Child Adolesc Psychiatry. 2021.
MOTIVATION AND COGNITIVE ABILITIES AS MEDIATORS BETWEEN POLYGENIC SCORES AND PSYCHOPATHOLOGY IN CHILDREN.
Pat N, Riglin L, Anney R, et al.
Objective: Fundamental questions in biological psychiatry concern the mechanisms that mediate between genetic liability and psychiatric symptoms. Genetic liability for many common psychiatric disorders often confers transdiagnostic risk to develop a wide variety of psychopathological symptoms through yet unknown pathways. This study examined the psychological and cognitive pathways that might mediate the relationship between genetic liability (indexed by polygenic scores; PS) and broad psychopathology (indexed by p factor and its underlying dimensions).
Method: First, which of the common psychiatric PSs (major depressive disorder [MDD], attention-deficit/hyperactivity disorder [ADHD], anxiety, bipolar disorder, schizophrenia, autism) that were associated with p factor were identified. Then focused was shifted to 3 pathways: punishment sensitivity (reflected by behavioral inhibition system), reward sensitivity (reflected by behavioral activation system), and cognitive abilities (reflected by g factor based on 10 neurocognitive tasks). We applied structural equation modeling on the Adolescent Brain Cognitive Development (ABCD) Study dataset (n = 4,814; 2,263 girls; 9ΓÇô10 years old).
Results: MDD and ADHD PSs were associated with p factor. The association between MDD PS and psychopathology was partially mediated by punishment sensitivity and cognitive abilities (proportion mediated = 22.35%). Conversely, the influence of ADHD PS on psychopathology was partially mediated by reward sensitivity and cognitive abilities (proportion mediated = 30.04%). The mediating role of punishment sensitivity was specific to emotional/internalizing. The mediating role of both reward sensitivity and cognitive abilities was specific to behavioral/externalizing and neurodevelopmental dimensions of psychopathology.
Conclusion: This study provides a better understanding of how genetic risks for MDD and ADHD confer risks for psychopathology and suggests potential prevention/intervention targets for children at risk

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J Am Acad Child Adolesc Psychiatry. 2021.
META-ANALYSIS: DOSE-DEPENDENT EFFECTS OF METHYLPHENIDATE ON NEUROCOGNITIVE FUNCTIONING IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Vertessen K, Luman M, Staff A, et al.
Objective: Neurocognitive deficits are at the heart of explanatory models of attention-deficit/hyperactivity disorder (ADHD), and lead to significant impairments in daily life. Determining the dosing effects of methylphenidate (MPH) on a broad range of neurocognitive functions and investigating possible impairing effects of high doses is therefore important.
Method: Placebo-controlled trials were included that investigated MPH dosing effects on neurocognitive functions in children and adolescents (aged 5-18 years) diagnosed with ADHD. Effect sizes (standardized

mean differences [SMDs]) were calculated for different neurocognitive functions (baseline speed, variability in responding, nonexecutive memory and executive memory, inhibitory control, and cognitive flexibility) and, if available, for ADHD symptoms. Meta-regression analysis were used to investigate linear effects of dose (mg/kg/dose), and separate meta-analyses compared SMDs for 3 MPH dose ranges: low (0.10-0.30 mg/kg/dose), medium (0.31-0.60 mg/kg/dose), and high (0.61-1.00 mg/kg/dose).
Results: A total of 31 studies fulfilled inclusion criteria, comprising 804 children with ADHD. Methylphenidate had beneficial effects on all neurocognitive functions (d = 0.20-0.73). Significant linear dosing effects were found for ADHD symptoms and lower-order neurocognitive functions (baseline speed, variability in responding, nonexecutive memory), with greater enhancement of functioning with increasing dose. No dosing effects were found for higher-order neurocognitive functions (executive memory, inhibitory control, and cognitive flexibility). No detrimental effects of MPH were found on any of the investigated functions.
Conclusion: Methylphenidate was superior to placebo in improving ADHD symptoms and a broad range of neurocognitive functions; however, effects sizes regarding the effects of dose vary substantially between functions. Our data highlight the importance of considering both neurocognitive and symptomatic aspects of ADHD in clinical practice

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J Am Acad Child Adolesc Psychiatry. 2021;60:1367-81.
SYSTEMATIC REVIEW: ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND INSTRUMENTAL LEARNING.
Hulsbosch AK, De Meyer H, Beckers T, et al.
Objective: Although instrumental learning deficits are, among other deficits, assumed to contribute to attention-deficit/hyperactivity disorder (ADHD), no comprehensive systematic review of instrumental learning deficits in ADHD exists. This review examines differences between ADHD and typically developing (TD) children in basic instrumental learning and the effects of reinforcement form, magnitude, schedule, and complexity, as well as effects of medication, on instrumental learning in children with ADHD.
Method: A systematic search of PubMed, PsyINFO, CINAHL, EMBASE+EMBASE CLASSIC, ERIC, and Web of Science was conducted for articles up to March 16, 2020. Experimental studies comparing instrumental learning between groups (ADHD versus TD) or a manipulation of reinforcement/medication within an ADHD sample were included. Quality of studies was assessed with an adapted version of the Hombrados and Waddington criteria to assess risk of bias in (quasi-) experimental studies.
Results: A total of 19 studies from among 3,384 non-duplicate screened articles were included. No difference in basic instrumental learning was found between children with ADHD and TD children, nor effects of form or magnitude of reinforcement. Results regarding reinforcement schedule and reversal learning were mixed, but children with ADHD seemed to show deficits in conditional discrimination learning compared to TD children. Methylphenidate improved instrumental learning in children with ADHD. Quality assessment showed poor quality of studies with respect to sample sizes and outcome and missing data reporting.
Conclusion: The review identified very few and highly heterogenous studies, with inconsistent findings. No clear deficit was found in instrumental learning under laboratory conditions. Children with ADHD do show deficits in complex forms of learning, that is, conditional discrimination learning. Clearly more research is needed, using more similar task designs and manipulations

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Med Hypotheses. 2021;157.
NEUROINFLAMMATION AS A POSSIBLE LINK BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND PAIN.
Kerekes N, et al.
Attention-deficit/hyperactivity disorder (ADHD) and pathological pain are two complex syndromes of multifactorial origin. Despite their prevalence and broad impacts, these conditions are seldom recognized and managed simultaneously. The co-existence of neuropsychiatric conditions (such as ADHD) and altered pain perception and chronic pain has been noted in children, and the comorbidity of ADHD and chronic pain is well documented in adults. Pathophysiological studies have suggested dysfunction of the dopaminergic system as a common neurochemical basis for comorbid ADHD and pain. Considerable evidence supports the role of neuroinflammation in the pathophysiology of both. We suggest that central neuroinflammation

underlies altered pain perception and pain sensitization in persons with ADHD. Based on our hypothesis, targeting neuroinflammation may serve as a potential new therapeutic intervention to treat ADHD and comorbid pain in children and adolescents and a preventive strategy for the development of chronic pain in adults with ADHD

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Mol Psychiatry. 2021.

MEDICAL CONDITIONS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS FROM EARLY CHILDHOOD TO ADOLESCENCE.

Galera C, Cortese S, Orri M, et al.

The comorbidity between physical and mental health conditions is challenging and frequently goes unrecognized in practice. Associations between Attention-Deficit/Hyperactivity Disorder (ADHD) and physical conditions have been reported in youth. However, prior research failed to: (1) address the patterns of associations in early childhood, middle childhood, and adolescence within the same population sample; (2) consider a large set of physical disorders at the same time; (3) take confounders into account. Our goal was to assess the associations between ADHD symptoms and a broad set of physical conditions across developmental periods. This birth cohort study (n = 2057) is the first to explore the associations between ADHD and a wide range of medical conditions by encompassing the whole early development from 5 months to 17 years in the same sample and relying on innovative network analyses. We found significant associations between ADHD symptoms and several physical conditions, some of which were observed in early childhood, middle childhood, and adolescence (e.g., asthma, sleep problems) or were confounded by socioeconomic status or psychiatric comorbidities (e.g., body mass index, dental caries). The study calls for an effective integrated care model encompassing mental and general healthcare across the developmental period

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NeuroImage. 2021;245.

EMOTION DYSREGULATION AND INTEGRATION OF EMOTION-RELATED BRAIN NETWORKS AFFECT INTRAINDIVIDUAL CHANGE IN ADHD SEVERITY THROUGHOUT LATE ADOLESCENCE.

Viering T, Hoekstra PJ, Philipsen A, et al.

The course of attention deficit hyperactivity disorder (ADHD) from adolescence into adulthood shows large variations between individuals; nonetheless determinants of interindividual differences in the course are not well understood. A frequent problem in ADHD, associated with worse outcomes, is emotion dysregulation. We investigated whether emotion dysregulation and integration of emotion-related functional brain networks affect interindividual differences in ADHD severity change. ADHD severity and resting state neuroimaging data were measured in ADHD and unaffected individuals at two points during adolescence and young adulthood. Bivariate latent change score models were applied to investigate whether emotion dysregulation and network integration affect ADHD severity changes. Emotion dysregulation was gauged from questionnaire subscales for conduct problems, emotional problems and emotional lability. Better emotion regulation was associated with a better course of ADHD (104 participants, 44 females, age range: 12ΓÇô27). Using graph analysis, we determined network integration of emotion-related functional brain networks. Network integration was measured by nodal efficiency, i.e., the average inverse path distance from one node to all other nodes. A pattern of low nodal efficiency of cortical regions associated with emotion processing and high nodal efficiency in subcortical areas and cortical areas involved in implicit emotion regulation predicted a better ADHD course. Larger nodal efficiency of the right orbitofrontal cortex was related to a better course of ADHD (99 participants, 42 females, age range: 10ΓÇô29). We demonstrated that neural and behavioral covariates associated with emotion regulation affect the course of ADHD severity throughout adolescence and early adulthood beyond baseline effects of ADHD severity

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Neuropsychiatr Enfance Adolesc. 2021;69:259-64.

MATERNAL SENSITIVITY AS A SPECIFIC FACTOR ASSOCIATED WITH THE RISK OF CO-OCCURRING DIAGNOSTICS AMONG PRESCHOOL CHILDREN.

Langlois V, Mubarak A, Cognard-Bessette S, et al.

Introduction: Co-occurrence of mental health diagnoses (dx) refers to the presence of two or more dx in the same child and may imply a more complex profile of symptoms and be more difficult to treat. Treatments for children with co-occurring dx often appear successful for some of the symptoms, while other symptoms persist with clinical efforts. Although it is well documented that an early onset of disorders in the preschool period is associated with numerous adverse outcomes in the middle childhood or adolescence periods (e.g., antisocial behavior, peer rejection), little is known about risk and protective factors associated with the co-occurrence of psychopathological disorders in preschool children.

Objective: To better identify intervention leverages for the treatment of these children, this study examines whether the quality of the family environment (maternal sensitivity, stress and depressive symptoms) is associated with the presence of co-occurring psychiatric dx among preschool age children. Participants: During four years, parents and children (1-5 years old) were approached at a specialized psychiatric clinic at the Sainte-Justine University Hospital Center in Montreal. An assessment and observation protocol was administered to a third of these families. Our study comprises the 54 children and their parents who participated to this protocol. In this sample, 37% of the children were diagnosed with an attention deficit hyperactivity disorder, 24% with a disruptive disorder, 39% with an oppositional defiant disorder and 46% with an anxiety disorder. Overall, 42 children (78%) were diagnosed with two or more dx. Method: Maternal sensitivity was observed during the very well-validated Strange Situation Procedure. Mothers completed questionnaires on parental stress and their depressive symptoms. Children were diagnosed by the clinic's psychiatrists.

Results: Analyses showed clinical level difficulties of sensitivity (39%), stress (67%) and depression (43%) in a significant portion of the mothers. Parental stress and depression were not associated with co-occurring dx in children; however, less sensitive mothers were more likely to have children with more than one dx. Precisely, children of less sensitive mothers were more than twice as likely to present co-occurring disorders as children with more sensitive mothers.

Conclusions: Parental sensitivity, i.e., the ability to observe, interpret correctly and respond in a timely and appropriate manner to the child needs, is more problematic in mothers of children with a more complex symptomatology. This study highlights the importance of parental involvement in the treatment of these preschool children. ParentΓÇôchild dyadic interventions, such as the Attachment Video feedback Intervention (AVI), to optimize parental sensitivity are discussed

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Neuropsychology. 2021;35:809-21.

DEVELOPMENT OF EXECUTIVE FUNCTIONING FROM CHILDHOOD TO YOUNG ADULTHOOD IN AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A 10-YEAR LONGITUDINAL STUDY.

Fossum IN, Andersen PN, +ÿie MG, et al.

Objective: This 10-year longitudinal study investigated the developmental trajectories of executive functioning (EF) in individuals with autism spectrum disorder (ASD) or attention-deficit/hyperactivity disorder (ADHD), compared to typically developing (TD) individuals from childhood into young adulthood.

Method: There were 173 participants at baseline (T1; ASD = 38 (eight with co-occurring ADHD), ADHD = 85, TD = 50; Mage = 11.7 years, SD = 2.1), 168 at 2-year follow-up (T2) and 127 at 10-year follow-up (T3). Participants were assessed with three neuropsychological tests aimed at capturing central components of EF: working memory/Letter-Number Sequencing Test (LNS), inhibition/Color–Word Interference Test, Condition 3 (CWIT3), and exibility/Trail Making Test, Condition 4 (TMT4). Test results were analyzed using linear mixed models (LMM).

Results: At baseline, the TD participants outperformed the ASD and ADHD participants on all three tests. From T1 to T2, the ASD participants had less improvement than the ADHD and TD participants on the LNS test (p =.007 and.025, respectively), while having more improvement on the CWIT3 relative to the TD participants (p =.027). From T2 to T3, the ADHD participants had less improvement on the LNS test than the ASD and TD participants (p =.004 and.021, respectively).

Conclusions: The ASD and ADHD groups mainly displayed similar maturation on the neuropsychological measures, and displayed continuous impairment relative to the TD group. The need for support and facilitation of EF in school, workplace, and social arenas might continue into young adulthood among certain individuals with ASD and ADHD

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Nutrients. 2021;13.

THE ROLE OF IRON AND ZINC IN THE TREATMENT OF ADHD AMONG CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW OF RANDOMIZED CLINICAL TRIALS.

Granero R, Pardo-Garrido A, Carpio-Toro IL, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder common from childhood to adulthood, affecting 5% to 12% among the general population in de-veloped countries. Potential etiological factors have been identified, including genetic causes, environmental elements and epigenetic components. Nutrition is currently considered an influ-encing factor, and several studies have explored the contribution of restriction and dietary supplements in ADHD treatments. Iron is an essential cofactor required for a number of functions, such as transport of oxygen, immune function, cellular respiration, neurotransmitter metabolism (dopamine production), and DNA synthesis. Zinc is also an essential trace element, required for cellular functions related to the metabolism of neurotransmitters, melatonin, and prostaglandins. Epidemiological studies have found that iron and zinc deficiencies are common nutritional deficits worldwide, with important roles on neurologic functions (poor memory, inattentiveness, and impulsiveness), finicky appetite, and mood changes (sadness and irritability). Altered levels of iron and zinc have been related with the aggravation and progression of ADHD. Objective: This is a systematic review focused on the contribution of iron and zinc in the progression of ADHD among children and adolescents, and how therapies including these elements are tolerated along with its effectiveness (according to PRISMA guidelines). Method: The scientific literature was screened for randomized controlled trials published between January 2000 to July 2021. The databases con-sulted were Medline, PsycINFO, Web of Science, and Google Scholar. Two independent reviewers screened studies, extracted data, and assessed quality and risk of bias (CONSORT, NICE, and Cochrane checklists used). Conclusion: Nine studies met the eligibility criteria and were selected. Evidence was obtained regarding the contribution of iron-zinc supplementation in the treatment of ADHD among young individuals. The discussion was focused on how the deficits of these elements contribute to affectation on multiple ADHD correlates, and potential mechanisms explain-ing the mediational pathways. Evidence also suggested that treating ADHD with diet interventions might be particularly useful for specific subgroups of children and adolescents, but further investigations of the effects of these diet interventions are needed

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Paediatr Perinat Epidemiol. 2021;35:10.

ASSOCIATION OF SWEETENED CARBONATED BEVERAGE CONSUMPTION DURING PREGNANCY AND ADHD SYMPTOMS IN THE OFFSPRING. A STUDY FROM THE NORWEGIAN, MOTHER, FATHER AND CHILD COHORT STUDY (MOBA).

Kvalvik L, et al.

Purpose: Intrauterine exposures influence offspring health and development. We investigated maternal intake of sweetened carbonated beverages (SCB) during pregnancy and its association with ADHD symptoms in children.

Methods: This study was based on the Norwegian Mother, Father and Child Cohort Study (MoBa) and the Medical Birth Registry of Norway. Maternal diet mid-pregnancy was assessed using a food frequency questionnaire (FFQ). All women who responded to the FFQ and a questionnaire when children were 8 years of age were included (n = 39 870). The exposure was defined as maternal intake (daily servings) of SCB, using no daily intake as reference. Outcome was offspring ADHD symptoms, evaluated as a continuous standardized ADHD score and as a binary outcome of six or more ADHD symptoms vs. five symptoms or less. Associations were analysed using linear mixed regression models and log-binomial regression, adjusted for relevant confounders.

Results: The adjusted regression coefficients for the standardized ADHD offspring symptom score were 0.003 (95% confidence intervals (-0.47 to 0.48)), 0.54 (0.08 to 1.00) and 0.39 (-0.24 to 1.01) for maternal intake of 1 glass, 2-3 glasses and 4 or more glasses of SCB, respectively. The adjusted relative risks were

1.01 (0.78 to 1.29), 1.27 (1.04 to 1.56) and 1.18 (0.92 to 1.51), for drinking 1, 2-3 and 4 or more glasses daily, respectively compared to women with no daily intake of SCB.
Conclusion: In a large pregnancy cohort with offspring followed up until 8 years of age, we found a positive association between high maternal intake of SCB and offspring ADHD symptoms. The results suggest a weak underlying relationship between maternal intake of SCB and offspring ADHD

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Pakistan Journal of Medical and Health Sciences. 2021;15:1668-71.
ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG ENGLISH LANGUAGE LEARNERS OF STERILIZATION PROGRAM AMIDST COVID-19.
Khan IA.
Background: This study explored the prevalence of Attention Deficit Hyperactivity Disorder (ADHD) among the students of ΓÇÿsterilization program while learning English language amidst COVID-19 in Saudi Arabia. Aim: To diagnose ADHD among the learners, and later propose some digital strategies to motivate the learners for resilience.
Methods: A qualitative exploratory study was undertaken in April, 2020. A diagnostic tool was administered to 41 students pursuing Sterilization program at king Abdulaziz University in Kingdom of Saudi Arabia (KSA). Later, learners with ADHD (N=9) were selected for in-depth study. Data was collected using the ADHD self-report scale V1.1 screener.
Results Five professors from the concerned department were purposively selected for the interviews for qualitative analysis using thematic analysis. Confidentiality and anonymity was ensured as per the ethical standard. Many students demonstrate signs of ADHD, therefore there is a need of assessment and intervention. Teachers, counselors and managers need to take care of such learners.
Conclusions: Conclusions were drawn that students with ADHD need relevant interventions in general and specific pedagogy

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Pediatr Drugs. 2021;23:403-09.
VILOXAZINE: PEDIATRIC FIRST APPROVAL.
Lamb YN.
Viloxazine (QELBREEΓäó), a selective norepinephrine reuptake inhibitor, is being developed by Supernus Pharmaceuticals as a non-stimulant for the treatment of attention-deficit/hyperactivity disorder (ADHD) in pediatric and adult patients. This is a novel formulation of a pharmacological agent formerly marketed in Europe for the treatment of depression in adults. Viloxazine received its first pediatric approval in April 2021 in the USA for the treatment of ADHD in pediatric patients aged 6ΓÇô17 years. Approval was based on positive results from a series of short-term phase III clinical trials in which viloxazine improved the severity of ADHD symptoms in children and adolescents with diagnosed ADHD. Viloxazine is available as extended-release capsules for once-daily oral administration. This article summarizes the milestones in the development of viloxazine leading to this first pediatric approval for ADHD

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2022;113.
IDENTIFY ABERRANT WHITE MATTER MICROSTRUCTURE IN ASD, ADHD AND OTHER NEURODEVELOPMENTAL DISORDERS: A META-ANALYSIS OF DIFFUSION TENSOR IMAGING STUDIES.
Zhao Y, Yang L, Gong G, et al.
Background: Neurodevelopmental disorders (NDDs) usually present overlapping symptoms. Abnormal white matter (WM) microstructure has been found in these disorders. Identification of common and unique neural abnormalities across NDDs could provide further insight into the underlying pathophysiological mechanisms.
Methods: We performed a voxel-based meta-analysis of whole-brain diffusion tensor imaging (DTI) studies in autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD) and other NDDs. A systematic literature search was conducted through March 2020 to identify studies that compared measures of WM microstructure between patients with NDDs and neurotypical controls. Peak voxel coordinates were

meta-analyzed via anisotropic effect size-signed differential mapping (AES-SDM) as well as activation likelihood estimation (ALE).
Results: Our final sample included a total of 4137 subjects from 66 studies across five NDDs. Fractional anisotropy (FA) reductions were found in the splenium of the CC in ADHD, and the genu and splenium of CC in ASD. And mean diffusivity (MD) increases were shown in posterior thalamic radiation in ASD. No consistent abnormalities were detected in specific learning disorder, motor disorder or communication disorder. Significant differences between child/adolescent and adult patients were found within the CC across NDDs, reflective of aberrant neurodevelopmental processes in NDDs.
Conclusions: The current study demonstrated atypical WM patterns in ASD, ADHD and other NDDs. Microstructural abnormalities in the splenium of the CC were possibly shared among ASD and ADHD

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Psychiatr Pol. 2021;55:887-900.
PARAFUNCTIONS, SIGNS AND SYMPTOMS OF TEMPOROMANDIBULAR DISORDERS (TMD) IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): THE RESULTS OF THE SOPKARD-JUNIOR STUDY.
Suligowska K, Mikietynska M, Pakalska-Korcala A, et al.
Aim. The aim of the study was to compare the prevalence of parafunctions and signs and symptoms of TMD in a population group of children with and without ADHD.
Material and methods. The study included all 5th grade children of all public primary schools in Sopot (untreated, unguided children). The reporting rate was 91%. At the first stage of the psychological-psychiatric study both parents and children filled in the CBCL and YSR questionnaires. At the next stage, in the group of children selected during the screening, a qualified child psychiatrist conducted a semi-structured diagnostic interview K-SADS-PL and diagnosed ADHD. Parafunctions, signs and symptoms of TMD were assessed by conducting a direct interview with a child and a clinical examination by a dentist.
Results. There were significant differences ($p < 0.05$) between children with ADHD and without ADHD associated with parafunctions such as chewing gum (76.47% vs. 46.07%), nail biting (70.59% vs. 40.45%) and bruxism (52.54% vs. 26.22%), the number of signs and symptoms of TMD (1 sign or symptom 0.0% vs. 32.21%; 4 7 signs or symptoms 17.65% vs. 3.75%).
Conclusions. In children with ADHD, symptoms of temporomandibular joint disorders and parafunctions were significantly more frequent. These studies suggest that children with ADHD constitute a group of increased risk for TMD in the future. Interdisciplinary treatment of an ADHD patient by a psychiatrist and a dentist is necessary

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Psychiatr Invest. 2021;18:818-24.
ASSOCIATION BETWEEN TIC AGGRAVATION AND METHYLPHENIDATE IN YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Cha JY, Joung YS, Oh S, et al.
Objective This study aimed to determine the tic aggravation event rate and cumulative incidence rate in the use of methylphenidate (MPH) treatment in attention-deficit/hyperactivity disorder (ADHD) and the factors that influence tic aggravation.
Methods We conducted a retrospective chart review of children and adolescents aged between 6 to 15 years, who were diagnosed with ADHD from January 2017 to December 2019. A total of 121 subjects were included. The MPH dosage, psychiatric family history, co-morbidity and past history of tics were assessed through chart review and the psychological examinations data were included. Collected data were analyzed using Cox regression and Kaplan-Meier survival analysis.
Results Tic aggravation event rates without a past history of tics were 2.9% with MPH treatment in ADHD. Past history of tics, total MPH dosage and age were the factors associated with tic aggravation ([HR 21.46, $p<0.001$], [HR 0.94, $p=0.023$], [HR 0.79, $p=0.021$] for each). Cumulative incidence of tic aggravation was different between groups with or without past tic history. When treated with MPH, all tic aggravation appeared within approximately eight months but for subjects with a past history of tic, aggravation showed within approximately six months ($p<0.001$).

Conclusion Tic aggravation event rate was significantly low especially in the group without a past history of tics with the use of MPH in ADHD. However, a thorough assessment of past history of tics, and close monitoring during the first six-eight months of treatment with MPH is needed to avert a potential worsening of tics

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Psychoneuroendocrinology. 2021;131.

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

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

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

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QJM. 2021;114.

PATHWAY TO SERVICE AND DURATION OF UNTREATED ATTENTION DEFICIT, HYPERACTIVITY DISORDER AMONG CHILDREN PRESENTED TO A GOVERNMENTAL, MENTAL HEALTH HOSPITAL IN EGYPT.

Ramy HA, Hashem RE, Khamis ME, et al.

Background ADHD is one of the most common neurodevelopmental disorders. Despite the presence of evidence based approved diagnosing and treatment tools for ADHD, there still is an underdiagnoses and underutilization of these services. Untreated ADHD, unlike what some families may believe, doesn't go away on its own, in fact, the condition may get worse with age, affecting more domains of the child's life as an adolescent and later on as an adult. In addition, untreated ADHD impacts not only the patient, but also the family and the society as a whole.

Objective Objective to investigate different routes that parents take before reaching the child and adolescence psychiatric services. And to further explore various reasons for any delay in seeking psychiatric help. In addition we aimed to estimate the duration of untreated ADHD before patients receive proper psychiatric service and treatment.

Patients and Methods A total of 350 cases were recruited in a cross sectional study that took place at the Child and Adolescence outpatient clinic at Abbassia mental health hospital in Cairo, Egypt.

Results Results showed that the average delay in seeking Child and Adolescence psychiatric service and the duration of untreated ADHD was 3-¦2 years. The majority of parents, 27.1%, first consulted pediatricians as regards to their child's symptoms. The most commonly reported source of referral was school teachers in 23.1%. The most distressing symptom stated by 28.1% of parents was impulsivity. Stigma of mental illness was the most frequently reported reason for delay in reaching out for psychiatric service.

Conclusion Conclusion we concluded that parents tend to take other routes through different professions before reaching Child and Adolescence Mental Health Services, this causes subsequent delay in receiving diagnosis and treatment for ADHD. In Addition, it was concluded that sociocultural beliefs affected parent's pattern of help seeking

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Res Autism Spectr Disord. 2021;89.

BRAIN-COMPUTER INTERFACE BASED ATTENTION AND SOCIAL COGNITION TRAINING PROGRAMME FOR CHILDREN WITH ASD AND CO-OCCURRING ADHD: A FEASIBILITY TRIAL.

Teo SHJ, Poh XWW, Lee TS, et al.

Background: Current treatment practices for comorbid conditions of autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) remain limited. This study examined the feasibility of an EEG brain-computer interface (BCI) programme for children with ASD and co-occurring ADHD.

Method: Twenty children were randomised to the intervention or waitlist-control group. Intervention consisted of thrice-weekly sessions of BCI-based training over 8 weeks. Both groups were followed up 4 weeks later. The BCI-based programme comprised of a series of attention and gaze-modulated games aimed to train social cognitive skills.

Results: All participants completed at least 20 training sessions and none dropped out of the study. No severe adverse events were reported. Side effects included mild headaches, fatigue, irritability and self-injurious behaviours. All were addressed within the same session. Feedback from therapists indicated that participants interest and motivation could be sustained with appropriate supports. Change scores indicated greater improvement in the intervention group compared to the waitlist-control on ADHD symptoms as measured on the ADHD rating scale; no significant differences were observed on social deficits on the Social Responsiveness Scale (SRS). Pooled data suggests that pre-post improvements could be maintained.

Conclusions: Findings indicate the BCI-based program is tolerable for most participants. Positive effects were also reported for ADHD symptoms. A future large clinical trial will incorporate appropriate controls to ascertain the efficacy of our training programme

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Rev Neurol. 2021;73:233-40.

FACTORS RELATED TO TEACHER KNOWLEDGE ABOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Herrera-Gutierrez E, Mart+¡nez-Frutos MT.

Introduction. Studies on teachers' knowledge about attention deficit/hyperactivity disorder (ADHD) are not abundant in the literature. The little research done indicates low or moderate scores.

Aim. To examine the knowledge of Childhood, Primary, and Secondary Education teachers on ADHD, as well as to study possible differences attributable to the previous training, the experience in the disorder and other sociodemographic variables. Subjects and methods. A sample of 130 teachers from the Region of Murcia (Spain) was administered a knowledge questionnaire about ADHD and sociodemographic variables were recorded.

Results. The teachers answered correctly to more than half of the items in the questionnaire (63,9%). The Symptoms/ Diagnostic scale reached the highest percentage of correct answers (69,1%) and the Etiology scale the lowest (32%). The female teachers showed superior knowledge to the male teachers in all dimensions of the questionnaire. Those teachers who had received training on the disorder presented a higher level of knowledge. In addition, teachers who had previous professional experience showed superior knowledge than those without such experience. According to the teaching specialty, no statistically significant differences were obtained almost in any of the dimensions of the questionnaire. The age group that showed a higher level of knowledge about ADHD was 27-32 years old.

Conclusion. The results point to the need for better training on knowledge and attitudes of teachers towards ADHD that facilitate the early detection of these cases and their specialized care at different educational levels

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World J Biol Psychiatry. 2021.

DIFFERENTIATING BRAIN FUNCTION OF PUNISHMENT VERSUS REWARD PROCESSING IN CONDUCT DISORDER WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Baumann S, Hartz A, Scharke W, et al.

Objectives: Conduct disorder (CD) and attention-deficit/hyperactivity disorder (ADHD) are reported to co-occur in about 30-50% of affected individuals. Research suggests that poor reinforcement-based decision-making may contribute to impaired social functioning in both youths with CD and ADHD. Considering its

frequent co-occurrence this raises the question whether decision-making deficits in both disorders have a disorder-specific and/or shared neurobiological basis.
Methods: 138 participants with CD, ADHD, or CD + ADHD, and typically developing controls (TDCs) aged 9-18 years (48% girls) were included in the study. Participants completed a reinforcement-based decision-making task in the fMRI scanner, investigating decision-making capabilities under different reinforcement contingencies (i.e. punishment vs. reward). Whole-brain and ROI analyses were used to test for potential group differences.
Results: For punishment versus reward contingencies, relative to TDCs, youths with CD + ADHD displayed lower brain activity in dorsal striatum (incl. caudate), middle temporal gyrus (MTG), inferior frontal gyrus (IFG) and lateral occipital cortex, and they showed lower activity in dorsal striatum (incl. putamen), orbitofrontal cortex (OFC) and IFG relative to participants with ADHD. All other group comparisons were found to be non-significant.
Conclusions: Participants with comorbid CD + ADHD are neurobiologically the most severely impaired group regarding reinforcement-based decision-making, particularly in response to punishment

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Rocco et al. BMC Psychiatry (2021) 21:575
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BMC Psychiatry

RESEARCH ARTICLE Open Access

Time of onset and/or diagnosis of ADHD in European children: a systematic review

Ilaria Rocco[1*], Barbara Corso[1], Maurizio Bonati[2] and Nadia Minicuci[1]

Abstract

Background: Attention-Deficit/ Hyperactivity Disorder (ADHD) is one of the most common childhood neurobehavioral conditions. Symptoms related to this disorder cause a significant impairment in school tasks and in the activities of children's daily lives; an early diagnosis and appropriate treatment could almost certainly help improve their outcomes.
The current study, part of the Models Of Child Health Appraised (MOCHA) project, aims to explore the age at which children experience the onset or diagnosis of ADHD in European countries.

Methods: A systematic review was done examining the studies reporting the age of onset/diagnosis (AO/AD) of ADHD in European countries (28 European Member States plus 2 European Economic Area countries), published between January 1, 2010 and December 31, 2019. Of the 2276 identified studies, 44 met all the predefined criteria and were included in the review.

Results: The lowest mean AO in the children diagnosed with ADHD alone was 2.25 years and the highest was 7.5 years. It was 15.3 years in the children with ADHD and disruptive behaviour disorder. The mean AD ranges between 6.2 and 18.1 years.

Conclusions: Our findings indicate that there is a wide variability in both the AO and AD of ADHD, and a too large distance between AO and AD. Since studies in the literature suggest that an early identification of ADHD symptoms may facilitate early referral and treatment, it would be important to understand the underlying reasons behind the wide variability found.

Trial registration: PROSPERO registration: CRD42017070631.

Keywords: ADHD, Neurodevelopmental disorders, Children, Onset, Diagnosis

Background

Attention-Deficit/Hyperactivity Disorder (ADHD), which is one of the most common childhood neurobehavioral conditions, has been characterized by continually increasing global prevalence rates over the past few decades [1]. A global consensus on the ADHD prevalence rate in children and adolescents has yet to be reached: meta-regression analyses have estimated the worldwide rate at between 5.29% [2] and 7.1% [3], but according to one comprehensive meta-analysis, the best-estimate prevalence rate of study based on case definition was 1.4%, (range: 1.1–3.1) [4].

These conflicting figures have triggered the hypothesis that ADHD is either over diagnosed [5, 6], underdiagnosed, missed, or undertreated [7].

Children with unmanaged ADHD often experience unnecessary impairments and detrimental long-term consequences leading to high personal and societal costs [8, 9]. Early identification and effective management could significantly improve the functioning and overall quality of life of these children and their families.

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Healthcare professionals specialized in child psychology, including the American Academy of Paediatrics, advise screening for the disorder early as the preschool period [10] so that those affected can be treated precociously permitting them to achieve their full potential in school and at home [11].

Multiple factors may affect the perception of the disorder by family members and healthcare providers and thus the timing of its diagnosis and treatment [7]. Moreover, there are numerous factors intrinsic to childhood or adolescence that could affect the diagnosis of ADHD including gender, age, race, socioeconomic status, and severity of symptoms [12, 13].

Parents play a central role in recognizing behavioural problems early in their children, their perception, awareness and acceptance of the disease, as their decision to accompany the child to a specialist [14]. Once parents decide to seek help, they need to be able to access specialised care for a timely and accurate diagnosis as well as optimal disease management strategies. Although there is an operationalized psychodynamic diagnostic process, no objective test is at yet available and substantial controversy exists regarding the challenge of formulating a correct diagnosis [15, 16]. In fact, conflicting views continue to exist with regard to the symptoms and psychometric features leading to a diagnosis of ADHD diagnosis [17–19].

Many clinicians depend on and utilize the Diagnostic and Statistical Manual of Mental Disorders (DSM) [20] for guidance in making diagnoses, even if general diagnostic issues (e.g. model of diagnosis and level of impairment) need of better clarification [17] also using different diagnostic criteria, such as the International Classification of Diseases (ICD) and the Research Domain Criteria.

Although the heterogeneity in the methodology of diagnosing of ADHD has resulted in a high variability in prevalence rates around the world [21], differences linked to age at diagnosis (AD) or onset (AO) of ADHD need to be investigated.

Within the Models Of Child Health Appraised (MOCHA) project [22], which has been critically assessing the existing models of primary care for children in 30 European countries (28 European Member States plus 2 European Economic Area countries), Minicuci et al. [23] have been involved in investigating the AO and AD of ADHD.

The current work set out to examine the studies involving children with ADHD in European countries that report their age at onset or diagnosis.

Methods

Following a systematic review approach and a standardized method of Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [24], we searched for studies that reported the AO or AD of ADHD. The review protocol was registered in the PROSPERO database (registration number CRD42017070631). The PRISMA checklist for this systematic review is presented in Additional file 1.

We searched the Medline (PubMed) database for studies in the literature examining ADHD onset or diagnosis published between January 1, 2010 and December 31, 2019. It was decided to limit the review to the last decade because it is the one in which the clinical guideline's recommendations previously produced by many parties had to be consolidated also with the fifth revision of the *DSM started in 2000 and finished in 2013* [25]. The search terms used were: "ADHD", "Attention deficit", "Hyperactivity Disorder" and "Attention disorder" in the title or abstract, combined with "age", "onset" or "diagnosis" and "child" or "adolescent" in the text word (see Additional file 1 for details). Any study not in English were excluded. In order to include all studies reporting ADHD AO/AD, no exclusion criteria was applied to diagnostic criteria/tools used for participants' diagnosis in the studies reviewed. The diagnostic criteria or tools adopted in each included study, as well as the inclusion and exclusion criteria followed to select the study sample, have been examined at a later time with other relevant characteristics.

The abstracts of all the articles were read and the full version of the papers for those seemingly fulfilling the selection criteria were retrieved.

Studies were included in this review if they reported the AO or AD for ADHD and were conducted in or referred to data from a European country.

We utilized a standardized form for data extraction that included the following items: the authors' names, the year of publication, the country in which the study was performed, the journal in which the study was published, the type of study, the aim of the study, the year in which the study was performed, the types of persons composing the study sample (including age and sample size), the diagnostic criteria adopted for the diagnosis, and, of course, the AO/ADs.

Two of the authors (IR and BC) screened all the articles; any differences in viewpoints that arose were resolved through discussion with the third author (NM).

Results

The initial PubMed search yielded 2276 studies (Fig. 1). After the abstracts were screened, a total of 1163 articles were excluded, mainly because the population studied and/or the geographic area (did not meet our criteria, in the former case for age, in the latter it referred to studies outside Europe). Out of the 1113 full-text articles reviewed, 49.1% were carried out outside Europe and

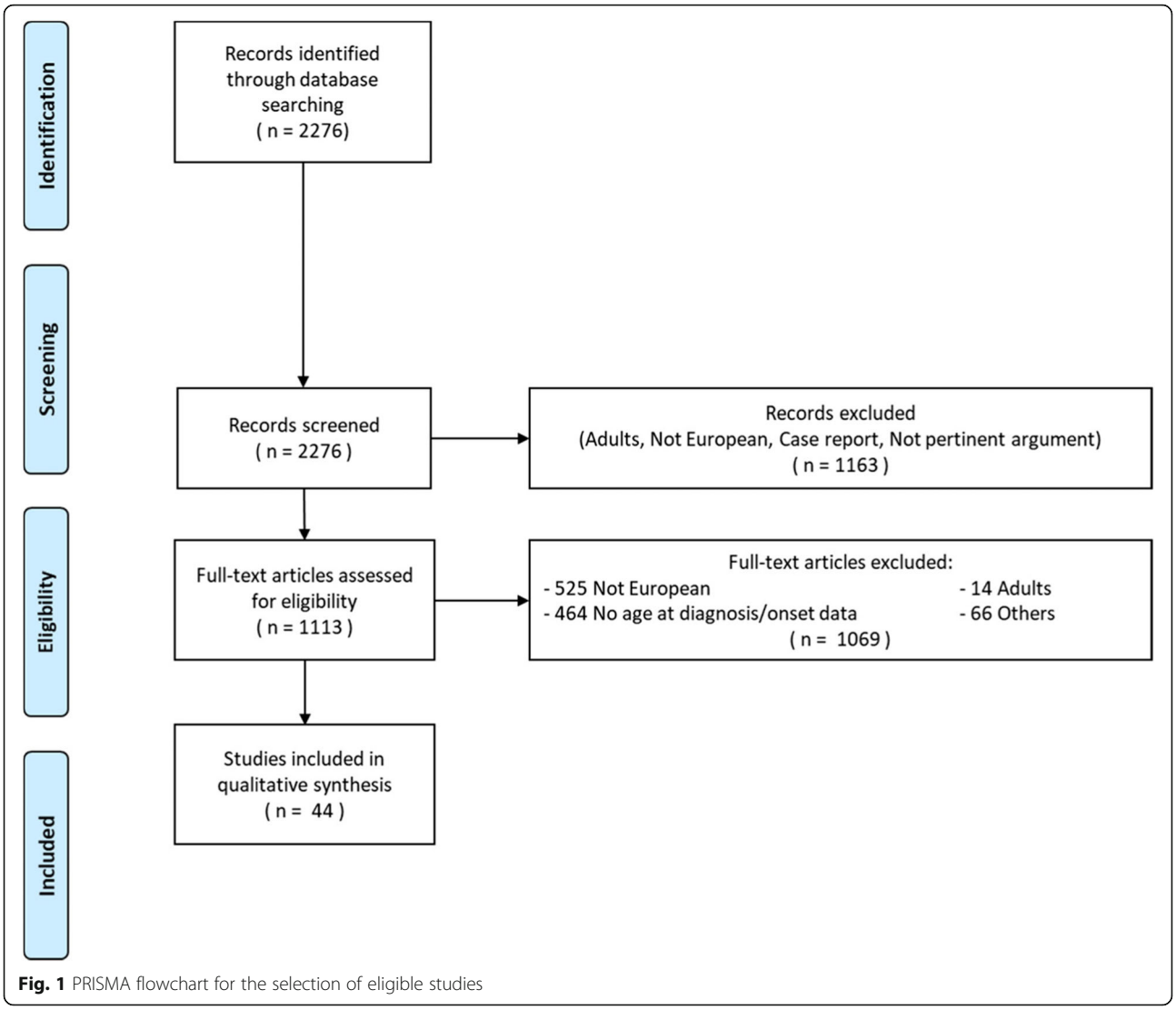

Fig. 1 PRISMA flowchart for the selection of eligible studies

43.4% did not report AO or AD. Forty-four articles met our inclusion criteria for this review.

Study characteristics

The characteristics of the studies included are outlined in Table 1. Twenty-three articles were published in 2010–15 and 21 articles in 2016–19.

One article reported both the AD and the AO, 34 studies reported only the AD, and 9 reported only the AO. The majority of the studies included in this review were conducted in Sweden (7 articles) and in Germany (5 articles), followed by 3 countries publishing 4 articles each.

Table 2 provides a full list of the 44 studies mentioned here, in the order of their publication date; its chronological number is also used throughout the text in all subsequent references to that article.

Diagnostic criteria

In the majority of the articles, the diagnostic criteria used to define ADHD symptoms or to formulate a diagnosis of ADHD was the DSM. One study conducted in Sweden [31] reported that the DSM criteria in the DSM-III-R [70] and in the DSM-IV [71] were used before and after 1994 respectively; while in the study of van Lieshout et al. [53] the DSM-IV and DSM-5 [72] were adopted. In eight papers the 4th edition (DSM-IV) was adopted, in five papers the "text revision" of the DSM-IV, namely the DSM-IV-TR [73], was used. The DSM-IV items of the Conners' teacher questionnaire were used with the Parental Account of Childhood Symptoms (PACS) interview in the study by Muller and colleagues [32].

The Composite International Diagnostic Interview (CIDI) version 3.0 was used to determine the presence of ADHD according to the DSM-IV criteria in the article

Table 1 Characteristics of the 44 studies included in qualitative synthesis

Characteristics	n (%)
Year of publication	
2010–2011	7 (15.9)
2012–2013	10 (22.7)
2014–2015	6 (13.7)
2016–2017	11 (25.0)
2018–2019	10 (22.7)
Country	
Germany	5 (11.4)
Sweden	7 (15.9)
Denmark	4 (9.1)
Netherlands	3 (6.8)
Finland	4 (9.1)
France	3 (6.8)
Italy	3 (6.8)
Norway	3 (6.8)
Czech Republic	1 (2.1)
Greece	1 (2.1)
Ireland	1 (2.1)
Spain	1 (2.1)
UK	4 (9.1)
Mix	4 (9.1)
Outcome	
Age at diagnosis	34 (77.3)
Age at onset	9 (20.5)
Both	1 (2.1)
Total	44 (100.0)

by Tuithof and collaborators [36]. Developed by the World Health Organization, the CIDI is a fully structured, lay administered interview used worldwide that has been shown to be a reliable and valid instrument [74].

We also identified 15 papers using the ICD to define ADHD symptoms or to make an ADHD diagnosis. Among these papers, one article [47] used both the 9th [75] and 10th [76] editions; the remaining articles used the 10th edition.

In three articles, multiple sources of information were taken into consideration for the diagnosis of ADHD. The diagnostic criteria of the DSM-IV and the ICD-9/ICD-10 were adopted and the results of Conner's questionnaire were considered in the six countries involved in the study by Hodgkins and collaborators [39]. In the article by Chen and collaborators [57], the individuals who were diagnosed with hyperkinetic disorder (ICD-9, ICD-10) or ADHD (DSM-IV) were defined as ADHD cases; in Bahmanyar et al. [38] the ICD-10 and DSM-IV were adopted.

The semistructured Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL) is a DSM-IV-based diagnostic interview procedure that was used in some of the articles to support ADHD diagnosis [41, 53, 59].

Two studies [65, 66] used Read codes for an ADHD diagnosis. Read codes are clinical terminology developed in the UK by the National Health Service (NHS) based on clinical parameters and usage.

Read codes have become the de facto standard for coding diagnoses, operations, and procedure for all national data sets and statistics on hospital and community health services in the UK.

Lastly, the diagnostic criteria utilized were not specified in six articles. In three papers [43, 45, 58], parents/caregivers of children and adolescents were asked if their children had ever been diagnosed with ADHD by a doctor or other healthcare professional; in a paper by Caci and colleagues [49] the physicians treating children with ADHD were asked to select patients to enrol in the study; finally, the patients were identified from the psychiatric cases and drug registers in two articles [48, 64].

Age at onset

Eight out of 10 of the studies presenting information on the AO reported the mean, median or age range at symptom onset in the sample of children being studied [26, 29, 35, 36, 41, 49, 51, 53]. The lowest AO was reported by a Dutch study examining a sample made up of 347 patients with combined ADHD, whose ages were between 5 and 19 years; the first ADHD symptom appeared at a mean age of 2.25 years [53]. The highest AO was reported in a study referring to children in Finland: it was 7.5 years in the children with only ADHD diagnosis and 15.3 years in the children with comorbid ADHD and disruptive behaviour disorder (DBD) [41].

The study by Muller and colleagues [32] reported the time of ADHD detection rather than the time of symptom onset which was analysed by comparing probands with combined ADHD with their siblings without ADHD diagnosis or to different subtypes of ADHD.

Polanczyk et al. [28] focused on the implications of extending the ADHD AO criterion from ages 7 to 12 years, since the variation would lead to a negligible increase in ADHD prevalence (0.1% in their cohort) by age 12.

Age at diagnosis

Thirty-two of the 35 studies presenting information on the AD of ADHD reported its mean, median, range or distribution, one study presented the peak of the ADHD incidence in males and females [63]; in two other studies, information on the AD was inferred through the

Table 2 List in chronological order of the 44 studies included here

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
Bernardi et al. (2010) [26]	Italy	Cross-sectional (January 2004–January 2008)	To compare bipolar disorder (BD) patients with/without ADHD diagnosis in childhood on clinical and temperamental characteristics.	100 patients with BD, 18 of which with ADHD (10 remitted (aADHD-BD) and 8 persistent (cADHD-BD) in adulthood)	Exclusion criteria were: (1) any clinically significant medical conditions, organic brain disorders, (2) current substance/ alcohol abuse or dependence (in the last 6 months), since it may precipitate BD episodes and impair ADHD symptoms at present increasing their intensity; and (3) any lifetime comorbid mental disorders (except previous secondary symptoms of anxiety or substance abuse as based on temporal onset and symptoms severity in remission from at least 6 months), unwillingness or inability to comply with study assessments, or inability to provide informed consent.	Inclusion criteria were: (1) an age range of at least 18 and no greater than 30 years to avoid a retrospective ADHD diagnosis time that was potentially too long; (2) remission of BD for at least 3 months, as assessed by Young Mania Rating Scale and Hamilton Depression Scale scores, in order to reduce possible diagnostic confounders of symptom overlap between ADHD and acute mania; and (3) the presence of at least one parent able to describe the patient's lifetime course of disease symptoms, in order to confi rm. th e age of onset of ADHD. The presence of at least one parent was considered necessary also to report about the onset and the course of BD symptoms and to distinguish them from symptoms of oppositional defi ant disorder or conduct disorder.	DSMIV-TR (Supported by the WURS)	AO (Mean ± SD, years): -Overall: 6.50 ± 1.04; cADHD: 6.75 ± 0.88; aADHD 6.30 ± 1.15.
Kopp et al. (2010) [27]	Sweden	Descriptive	To clinically describe girls referred for problems with social interaction, attention/ academic problems, or tics, comparing symptomatology and comorbidity.	60 clinic girls aged 7 to 16 years with a tested FSIQ ≥80 were selected and matched for age with 60 randomly selected schoolgirls.	Girls with previously diagnosed LD (FSIQ ≤70) had been excluded. However, after full assessment, 12 clinic girls were found to meet criteria for LD (9 of whom were less than age 7 at referral). They were retained because they had not been diagnosed or		DSM-IV; Griffiths; WPPS IR; WISC-III; WAIS-R; 10-Item Conners' Scale; CTRS-R:L; FTF; ASSQ; DSRS; GAF; Severity of Psychosocial Stressors Scale, Children and Adolescents; ADI-R; CAPA; VABS-DLS; ADOS-G	AD (Mean ± SD, years): -Among the clinic girls with ADHD diagnosis ($n = 46$), 13.0 ± 3.4; Among the matched clinic girls with ADHD diagnosis (n = 34): 12.7 ± 2.6.

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
					suspected of LD before entering the study. Other exclusion criteria were defined as parental inadequate command of the Swedish language and serious physical disorders (e.g., cerebral palsy and severe epilepsy).			
Polanczyk et al. (2010) [28]	UK	Prospective longitudinal (From 1999 to 2000, 7 years follow-up)	To test the implications of extending the ADHD AO criterion from age 7 to 12.	66 met full ADHD criteria; 2 met ADHD criteria, except AO criterion; 1183 without ADHD, symptom onset before age 7 years; 181 without ADHD, symptom onset between ages 7 and 12 years; 547 without ADHD, never had symptoms.			Mother and teacher reports symptoms according to DSM-IV.	At age 12, 66 children (3.3%) met full diagnostic criteria for ADHD, including AO criterion. Among the 181 children with AO between age 7 and 12 years, only 2 met full diagnostic criteria for ADHD (except the AO criterion).
Prihodova et al. (2010) [29]	Czech Republic	Case control (2007)	To evaluate the sleep macrostructure in the ADHD group comparing with controls.	31 patients with ADHD and 26 matched controls (age range 6–12 years).		The enrollment criteria were as follows: (1) ADHD diagnosed on the basis of DSM-IV, (2) no previous pharmacological treatment for ADHD, (3) no history of any chronic physical condition (including obesity), chronic sleep disorder, neurological or other psychiatric disorders (including mental retardation and autism) based on a complete pediatric report and on a neurological and psychiatric examination, (4) no current medication (psychotropic or general) and (5) the patient's and his/her parents' willingness to participate in the study	DSM-IV and Children's Psychiatric Rating Scale; CPRS; CBCL; CMAS; CDI; WISC-III	Parentally reported AO was between 4 and 6 years.

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
						and informed consent signed by the parents. All participants were in the prepubertal or early pubertal stages as assessed by Tanner scale. All were of Caucasian origin. They underwent psychological, psychiatric and neurological testing. Information about their sleep habits and sleep disturbances was collected from the parents and children by means of a detailed clinical interview and Pediatric Sleep Questionnaire.		
Berek et al. (2011) [30]	Germany	Multicentre, prospective, open-label, single-arm, non-interventional	To compare clinical and health-related quality of life outcomes between children and adolescents treated with Methylphenidate	822 patients with ADHD. Among these, 785 have valid data on age at diagnosis: 565 children (6–12 years) and 220 adolescents (13–18 years).		Children and adolescents aged 6–18 years who had a confirmed diagnosis of ADHD by ICD-10 criteria, and in whom treatment with OROS® MPH was medically indicated and planned by the treating physician, were eligible to participate in the studies.	ICD-10	AD (Mean ± SD/ Median/[Range]), years: -Overall: 8.06 ± 2.49/8.0/ [1.0–16.0]; −Children: 7.31 ± 1.85/7.0/[2.0–12.0]; −Adolescents: 9.97 ± 2.86/10.0/[1.0–16.0].
Gustafsson and Källén (2011) [31]	Sweden	Population-based (Study initiated in 2005)	To evaluate the impact of pre- and perinatal factors on the risk of developing ADHD.	237 children with ADHD diagnosis and 31,775 typically developing children, born between 1986 and 1996	Individuals for whom no linkage was possible (e.g. children who were born abroad) or children who were born in Sweden but outside Malmo¨ were not included in the final analysis.		DSM-III-R before 1994 and DSM-IV from 1994 onwards	AD varied between 5 and 17 years, with most children diagnosed between 8 and 12 years of age.
Muller et al. (2011) [32]	Belgium, Germany, Ireland, the Netherlands, Spain, Switzerland, UK and Israel	Large multi-centre (recruitment between April 2003 and April 2007)	To analyse the International Multicentre ADHD Genetics sample with respect to demographic features and psychopathological characteristics.	The sample consisted of 1068 probands with the combined type of ADHD and 1446 'unselected' siblings. Age (Mean ± SD) = 10.8 ± 3.1 years.	Families were excluded from genetic analyses, if either the proband or the participating sibling had an IQ < 70, a diagnosis of schizophrenia or	Recruited families had at least one child with diagnosed or suspected combined type Attention Deficit-Hyperactivity Disorder (ADHD-CT). Further	PACS interview and the DSM-IV items of the CTRS questionnaire	Age at detection of Inattention (I) and Hyperactivity/ Impulsivity (H/I) symptoms (Mean [Range]), years: -Siblings (No diagnosis) I: 6.19

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
					autism, a neurological disorder of the central nervous system or a genetic disorder that might mimic ADHD based on both history and clinical assessment. Children with classical or atypical autism were excluded from the IMAGE project because some genetic regions are known to be associated both with autism and ADHD. There was no rule for assigning proband status to a certain child of a family when several children fulfilled criteria for ADHD-CT.	entry criteria for assessment were: white Caucasian ethnicity of all participants, availability of one or more sibling, children between the ages of 5 and 17 years, participation of a minimum of four family members including one parent, and consent of all persons to give blood samples or buccal swabs for DNA extraction.		[1–16]; H/I:3.93 [1–15]; −Siblings (Hyperactive/Impulsive) I: 4.31 [1–11]; H/I: 3.13 [1–6]; −Siblings (Inattentive) I: 4.80 [1–6]; H/I: 3.56 [0–10]; −Siblings (Combined) I: 4.07 [0–10]; H/I: 2.8 [0–7]; −Siblings (All subtypes) I: 4.59 [0–16]; H/I: 3.09 [0–15]; −Probands (Combined) I: 4.22 [0–12]; H/I:2.36 [0–11]. *N.B.: The same data available also by gender*
Durá-Travé et al. (2012) [33]	Spain	Follow-up (Between January and December, 2009)	To determine the repercussions of drug therapy with osmotic-release oral system methylphenidate during 4 years on the weight and height curve of these patients.	187 ADHD patients under treatment with osmotic-release oral system methylphenidate for at least 48 months since their diagnosis. Among them, 158 combined subtype (84.5%) and 29 inattentive subtype (15.5%). Age at baseline (Mean ± SD) = 8.14 ± 1.60 years	The patients who had stopped treatment during school holidays or summer periods were excluded.		DSM-IV	AD (Mean ± SD), years = 8.14 ± 1.60; 84.5% of patients were diagnosed during school age (6–10 years), 10.5% during preschool age (< 6 years), and 5% of patients during adolescence (> 10 years). There were no significant differences in AD regarding sex and clinical subtype.
Garbe et al. (2012) [34]	Germany	Population-Based Cohort (From a first diagnosis of ADHD in 2005, until discontinuation of insurance, death, or December 31, 2008)	To evaluate drug treatment of ADHD in children and youth in Germany with respect to the time until treatment, the initial treatment choice, switches between drugs, and persistence of drug treatment.	6210 children and adolescents 3–17 years of age, with a first diagnosis of ADHD in 2005.They had either received one inpatient or at least two outpatient ICD-10 GM diagnoses within a time interval of 365 days.		Subjects were required to be continuously ensured for at least 12 months before the date of cohort entry.	ICD-10 GM (German modification)	AD (years) M F T 3–5 9.0 7.6 8.7 6–8 36.3 34.9 36.0 9–11 31.3 36.4 32.5 12–14 18.1 14.3 17.2 15–17 5.3 6.8 5.6 Total 100,100,100
Kirov et al. (2012) [35]	Germany		To investigate sleep architecture in children with ADHD by	20 unmedicated children with ADHD combined type (8–15	Exclusion criteria for both healthy children and children with		DSM-IV; clinical tests for neurological and internal	Mean [range] AO = 5.9 [4–8] years

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
			targeting the first-night effect as a possible confounder.	years old; mean 11.24, SD 2.31) and 19 healthy controls, matched for age and gender.	ADHD were the presence of internal diseases and neurological problems not associated with ADHD. Subjects with total IQ less than 80 also were excluded. Further exclusion criteria applied for the controls were current sleep problems. Also, none of the controls met any DSM-IV criteria for the presence of any psychiatric disorder. Patients who met DSM-IV criteria for the presence of psychiatric disorders different from ADHD were excluded.		diseases,including routine electroencephalogram and electrocardiogram	
Tuithof et al. (2012) [36]	the Netherlands	Survey (Between November 2007 and July 2009)	To investigate the childhood ADHD association with prevalence and onset of 3 stages of alcohol use (alcohol initiation, regular alcohol use, and alcohol use disorder) and the conduct disorder role in this association.	3309 respondents aged 18–49 years (mean age 32). Childhood ADHD was present in 74 of the respondents.			CIDI (version 3.0) was used according to DSM-IV criteria	The mean AO of ADHD was 6.7 (95% CI: 5.4–8.0) years
Andreou and Trott (2013) [37]	Greece	Matched case-control	To examine the performance of adults, diagnosed with ADHD in childhood, on semantic and phonemic verbal fluency tasks.	30 university students diagnosed with ADHD in childhood (26 combined type and 4 hyperactive impulsive type) and 30 controls. Mean years of age 20.5, SD = 1.5		Students of both groups must have met the following criteria: (a) entered the Greek university through the national Greek system of exams, (b) reported Greek as their native language, (c) were free from medications known to affect the central nervous system, and (d) had no history of neurological or psychiatric disease.Students who	DSM-IV;ADHD questionnaire adapted from Conners' Hyperactivity Index	The mean AD was 6.2 years of age, SD = 0.9.

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
						were included in the ADHD group must have also met the following criteria: (a) had received an ADHD diagnosis in childhood, according to DSM-IV criteria and (b) obtained a high score in the ADHD questionnaire adapted from Conners' Hyperactivity Index. Students who were included in the control group must have obtained a low score		
Bahmanyar et al. (2013) [38]	Sweden	Follow-up (From January 1, 2006 until December 31, 2009)	To describe the paediatric population with ADHD and their pharmacological treatment.	7931 individuals who, for the first time, were diagnosed or medically treated for ADHD before 19 years of age during 2006–2007		All patients who, for the first time, received a diagnosis of ADHD or treatment for ADHD before 19 years of age in Sweden between January 1st, 2006 and December 31st, 2007 were identified using the National Patient Register and the Prescribed Drug Register.	ICD-10, DSM-IV	The mean age of incident paediatric patients with a recorded ADHD diagnosis or treatment for ADHD is 12.0 years (SD = 3.7).
Hodgkins et al. (2013) [39]	France, Germany, Italy, the Netherlands, Spain and UK	Retrospective chart-review (ADHD diagnosis between January 2004 and June 2007 followed up until 2009)	To descriptively illustrate variation in physician practice patterns in the management of ADHD in various Western European countries.	340 physicians reviewed and abstracted charts for 779 patients (130 France, 151 Germany, 144 Italy, 74 the Netherlands, 134 Spain, 146 UK). Each physician managed approximately 20 patients aged 6 to 12 years and 15 patients aged 13 to 17 years.	Patient charts were excluded if there was evidence of enrolment in a randomized clinical trial.	Physicians were screened as eligible for inclusion in the study if they were engaged in clinical practice for between 3 and 30 years, managed the treatment of at least five ADHD patients (aged 6–17 years) per month and were responsible for making ADHD treatment decisions. Physicians were required to identify the most recent ADHD patients (up to a maximum of	DSM-IV; ICD-9/ICD-10; ADHD Connors Test	Mean (SD)/Median/ Range AD: -Overall: 8.9 (2.6)/9/ [2–15] years -France: 9.1 (2.5)/9/ [3–14] years -Germany: 8.4 (2.1)/8/ [2–15] years -Italy: 8.7 (2.9)/8/ [4–14] years -the Netherlands: 8.6 (2.6)/9/ [4–15] years -Spain: 9.0 (2.3)/9/ [3–15] years -UK 9.3 (2.8)/9/ [4–15] years

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
						five patients aged 6–17 years) that they had seen at the time of the review. In order for patients to be included in the study, they should have had a documented diagnosis of ADHD between January 2004 and June 2007 and have had at least 2 years of follow-up post-diagnosis. Patients were also required to have received either pharmacological treatment or BT following the ADHD diagnosis.		
McCarthy et al. (2013) [40]	Ireland	Case control	To explore the resting-state functional connectivity in ADHD and to determine the localization and specificity of ADHD related connectivity differences between adults diagnosed with ADHD in childhood and controls by examining 5 predefined neural networks.	16 adults with combined-type ADHD who underwent careful clinical assessment as children, mean (SD) age at diagnosis: 8.9 (2.1) years; 16 healthy matched controls	Exclusion criteria consisted of previous head injurywith loss of consciousness, comorbid psychiatric disorder or disease, a history of hydrocortisone use, and current alcohol or substance abuse and/or dependency.		Structured Clinical Interview for DSM-IV Axis I Disorders	Mean (SD) AD = 8.9 (2.1) years
Nordström et al. (2013) [41]	Finland	Prospective (From birth, between July 1, 1985 and June 30, 1986, to December 31, 2010)	To complete previous findings about the comorbidity of Disruptive behaviour disorder (DBD) and ADHD and to compare the diagnoses based on a clinical evaluation using K-SADS-PL and the register data.	44 only DBD diagnosis; 91 only ADHD; 72 comorbid DBD and ADHD; 250 no DBD or ADHD. A total of 457 adolescents participated.	Adolescents who were neither ADHD cases nor controls were excluded from analyses.		K-SADS-PL; SWAN scale	The median AO of the psychiatric disorders among adolescents with only DBD was 14.9, IQR (interquartile range) = [6.4–18.9], with only ADHD 7.5, IQR = [4.3–15.1] and with comorbid DBD and ADHD 15.3 (IQR = 8.6–20.3).
Socanski et al. (2013) [42]	Norway	Retrospective chart-review	To investigate the prevalence and characteristics of epilepsy in a large, unselected cohort of children with ADHD.	607 children (82.4% males) aged 6–14 years with ADHD were identified. Of these 14 (2.3%) had a history of epilepsy and 13 of	Patients with IQ below50 and those meeting criteria for pervasive developmentaldisorder were excluded		DSM-IV-TRCBCL; CPRS; CTRS; ADHD rating scale IV	Mean (SD) AD of ADHD, years: Total sample 9.4 (2.5); Children with epilepsy 8.2 (2.3); children without epilepsy 9.4

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
				these had active epilepsy				(2.5) (p-value = 0.07).
Caci et al. (2014) [43]	France, Germany, Italy, the Netherlands, Spain and UK	Cross-sectional (From May 2010 to June 2010)	To assess the degree to which ADHD impairs patients' everyday lives and to identify the areas of life most affected by the condition.	959 children/ adolescents aged < 20 were included in the analyses: 535 with ADHD (ADHD group) and 424 without ADHD (control group).	Respondents who provided implausible or impossible answers (e.g. reporting a time to diagnosis that exceeded the age of the child) were excluded, as well as the UK control group (as child age was not collected). Analyses focus on a subgroup of respondents who reported on children/ adolescents aged 6 years (respondents with children aged 5 years or younger were excluded).		Caregiver-reported diagnosis	Mean (SD) AD was 7.0 (2.8) years, ranging from 6.3 (2.1) years in Germany to 7.6 (3.1) years in the Netherlands. Diagnosis was obtained following the consultation of 2.7 (2.6) doctors, ranging from 2.3 (1.8) in the Netherlands to 3.2 (4.0) in France, over a mean period of 20.4 (23.9) months, ranging from 12.2 (19.0) in Spain to 31.8 (30.0) in the UK.
Dalsgaard et al. (2014) [44]	Denmark	Prospective population-based (From birth until date of death or December 31, 2010)	To examine whether gender and injuries in early childhood were associated with later being prescribed ADHD medication in 3 groups of patients (with ADHD, ASD, and OPD).	Within the cohort of all persons born in Denmark between 1990 and 2001 (n = 852,711), three mutually exclusive groups of patients was identified: 11553 ADHD, 9698 ASD or 48,468 OPD			ICD-10	Age at first psychiatric diagnosis of: - ADHD: Mean (SD) = 9.81 (3.85) - ASD: Mean (SD) =8.40 (4.06) - OPD: Mean (SD) = 11.40 (5.26)
Genuneit et al. (2014) [45]	Germany	Population-Based prospective birth cohort (From birth in 2000/2001, with follow-up up to age 11)	To investigate the association between Atopic Eczema and ADHD diagnosis, to further determine the temporal sequence, especially with respect to the ages at diagnosis.	770 children. The cumulative incidence of ADHD was 6.2% up to age 11 years (n = 48).	We excluded women who left the hospital immediately after birth, gave birth at < 32 gestational weeks, had a child of < 2500 g, or whose infant was transferred to pediatric care after delivery. We also excluded women who were not speaking German, Turkish, or Russian, the languages in which study material and questionnaires were available.		Parental-reported diagnosis and medication	Among the 48 children with ADHD, 21 were diagnosed up to age 8 years and 27 were diagnosed between 9 and 11 years.

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
Steinhausen and Bisgaard (2014) [46]	Denmark	Representative study based on a large nationwide psychiatric sample (ADHD diagnosis in the years between 1994 and 2010)	To investigate the risk of various medications in comparison to a control group of non-medicated patients with ADHD, and furthermore risk factors including various co-morbid disorders, duration of medication, age at onset of medication, and year of birth for developing SUD.	20,742 ADHD patients aged between 3 and 60 years			ICD-10	The mean AD was 15.20 (SD = 10.08) years.
Sucksdorff et al. (2015) [47]	Finland	Nationwide, nested, case-control (Born between January 1, 1991, and December 31, 2005, followed until December 31, 2011)	To examine the association between gestational age and ADHD by each gestational week. To study the association of weight for gestational age and ADHD.	10,321 children with ADHD were included in the study. Each patient was matched with 4 controls.	Children who had received an ADHD diagnosis before the age of 2 years, but not after that, were excluded. Children diagnosed with severe or profound mental retardation also were excluded. Children for whom information on gestational age or birth weight was not available or clearly inaccurate were excluded.		ICD-9 from 1987 to 1995; ICD-10 since 1996. 88% of subjects met DSM-IV criteria	The mean AD was 7.6 years (SD 2.9 years, range: 3–19 years).
van den Ban et al. (2015) [48]	the Netherlands	Cohort of ADHD patients diagnosed between January 1999 and December 2010	To analyse differences in starting and discontinuation of ADHD medication between native Dutch youth and those with a Moroccan, Turkish or Surinam cultural background with ADHD	817 (11.6% of total patients) patients that had a diagnosis of ADHD. All patients were younger than 19 years at the time of diagnosis. 598 patients were Dutch natives, 143 Moroccans, 52 Turks and 24 of Surinam's.		younger than 19 years at the time of diagnosis. Had at least 6 months of history in the composed database before the ADHD diagnosis and could be followed for at least 6 months afterwards.	Diagnosis of ADHD at Altrecht (a large institute for mental health care) identified from the Psychiatric Casus Register.	Almost 60% of the patients are diagnosed at the age of 6–11 year old. Mean (SD) age at ADHD diagnosis, years: -Overall: 10.1 (3.5); −Dutch natives: 10.1 (3.5); Moroccans: 9.8 (3.3); Turks: 11.4 (3.8); −Surinam's: 10.7 (3.7). Total sample age at ADHD diagnosis: 0–5 yrs. 5.6%; 6–11 yrs. 62.8%; 12–18 yrs. 31.6%. Dutch natives age at ADHD diagnosis: 0–5 yrs. 6.2%; 6–11 yrs. 63.0%; 12–18 yrs. 30.8%.

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
								Maroccan age at ADHD diagnosis: 0–5 yrs. 4.9%; 6–11 yrs. 67.1%; 12–18 yrs. 28.0%. Turkish age at ADHD diagnosis: 0–5 yrs. 3.8%; 6–11 yrs. 50.0%; 12–18 yrs. 46.2%. Surinam age at ADHD diagnosis: 0–5 yrs. 0.0%; 6–11 yrs. 58.3%; 12–18 yrs. 41.7%.
Caci et al. (2016) [49]	France	Multicentric, cross sectional (Between November 4, 2013 and January 31, 2014)	To describe the health care trajectories in a sample of French children with ADHD	All the 473 patients in the series were under age of 18 (median age was 11.0 years); 382 were boys (81%).	no exclusion criterion was defined	under the age of 18 in whom ADHD diagnosis had been confirmed by the clinician	ADHD diagnosis confirmed by physician	AD: Mean (SD) = 8.07 (2.19); Median = 7.5. AO noticed by caregivers: Mean (SD) = 4.45 (2.25). Age at the first symptoms noticed outside the family: Mean (SD) = 5.00 (2.30).
Lemcke et al. (2016) [50]	Denmark	Longitudinal (from birth until their first ADHD diagnosis or to the end of follow-up on 8 February 2012)	To investigate if children that are later diagnosed with disorders of attention and activity, already early in life have deviations in early development that can differentiate them from children with typical development.	2034 ADHD (F90.0, F90.1, F98.8) cases were included in the study, which corresponds to 2.7% of the study population. 24 children diagnosed with ADHD before 3 years of age were excluded. Mean (SD) [Range] age at end of follow-up, years: ADHD cases 11.4 (1.30) [8.7–13.9]; Study cohort 11.3 (8.6) [13.9–1.35].	children diagnosed with ADHD before 3 years of age were excluded. Indication for treatment was narcolepsy were removed from the cohort.		ICD-10	Mean (SD) [Range] AD, years = 8.4 (1.98) [3.0–13.4]
Rheims et al. (2016) [51]	France	Multicentre prospective observational (Enrolment between November 2011 and September 2014, follow-up 12–16 week)	To investigate the association between the presence of ADHD and the type of epilepsy, the duration of epilepsy, the seizure frequency, the antiepileptic treatments, the co-occurrence of other psychiatric	160 patients aged between 6 and 16 years completed the follow-up, including 58 in whom Methylphenidate (MPH) had been initiated at study entry. 68 children (42.5%) had ADHD-I and 92 (57.5%) had ADHD-C.		(1) age ≥ 6 years and < 16 years; (2) patients having epilepsy according to International League Against Epilepsy (ILAE) classification14 regardless of underlying epilepsy syndrome, seizure frequency, or ongoing	DSM-IV ADHD-RS	Mean ± SD AO of ADHD symptoms, years: - Overall sample: 5.4 ± 1.9, range= [2–13] - Patients not treated: 5.3 ± 1.8 years - Patients treated with MPH: 5.6 ± 2.1

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
			comorbidities.			antiepileptic drug treatment; (3) diagnosis of ADHD of Inattentive subtype (ADHD-I) or combined Inattentive/ Hyperactive-Impulsive subtype (ADHD-C) according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria except for the criterion of onset before age of 715; (4) no ongoing specific ADHD treatment, including methylphenidate and atomoxetine.		
Sollie and Larsson (2016) [52]	Norway	Follow-up 2007–2008	To examine the associations between child symptoms, demographic variables and the following parent and family characteristics.	Parents of 214 children (mean age at follow-up: 12.6 years, SD = 2.1) with Hyperkinetic disorders recruited from five child and adolescent mental health out-patient clinics.		children with Hyperkinetic disorders	ICD-10 DBRS	Mean age at follow-up: 12.6 years, SD = 2.1. The mean interval from the time of diagnosis to follow-up was 3.7 years (SD = 2.2) and ranged from 1 to 10 years.
van Lieshout et al. (2016) [53]	the Netherlands	Follow-up (Enrolment between 2003 and 2006, follow-up on average 6 years)	To investigate ADHD persistence rates, comorbidity rates, symptom severity, overall functioning and the impact of continued pharmacological treatment.	347 participants with ADHD-combined type aged 5–19 years. Mean age at baseline was 11.4 years (SD = 2.8) and mean age at follow-up was 17.4 (SD = 2.8).		age of 5–19 years, Caucasian descent, IQ ≥70, no diagnosis of autism, epilepsy, general learning difficulties, brain disorders and known genetic disorders. Only participants with a diagnosis of ADHD/C based on the algorithm at baseline were included in the current study.	DSM-IV, DSM-5 CPRS-R:L; CTRS-R:L; CAARS-S:L; SDQ; PACS, symptoms as defined by DSM-IV-TR, K-SADS-PL	Mean AO of the first symptom = 2.25 (SD = 1.52) years.
Abel et al. (2017) [54]	Norway	Large Prospective Cohort of women pregnant in their first	To explore the association between iodine intake from food in pregnancy (as a proxy for long-term iodine intake and	77,164 mother-child pairs were included in this study. ADHD diagnosis was registered in 1725 children (2.2%) by December 2015			ICD-10	The median AD was 8.2 years (IQR: 7.0, 9.5 years).

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
		trimester from all over Norway during the years 1999 to 2008.	status) and (i) risk of specialist-diagnosed ADHD in the child and (ii) maternal report of child ADHD symptoms at eight years of age.					
Bachmann et al. (2017) [55]	Germany	Observational; Nationwide routine data of patients diagnosed between 2009 and 2014	To investigate frequency of diagnosis and treatment for ADHD in children, adolescents, and adults, changing between 2009 and 2014 and transition.	In 2009 there were 214,110 members of the Germany's largest statutory health insurance company aged between 0 and 69 years (71.4% male, mean age 13.5 [± 31.9] years) with a diagnosis of ADHD; in 2014 there were 274,982 (69.7% male, mean age 14.6 [± 35.1] years).		all insurants with a diagnosis of ADHD who were 15 years old in 2008 and who had been continuously insured until 2014.	ICD-10	Graphical representation of ADHD diagnoses in insureds for 2009 and 2014 by age and sex, based on routine data (administrative prevalence). Modal class: 10–14 years
Balboni et al. (2017) [56]	Italy	A posteriori investigation of information derived from a national database	To investigate which item subsets of the Vineland-II can discriminate children with ADHD or specific learning disorders from peers with typical development.	24 children with ADHD (5–14 years), 61 elementary students with specific learning disorders (6–11 years), and 85 controls with typical development (5–14 years).		Italian native speakers and attended a regular education program. T	DSM-IV-TR diagnosis of ADHD was based on a testing battery assessing attentional and executive functions and on questionnaires given to parents and teachers to evaluate the presence of psychological problems. WISC-III	Children received the diagnosis of ADHD at a mean age of 9 years (range: 5–15 years).
Chen et al. (2017) [57]	Sweden	Cohort (born between 1985 and 2006, followed from their third birthday to 31 December 2009 for ADHD diagnosis)	To estimate the strength and pattern of the familial aggregation of ADHD with greater precision than previously reported.	During the follow-up, 31,865 out of 1,656,943 individuals received ADHD diagnosis			ICD-9 during 1987–1996 and ICD-10 from 1997 onwards; or DSM-IV	Graphical representation of cumulative incidence of ADHD diagnosis among all siblings and all cousins. Median class: 10–15 years
Pohlabeln et al. (2017) [58]	Belgium, Cyprus, Estonia, Germany, Hungary, Italy, Spain and Sweden	Prospective multi-centre cohort	To investigate whether in addition to established early risk factors other, less studied pre-, peri-, and postnatal influences, like gestational	A total of 15,577 children from 8 European countries were included in the analyses (age range: 2–11.9 years, mean age: 6.2 years, SD: 1.9 years).			Parent-reported ADHD diagnosis by a physician or medical health professional	AD: ≤ 4 *n* = 13 (6.8%) (4–6] *n* = 34 (17.7%) (6–8] *n* = 93 (48.4%) ≥ 8 *n* = 52 (27.1%)

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
			hypertension or neonatal respiratory disorders and infections, may increase a child's risk of developing ADHD.	192 (15 Belgium, 28 Cyprus, 22 Estonia, 42 Germany, 35 Hungary, 8 Italy, 33 Spain and 9 Sweden) were classified as affected by ADHD.				
Sayal et al. (2017) [59]	Finland	Nationwide population-based	To investigate whether relative age is associated with ADHD diagnosis in a country where prescribing rates are low and whether any such association has changed over time or relates to comorbid disorders.	6136 children born between Jan 1, 1991, and Dec 31, 2004, who were diagnosed with ADHD from age 7 years onwards.	children with severe or profound intellectual disability	children diagnosed with ADHD from age 7 years onwards.	ICD-10	The mean AD in the sample was 9.4 years (standard deviation: 2.4; range: 7–19 years).
Bonati et al. (2018) [60]	Italy	Clinical multicentre; review of patient medical records between September 2011, and December 2017	To confirm the association between relative age (defined as the child's age within their school year) and ADHD in a different additional national context.	4070 children from age 6 years onwards. 2856 of 4070 subjects evaluated (70%) met the diagnostic criteria for ADHD.	children with severe or profound intellectual disability were excluded	children diagnosed with ADHD from age 6 years onwards.	DSM-IV-TR WISC-III; K-SADS, CBCL, CPRS-R, CTRS-R, CGI-S	The mean AD was 9.3 years (SD 2.5, range 6–17).
Cornu et al. (2018) [61]	France	Double-blind placebo-controlled randomised trial between 2009 and 2011	To investigate the effects of omega-3 supplements in children with ADHD.	162 children aged 6–15 years (Treated $n = 80$; Placebo $n = 82$)	known intolerance to omega-3 fatty acids, intake of fatty acid/fish oil dietary supplements for more than 1 week during the 3 months preceding inclusion, or MPH or other ADHD drug during the month preceding inclusion. Children who required MPH treatment were also excluded to ensure equipoise.	children and adolescents aged 6–15 years referred for hyperactivity symptoms to five reference centres for learning disabilities in France.	DSM-IV-TR CGI-S	Mean (SD) AD: DHA–EPA 7.0 (3.0); Placebo 6.9 (2.9)
Prasad et al. (2018) [62]	UK (England)	Population-based cohort study	To provide estimates of the risk of fractures, thermal injuries, and poisonings in young people with/ without ADHD	15,126 young people with and 263,724 without ADHD		CYP aged 3 to 17 years during the study period of 1998–2012, with at least one diagnosis code or at least one drug code for ADHD in the CPRD, were included in the	ICD-10	AD: 3–4 years 7.7% 5–9 years 51.2% 10–14 years 35.4% 15–17 years 5.7%

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
						population of CYP with ADHD.		
Dalsgaard et al. (2019) [63]	Denmark	Cohort study included all individuals born from January 1995 through December 2016 and followed up from birth until December 2016	To estimate age- and sex-specific incidence rates and risks of being diagnosed with any mental disorder during childhood and adolescence	99,926 individuals were diagnosed with a mental disorder before 18 years of age. Among these, 30,776 had ADHD diagnosis			ICD-10-DCR	Incidence peaked earlier in boys than girls in ADHD (8 vs 17 years of age)
Granström et al. (2019) [64]	Sweden	Nationwide, population-based cohort study with an observational period from January 1964 to December 2013.	To assess if individuals with Hirschsprung disease have an increased risk for ADHD	739 individuals with HSCR and 7390 controls. Twenty-six of the individuals with HSCR and 202 of the 7390 controls had ADHD.	Exclusion criteria were applied only to HSCR to avoid including neonates with suspected HSCR admitted for rectal suction biopsies where the biopsies turned out to be negative or patients admitted only to a hospital not providing pediatric surgery.		Prescription of any drug used in the treatment of ADHD used as a proxy for the diagnosis.	The mean age at diagnosis of ADHD was not different between the groups, 18.1 years (SD = 8.4) vs 16.7 years (SD = 7.8), $p = 0.39$.
Hoang et al. (2019) [65]	UK	Cross-sectional database study of a national surveillance network of children under 19 years of age between January and December 2016	To describe variations in age of ADHD diagnosis and stimulant prescribing among general practitioner practices in a nationwide network and identify factors that might account for these variations.	3470 children with a coded diagnosis of ADHD		3470 children under 19 years of age with a coded diagnosis of ADHD within the RCGP RSC network were included in the study	Read code	The mean age of first ADHD diagnosis was 10.5 years (95% CI 10.1 to 10.9, median 10, IQR 9.0–11.9)
Root et al. (2019) [66]	UK	Population-based cohort study used electronic record data collected before January 3, 2017, from more than 700 general practices	To estimate the associations with intellectual disability and ADHD and investigate association between relative age and childhood depression.	1,042,106 children aged 4 to 15 years	Children receiving an outcome diagnosis before study entry or with missing sex were excluded.	all children who were registered before January 3, 2017, at a general practice contributing high-quality data to the Clinical Practice Research Datalink (CPRD), and younger than 16 years at the last data collection at that general practice. Children were	Read code	Median age at ADHD diagnosis was 8.0 years (IQR, 6.7–9.7)

Table 2 List in chronological order of the 44 studies included here *(Continued)*

Reference	Country	Type of Study (Year)	Aim	Sample description	Exclusion criteria	Inclusion criteria	Diagnostic criteria and tools	Outcome
						included from their imputed fourth birthday or from 12 months after registering at a practice contributing research quality data to CPRD, if later.		
Sun et al. (2019) [67]	Sweden	Prospective cohort study used national registers to identify individuals born from January 1983, through December 2009	To investigate the all-cause and cause-specific mortality risks in ADHD and to explore the potential role of psychiatric comorbidities	2,675,615 individuals with a mean (SD) age at study entry of 6.4 (5.6) years and a mean (SD) follow-up of 11.1 (3.1) years: 1374790 were male (57,919 with an ADHD diagnosis) and 1,300,825 were female (28,751 with an ADHD diagnosis).		all individuals born in Sweden from January 1, 1983, through December 31, 2009, who were alive and residing in Sweden on their 1-year birthday or January 1, 2001 and followed up until death, emigration from Sweden, or December 31, 2013, with the oldest cohort member censored at 31 years of age.	ICD-10	The mean (SD) AD was 14.3 (5.7) years; 13.5 (5.5) years for male and 16.0 (5.6) for female individuals.
Sourander et al. (2019) [68]	Finland	Population-based case-control study	To investigate the association between maternal cotinine levels during pregnancy and ADHD diagnosis in offspring	1079 patients born between 1998 and 1999 and diagnosed with ADHD and 1079 matched controls			ICD-10	The mean AD was 7.3 years (SD: 1.9; range: 2–13.7 years).
Taylor et al. (2019) [69]	Sweden	Population based twin study focused on all birth cohorts between 1992 and 1999	To investigate the degree to which individuals first receiving community diagnoses of ADHD as adults would display discernible signs of neuropsychiatric impairments as children.	662 individuals with diagnoses of ADHD and 14,474 individuals were the comparison group	All diagnoses were required to have been assigned prior to the age of 18.	All diagnoses were required to have been assigned prior to the age of 18.	ICD-10	74 individuals diagnosed after age 18; 394 diagnosed between the ages of 12–18; 194 diagnosed prior to age 12

Attention-Deficit/Hyperactivity Disorder (ADHD); age of diagnosis (AD); age of onset (AO); ADHD Rating Scale-IV (ADHD-RS); Autism Diagnostic Interview-Revised (ADI-R); Autism Diagnostic Observation Schedule–Generic (ADOS-G); Autism Spectrum Screening Questionnaire (ASSQ); Bipolar Disorder (BD); Birleson Depression Self-Rating Scale (DSRS); Child and Adolescent Psychiatric Assessment (CAPA); Child Behavior Checklist for parents (CBCL); Children's Depression Inventory (CDI); Children's Manifest Anxiety Scale (CMAS); Clinical global impressions–severity scale (CGI-S); Composite International Diagnostic Interview (CIDI); Conners' Adult ADHD Rating Scales-Self-Report: Long Version (CAARS-S:L); Conners' Parent Rating Scale (CPRS); Conners' Parent Rating Scale-Revised: Long version (CPRS-R:L); Conners' Teachers' Rating Scale–Revised: Long Form (CTRS-R:L); Diagnostic and Statistical Manual of Mental Disorders (DSM); Disruptive Behaviour Disorder (DBD); Disruptive Behaviour Rating Scale (DBRS); Five to Fifteen (FTF) questionnaire; Global Assessment of Functioning Scale (GAF); Hyperactivity/Impulsivity (H/I); International Classification of Diseases (ICD); Methylphenidate (MPH); Parental Account of Childhood Symptoms (PACS); Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL); Strengths and Difficulties Questionnaire (SDQ); Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour (SWAN); Vineland Adaptive Behaviour Scales–Daily Living Skills domain (VABS-DLS); Wechsler Adult Intelligence Scale–Revised (WAIS-R); Wechsler Intelligence Scale for Children–Third Edition (WISC-III); Wechsler Preschool & Primary Scale of Intelligence–Revised (WPPSIR); Wender Utah Rating Scale (WURS).

graphical representations of the cumulative incidence of ADHD diagnosis among siblings and cousins [57] and of the prevalence of ADHD diagnosis in an insured population [55].

The age range in the 24 studies reporting the mean AD was 6.2 to 18.1 years. The lowest mean value, which was reported by Andreou and Trott [37], concerned a group of 30 university students living in Greece who were diagnosed with ADHD during childhood (26 a combined form and 4 a hyperactive impulsive form).

Granström et al. [64] reported the highest mean AD in 26 individuals with Hirschsprung disease and 7390 controls taking any drug for the treatment of ADHD according to the Swedish Prescribed Drug Register.

Two studies reported the mean age for ADHD diagnosis for a specific group of countries [39, 43]. Taking into consideration the same countries (i.e. France, Germany, Italy, the Netherlands, Spain and UK), the two studies identified Germany as the country with the lowest mean age and the UK [39] and the Netherlands [43] as the countries with the highest mean age.

Discussion

ADHD, one of the most common childhood neurodevelopmental disorders, is characterized by a pattern of inattention and/or impulsivity and hyperactivity, behaviours that can have a dramatic impact on children and on family life [77]. Since early identification of the disease is essential to optimize the quality of life of both the children themselves and their families, there is growing research interest in investigating the timing of diagnosis which can lead to prompt medical attention.

The current study set out to investigate age at the time of onset and/or diagnosis of ADHD in children living in European countries by examining the studies published between January 1, 2010 and December 31, 2019 reporting on the AO and AD of ADHD. The study's most important finding was that there is a wide variability in both.

Much of the variability could be attributed to discrepancies in study methods. Differences in study designs, ranging from case-control, cohort, to cross-sectional, could have affected the AO/AD as a cohort study could more accurately identify the AO and thus the incidence of ADHD with respect to a cross-sectional retroactive study basing its figures on parent reports.

The studies also show differences in sampling methods. Several studies, in fact, used convenience samples from clinic-based studies; others were based on registry data or medical records. It is reasonable to hypothesise that referred patient samples have lower AO/AD compared to community cohorts given the differences in the severity of the disorder in these populations.

The source of information (self-reported, parent-reported, teacher-reported, doctor-reported) can also significantly influence the figures on the AO/AD registered by the different studies. In a multi-country cross-section study by Caci et al. [43] which assessed the degree to which ADHD impairs patients' everyday lives, the diagnosis was caregiver-reported and the mean AD was 7.0 years, ranging from 6.3 years in Germany to 7.6 years in the Netherlands. The diagnosis was obtained following the consultation of a mean of 2.7 doctors, ranging from 2.3 in the Netherlands to 3.2 in France, over a mean period of 20.4 months, ranging from 12.2 in Spain to 31.8 in the UK.

The articles by Genuneit et al. [45] and Pohlabeln et al. [58] presented the parent-reported AD: in the first, 44% of the children included in the sample were diagnosed before the age of 8 years and the others between 9 and 11 years; in the second article the percentage of children diagnosed between 9 and 11 years fell to 17%. Although the age range as well as the source of information (parent-reported) of these two articles was the same, the differences in AD could probably be explained by the presence of a comorbidity, that is Atopic Eczema in the case of the first sample.

The presence of comorbidities is an exceedingly important consideration when ADHD diagnosis is being discussed. ADHD symptoms can overlap with those of other disorders, including autism spectrum disorder, disorders of mood and conduct, oppositional defiant disorder, learning difficulties, impaired motor control, poor executive functions (working memory, planning, organisation, and time management), communication difficulties, sleep disorders, tics/Tourette syndrome, epilepsy, and anxiety disorders, that commonly coexist with ADHD.

Socanski et al. [42], who compared the ADs of ADHD in a group of children with epilepsy and a control group, uncovered a statistically significant different in the mean ages: the children with epilepsy had a mean AD of 8.2 years, while those without epilepsy had a mean AD of 9.4 years (p-value = 0.07). This result suggests that children with comorbidities related to ADHD have a greater probability of being diagnosed with ADHD at a younger age, presumably because they already have access to some kind of healthcare services and are being monitored by medical specialists.

Thus, the characteristics of enrolled populations (exclusion/inclusion criteria) and the sample size enormously undermine the evaluation and comparison of studies as well as a formal summary of the results. The application of meta-analysis is also impossible due to the lack of publication by all the studies of the absolute values.

The criteria used to diagnose the condition is another important factor that could affect the heterogeneity in the studies considered.

The two main diagnostic systems currently being used are the ICD-10 and the DSM-V [72]. Both systems require that symptoms be present in several settings, for example school/work, home life and leisure activities, and that the onset of symptoms be evident in early life, although this criterion has not yet received a consensus among specialists and has changed over the last decades. For the DSM-V, onset is expected to occur by the age of 12 years; for the ICD-10 and the DSM-IV by the age of 7 years. Since AO itself is one of the criteria of a diagnosis of ADHD in the studies included in our analysis, the AD falls within the ages determined by the diagnostic criteria.

Several research teams have been concerned about the implications of increasing the age of onset to 12 years [78]. Some investigators seem favourable to adopting the new criteria since it has increased the number of ADHD patients receiving help [79]. Other researchers believe that parents' inability to recall the AO prior to 7 years might give false negative results and reduce some of the diagnostic relevance connected to recalling the AO [80]. A revision of AO criteria should in any case be based on studies assessing the performance of different diagnostic criteria in the population [79].

Strengths and limitations

To our knowledge, this study represents the first systematic review of the AO and AD of ADHD in European countries. Although we did adhere to PRISMA guidelines [24] to ensure methodological rigour, the study does have a number of potential limitations.

The first is that studies not published in English as well as those not available in PubMed were not taken into consideration.

We would also like to point out that the 44 articles included in this systematic review refer to studies conducted in 13 European countries.

Despite these limitations, and those methodological of analysed studies, the review offers new insights into the timing of the onset and diagnosis of ADHD.

Conclusions

One of the key functions of primary care is to recognize the symptoms of an illness at an early stage. As far as childhood illnesses are concerned, neurodevelopmental disorders are relatively common and increasing in Europe. Early diagnosis makes it possible to contemplate and implement opportune treatment strategies thus reducing, in this case, some of ADHD's adverse current and future consequences in the child and family. This study provides a preliminary overview on the timing of the onset and the diagnosis of ADHD in children living in European countries. The long term validity and heterogeneity of the classification systems used to guide diagnoses and the factors behind the social, cultural and genetic differences affecting the timing of identification of the syndrome need further analysis. The fact that Germany has a much earlier AO and AD with respect to the UK and the Netherlands is just one example of differences that need to be clarified. Studies in the literature suggest that identifying ADHD symptoms early on can facilitate early referral and treatment, and thus limit its cost in personal and societal terms [81, 82]. To optimize the quality of the service and of the care delivered is the task of both policymakers and clinical experts. To guarantee an equal standard of care for all children and adolescents with ADHD is a pressing need to reduce the times to complete the diagnostic path, and promptly star with appropriate therapy [83]. However, further studies are necessary to uncover the underlying reasons for the large variability observed in both AO and AD, and reducing the distance between the onset and the diagnosis of ADHD.

Abbreviations

ADHD: Attention-Deficit/Hyperactivity Disorder; AD: Age of diagnosis; AO: Age of onset; ADHD-RS: ADHD Rating Scale-IV; ADI-R: Autism Diagnostic Interview-Revised; ADOS-G: Autism Diagnostic Observation Schedule–Generic; ASSQ: Autism Spectrum Screening Questionnaire; BD: Bipolar Disorder; DSRS: Birleson Depression Self-Rating Scale; CAPA: Child and Adolescent Psychiatric Assessment; CBCL: Child Behavior Checklist for parents; CDI: Children's Depression Inventory; CMAS: Children's Manifest Anxiety Scale; CGI-S: Clinical global impressions–severity scale; CIDI: Composite International Diagnostic Interview; CAARS-S:L: Conners' Adult ADHD Rating Scales-Self-Report: Long Version; CPRS: Conners' Parent Rating Scale; CPRS-R:L: Conners' Parent Rating Scale-Revised: Long version; CTRS-R:L: Conners' Teachers' Rating Scale–Revised: Long Form; DSM: Diagnostic and Statistical Manual of Mental Disorders; DBD: Disruptive Behaviour Disorder; DBRS: Disruptive Behaviour Rating Scale; FTF: Five to Fifteen questionnaire; GAF: Global Assessment of Functioning Scale; H/I: Hyperactivity/Impulsivity; ICD: International Classification of Diseases; MPH: Methylphenidate; MOCHA: Models Of Child Health Appraised; PACS: Parental account of childhood symptoms; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; K-SADS-PL: Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version; SDQ: Strengths and Difficulties Questionnaire; SWAN: Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour; VABS-DLS: Vineland Adaptive Behaviour Scales–Daily Living Skills domain; WAIS-R: Wechsler Adult Intelligence Scale–Revised; WISC-III: Wechsler Intelligence Scale for Children–Third Edition; WPPSIR: Wechsler Preschool & Primary Scale of Intelligence–Revised; WURS: Wender Utah Rating Scale

Supplementary Information

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Additional file 1. PRISMA checklist.

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Authors' contributions

IR and BC screened all the articles present in this review; IR wrote the manuscript; IR, BC, MB interpreted the data; all authors revised and approved the final manuscript.

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Availability of data and materials
The data used to support the findings of this study are included within the article.

Declarations

Ethics approval and consent to participate
Not applicable.

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Competing interests
The author(s) declare that there is no conflict of interest regarding the publication of this paper.

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Publisher's Note

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Systematic Review

Biological Bases of Empathy and Social Cognition in Patients with Attention-Deficit/Hyperactivity Disorder: A Focus on Treatment with Psychostimulants

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Abstract: In recent years, there has been growing interest in investigating the effect of specific pharmacological treatments for ADHD not only on its core symptoms, but also on social skills in youths. This stands especially true for ADHD patients displaying impulsive aggressiveness and antisocial behaviors, being the comorbidity with Disruptive Behavior Disorders, one of the most frequently observed in clinical settings. This systematic review aimed to synthesize research findings on this topic following PRISMA guidelines and to identify gaps in current knowledge, future directions, and treatment implications. Search strategies included the following terms: ADHD; methylphenidate and other ADHD drugs; empathy, theory of mind and emotion recognition. Full-text articles were retrieved and data from individual studies were collected. Thirteen studies were finally included in our systematic review. Ten studies assessing changes in empathy and/or theory of mind in patients with ADHD treated after pharmacological interventions were identified. Similarly, seven partially overlapping studies assessing changes in emotion recognition were retrieved. Despite a great heterogeneity in the methodological characteristics of the included studies, most of them reported an improvement in emphatic and theory of mind abilities in youths with ADHD treated with psychostimulants and nonstimulant drugs, as well as positive but less consistent results about emotion recognition performances.

Keywords: empathy; theory of mind; emotion recognition; ADHD; disruptive behavior

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1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders, with a pooled worldwide prevalence of 7.2% among children and adolescents [1]. In addition to the core symptoms of inattention, hyperactivity, and impulsivity [2], subjects with ADHD frequently exhibit difficulties in establishing and keeping relationships with peers and are perceived as less socially competent than peers [3]. Particularly, they tend to show a high rate of social and interpersonal problems during their whole life span, since reduced social cognition skills are usually found to be highly associated with the disorder, which may be considered to be an independent risk factor for negative outcome and poor quality of life in ADHD [3].

Interestingly, ADHD core symptoms per se may interfere with adequate social interactions. Indeed, attention deficits interfere with a proper coding and interpretation of social information, i.e., focusing and sustaining attention during conversations or appropriately reading social cues during play [4]. On the other hand, impulsivity involves inappropriately intruding in conversations or play, and disinhibition of motor, verbal, and behavioral responses can lead to fewer opportunities for social interaction due to peer rejection [5].

Moreover, ADHD is commonly associated with the presence of comorbid disruptive behavior disorders such as Oppositional Defiant Disorders (ODD) and/or Conduct Disorders (CD) that may further worsen social impairments and maladjustment [6]. Interestingly, deficits in social cognition skills may be even more challenging when ADHD presents with comorbid ODD/CD [7].

1.1. Empathy and Related Constructs

Social cognition is essential for successful social interaction and, as a whole, refers to the ability to understand other people's behaviors. It involves codification, representation and interpretation of social cues and includes (1) recognizing others' affects from face and prosody perception (i.e., emotion recognition), (2) making inferences regarding others' mental states (i.e., theory of mind (ToM)), (3) sharing and understanding the emotional perspective of others (i.e., empathy) [3]. More complex social cognition abilities include humor processing and further steps of the social information-processing model [8], from which biases may lead individuals to assume the hostile attributions of another's ambiguous behavior and generate aggressive or ineffective solutions to social problems.

Empathy is a complex multidimensional construct including an affective component—affective empathy (AE)—that is, the capacity of sharing emotions and responding to emotional displays of others, and a cognitive one—cognitive empathy (CE)—namely, the ability to understand the perspective of another person [9–13]. AE may involve several related underlying processes, including, among others, emotional contagion, emotion recognition, and shared pain [14]; on the other hand, CE involves making inferences regarding the other's affective and cognitive mental states [15].

These two components may have different neuroanatomical correlates, the former implying the contribution of limbic and paralimbic structures and developing earlier than the latter, which assumes, in turn, a fine-tuned maturation of prefrontal and temporal networks [16]. However, in a study on the anatomical correlates of empathy in patients with focal brain injuries, Shamay-Tsoory and colleagues [17] demonstrated that prefrontal lesions, especially those involving the orbitofrontal and ventromedial regions, were significantly associated with impairments in both cognitive and affective empathic skills, while lesions involving right parietal areas were also associated with deficient empathy. The distinction between the emotional and cognitive empathic subprocesses may also relate to different neurobiological systems. It has been suggested, indeed, that the oxytocinergic system, which has been associated with attachment and pair bonding, may modulate emotional but not cognitive empathy [18], whereas dopaminergic circuitry is associated with cognitive aspects of empathy [19].

Although the two systems work independently, as previously suggested by the Perception–Action Model of empathy [20,21], they interact with each other. The affective component is, indeed, regarded as a bottom-up automatic process, while the cognitive component may be better represented as a top-down modulator. Nonetheless, they also work in synergy with several other distinct but integrated components of social cognition, among which the theory of mind (ToM) stands out first. ToM is defined as the ability to make inferences regarding others' mental states—their knowledge, needs, intentions, and feelings—and is mediated by dissociable though interacting cognitive and affective aspects [22], whereas cognitive ToM, for instance, assessed through the so-called False Belief task, is thought to require cognitive understanding of the difference between the speaker's knowledge and that of the listener. Affective ToM, for example, tested with Faux Pas and Irony tasks, is supposed to require, in addition, an empathic appreciation of the listener's emotional state [23]. ToM functioning critically involves a complex neural network including the medial prefrontal cortex, the superior temporal sulcus region, the temporal pole, and the amygdalae [24–26], and has also been linked to the integrity of the dopaminergic and serotoninergic systems [24].

On the other side, the appropriate recognition of emotional cues represents a fundamental milestone in the early development of social cognition skills. Indeed, the ability

to identify emotions from facial expressions and prosody is acquired during childhood and further develops during adolescence. Besides, nonverbal channels of communication seem to play an important role in helping individuals to interact appropriately with each other. Intact emotion recognition is required for the inhibition of aggressive behavior and its deficiencies might lead to aggressive reactions toward others [27]. At the same time, impaired recognition of facial emotions has been suggested to play a central role for social malfunctioning, being a potential cause of low social competence and low popularity in peer groups [28]. In other words, social adaptation is poorer in those who tend to identify emotional expressions less accurately [29].

In healthy individuals, facial expressions usually elicit neural changes over frontotemporal and parieto-occipital cortices, while right-sided peri-sylvian areas are engaged in the processing of emotional prosody [3]. Face emotion recognition has also been linked to temporal, prefrontal (e.g., orbitofrontal), and anterior cingulate regions, as well as the amygdala and the basal ganglia [30]. Finally, a connection between the perception of emotions and the dopaminergic pathway has been demonstrated [31].

1.2. Social Cognition in ADHD

Clinical evidence suggests several psychopathological disorders to be characterized by deficits in social cognition [32,33]. Importantly, empathy/ToM deficits have been implicated, indeed, in neurodevelopmental conditions in childhood and adolescence, among which Autism Spectrum Disorder (ASD) [34–37] and ODD/CD with limited prosocial emotions i.e., callous–unemotional traits [38,39] are the most studied. Empathy and ToM may be also compromised in a proportion of youths with ADHD. Clinical practice usually reveals low levels of social perspective taking and ToM in ADHD children [6,40,41]. Indeed, young people with ADHD may have low CE attitudes, as demonstrated, for instance, by the frequently observed unawareness of other children playing the same game [42]. In this regard, a recent meta-analysis on social cognition findings in ADHD [43] revealed that especially ToM was significantly impaired in ADHD patients. Interestingly, they also reported that social cognition deficits in ADHD lied intermediately between ASD and healthy controls [43].

On the other hand, several studies have also demonstrated that children with ADHD exhibited AE deficits compared to healthy controls [6,41,44], either assessed as trait using parent reports [45] or as a state assessed with affective responses to vignettes [41]. Presumably, a global empathy deficit can be detected in ADHD, involving both components, as shown by Maoz and colleagues [46] through self-report assessments. Interestingly, in another study from the same research group [47], differences in the empathic profile were identified between the Combined (ADHD-C) and the Inattentive (ADHD-I) subtypes of ADHD, with greater impairment in the former.

Children and adolescents with ADHD also exhibit an impaired emotion recognition ability and a nonverbal receptive language deficit [5,48,49], which denotes a difficulty in detecting and interpreting social clues and generates impaired social interactions and interpersonal problems. In particular, individuals with ADHD are significantly poorer in identifying emotional expressions, especially the negative effects of fear, anger and sadness, likely originating from a primary deficiency in encoding social cues and selectively inhibiting irrelevant information in ADHD [43,50].

According to Uekermann and colleagues [3], empathy deficits in ADHD might be explained, at least in part, by the impulsive response modalities typically found in these patients, and thus may be linked to dysfunctions of the fronto-striatal brain networks, functionally related to empathic processing and executive functioning. Interestingly, Barkley [51] argues that deficits in behavioral inhibition might impair social cognition skills, but how much they could affect empathic abilities still remains an unsolved question. In this respect, several studies have demonstrated a significant positive correlation between empathic skills and executive functions in both healthy subjects [52] and clinical samples [7,53,54]. Interestingly, a recent meta-analysis on healthy individuals [52] revealed that

executive functioning, i.e., working memory, cognitive flexibility, and sustained attention, was more strongly related to CE; besides, AE was still closely related to inhibitory control. Conversely, Cristofani and colleagues [7] identified an opposite trend in ADHD patients and speculated that these subjects are somewhat constrained by their executive dysfunction in an underdeveloped empathic attitude, which would be limited to the expression of emotional contagion.

1.3. The Systematic Review

Recent literature has suggested that pharmacological interventions in ADHD patients may provide beneficial effects on social cognition deficits. Indeed, psychostimulants, including methylphenidate (MPH), and amphetamines, the gold-standard drug treatment for ADHD [55], have been likely associated with improvements in social judgment and interpersonal relationships [56,57], as well as in empathy and ToM in youths with ADHD [46,47,58–62]. Interestingly, MPH administration has been shown to promote empathy-like behaviors and sociability and reduce aggressiveness in a mouse model of callousness [63]. Moreover, it has been suggested that MPH treatment may possibly provide an improvement in emotion recognition [28,50]. Nonetheless, the evidence on the efficacy of psychostimulants on empathy and ToM, as well as on emotion recognition, is still under debate [64]. Thus, the aim of the present study was to systematically review the available literature on the topic in order to clarify whether the gold-standard drug treatment for ADHD may exert its effects on empathy and related constructs, through and beyond its well-known effects on the core symptoms of the disorder.

2. Materials and Methods

2.1. Search Strategy

The aim of the present study was to perform a systematic review of the literature on the effects of psychostimulants and nonstimulant drugs on empathy and related constructs in patients with ADHD. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines; the corresponding checklist is available in Supplementary Table S1. The protocol of the present systematic review was preregistered on PROSPERO (CRD42021247024). Three bibliographic databases were searched, namely PubMed, Scopus, and Web of Science, from the inception date to the 10 August 2021. A search strategy was developed including three groups of terms related to the following semantic fields: (1) ADHD; (2) Methylphenidate or other psychostimulants and nonstimulant drugs for ADHD; (3) Social Cognition, Empathy, Theory of Mind and Emotion Recognition. The full search strategy, along with the details of the bibliographic search, is available in Supplementary Table S2. The strategy was thus to include all relevant articles relating to Group 1 and Group 2 and Group 3; terms were consistently adapted for each database. Results of the bibliographic search were then downloaded into Mendeley software, and two authors (GS and PF) reviewed and discussed the scoping search which included both original studies and reviews. If a previous review was already available on the topic, its reference list was carefully searched to retrieve primary studies. Reference lists of the studies included in the final search were also thoroughly inspected to identify relevant citations.

2.2. Screening Procedure

Our search strategy was used to retrieve potentially relevant abstracts; duplicates from different bibliographic databases were initially removed, whereas additional records were identified through reference lists and the inspection of screened articles, as stated above, were also included. Two researchers (GS and PF) screened all titles and abstracts to identify relevant articles. Full texts of selected papers were then retrieved and carefully screened to finally identify the included studies according to eligibility criteria. Any disagreements were resolved by consensus. The PRISMA flowchart (Figure 1) shows the process of identification and selection of papers. Inclusion criteria were defined in order to retrieve

clinical studies aimed at assessing the effects of MPH and other psychostimulants and nonstimulant drugs on empathy, theory of mind, and emotion recognition in patients with ADHD, as follows:

(1) Study design: any type of clinical trial;
(2) Comparison: either case versus control, drug versus placebo or pre-to peri-/post-treatment;
(3) Participants: patients non-retrospectively diagnosed with ADHD according to the international classification systems DSM-IV, ICD-9, or later versions; no restriction for participants' age, gender, or IQ;
(4) Intervention: either one-day, single-dose administration or prolonged daily administration of psychostimulants (e.g., Methylphenidate) or nonstimulant drugs (e.g., Atomoxetine);
(5) Measures: any type of measurement (i.e., tasks, rating scales, and parent- or self-rated questionnaires) assessing empathy, theory of mind, and emotion recognition.

Exclusion criteria are detailed in Figure 1 and Supplementary Table S2. Briefly, in order of exclusion, they have been defined as follows: (1) Not clinical trial; (2) Absence of adequate comparison; (3) Subjects not diagnosed with ADHD; (4) Retrospective diagnosis of ADHD; (5) Clinical diagnosis not based on DSM-IV, ICD-9, or later versions; (6) Not intervention with psychostimulant/nonstimulant drugs; (7) Not assessment of empathy, theory of mind, and emotion recognition.

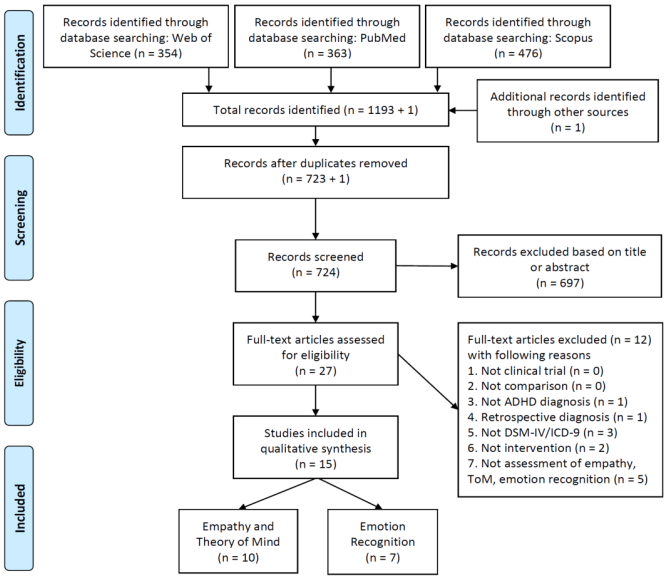

Figure 1. PRISMA flowchart showing the process of identification and selection of studies.

2.3. Data Collection

For each included study, we extracted relevant information, whenever available, including sample size, demographic data (age and gender), ADHD diagnosis and subtypes, intellectual functioning and psychiatric comorbidities, previous and current medication (including dosage and administration), follow-up duration, as well as information about the clinical measure used to assess changes in empathic competencies and related constructs and main findings of the study. When datasets were not fully available, authors of the included studies were contacted to attain the relevant data. Extracted information are available in Tables 1 and 2. Included studies were classified according to the examined construct as follows: (1) empathy and theory of mind and (2) emotion recognition. Emotion recognition is an underlying process related to the affective empathy, often investigated separately from the construct of empathy and theory of mind; for this reason, we decided to group studies into two classification types. Articles were also grouped according to the study design, either (1) single-dose administration of the drug with one-day follow-up or (2) daily administration of the medication with prolonged follow-up.

Table 1. Summary findings of the included studies: empathy and theory of mind.

Study	N	Gender	Age	ADHD	Comorbidity	Treatment	Assessment	Outcome
Coelho et al., 2017 [65]	60 ADHD (30 C, 30 I)	48/12	7–14 (unimodal group = 10.13) (multimodal group = 10.2)	no other medications when recruited	ID excluded	unimodal-medication only vs. multimodal medication + CBT for 20 weeks (prolonged release-MPH 20 mg)	Children's Social Skills Multimedia System	Multimodal treatment showed more improvement in frequency indicators on empathy.
Demirci and Erdogan, 2016 [58]	60 ADHD (21 C, 17 H/I, 22 I) 60 HCs	35/25 ADHD 35/25 HCs	8–15 (ADHD = 10.8) (HCs = 10.8)	drug-naive	ID, ASD, CD excluded	pharmacological treatment for 12 weeks: −38 OROS-MPH (final dose 1.2 mg/kg/day) −32 ATX (final dose 1.2 mg/kg/day)	RMET	The ADHD sample had significantly lower scores in RMET than HCs. ADHD-H/I had a lower number of correct answers in the RMET than ADHD-I. After OROS-MPH/ATX treatment, the ADHD sample showed a significant improvement in RMET.
Fantozzi et al., 2021 [62]	61 ADHD (50 C, 11 I)	51/10	6–17 (10.3)	drug-naive	ID, ASD excluded 14 SLD; 9 ODD; 4 MD; 2 LD; 1 AD; 1 tics; 1 dyspraxia	MPH treatment for 6 months (final dosage 31.6 ± 15.1 mg/day)	BES	Significant improvement in AE and CE. Changes in attention symptoms predicted changes in AE but not in CE.
Golubchik and Weizman, 2017 [59]	52 ADHD		8–18	psychostimulant-medication naive	ID, ASD, schizophrenia, bipolar disorder, suicidal ideation excluded 26 ODD	MPH treatment for 12 weeks (0.5–1 mg/kg/day)	EQ-C	Significant improvement in EQ scores in both groups (ADHD and ADHD/ODD). Only in the ADHD group, a significant correlation between changes in ADHD-RS and in EQ-C was found.
Golubchik and Weizman, 2019 [66]	25 ADHD	21/4	7–17 (10.8)		ID, ASD, psychosis, bipolar disorder excluded	single dose of MPH (1 mg/kg)	RMET	No improvement of RMET.
Gumustas et al., 2017 [60]	65 ADHD 61 HCs	53/12 ADHD 46/15 HCs	8–14 (ADHD = 10.86) (HCs = 11.21)	drug-naive	ID, ASD, psychosis, mood disorders, anxiety disorders, ODD excluded	OROS-MPH treatment for 12 weeks (0.83 ± 0.21 mg/kg/day)	BEI (trait empathy) GEM-PR (trait empathy) ERT (state empathy)	No significant statistical differences in trait and in state empathy skills in the two groups. Following the MPH treatment, the ADHD group showed a significant increase in the ERT (state empathy) interpretation sub-score.
Levi-Shachar et al., 2019 [61]	50 ADHD 40 HCs	28/22 ADHD 22/18 HCs	6–12 (ADHD = 9.42) (HCs = 8.95)	psychotropic medication free	psychosis, affective disorders, CD, substance abuse disorder excluded	single dose of short-acting MPH (0.3–0.5 mg/kg)	ToM test	The ADHD sample displayed significantly poorer ToM performance compared with HCs. Following MPH administration, the ToM performance of the ADHD sample normalized.

Table 1. *Cont.*

Study	N	Gender	Age	ADHD	Comorbidity	Treatment	Assessment	Outcome
Levi-Shachar et al., 2021 [67]	50 ADHD	28/22 ADHD	6–12 (ADHD = 9.42)	psychotropic medication free	psychosis, affective disorders, CD, substance abuse disorder excluded	single dose of short-acting MPH (0.3–0.5 mg/kg)	ToM test FPR	Negative association between severity of behavioral ADHD domains and impairment in ToM. Administration of MPH improved ToM performance, with the greatest improvement in children with more severe behavioral symptoms.
Maoz et al., 2013 [47]	24 ADHD (11 C, 13 I)	16/8	6–12 (10.2)		ID, psychosis, bipolar disorder, major depression, DBD, substance abuse disorder excluded	single-dose of long-acting MPH	IRI FRP TCT	Significant improvement in ToM performance.
Maoz et al., 2019 [46]	24 ADHD 36 HCs	6/8 ADHD 19/17 HCs	6–12 (ADHD = 10.29) (HCs = 9.37)	psychotropic medication free	ID, psychosis, bipolar disorder, major depression, CD, substance abuse disorder excluded	single dose of long-acting MPH	IRIFRP	The ADHD sample showed lower levels of self-reported empathy and FRP scores compared with HCs. In ADHD sample, MPH administration improved FRP scores to a level equal to that in HCs.

Abbreviations: AE, Affective Empathy; ADHD, Attention Deficit/Hyperactivity Disorder; ADHD-RS, Attention Deficit/Hyperactivity Disorder-Rating Scale; ASD, Autism Spectrum Disorder; ATX, Atomoxetine; BEI, Bryant Bryant Index of Empathy; BES, Basic Empathy Scale; C, Attention Deficit/Hyperactivity Disorder-Combined subtype; CE, Cognitive Empathy; CD, Conduct Disorder; EQ-C, Empathizing Quotient-Children's version; ERT, Empathy Response Task; FPR, Faux-Pas Recognition task; GEM-PR, Griffith Empathy Measurement-Parent Rating; H/I, Attention Deficit/Hyperactivity Disorder-Hyperactive/Impulsive subtype; HCs, Healthy Controls; I, Attention Deficit/Hyperactivity Disorder-Inattentive subtype; ID, Intellectual Disability; IRI, Interpersonal Reactivity Index; RMET, Reading the Mind in the Eyes Test; MPH, Methylphenidate; ODD, Oppositional Defiant Disorder; OROS-MPH, long acting-Methylphenidate; SLD, Specific Learning Disability; TCT, ToM Computerized Task; ToM, Theory of Mind.

Table 2. Summary details of the included studies: Emotion Recognition.

Study	N	Gender	Age	ADHD	Comorbidity	Treatment	Assessment	Outcome
Demrici and Erdogan, 2016 [58]	60 ADHD (21 C, 17 H/I, 22 I) 60 HCs	35/25 ADHD 35/25 HCs	8–15 years (ADHD = 10.8) (HCs = 10.8)	drug-naive	ID, ASD, CD excluded	pharmacological treatment for 12 weeks: −38 OROS-MPH (final dose 1.2 mg/kg/day) −32 ATX (final dose 1.2 mg/kg/day)	BFRT	ADHD sample had significantly lower scores in BFRT than HCs. ADHD-H/I had a lower number of correct answers in BRFT than ADHD-C and I. After OROS-MPH/ATX treatment, the ADHD sample showed a significant improvement in BFRT.
Gumustas et al., 2017a [60]	65 ADHD 61 HCs	53/12 ADHD 46/15 HCs	8–14 years (ADHD = 10.86)(HCs = 11.21)	drug-naive	ID, ASD, psychosis, mood disorders, anxiety disorders, ODD excluded	OROS-MPH treatment for 12 weeks (0.83 ± 0.21 mg/kg/day)	DANVA-2	No significant statistical differences in facial expression recognition skills in the two groups. Following the MPH treatment, the ADHD group showed a significant decrease in the recognition error of anger and sadness expressions.

Table 2. *Cont.*

Study	N	Gender	Age	ADHD	Comorbidity	Treatment	Assessment	Outcome
Hall et al., 1999 [68]	15 ADHD (13 C, 2 H/I) 15 ADHD/LD (14 C, 1 H/I) 15 no ADHD or LD	36/9	7–10 years	the ADHD sample was taken MPH (Ritalin) for at least a month at the time of the study	ID excluded	the DANVA was administered twice to each child in the ADHD and ADHD/LD groups: once while the ADHD and ADHD/LD participants were on medication and once off medication	DANVA SPBRS	The ADHD/LD group demonstrated significant difficulty in comparison to their peers in perceiving paralanguage cues effectively. The ADHD/LD group showed significant improvement on the Postures and Paralanguage subtests during on-medication conditions.
Schulz et al., 2018 [69]	25 ADHD (17C, 8I)	14/9	19–52 years (34.8 ± 9.8)	2 participants were on medication at intake, 9 had a history of previous stimulant treatment (2 of whom had also previously been treated with nonstimulant medication)	psychosis, BD, PTSD, substance use disorderexcluded	3 to 4 weeks of LDX (mean maintenance dose = 64 mg/day–SD = 13 mg) treatment and 3 weeks of medication in a randomized, counterbalanced, hybrid crossover design	participants were scanned twice with event-related fMRI while performing an emotional go/no-go task	No significant differences between the two treatment arms. LDX was associated with an increase in fMRI activation in the right amygdala and reduced interactions with the orbital aspect of the left inferior frontal gyrus specifically for responses to sad faces.
Schwenck et al., 2013 [70]	56 ADHD (10C,2H/I,44I) 28 ADHD-MD− 28 ADHD-MD+ 28 CG	19/9	8.2–17.3 years (MD− = 12.36) (MD+ = 12.31) (CG = 12.49)	47 children in the ADHD group were taken MPH at the time of the study (one child was additionally taken ATX), 6 drug-naive	ID, ASD, ODD, CD excluded	cross-sectional design study	MT	No differences found between ADHD-MD−, ADHD-MD+ and CG on emotion recognition.

Abbreviations: ADHD, Attention Deficit/Hyperactivity Disorder; ADHD-MED-, Attention Deficit/Hyperactivity Disorder no medication; ADHD-MED+, Attention Deficit/Hyperactivity Disorder with medication; ASD, Autism Spectrum Disorder; ATX, Atomoxetine; BD, Bipolar Disorder; BRFT, Breton Face Recognition Test; C, Attention Deficit/Hyperactivity Disorder-Combined subtype; CD, Conduct Disorder; CG, control group; DANVA, Diagnostic Analysis of Nonverbal Accuracy; ERP, event related potential; FEFA, Frankfurt Test and Training of Facial Affect; fMRI, functional magnetic resonance imaging; H/I, Attention Deficit/Hyperactivity Disorder-Hyperactive/Impulsive subtype; HCs, Healthy Controls; I, Attention Deficit/Hyperactivity Disorder-Inattentive subtype; ID, Intellectual Disability; LD, Learning Disability; LDX, lisdexamfetamine; MPH, Methylphenidate; MT, Morphing Task; ODD, Oppositional Defiant Disorder; OROS-MPH, long acting-Methylphenidate; PTSD, Post Traumatic Stress Disorder; SD, standard deviation; SPBRS, Social Perception Behavior Rating Scale.

3. Results

Details of the screening process and the identification and selection of papers are available in Figure 1, along with the main reasons for exclusion. In summary, 1193 abstracts were initially retrieved using our search strategy, plus one additional record identified in the reference lists of the studies included in the final search. After duplicates removal, 724 records were screened by two authors (G.S. and P.F.) and any disagreement was resolved by consensus. Twenty-seven full-text articles were carefully assessed for eligibility, of which 12 were excluded. Fifteen articles were finally included in our systematic review and were non-mutually subdivided into two partially overlapping groups as follows: (1) empathy and theory of mind (n = 10 studies); (2) emotion recognition (n = 7 studies).

3.1. Empathy and Theory of Mind

Ten studies [46,47,58–62,65–67] assessing the effects of MPH (either immediate-release or long-acting formulations) on empathy and ToM in young patients with ADHD were finally identified. One study [58] also assessed the effects of atomoxetine (ATX) treatment, while another one [65] compared unimodal (medication only) versus multimodal (medication plus cognitive behavioral therapy).

All studies were conducted on children and adolescents aged 6 to 18 years old. Diagnoses were based on DSM-IV or DSM-5 systems [2] and included different proportions of ADHD subtypes. Intelligence was on average, while other psychiatric comorbidities were excluded based on standardized criteria, except for the study by Fantozzi and colleagues [62], which also included patients with ADHD and comorbid with language disorders, verbal dyspraxia, Specific Learning Disabilities, tics, affective disorders, and behavioral disruptive disorders, and for the study by Golubchik and Weizman [59], which also included youths with ADHD and comorbid with ODD. Further details of the studies are reported in Table 1.

Five studies [46,47,61,66,67] examined the effect of a single-dose administration of MPH on children and adolescents with ADHD who were already regularly taking the medication at the time of the study. Particularly, one study [47] revealed an improvement in cognitive and affective ToM, as measured with two ToM tests, the Faux Pas Recognition task and the ToM Computerized task, in a group of young patients with ADHD after a single MPH dose administration. The same research group [46] later replicated their findings through a self-report measure, the Interpersonal Reactivity Index, and the Faux Pas test demonstrating that ADHD patients, who initially displayed significant deficits in empathy/ToM skills, improved their performances after a single dose of MPH until they matched their healthy peers.

A recent study [61] corroborated these findings by examining the effect of a single dose of MPH versus placebo on different ToM task performances in a group of children with ADHD versus healthy controls in a double-blind controlled trial. ToM abilities in ADHD children, while initially poorer, normalized only after MPH administration and differences between the two groups were no longer found. The same research group, analyzing later the same ADHD sample [67], found a correlation between the severity of the ADHD behavioral symptoms and deficits in ToM. The authors also found that the administration of a single dose of MPH improved ToM performance, especially in children with more severe behavioral symptoms. Conversely, another research group [66] revealed no significant single-dose MPH effects in children with ADHD on ToM performances, as measured through the commonly used Reading the Mind in the Eyes test.

Five additional studies [58–60,62,65] evaluated the effects of mid-term treatment with daily drug administrations in ADHD patients. Notably, all five studies agreed in demonstrating a significant improvement in empathy/ToM performance after drug treatment. Particularly, a significant increase in empathic abilities, as measured by the Empathizing Quotient, was shown after 12 weeks of daily treatment with MPH [59]; it should be noted, however, that half of the included patients were also diagnosed with comorbid ODD, which implied even lower baseline scores than the ADHD-only group. Though they

did not confirm such improvement in trait empathy by means of two paper-and-pencil questionnaires, the Bryant Index of Empathy and the Griffith Empathy Measure-Parent Rating, Gumustas and colleagues [60] found a significant increase in state empathic skills, as measured through the Empathy Response Task, after 12 weeks of MPH treatment in drug-naïve children and adolescents with ADHD. Recently, our research group [62] conducted a study on a sample of drug-naïve young patients with ADHD, naturalistically treated with MPH monotherapy and followed up for 6 months, who showed a significant improvement in AE and CE scores measured with the Basic Empathy Scale. The authors also found that changes in attention symptoms predicted changes in AE but not in CE.

Interestingly, a multimodal approach including drug treatment plus cognitive behavior therapy resulted in significantly greater improvements in frequency indicators on skillful reactions of empathy than the medication-only approach in ADHD patients [65]. Finally, ATX demonstrated a similar effectiveness on ToM skills, as measured with the Reading the Mind in the Eyes test, in a group of young drug-naive patients with ADHD, as compared with long-acting MPH administered for 12 weeks [58].

3.2. Emotion Recognition

Seven studies [31,50,58,60,68–70] assessing the effects of psychostimulants and non-stimulant drugs on emotion recognition abilities in individuals with ADHD were finally identified. Most of the studies were conducted on children and adolescents aged 7 to 17 years old, except for one study [69] that included adult patients. Diagnoses were based on DSM-IV and, in one case [31], on the ICD classification system, and included different proportions of ADHD subtypes; intelligence was generally on average, whereas other psychiatric comorbidities were excluded based on standardized criteria except for two studies [50,68] that included learning disabilities and internalizing disorders, respectively. Further details of the studies are reported in Table 2.

Two studies [31,68] examined the effect of a single-dose administration of MPH on children with ADHD who were already taking the medication regularly at the time of the study. Particularly, the former study [68] compared 30 ADHD patients with and without learning disabilities (LD) to 15 matched controls with no ADHD nor LD and found that, while at baseline only ADHD patients with comorbid LD demonstrated greater difficulties in perceiving paralanguage gesture cues than the other groups, as assessed through the Diagnostic Analysis of Nonverbal Accuracy test, the effect of medication was to equalize such differences. On the other hand, the latter study [31] revealed no significant medication effects on 21 children with ADHD on facial affect recognition abilities, neither with pictures of faces nor with eye pairs for any type of emotions, as assessed through the Frankfurt Test and Training of Social Affect.

Four studies [50,58,60,70] evaluated the effect of a mid-term treatment with daily administration of MPH. The oldest study [50] revealed significant improvements in fear and anger recognition in thirty-three patients with ADHD and comorbid anxiety and depression symptoms—either drug-naïve or under MPH treatment suspended at least three days before the testing session—after four weeks of daily treatment with MPH. Nonetheless, despite such improvements, ADHD patients still displayed deficits in emotion recognition abilities compared to healthy controls. Conversely, in a cross-sectional design study [70], the authors found no significant effects of MPH on emotion recognition reaction times and the number of correct answers in twenty-eight treated versus twenty-eight untreated ADHD patients compared to healthy controls, by means of a morphing task implemented from the Karolinska Directed Emotional Faces Set. The only difference approaching statistical significance concerned the number of sad faces mistaken as angry after MPH treatment.

Two more recent studies [58,60] compared a sample of more than 60 drug-naïve patients treated with MPH for 3 months to matched healthy controls and found significant improvements in emotion recognition abilities, as assessed through the Diagnostic Analysis of Nonverbal Accuracy (for sadness and anger only) and the Benton Face Recognition

tests, respectively. Interestingly, the former study [58] confirmed a similar trend also for ATX. Finally, only one study [69] assessed the effects of a 4-week treatment with lisdexamfetamine (LDX) versus placebo in 25 adult patients with ADHD on performances of a mixed task evaluating executive functioning and emotion recognition abilities (i.e., Face Emotion Go/No-Go Task). The authors revealed no significant differences between the two treatment arms; it should be noted, however, that some patients were previously treated with MPH suspended at least 2 weeks before the testing session.

4. Discussion

The present systematic review aimed to synthesize research findings on the effect of psychostimulants and nonstimulant drugs on social cognition in patients with ADHD. As far as we know, our study is the first review that systematically and specifically addressed this topic; former narrative but still comprehensive reviews [3,6] were respectively focused on social dysfunctions in ADHD, with the contribution of comorbid disruptive behavior disorders (i.e., ODD/CD) to social impairments, and on the link between social cognition deficits in ADHD and evidence from neuroimaging and lesion studies. Here, we complementarily aimed at looking for the available evidence from scientific literature on the impact of pharmacological interventions on empathy, theory of mind, and emotion recognition in ADHD. The research interest on such a topic is quite recent since the oldest studies retrieved through our search date back to 1999 for emotion recognition [68] and even later for empathy/ToM [47]. Unfortunately, for this reason, the number of studies dedicated to the assessment of social cognition in ADHD is still limited and even less on the effects of pharmacological treatment.

Most of the studies we identified through our search were conducted on children as expected, since ADHD is a neurodevelopmental condition with greater incidence in childhood [71] and social cognition deficits may become attenuated from adolescence on [53], while only one study was performed on adults [69]. Nonetheless, longitudinal studies are missing to investigate the developmental trajectories of social cognition skills from early childhood to adulthood, thus highlighting a still underexplored field of research on this topic. Study samples included, when clinical details were available, both Combined and Inattentive presentations of ADHD, whereas the Hyperactive/Impulsive type was typically underrepresented; in one study [68], a group of patients with ADHD and comorbid learning disabilities was compared to a pure ADHD group, while DBD and other comorbidities were generally excluded with some notable exceptions [31,50,59,62]. Most studies also included a comparison group variably consisting of healthy or clinical controls without ADHD.

As for the assessment of empathy and ToM, both paper-and-pencil questionnaires, including self (e.g., Basic Empathy Scale) and parent reports (e.g., Griffith Empathy Measurement), and standardized tests (e.g., Reading the Mind in the Eyes Test) were used. On the other hand, only standardized tasks were used instead to assess the emotion recognition abilities of participants (e.g., Diagnostic Analysis of Nonverbal Accuracy). Among the available treatment options for ADHD, most studies assessed the effect of psychostimulants, and first of all MPH, which represents the gold-standard pharmacological intervention for the disorder [55]. Schulz and colleagues [69], instead, evaluated the impact of LDX—an amphetamine derivative—while the study conducted by Demirci and Erdogan [58] was the only one that applied a selective noradrenaline reuptake inhibitor, namely ATX. Finally, Coelho and colleagues [65] assessed the efficacy of a multimodal treatment (medication plus cognitive-behavioral therapy) to investigate a possible additive effect of both types of intervention on social skills.

Study designs significantly varied across the included papers, most of which were based on longitudinal trials. Indeed, several studies assessed the effect of a mid-term treatment with MPH and/or other pharmacological and non-pharmacological interventions administered on a regular daily basis for 3–12 weeks to 4–6 months, typically in drug-naïve ADHD patients, except for a few samples including individuals previously exposed to

psychostimulants that were washed-out from 3 days to 1 month prior to testing. Some additional studies assessed the effects of a single-dose administration of MPH, either alone or versus placebo in drug-naïve ADHD patients or subjects that were already regularly taking drugs, whereas only one study [70] applied a cross-sectional design on drug-naïve ADHD patients versus MPH-treated ones.

Eight studies demonstrated significant improvements in empathy and/or ToM skills after a single-dose administration or prolonged treatment [46,47,58–62]. Interestingly, Coelho and colleagues [65] observed a significant effect of a multimodal treatment including medication combined with CBT on measures of social skills. Notably, the only study in which the authors did not find any significant improvement of ToM skills after a single-dose administration of MPH was the one by Golubchik and Weizman [66]. When compared to healthy controls, patients with ADHD displayed significantly lower baseline performances on empathy/ToM measures that greatly improved after pharmacological intervention until they reached those obtained by the comparison group [46,58,61]; interestingly, the greater baseline impairments were identified in Hyperactive/Impulsive and Combined types than in the Inattentive one.

As for emotion recognition abilities, most studies showed a significant improvement after the implementation of pharmacological treatment [50,58,60,68], while one study [31] found a non-significant improvement. Only two studies did not reveal a beneficial effect, though neither was it detrimental, of drugs on the emotion recognition skills in ADHD patients [69,70]; however, the former assessed the effects of LDX, which is not considered the first-line treatment option for the disorder, while the latter was based on a cross-sectional design. Interestingly, Gumustas and colleagues [60] revealed that, following the treatment with MPH, the ADHD group showed a significant improvement in the recognition of anger and sadness expressions. When compared to controls, patients with ADHD exhibited significantly lower baseline performances on emotion recognition that improved after pharmacological implementation until they reached those obtained by the comparison group.

Based on our review, we could speculate that, in patients with ADHD, drug treatment improves social cognition skills, namely emotion recognition, empathy and ToM abilities. Psychostimulant treatment has been also likely associated with a long-term improvement in prosocial behavior and other outcomes of social functioning [72], including social judgment and interpersonal relationships [56]. Empathy is a critical facilitator of prosocial behavior and is disrupted in ADHD patients, as previously reported in Section 1; however, the beneficial impact of pharmacological interventions on social cognition and functioning is likely to result from their effects on brain circuitries known to be involved in ADHD, possibly, but speculatively, not exhaustively mediated by the effects on the core symptoms of the disorder. In the subsequent paragraphs, we try to illustrate a theoretical framework linking psychostimulants mechanisms of action to social cognition outcomes in ADHD that could be hypothesized based on literature findings, which is depicted in Figure 2.

Structural and functional neuroimaging studies have documented abnormalities in brain anatomy and function in individuals with ADHD [73–75]. Meta-analyses of magnetic resonance imaging (MRI) studies show smaller volumes in the ADHD brain, most consistently in the basal ganglia [74,76]. Functional abnormalities are reported by a meta-analysis of 55 task-based functional MRI (fMRI) studies [73], reporting that children with ADHD show a hypoactivation in the fronto-parietal and ventral attentional networks, involved in attention and goal-directed behaviors, and a hyperactivation in the sensorimotor network and default-mode network, involved in lower-level cognitive processes [77]. In high-functioning, drug-naive young adults with ADHD, resting-state fMRI revealed altered connectivity in the orbitofrontal-temporal-occipital and frontal-amygdala-occipital networks, relating to inattentive and hyperactive/impulsive symptoms, respectively, compared with matched controls [78]. Structural MRI studies on children and adolescents with ADHD demonstrated that chronic naturalistic stimulant treatment was associated with attenuation of ADHD-related brain structural abnormalities, the more

consistent findings in frontal, striatal, cerebellar and corpus callosum regions [79]. In the review by Spencer et al. [79], analyzed fMRI studies revealed most consistent findings for striatum and anterior cingulate cortex. In the review by Faraone [78], the author reported that MPH treatment was associated with an increased activation of the parietal and prefrontal cortices and with an increased deactivation of the insula and posterior cingulate cortex during visual attention and working memory tasks. The same author indicated that MPH exposure altered connectivity strength across various cortical and subcortical networks.

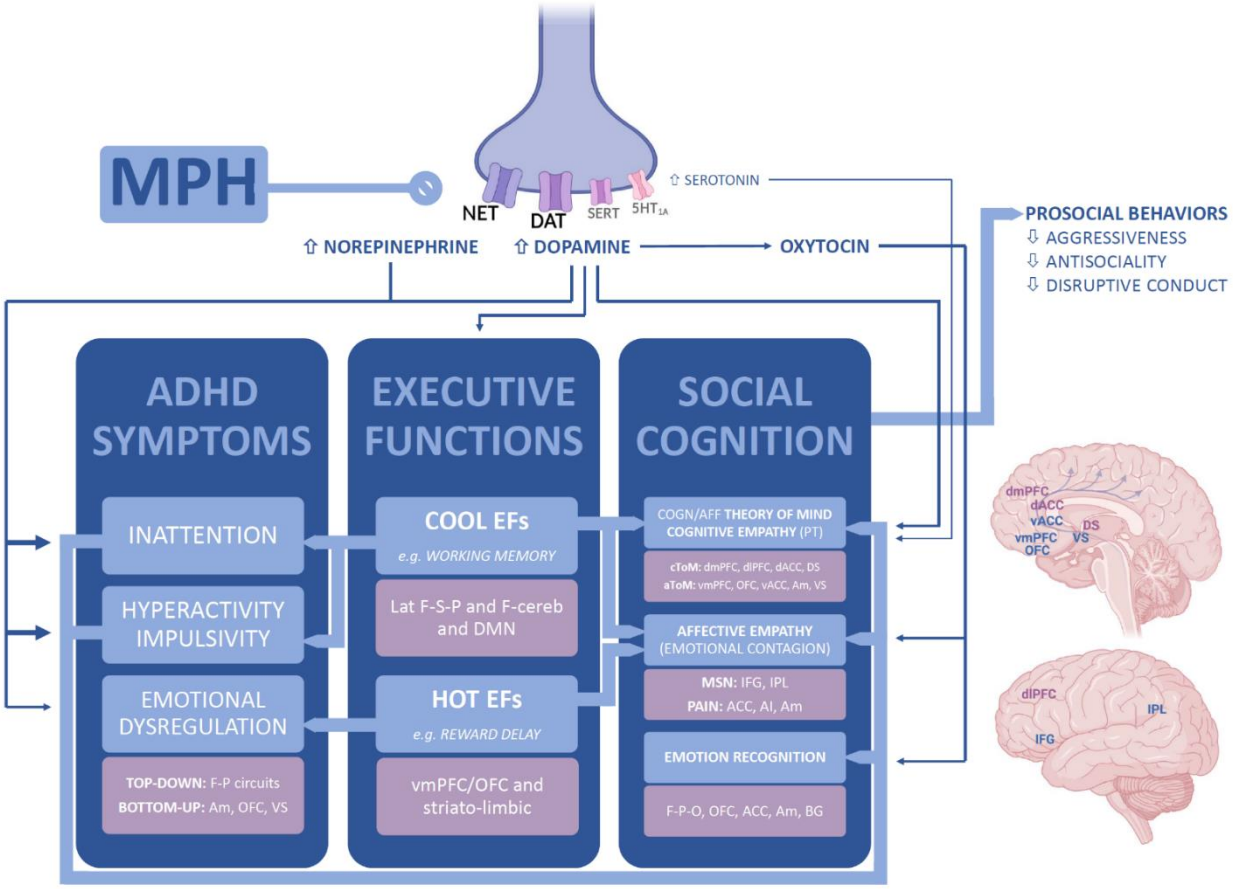

Figure 2. Proposed neurobiological pathways linking methylphenidate pharmacodynamic effects and changes in social cognition in patients with ADHD.

Interestingly, it has been suggested that the efficacy of psychostimulants on the core symptoms of the disorder—i.e., inattention, hyperactivity, and impulsivity—is due to the increased central dopaminergic and noradrenergic activity in the brain regions that include the cortex and the striatum, regions involved in the regulation of attentional and behavioral outcomes [80]. ADHD patients have, indeed, deficits in higher-level cognitive functions necessary for mature adult goal-directed behaviors, that is executive functioning (EF), which are known to be mediated by later developing fronto-striato-parietal and fronto-cerebellar networks [81]. The most consistent deficits are in the so-called "cool" EF, such as motor response inhibition, working memory, sustained attention, response variability, and cognitive switching [81–84], as well as in temporal processing (i.e., motor timing, time estimation, and temporal foresight), with the most consistent deficits in time discrimination and estimation tasks [85,86]. However, impairment has also been found in so-called "hot" EF of motivation control and reward-related decision making, as measured in temporal discounting and gambling tasks, albeit with more inconsistent findings [82,86–88].

Among these, emotion regulation (ER) is also known to be affected in ADHD patients. According to what Posner and colleagues [89] termed the "dyscontrol hypothesis", ER

deficits—or simply emotional dysregulation (ED)—in ADHD arise from impairments in hot EF. ED is an altered ability to modulate emotional states in an adaptive and goal-oriented way, with excitability, ease anger, and mood lability [90], which should be considered as pivotal components of ADHD [91]. More specifically, deficits in top-down inhibitory processes, which are found in a sizeable portion of individuals with ADHD, would lead to abnormal emotional reactions, whilst emotional processing per se would be largely normal. The concept proposed by Barkley of "deficient emotional self-regulation" should be considered within this model [92]. Alternatively, the affectivity hypothesis posits that emotional processing per se is abnormal, due to dysfunctions in bottom-up circuits, encompassing the amygdala, the orbitofrontal cortex, and the ventral striatum that processes emotional stimuli.

Interestingly, previous studies demonstrated a positive correlation between EF/ER and empathy/ToM competences in healthy subjects (for a recent review on the topic, please refer to [52]); inhibitory control, working memory, and cognitive flexibility were more strongly related to cognitive empathy, while only inhibitory control was closely related to the affective component. Conversely, a recent paper by our research group [7], which assessed the reciprocal relationship between empathic attitudes and executive functioning in ADHD patients with comorbid conditions, indicated that this latter was more strongly related to the affective empathy. Moreover, a recent meta-analysis [93] that examined the effects of MPH on executive functions in children, youths, and adults with ADHD found that the effects on response inhibition, working memory, and sustained attention were small to moderate. Thus, one may speculate that MPH has a positive effect on EF that, in turn, constitutes a possible mediator for the improvement of empathy and social abilities in youths with ADHD.

From a neuroanatomical point of view, strong evidence supports a model of two separate, yet interacting, systems for empathy, as previously mentioned in Section 1. AE would rely on a large brain network that includes the anterior cingulate cortex, anterior insula, inferior parietal lobule, and inferior frontal gyrus, with its mirror neuron system involved in motor imitation and emotional contagion [14,94]. On the other hand, CE/ToM is subserved by prefrontal and temporal networks: the cognitive ToM network engages the dorsomedial prefrontal cortex, dorsal anterior cingulate cortex, and dorsal striatum; the affective ToM network engages the ventromedial prefrontal cortex, orbitofrontal cortices, ventral anterior cingulate cortex, amygdala, and ventral striatum [94]. A functionally interactive dorsal and ventral attention/selection system at the temporoparietal junction and anterior cingulate cortex modulates the ability to distinguish between self and other mental states [24]. From a neurochemical point of view, AE is modulated in part by oxytocinergic projections [33], while, on the other hand, CE/ToM functioning is dependent on the integrity of the dopaminergic and serotoninergic systems [24].

Pharmacological treatments, especially with MPH, through a direct modulation of central dopaminergic and noradrenergic transmission in cortex and striatum, an indirect action on other neuropeptides such as oxytocin, and by regulating neural activity in these systems acting on top-down and only partly on bottom-up circuits [90], can concurrently improve empathy, theory of mind, executive and emotional regulation in youths with ADHD (see Figure 2). On the other hand, we may speculate that a possible mechanism explaining the social effect of psychostimulants in ADHD youths may be a positive effect of improved attention and EF on empathic abilities.

Little literature evidence is available to discern whether the impacts of stimulants on social cognition could be mediated by the complementary effects on the different core symptoms of ADHD, namely inattention and hyperactivity/impulsivity. Indeed, the studies conducted so far have not specifically addressed the effects of MPH on different ADHD subtypes, but it may be argued that different subtypes could present different empathy profiles. Children with a predominant Inattentive subtype are typically less aggressive and less likely to have comorbid ODD/CD than children with the combined or the Hyperactive/Impulsive subtype that seem to be less empathic than youths with the

inattentive one [46,58]. We could speculate that the Inattentive and Hyperactive/Impulsive profile lies intermediate between two extremes, the latter being substantially overlapping with that of ODD/CD. The very few fMRI studies that compared non-comorbid ADHD and ODD/CD children showed that ADHD is associated with dorsolateral prefrontal and inferior frontal under-activation, while ODD/CD was associated with paralimbic under-activation in orbitofrontal, limbic, and superior temporal regions [83,85,88].

Empathy deficits have been implicated in several neurodevelopmental disorders, among which ASD is the most studied [9,95]. Some authors have speculated that performances of individuals with ADHD on social cognition tasks lies intermediate between ASD and healthy controls [43]. Socioemotional problems in ADHD are associated with a more negative prognosis, notably interpersonal and educational problems and an increased risk of developing other psychiatric disorders, while on the other hand, attentional problems at a very early age have been supposed to precede the onset of clinical manifestations of ASD, ADHD, or both disorders [96]. In this perspective, the association between ASD and ADHD traits may be featured by shared attention-related problems (inattention and attentional switching capacity) and biological pathways involving attentional control may be a key factor in the overlapping conditions [97,98]. Future studies are welcome to explore the effects of MPH on empathy/ToM and emotion recognition also in patients with co-occurring ASD.

The current review indicates several limitations of the studies on this topic. First, the limited number of eligible studies. Second, the heterogeneity of the recruited samples and the study protocols (single dose of MPH versus mid-term treatment). Third, the use of self- and parent-rated measures of empathy, which should be integrated with experimental paradigms. In future investigations, empathy/ToM abilities and emotion recognition skills should be assessed in separate samples of ADHD patients including the Inattentive, Hyperactive/Impulsive, and Combined subtype carefully matched on age, gender and medication status. In addition, it would be interesting to investigate possible different responses on the bases of the comorbidity such as other neurodevelopmental disorders, specially ASD, or psychiatric comorbidity.

5. Conclusions

This review provides a contribution for a better understanding of the possible effects of the MPH. Some evidence support the notion that the timely and affective treatment of ADHD symptoms may have beneficial effects not only on core symptoms of ADHD, but also on the social difficulties of youths with ADHD. Future studies on the association of several measures of empathy with comorbid disorders, such as ASD and disruptive behavioral problems, are warranted. At the same time, future studies concerning gender effects are desirable. One important issue for future studies would be the question of whether empathy/Tom/emotion recognition impairments can be observed in all subtypes and, in this case, whether the underlying mechanisms are the same for ADHD subtypes.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/brainsci11111399/s1, Table S1: PRISMA checklist, Table S2: search strategy.

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Research paper

The assessment of cyclothymic-hypersensitive temperament in youth with mood disorders and attention deficit hyperactivity disorder

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ABSTRACT

Background: Cyclothymic-hypersensitive temperament (CHT) has been related to both depression and bipolarity, as well as to suicidality. Recently, a psychometrically sound way of assessment has been validated in youth (Cyclothymic-Hypersensitive Temperament Questionnaire, CHTQ), but data on clinical populations are still scant. Aim of our study is to further explore the structure and other psychometric properties of the revised version of CHTQ and its clinical implications in clinical samples.

Methods: The study is based on a dataset of patients with unipolar depression, bipolar disorder and attention deficit and hyperactivity disorder (ADHD) (243 patients, 135 males, mean age 14.22 ± 2.16 years, age range 9–18 years), compared to a community sample of adolescents (398 subjects, 95 boys, mean age 15.47 ± 1.96 years, age range 10–18 years)

Results: The two-correlated factor structure of CHT has been confirmed, with a moodiness/hypersensitiveness factor, correlated with internalizing symptoms, and an impulsiveness/emotional dysregulation factor, correlated with externalizing symptoms. All CHTQ scores correlate with global functioning. CHTQ total scores discriminate patients from healthy controls. Only CHTQ impulsiveness/emotional dysregulation subscale score is higher in bipolar patients, compared to unipolar depression and ADHD, whereas neither CHTQ moodiness/hypersensitiveness subscale score nor CHTQ total score discriminate between clinical groups.

Limitation: Data on current mood states are unavailable. Patients were recruited in a third level clinic. The unipolar depression group is relatively small.

Conclusion: CHT may be a rapid and reliable screening and diagnostic tool in the clinical practice with youth, exploring the cyclothymic dimension in different psychiatric disorders.

1. Introduction

Affective temperaments (i.e., depressive, hyperthymic, cyclothymic, irritable, and anxious) are possible precursors of mood disorders, and they can also affect the presentation of symptoms, the specific clinical phenotype, and the outcome (Akiskal and Pinto, 1999; Guerreiro et al., 2013; Rihmer et al., 2010; Parker et al., 2012). Among these, cyclothymic temperament has received the greatest attention. It is characterized by the highest level of emotional and behavioral instability and over-reactivity (Perugi and Akiskal, 2002), and it can be interpreted as a neurodevelopmental disorder of the affective domain (Perugi et al., 2015; Perugi et al., 2017). This neurodevelopmental approach overlaps cyclothymia, in the wide range from a temperamental disposition to a disorder, when expressed in his extreme form, to the concept of emotional dysregulation (Faraone et al., 2019; Cole et al., 2019; Perugi et al., 2017). Cyclothymic subjects display a wide range of psychopathological phenomena, in emotional, interpersonal and behavioral domains, that are difficult to catch within a DSM-based perspective. Mood swings from mild to moderate depressive symptoms to brief and often under-recognized, hypomanic phases; the affective state is

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extremely reactive to external stimuli, irritable and with deficient self-regulation; anxiety (mainly separation and panic) and low impulse control are both usual features; heightened interpersonal sensitivity is the typical interpersonal style (Sesso et al., 2021); self-harm, non-suicidal self-injuries and suicide attempt, as well as substance use and behavioral addictions, may occur later in life (Akiskal, 1995; Perugi et al., 2015; Perugi et al., 2017; Masi et al., 2018). These heterogeneous psychopathological manifestations lead some authors to extend its conceptualization in the more comprehensive construct of cyclothymic-hypersensitive temperament (CHT), which better accounts for the typical interpersonal style and the heightened reactivity to environment (Akiskal, 1995; Kochman et al., 2005; Van Meter et al., 2012; Pisano et al., 2020). Most studies come from adult literature on affective temperaments, while few of them are focused on youth population. Some of these found CHT to be linked to bipolarity and suicidality (Kochman et al., 2005), to non-suicidal self-injuries (Masi et al., 2018), and to externalizing and internalizing psychopathological symptoms (Pisano et al., 2020; Masi et al., 2021; Sesso et al., 2021). CHT traits were found to correlate with the three scores (total, mania and depression) of the Bipolar Prodrome Symptom Interview and Scale-Prospective (BPSS-P; Correll et al. 2014), developed to assess the prodromal symptoms of bipolar disorder in adolescents.

The paucity of studies on youths may be related to the uncertainty on the conceptualization of the cyclothymia construct in the developmental period, and the lack of a psychometrically sound assessment measure. The structure of the cyclothymic construct has been recently explored in the general youth population (Pisano et al., 2020), using the CHT questionnaire (CHTQ), a self-reported scale based on Temperament Evaluation in Memphis Pisa and San Diego (TEMPS) (for a review see Elias et al., 2017), adapted for youths from 7 to 18 years (Kochman et al., 2005). First, based on inspection of factor loadings of each item, a refined 22-items version of the scale was proposed. Second, based on explorative and confirmatory factor analyzes, a two-correlated factor structure which better fits the data was proposed, with one factor more related to externalizing symptoms (named impulsiveness/emotional dysregulation), and a second factor more related to internalizing symptoms (named moodiness/hypersensitiveness). Lastly, authors proposed a cut-off score for the total scale of 15 for females and of 17 for males that were associated with the likelihood of psychopathological symptoms of clinical relevance (Pisano et al., 2020). Despite this advance, several shortcomings still exist. The study was based on a single community sample of youths aged from 10 to 14 years; thus, results cannot be generalized to clinical samples and to youth in late adolescence. Furthermore, the study did not investigate clinical correlates, such as the related functional impairment.

Consequently, the present study aimed to replicate and extend previous findings by analysing new independent samples of older youths from both healthy and clinical populations. In the latter case, we used a large mood disorder sample, attending a third level clinical centre, as well as an ADHD sample. More specifically, the aims of the present study were: (a) to verify the replicability of the factorial structure and psychometric properties of CHTQ in 10 to18 year-old youth, hypothesizing the same two- factors structure (impulsiveness/emotional dysregulation and moodiness/hypersensitiveness factor) in both populations, and investigating if the scale was invariant and equally reliable across the two groups; (b) to further asses the criterion validity of the CHTQ scales. To this latter aim, as regards the total score, the correlations with psychopathological problems, measured by means of the Child Behavior Checklist (CBCL), and the global functioning, measured by means of the Children's Global Assessment Scale (CGAS), were investigated. We expected a positive correlation between CHTQ total score and CBCL total score, whereas a negative correlation between CHTQ total score and the CGAS total score. As regards the two factors scores, the correlations with the externalizing and internalizing problems dimensions of the CBCL were considered. We expected that the impulsiveness/emotional dysregulation factor would be more strongly correlated with the externalizing dimension than the internalizing one, with the opposite pattern of associations for the moodiness/hypersensitiveness factor. Moreover, to further evaluate the construct validity of the CHTQ, we investigated if the total score discriminates between patients and controls, or between the different clinical groups. As regard the former comparison, in line with a previous study (Correll et al., 2014), we expected that the mean CHTQ total score will be higher in the clinical group than in the control group. Regarding the possible differences among clinical groups, inconsistent findings are reported in the literature, and they do not allow for a-priorihypotheses. As cyclothymia refers to bipolar diathesis (Perugi and Akiskal, 2002; Kochman et al., 2005; Parker et al., 2012), and cyclothymic temperament was found to be one of the temperament present prior the first manic/hypomanic episodes (Zeschel et al., 2015), one could expect a higher CHTQ score in patients with bipolar spectrum compared to the other groups. Inconsistently, in a sample of youth, Correll et al. (2014) found no differences between clinical groups (Non-mood, Unipolar, Mood Not Otherwise Specified [NOS], Bipolar NOS and Bipolar I/II/cyclothymic).

2. Methods

2.1. Participants

The dataset of the present study is composed of three different and independent datasets, two clinical and one school based. The first one (Masi et al., 2018) consists of data gathered from a clinical sample of 89 adolescents with mood disorders (30 males and 59 females, age range 11.5–17.5 years, mean age 15.2 ± 1.5 years), including patients with both unipolar major depression (UMD, $n = 21$, 23.5%) and bipolar spectrum disorders (BSD, $n = 68$, 76.4%). The second (Masi et al., 2021) includes 167 patients (114 males and 53 females, age range 9–18 years, mean age 13.8 ± 2.3 years) with attention deficit hyperactivity disorder (ADHD, 72 subjects: 62 males and 10 females, mean age 10.9 ± 2.2 years), BSD ($n = 82$ subjects: 42 males and 40 females, mean age 14,3 ± 2.1 years), and unipolar depression ($n = 13$ subjects: 10 males and 3 females, mean age 13,4 ± 1.9). Both these clinical groups were recruited from a third-level Department of Child and Adolescent Psychiatry and Psychopharmacology, the first from December 2015 to December 2016 and the second from March 2017 to June 2020. All diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders – Fifth edition (DSM-5; APA, 2013), based on medical history, clinical observations, and the semi-structured interview Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL; Kaufman et al., 1997), administered by trained child psychiatrists to both patients and parents. Exclusion criteria for both clinical groups were as follows: older than 18 years old or younger than 9 years old; presence of comorbid intellectual disability, as detected through formal psychometric assessment (either the Full-Scale Intelligence Quotient or the General Ability Index below 85 at the Italian version of the Wechsler Intelligence Scale for Children-fourth edition, Wechsler, 2003); presence of comorbid Autism Spectrum Disorders, Schizophrenia Spectrum and other Psychotic Disorders. The third group was a healthy control (HC) group recruited on a voluntary basis upon engagement of a nearby Junior High School and included all adolescents without known psychiatric disorders and/or intellectual disabilities. Schools and research staff explained the aims and the procedures of the research. It consists in a range of questionnaires on which our research team is working, including CHTQ among others. After excluding subjects with missing data on CHTQ (2 patients in ADHD group, 1 in UMD, 10 in BD), the resulting dataset comprised 641 participants: the clinical group included 243 patients, (135 boys and 108 girls, mean age 14.22 ± 2.16 years, age range 9–18) distributed across three clinical groups (70 in the ADHD group, 33 in the group with Unipolar Depression, and 140 in the group with Bipolar Spectrum Disorder group). The control group included 398 subjects (95 boys and 303 girls, mean age 15.47 ± 1.96 years, age range 10–18). Demographic and clinical characteristics of the

four groups are reported in Table 1.

Regardless of the groups, all participants and parents were informed about assessment instruments, and participated voluntarily in the study after written informed consent was obtained for assessment procedures from parents of all subjects. The Regional Ethics Committee for Clinical Trials of Tuscany (section: Paediatric Ethics Committee at Meyer Children' Hospital of Florence) approved the study.

2.2. Measures

Cyclothymic-Hypersensitive Temperament Questionnaire (CHTQ). The Italian version of Cyclothymic-Hypersensitive Temperament scale for children/adolescents aged 7–18 years (Masi et al., 2018) is based on Akiskal's construct of cyclothymic temperament in adults (Akiskal and Mallaya, 1987) and on Temperament Evaluation of Memphis, Pisa, Paris, and San Diego questionnaire, Cyclothymic Subscale (TEMPS-A; Akiskal and Akiskal, 2005). The original version of CHTQ (Hantouche et al., 2001; Kochman et al., 2005) consists of 25 questions exploring the presence of temperamental characteristics of the patient, the presence of a possible emotional instability, and emotional predisposition associated with mood swings and impulsiveness (e.g. "I alternate between feeling low and high according to what is going on around me"; "I am sometimes bubbling with energy, and at other times sluggish"; "When watching a film, I often get overemotional"; "I can't help crying, being scared, or laughing"; "When I'm irritated, I can do stupid things I wouldn't have done otherwise"). For each item, the participants have to answer "yes'' or "no'', corresponding respectively to a score of 1 or 0. In this study, the 22-items version was used (Pisano et al., 2020), excluding three items (2, 8, 17) from the original version. The 22-item scale showed to measure two highly correlated factors (labelled impulsiveness/emotional dysregulation [I-ED] and a moodiness/hypersensitiveness [M-H] factor), that have good psychometric characteristics in terms of latent dimensionality, reliability (for the two subscales and for the total score) and measurement invariance (the scale was proven to provide full measurement invariance scores across age and classrooms factors). The English and Italian versions of the CHTQ are available in Supplementary Material 1.

Child Behavior Checklist – Parent Report Form (CBCL). The Italian version of CBCL-parent form is one of the most frequently used instruments for epidemiological and clinical studies with good psychometric properties (Achenbach, 1991; Frigerio, 1998). The scale is a standardized questionnaire, widely used in epidemiological and clinical studies, that assess behavior problems and competences of children aged 4–18 years. It consists of 118 items and is filled in by parents using a Likert type scale (0 = "not true"; 1 = "somewhat or sometimes true"; and 2 = "very or often true"). We here used the Total Problem Score, and two broad-band scores designated as Internalizing Problems and Externalizing Problems as external correlates of CHTQ total and subscale scores. CBCL was available for a subgroup of 192 patients.

Children's Global Assessment Scale (CGAS, Schaffer et al., 1983*)*, adapted from the Global Assessment Scale for adults, was used to assess global functioning in youth aged under 18 years old, with score between 1 and 100, based on a clinician's assessment of a range of aspects related to a child's psychological and social functioning. Ten categories range from 'extremely impaired' (1–10) to 'doing very well' (91–100). We have used the CGAS as external correlate of CHTQ total and subscale scores. CGAS was available for a subgroup of 184 patients.

Table 1
Demographic and clinical data ($N = 641$).

Statistics/Variables	ADHD	UMD	BSD	HC	*p*-value
N	70	33	140	398	–
Males, N (%) [a]	60 (85.7)	22 (66.7)	53 (37.9)	95 (23.9)	< 0.001
Age, M (SD) [b]	13 (2.3)	14.6 (1.8)	14.7 (1.9)	15.5 (1.9)	< 0.001
Comorbid ADHD, N (%) [a]	–	10 (29.4)	56 (37.5)	–	Ns
Other comorbidities, M (SD) [b]	0.77 (0.93)	2.14 (1.40)	2.22 (1.28)	–	< 0.001
Single AD, N (%) [a]	9 (12.86)	9 (27.27)	38 (27.14)	–	< 0.001
Multiple AD, N (%) [a]	7 (10.00)	12 (36.36)	49 (35.00)	–	
OCD and/or Tics, N (%) [a]	7 (10.00)	5 (15.15)	22 (15.71)	–	ns
ODD and/or CD, N (%) [a]	20 (28.57)	17 (51.52)	80 (57.14)	–	< 0.001
Eating Disorders, N (%) [a]	1 (1.43)	1 (3.03)	9 (6.43)	–	ns
Missing data					
CBCL, N (%) [a]	32 (45.70)	1 (3.03)	18 (12.86)	–	–
CGAS, N (%) [a]	19 (27.14)	4 (12.12)	36 (25.71)	–	–

Note. AD = Anxiety Disorder; ADHD = Attention Deficit and Hyperactivity Disorder; BSD = Bipolar Spectrum Disorder; CD = Conduct Disorder; HC = Healthy Controls; *M* = Mean; *N* = Number; OCD = Obsessive Compulsive Disorder; ODD = Oppositional Defiant Disorder; SD = Standard Deviation; UMD = Unipolar Mood Disorder. Demographic (number of subjects, age and gender) and clinical variables (comorbid ADHD and other psychiatric comorbidities) are compared across the four clinical groups. Data are presented either as [(a)] absolute number [N] (percentage [%]) for dichotomous variables or [(b)] mean [M] (standard deviation [SD]) for continuous variables; *p*-values refers to statistical analyzes as reported in detail in the main text (either χ^2 test or Fisher test for dichotomous variables, Analysis of Variance with Tukey's post-hoc test for continuous variables). *** *p*-values < 0.001. Tukey Post-Hoc comparisons for ANOVA: Age: ADHD < UMD ≈ BSD ≈ HC; Other Comorbidities: ADHD < UMD ≈ BSD.

2.3. Data analysis

The data analyzes were firstly carried out to describe the characteristics of the samples and then to investigate the factorial structure and the measurement invariance of the CHTQ, and the validity of CHTQ scores. Confirmatory factor analysis (CFA) and measurement invariance (MI) analysis were performed with LISREL 8.71 software. All the other analyzes were performed with R 4.0.2 software.

Clinical and Demographic Characteristics of the Sample. To compare clinical and demographic characteristics of the sample, the χ^2 test was used to detect significant differences (p-value < 0.05) for variables, such as gender and clinical comorbidities. When more than 20% of observations had expected frequencies less than 5, Fisher's exact test was performed. Analyzes of variance (ANOVA) was conducted to assess significant differences (p-value < 0.05) between clinical and demographic variables with continuous distribution. A Tukey post-hoc test was utilized whenever the ANOVA led to a statistically significant result to retrieve significant comparisons between variables.

Confirmatory factor analysis. To verify the replicability of the two-correlated factors structure (impulsiveness/emotional dysregulation and moodiness/hypersensitiveness factor; see Pisano et al., 2020) of the 22-item CHTQ in both considered samples (controls and patients), a robust confirmatory factor analysis was carried out on data collected for each sample. To assess the fit of the data to the model (Kline, 2011), the maximum likelihood chi-square test (*ML*χ2), the root mean square error of approximation index (*RMSEA*), the comparative fit index (*CFI*) and the non-normed fit index (*NNFI*) were used. For *ML*χ2 test values associated with $p > .05$ were considered well-fitting models; for the *RMSEA* index, values up to 0.08 or lower were considered indicating good fitting models; for the *CFI* and for the *NNFI* indices, values > 0.90 were considered as indicating adequate fit of the model to the data. Finally, the difference in *ML*χ^2 statistics (*ML*χ^2_{diff}), and *CFI* (*CFI*$_{\text{diff}}$) values were used to test the relative fit of nested models (Putnick and Bornstein, 2016).

Measurement invariance. Measurement invariance (MI) across groups

was verified. Invariance was analyzed according to the guidelines in the literature (Putnick and Bornstein, 2016). In particular, configural, metric, scalar, and residual invariance were tested by comparing covariance matrices computed as a function of the group: controls (n = 398) and patients (n = 243). The robust *ML* estimation method was used to estimate parameters, and the same goodness-of-fit statistics as in the *CFA* were considered to verify the invariance of the matrices.

Reliability. Reliability of the 22-item CHTQ was evaluated separately in each sample (controls and patients) by computing both Cronbach's alpha and omega (ω_t) for ordinal measures (Revelle and Condon, 2019).

Criterion validity. To evaluate the concurrent validity of the CHTQ scores, Pearson's correlation coefficients between the CHTQ scores and the criterion measure were computed. The CGAS and CBCL scores were considered as external criterions.

To explore the construct validity of the CHTQ by testing if the scores (M-H, I-ED and Total scores) discriminate between patients and controls, or between the different clinical groups, over and above gender and age differences, 2 between-subject *MANCOVA*s were carried out. The first to compare patients and controls (2-level), whereas the second analysis was carried out to compare the patients of the three clinical groups (3-level). In both analyzes the three CHTQ total scores were considered as the dependent variables, gender and age were included as covariate (control variables). The Sidak correction was used to analyze post hoc effects, and the magnitude of the significant effects was indicated by partial eta squared (η^2_p).

3. Results

Clinical and Demographic Characteristics of the Sample. Post-hoc comparisons are detailed in the table caption. As shown in the Table 1, the three clinical groups and the HC group significantly differed in terms of gender distribution ($p < .001$), with the ADHD (85.71%) and UMD (66.67%) groups exhibiting the greatest prevalence of males relative to the BSD (37.86%) and HC (23.87%) groups. Similarly, mean age differed across the four groups ($p < .001$), being ADHD (13.00 ± 2.27) patients significantly younger than UMD (14.64 ± 1.83), BSD (14.74 ± 1.94) and HC (15.47 ± 1.96). Comorbid ADHD was nearly equally represented in the two mood disorder groups ($p = .311$) being only slightly, but not significantly more represented in the BSD (37.5%) than the UMD (29.4%) group, whereas other associated psychiatric conditions were significantly more represented in the BSD and the UMD, than the ADHD group ($p < .001$). Specific clinical comorbidities, according to DSM-5, are listed in Table 1. Namely, both anxiety and disruptive behavior disorders were significantly more represented in the UMD and BSD groups than the ADHD ($p < .001$), while OCD/tics (p = .363) and eating disorders (p = .168) did not differ across clinical groups.

Confirmatory factor analysis. Results confirmed that the two-correlated factor model had adequate fit indices in both samples, *RMSEA* = 0.044, 90%*CI* [.036; 0.051], *CFI* = 0.982, $ML\chi^2$ (208, N = 398) = 1507.24, $p < .001$ and *RMSEA* = 0.027, 90%*CI* [.005; 0.039], *CFI* = 0.992, $ML\chi^2$ (208, N = 243) = 930.82, $p < .001$, respectively for the controls and the patients group. Parameter analysis showed that in both samples the two factors were strongly associated, $rs > 0.67$, supporting the notion that they can be considered as expressions of the same general dimension. The standardized factor loadings of the 22-item 2-factor model ranged from 0.15 to 0.82 for the impulsiveness/emotional dysregulation dimension, from 0.22 to 0.62 for the moodiness/hypersensitiveness dimension (see Table 2).

Measurement invariance. Measurement invariance analysis showed that the 22-item CHTQ is a fully invariant scale as a function of the population (see Table 3).

Reliability. The 22-item CHTQ showed good levels of internal consistency in both samples, as indicated by robust alpha and omega statistics computed for the impulsiveness/emotional dysregulation subscale, $\alpha s = 0.959$ and $\omega_t s = 0.876$, the moodiness/hypersensitiveness subscale, $\alpha = 0.959$ and $\omega_t = 0.969$, and the general dimension, $\alpha s = 0.959$ and $\omega_t s = 0.969$.

Table 2
Common metric standardized saturations of the 22-item CHTQ as a function of the factor (estimates come from the clinical and control groups merged).

	[a]Factor	
[§]Item	F1	F2
1. I often react intensely to minor upset	.583	
3. When I get upset, it's very hard for me to calm down	.686	
4. I have period of irritation during which I can lose control	.826	
5. I often experience intense emotions which I can feel all over my body (flushing, sweating, pounding heart)		.540
6. I experience all negative and positive emotions (both sadness or joy) more intensely than others		.644
7. When watching a film, I often get overemotional (I can't help crying, being scared, or laughing)		.300
9. My mood often changes without me knowing why		.660
10. Compared to my peers, when I get excited during the class recess, it is much harder for me to settle down upon return to the classroom	.412	
11. I am very excited during a video game, and it's very hard for me to calm down afterwards	.269	
12. I experience rapid shifts in mood and energy		.728
13. At times I have strong urge for risky or outrages behavior	.717	
14. When I'm irritated, I can do stupid things I wouldn't have done otherwise	.742	
15. I can feel depressed for a few days and then be in a good mood again		.662
16. After a big stressful situation it can take several days for me to recover my composure		.391
18. I often need to attract the attention of others to me	.159	
19. I am sometimes bubbling with energy, and at other times sluggish		.595
20. I know I have tendency to get worked up, or to lose my temper too quickly when I'm frustrated	.653	
21. I often experience severe, sudden emotions		.721
22. I can become strongly fond of a person I've just met		.223
23. Often I crave certain foods, cigarettes, alcohol or upper drugs	.369	
24. I often daydream about things people consider unrealizable		.455
25. I alternate between feeling overly confident and feeling unsure and self-critical		.696

Note. [§]Item number in the original 25-item CHTQ.
[a] F1: impulsiveness/emotional dysregulation; F2: moodiness/hypersensitiveness.

Criterion validity. The correlation analysis confirmed that the 22-item CHTQ score had adequate concurrent validity (Table 4). Indeed, as expected results showed that CHTQ total score had a positive and significant correlation with the CBCL total score, whereas a negative and significant correlation with the CGAS total score. Moreover, results showed that the impulsiveness/emotional dysregulation factor was correlated with the externalizing dimension but not with the internalizing one, whereas the opposite pattern of associations was observed for the moodiness/hypersensitiveness factor.

The 2-level between subject *MANCOVA* analysis comparing clinical and control groups showed a significant overall effect of the group on the CHTQ, Wilks' lambda = 0.916, $F(2636) = 29.04$, $p < .001$, multivariate $\eta^2_p = 0.084$. The follow up *ANOVA* showed that the effect was observed on all the CHTQ scores (see Table 5). Mean comparisons indicated that patients showed higher score than controls either on the two subscales or on the total score.

The 3-level between subject *MANCOVA* analysis comparing clinical and control groups showed a significant but small overall effect of the group on the CHTQ, Wilks' lambda = 0.955, $F(4474) = 2.77$, $p = .027$, multivariate $\eta^2_p = 0.023$. The follow up *ANOVA* showed that the effect was observed on the subscale Impulsiveness/Emotion dysregulation (see Table 6). Mean comparisons indicated that patients with BSD showed higher score than UNI, not significant were the differences between the ADHD and the other two groups.

Table 3
Invariance analysis of 22-item CHTQ as a function of the Group (Patients vs Controls): Multi-group hierarchical confirmatory factor analyzes goodness-of-fit indices (Patients $n = 243$; Controls $n = 398$).

Model	RMSEA	CFI	NNFI	MLχ^2	df	MLχ^2_{diff}	df_{diff}	CFI_{diff}	$RMSEA_{diff}$
Model A	.039	.985	.984	2438.06***	416	–	–	–	–
Model B	.039	.985	.984	2470.74***	436	32.68*	20[a]	0	0
Model C	.046	.977	.977	2730.75***	456	260.01***	20[b]	.008	.007
Model D	.045	.977	.978	2748.88***	478	14.13	22[c]	0	−0.001

Note. Controls = group including Healthy Controls (HC); Patients = group including the three clinical groups (ADHD, UMD and BSD). Model A: two-factor configural invariance (CI). Model B: two-factor CI and metric invariance (MI). Model C: two-factor CI, MI, and scalar invariance (SI). Model D: two-factor CI, MI, SI, and invariant uniquenesses (IU). [a]The reference model is Model A. [b]The reference model is Model B. [c]The reference model is Model C. *** $p < .001$ * $p < .05$.

Table 4
Correlations between Cyclothymic-Hypersensitive Temperament scores and the external criterions (CGAS and CBCL) in the patients group.

		CBCL		
CHTQ	CGAS	Total	Externalizing	Internalizing
Total	−0.306***[a]	.233***[b]	.166*[b]	160*[b]
Moodiness/ Hypersensitiveness	−0.280***[a]	.160*[b]	.054[b]	.172*[b]
Impulsiveness/ Emotional dysregulation	−0.244***[a]	.255***[b]	.254***[b]	.100[b]

Note. CHTQ = Cyclothymic-Hypersensitive Temperament Questionnaire; CGAS = Children's Global Assessment Scale; CBCL = Child Behavior Checklist (Parent Report Form).
[a] $n = 184$.
[b] $n = 192$; ***$p < .001$; *$p < .05$.

Table 5
Mean values and 95% Confidence Interval of Cyclothymic-Hypersensitive Temperament Questionnaire (CHTQ) scores as a function of the population (controls vs patients) and the scale.

	[4]Controls		[5]Patients	
CHTQ	M	95% CI	M	95% CI
[1] M-H	6.67	[6.39; 6.95]	7.60	[7.24; 7.97]
[2] I-ED	3.61	[3.37; 3.86]	5.22	[4.90; 5.54]
[3]Total score	10.28	[9.83; 10.73]	12.82	[12.24; 13.41]

Note.
[1] M-H = Moodiness/Hypersensitiveness subscale, $F(1637) = 14.95$, $p < .001$, $\eta^2_p = 0.023$.
[2] I-ED = Impulsiveness/Emotional Dysregulation subscale, $F(1637) = 58.16$, $p < .001$, $\eta^2_p = 0.084$.
[3] Total score, $F(1637) = 42.19$, $p < .001$, $\eta^2_p = 0.062$.
[4] Controls = group including Healthy Controls (HC; $n = 398$).
[5] Patients = group including the three clinical groups (ADHD, UMD and BSD; $n = 243$).

4. Discussion

In the present study we have initially explored the clinical significance of CHT. We firstly assessed the factor structure and psychometric properties of the CHTQ, previously explored in a community sample (Pisano et al., 2020), in a clinical sample of youth with ADHD and/or mood disorders, compared to healthy controls. Based on a confirmatory factor analysis, we were able to replicate a good fit of data for a two-factor structure of CHTQ, in both clinical and community samples. Consistently with a previous work (Pisano et al., 2020), the two factors, moodiness/hypersensitiveness and impulsiveness/emotion dysregulation, strongly correlated, supporting the notion that they are related dimensions of a same general "Cyclothymic" construct. Previous data on validity and reliability are confirmed in this study, replicating the same factor structure and other psychometric properties, resulting CHTQ fully invariant among samples and with good reliability indices. Taken together, these findings strongly support the use of CHTQ in a clinical context and in non-referred youth up to 18 years, underlining the conceptualization of cyclothymia as a multi-dimensional construct with at least two dimensions, that could refer to over-reactivity (Impulsiveness/Emotional dysregulation) and to mood instability (Moodiness/Hypersensitiveness) (see also Perugi et al., 2015). This may be particularly true and relevant in youth, given how intertwined may be emotional and behavioral symptoms, how unstable are the DSM-based disorders, and how undefined may be the borders between diagnosis (Ghazan-shahi et al., 2009; Perugi et al., 2017; Mc Elroy et al., 2018; Muratori et al., 2021).

Table 6
Mean values and 95% Confidence Interval of Cyclothymic-Hypersensitive Temperament Questionnaire (CHTQ) scores as a function of the clinical population (ADHD, UMD and BSD) and the scale.

	[4]ADHD		[5]UMD		[6]BSD	
CHTQ	M	95% CI	M	95% CI	M	95% CI
[1] M-H	6.47[a]	[5.79; 7.16]	7.14[a]	[6.23; 8.05]	7.24[a]	[6.78; 7.71]
[2]I-ED	4.63[a, b]	[4.03; 5.23]	4.37[a]	[3.57; 5.17]	5.50[b]	[5.09; 5.91]
[3]Total score	11.10[a]	[9.99; 12.21]	11.51[a]	[10.03; 12.99]	12.74[a]	[11.99; 13.50]

Note. Different letters indicate different means ($p < .05$).
[1] M-H = Moodiness/Hypersensitiveness subscale, $F(2238) = 1.56$, $p = .212$, $\eta^2_p = 0.013$.
[2] I-ED = Impulsiveness/Emotional Dysregulation subscale, $F(2238) = 4.28$, $p = .015$, $\eta^2_p = 0.035$.
[3] Total score, $F(2238) = 2.94$, $p = .055$, $\eta^2_p = 0.024$.
[4] ADHD = group including patients with Attention Deficit Hyperactivity Disorder ($n = 70$).
[5] UMD = group including patients with Unipolar Mood Disorder ($n = 33$).
[6] BSD = group including patients with Bipolar Spectrum Disorder ($n = 140$).

Another aim of the present study was to investigate the criterion validity of each CHTQ factors in a clinical sample. We found a clear pattern of correlations between the moodiness/hypersensitiveness factor with internalizing, but not externalizing symptoms of CBCL, as well as between the impulsiveness/emotion dysregulation factor and externalizing, but not externalizing symptoms CBCL Total problems score correlated with CHTQ Total. Similar findings were found using the internalizing and externalizing subscales of Strengths and Difficulties Questionnaire, with the limitation that both questionnaires are self-reported (Pisano et al., 2020). Here, we have replicated the findings using a multi-informant strategy and another widely used external criterion. This is crucial, as multi-informant assessment is usual in child and adolescent psychiatry and supports the validity of clinical information and research findings (for a review please see Martell et al., 2017). Interestingly, all CHTQ scores (total and subscales) also correlated with CGAS, a clinician-rated measure of functional impairment. This support the idea that the dimensions of CHT have relevant clinical implications, as they may be considered a marker of severity and alarm, and not only considered as a personality style (for a review see Parker

et al., 2012).

Further exploring the implications of CHTQ into a clinical context, we found that this instrument discriminates between clinical (as a whole) and community samples, as the likelihood of a clinical diagnosis is higher in those scoring higher in CHTQ. This is in line with Correll and colleagues (2014), who reported similar findings comparing healthy controls and youth with mood disorders. It should be noted that the mean of the total score of CHTQ in our community group is slightly higher than that reported by Correll and colleagues (2014), and much more similar to those reported in a previous study (Pisano et al., 2020). Sampling and cultural factors may account for this difference (e.g. the age range is clearly different).

More complex is the interpretation of the results on the comparison between diagnoses. According to the bidimensional conceptualization of CHT, we found a significant difference between diagnostic groups, as impulsiveness/emotional dysregulation factor is prevalent in bipolar youths rather than in other groups, whereas moodiness/hypersensitiveness is not. This is in line with previous studies conceptualizing impulsiveness as a state as well as a trait-like construct, and emotional dysregulation as core features of bipolar disorders (Swann et al., 2009; Marwaha et al., 2020; Masi et al., 2021). This may imply that a refined and more detailed measure of CHT is able to draw a more comprehensive picture of similarities and differences, in terms of components of temperament, among mood disorders.

On the contrary, the Total score of CHTQ was unable to discriminate among diagnoses, ADHD, Bipolar and Unipolar mood disorder. Correll et al. (2014) reported nearly identical findings. Similarly, ADHD and unipolar patients report a substantial level of CHT (Masi et al., 2018; Syrstad et al., 2020). On the other side, adult bipolar patients resulted to score higher in cyclothymic and hyperthymic temperament (Gassab et al., 2008). The issue remains to be resolved by further studies.

Our findings suggest that, although CHT have been traditionally associated to the bipolar spectrum, it may be better conceptualized as a trans-diagnostic dimension, not necessarily related to a specific disorder, associated with more severe impairment and with both externalizing and internalizing dimensions, probably linked to bipolarity via impulsiveness/emotional dysregulation.

Several limitations of our study have to be taken into account. First, the clinical sample is recruited from a third level clinic, and this may have selected more severe patients. Second, we did not systematically gather data on current mood states, especially for bipolar disorders, or treatments, either psychosocial or pharmacological, during the assessment, and this may have confounded the results. In this regard, CHT measures affective predisposition (e.g. traits) rather than current symptoms (e.g. states), and thus results can be reliable. Third, the samples size is relatively small, especially the unipolar depression group, and thus analyzes may not be enough powered, although sufficient to show significant effects that are also congruent with the hypotheses. Relatedly, clinical and control groups are not perfectly matched for age and gender, and thus future larger studies with better matched control group are needed. Fourth, we lack data on personality traits. It is known that cyclothymia shares features with borderline or other personality disorders (Van Meter et al., 2012); it may also represent the prodromal state for a subsequent, more evident, personality disorder. Whether or not CHTQ scores may be confounded by the presence of emerging borderline symptoms is still unknown, and future longitudinal studies are needed to explore this topic. Finally, as cyclothymia is a construct whose symptoms vary over time; again, a longitudinal study is needed to complete the description of its phenomenology as well as its stability.

Despite these relevant limitations, our data support the use of CHTQ as screening and diagnostic tool. The two-factorial structure is replicated in independent clinical and community samples, it is psychometrically sound, and it holds some relevant clinical meanings for the study of the bipolar diathesis in youths. Although to be empirically tested, CHTQ may be helpful in studying cyclothymic dimension in different disorders, beyond ADHD and mood disorders, including high-functioning autism spectrum disorders (Joshi et al., 2018), obsessive compulsive disorder (Hantouche et al., 2003), and disruptive behavior disorders (Tonacci et al., 2019). This approach, based on related reliable diagnostic instruments as CHTQ, may boost the research and the treatment of psychiatric patients with mixed emotional, interpersonal and behavioral symptoms that can be hardly included in specific DSM disorders.

Author agreement

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

CRediT authorship contribution statement

Simone Pisano: Resources, Data curation, Writing – original draft, Formal analysis. **Gianluca Sesso:** Resources, Data curation, Writing – original draft. **Vincenzo Paolo Senese:** Formal analysis, Writing – original draft. **Gennaro Catone:** Formal analysis, Writing – original draft. **Annarita Milone:** Resources, Data curation, Writing – original draft, Writing – review & editing, Supervision. **Gabriele Masi:** Writing – review & editing, Supervision.

Declaration of Competing Interest

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

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Supplementary materials

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La Cura della Lettura

Libri che divertono, che crescono, che curano: i servizi sanitari promuovono la lettura in famiglia.

Documenti di indirizzo e indicazioni operative per la promozione della lettura (età 0-6)

in Neonatologia e Terapia Intensiva Neonatale (TIN), in Oncoematologia pediatrica, nei disturbi del neurosviluppo e in modo integrato tra servizi sanitari, educativi, culturali e sociali.

Il progetto si realizza

a cura di

ACP Associazione Culturale Pediatri

in collaborazione con

Centro per la Salute del Bambino

Nati per Leggere

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LEGGIMI 0-6 Programma per la prima infanzia

I documenti di indirizzo e indicazioni operative sono stati realizzati a cura di

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INDICE:

Introduzione:

"Libri che divertono, che crescono, che curano: i servizi sanitari promuovono la lettura in famiglia" è il progetto proposto dall'Associazione Culturale Pediatri (ACP), sostenuto nel metodo e nell'organizzazione dal Centro per la Salute del Bambino (CSB), e approvato nell'ambito del bando CEPELL "Leggimi 0-6 2019" per la promozione della lettura nella prima infanzia.
Accanto a CSB sono partner nella realizzazione dell'iniziativa: ATS Brianza (Monza); Dipartimento Salute Provincia di Trento (Trento); Fondazione Pierfranco e Luisa Mariani (Milano); Oncoematologia Pediatrica P.O. Vito Fazzi ASL (Lecce); Oncoematologia Pediatrica IRCSS "Burlo Garofolo" (Trieste); TIN ASST Lecco (Lecco); TIN P. O. Melloni (Milano); TIN Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli" (Reggio Calabria); TIN Castellammare di Stabia, ASL Napoli 3 Sud (Castellammare di Stabia); TIN AOU Ospedale Civile Maggiore Borgo Trento di Verona (Verona); TIN SC Neonatologia dell'Università di Torino Città della Salute e della Scienza (Torino); Casa di Cura "Villa Immacolata" Provincia Romana O. CC. RR. Min. Inf. S. Martino al Cimino (Viterbo).

Oltre a rivolgersi realtà territoriali dove servizi educativi per l'infanzia 0-6 e biblioteche per bambini e ragazzi vanno implementati, il progetto si caratterizza per l'attenzione a tre gruppi di bambini in condizioni di vulnerabilità e con bisogni speciali: nati prematuri al di sotto delle 37 settimane di età gestazionale, bambini con malattia oncologica, bambini affetti da problemi di neurosviluppo. Nella convinzione che, quando i grandi leggono e (ri)leggono ai bambini, si crea una condizione di ascolto reciproco che diventa parte integrante del percorso di promozione dello sviluppo e di cura, offrendo anche la possibilità di immaginare un futuro diverso da quello insito in condizioni più impegnative in cui i bambini e le loro famiglie si vengono a trovare.

A partire da una attenta ricerca bibliografica (vedi evidenze scientifiche a pag.8) e organizzati in gruppi di lavoro dedicati, i partner coinvolti hanno elaborato specifici documenti di indirizzo e linee operative per la promozione della lettura 0-6 e per la loro applicazione in contesti definiti; sono stati proposti percorsi FAD e materiali formativi per gli operatori sanitari operanti nei diversi contesti coinvolti nel progetto (formazione effettuata nei mesi di ottobre e novembre 2021); sono stati predisposti angoli di lettura dedicati e attrezzati presso i servizi territoriali, gli ambulatori, le sale di attesa e i reparti ospedalieri. La scelta di libri più appropriati, raccolti in una bibliografia curata espressamente per i bambini in condizioni di particolare bisogno e vulnerabilità e per le loro famiglie è un'altra delle azioni qualificanti nell'ambito della rete che si intende attivare. Il documentario "La Cura della lettura" e alcuni video teaser realizzati nell'ambito del progetto rimandano alla concreta possibilità di realizzare il programma "Nati per Leggere" e alle conseguenti positive ricadute in situazioni di particolare fragilità.

È da segnalare anche che i materiali del progetto sono stati caratterizzati da un logo apposito.

Il documento di indirizzo e indicazioni operative per la promozione della lettura condivisa in Neonatologia e in Terapia Intensiva Neonatale è stato redatto intorno alla considerazione che i neonati pretermine sono particolarmente a rischio per i disturbi del linguaggio. La brevità dell'esposizione temporale in utero al linguaggio umano, lo stressante ambiente uditivo in TIN, la riduzione del linguaggio diretto al neonato, sia in termini quantitativi, sia per una alterata modalità di messaggi verbali a minor contenuto relazionale, dovuta alla rotazione degli operatori-caregivers del reparto, rispetto ai neonati accuditi in ambiente famigliare sono indicati come i principali fattori condizionanti il rischio. Come anche documentato dalla ricca bibliografia che accompagna il testo, la lettura condivisa ad alta voce, nel rispetto dei segnali comportamentali del neonato, si rivela una sicura strategia di intervento linguistico e per lo sviluppo neurocomportamentale nel bambino nato pretermine.
Il documento insiste sulle indicazioni precoci e continuative ai genitori, durante la degenza in reparto, e anche a casa, dopo le dimissioni: lo sviluppo del linguaggio e poi delle competenze per la lettura è sostenuto da esperienze ambientali favorenti, dalla frequente lettura interattiva in famiglia e da una buona disponibilità di libri.

I benefici possibili della lettura in ambiente ospedaliero, e più specificamente in oncoematologia pediatrica sono illustrati nel **documento di indirizzo e indicazioni operative per la promozione della lettura condivisa in oncoematologia pediatrica.**
Buoni risultati nella limitazione e nella cura dell'ansia nei bambini oncologici, sulla percezione del proprio funzionamento interpersonale, sulla sintomatologia depressiva, sull'adattamento alle cure e lo sviluppo di nuove strategie di coping, sono stati riportati in letteratura riguardo bambini ospedalizzati e in cura per malattia oncologica.
Viene ricordato anche che i libri, la lettura e il commento insieme agli adulti, agli operatori, ai genitori e anche tra pari, agiscono in maniera sensibile nel contrastare i possibili vissuti di solitudine e abbandono e la sintomatologia ansioso-depressiva ascrivibili al ruolo improvvisamente subordinato che sono costretti a vivere in conseguenza della malattia del familiare.
Nel documento vengono citate le esperienze di promozione della lettura già in atto in Italia nei centri AIEOP dotati di angoli lettura e vere e proprie biblioteche di reparto, dedicate ai ragazzi ma aperte anche alla lettura dei genitori e dei caregivers in generale.
Per quanto riguarda le esperienze svolte all'estero, è stata rintracciata una buona quantità di articoli scientifici inerenti ricerche svolte in setting ospedalieri che confermano i buoni risultati della biblioterapia in ospedale.

Il documento di indirizzo e indicazioni operative per la promozione della lettura condivisa nei disturbi del neurosviluppo rimanda sin dall'inizio a una revisione sistematica Cochrane condotta nel 2019 che ha analizzato le abilità di lettura in bambini e adolescenti con disabilità intellettiva (DI).
Per molto tempo si è creduto che bambini con DI non potessero imparare a leggere, e che quindi la lettura non fosse per loro appropriata. Le prospettive di arricchimento intellettivo e sociale in presenza di disturbi del neurosviluppo sono in seguito drasticamente cambiate, con la proposta di percorsi di istruzione formale alla lettura in bambini con disabilità intellettiva, simile a quella data ai pari, fino a pochi anni fa ritenuta inefficace.
Il documento sottolinea anche il supporto della tecnologia che ha portato grandi vantaggi nell'accesso alle risorse librarie: gli audiolibri, gli inbook, i lettori mp3, le applicazioni per smartphone e tablet hanno permesso di trovare e ritrovare il piacere della lettura a chi presenta deficit visivi, disabilità cognitive, disturbi del linguaggio o dell'apprendimento, quadri di funzionamento atipico.
Viene citata in particolare l'importanza della Comunicazione Aumentativa (CAA) come base per lo sviluppo di una lingua vera e propria per accedere ai libri anche in presenza di vulnerabilità e bisogni speciali.

Nelle indicazioni operative il documento propone una attenzione specifica al bambino straniero con difficoltà nell'area comunicativo-linguistica. Le modalità condivise di lettura possono facilitare in questi casi anche i genitori nell'acquisizione di più competenze lessicali e morfosintattiche, queste ultime tipicamente più ridotte in chi apprende una seconda lingua da adulto.

Il documento di indirizzo e indicazioni operative per la promozione della lettura condivisa 0-6 in modo integrato tra servizi sanitari, educativi, culturali e sociali sottolinea e illustra, come presupposti fondamentali e qualsiasi sia la tipologia di interventi da mettere in atto, alcuni elementi di carattere generale: equità, centralità del bambino e della famiglia, intersettorialità, metodo di lavoro, sostenibilità, efficacia, valutazione di impatto.
Facendo riferimento a iniziative già realizzate nelle provincie di Trento e Monza Brianza, vengono presentati brevemente, e a titolo di esempio, alcuni progetti di promozione della lettura 0-6 che vedono sviluppata la rete territoriale e che interessano i servizi educativi per la prima infanzia, i reparti ospedalieri di neonatologia e pediatria, i consultori, i centri vaccinali, i pediatri di famiglia, le biblioteche, i musei, le associazioni del terzo settore, i comuni, le istituzioni e altri servizi dedicati alle famiglie.
Sono azioni/modalità di lavoro ritenute efficaci per promuovere e sostenere la pratica della lettura precoce in famiglia in un territorio definito, sviluppando la rete e l'integrazione tra i servizi: la definizione dei ruoli, l'analisi del contesto territoriale di riferimento e delle attività che sono già in essere, la creazione di un gruppo di lavoro intersettoriale, la definizione del progetto, l'organizzazione di un "evento lancio" del progetto rivolto agli operatori e alla comunità, il supporto alle attività previste dal progetto (incontri operativi nei territori insieme alle diverse realtà coinvolte (sanitaria, educativa, sociale…), la rilevazione delle conoscenze/competenze in essere nelle diverse realtà interessate dal progetto, il monitoraggio dello stato di avanzamento del progetto.

Il percorso progettuale che ha portato alla stesura dei documenti di indirizzo si è avvalso, da subito, di un lavoro qualificato e collaborativo da parte di tutti i partner coinvolti, con le società scientifiche di riferimento, con operatori dell'ambito socio-sanitario, culturale ed educativo attivi in contesti diversi e portatori di uno sguardo allargato, che è alla base di interventi di promozione efficaci per la salute del bambino e della sua famiglia.

Federica Zanetto, presidente ACP

LE PIÙ RECENTI EVIDENZE SUI BENEFICI DELLA LETTURA CONDIVISA IN FAMIGLIA

Le evidenze scientifiche sui benefici della lettura condivisa e sui meccanismi attraverso i quali si producono si sono ulteriormente arricchite negli ultimi anni.
Riportiamo in queste righe un breve estratto preso dal rapporto dei vent'anni di Nati per Leggere in cui mettiamo in evidenza le più recenti ricerche sui benefici della lettura in età 0-6.

La lettura condivisa è ormai da tempo parte delle raccomandazioni formulate da agenzie internazionali e da gruppi professionali sui consigli da dare ai genitori per favorire lo sviluppo precoce del bambino (WHO, Unicef 2012; Walker 2015; Black 2017; Needlman 2017; Shonkoff 2010; Richter 2017).
La ricerca ha innanzitutto consolidato, grazie ad approcci sistematici, le evidenze sui benefici cognitivi, sullo sviluppo del linguaggio, in particolare quello recettivo (cioè la comprensione) che è ciò che per altro più incide sulle performance una volta che i bambini sono a scuola (Law 2019; Dowdall 2019).
Questo comporta un vantaggio quantificabile in 6-12 mesi nelle abilità di lettura e scrittura rispetto ai bambini di pari estrazione sociale che non hanno questa opportunità (Dowdall 2019). L'analisi di dati raccolti in ben 35 paesi e 100.000 bambini ai fini del sistema Unicef di valutazione della salute e dello sviluppo del bambino nei primi anni, ha evidenziato che i bambini che hanno almeno un libro in casa hanno quasi il doppio di probabilità di avere competenze di *literacy* e *numeracy* adeguate all'età (Manu 2019). Grazie anche alle nuove tecnologie di immagine, abbiamo compreso meglio i meccanismi attraverso i quali la lettura condivisa iniziata in età molto precoce e effettuata in famiglia, produce i suoi effetti sulle reti neurali che sostengono le diverse competenze e funzioni cognitive (Hutton 2015). Effetti benefici sono stati dimostrati sull'attenzione sostenuta (Vally 2014), aspetto importante se si considera che i bambini di oggi, al di là di specifici disturbi dello sviluppo quali l'ADHD, tendono ad avere crescenti difficolta nell'attenzione sostenuta, verosimilmente per l'eccesso di stimoli contemporanei che ne disturba la concentrazione. L'esercizio alla narrazione di storie in età precoce, in particolare con modalità dialogica, quindi con domande, sottolineature, tempi e spazi per l'intervento del bambino, può dunque facilitare l'attivazione dei circuiti neurali che controllano le competenze cognitive essenziali per la comprensione narrativa, tra le quali vi sono funzioni esecutive fondamentali quali l'attenzione, la pianificazione, il controllo dell'esecuzione, la flessibilità nella scelta delle strategie, la velocità di processamento e la memoria di lavoro.
Molto importanti sono inoltre i risultati di studi (più difficili da realizzare) che misurano i benefici sull'interazione madre-bambino, sul miglioramento del senso di autoefficacia delle madri (i padri sono stati fino ad oggi ben poco studiati) evidente anche quando questi ultimi sono in situazioni di difficolta o soffrono di depressione, e sullo stesso stato socio-emotivo del bambino (Albarran 2014; Murray 2016; Jimenez 2019; Mendelsohn 2018).
Gran parte degli studi più recenti confermano inoltre che sia i benefici sul piano cognitivo che quelli sul piano socio-relazionale sono sempre maggiori in bambini e genitori di stato socio-economico e culturale basso, venendo quindi a svolgere un effetto di contrasto all'insorgere precoce delle diseguaglianze.
La tabella che riportiamo qui di seguito riassume brevemente le evidenze forti disponibili sui benefici della lettura condivisa in età precoce.

Per il bambino	Per i genitori	Per entrambi e per le comunità
Cognitivi: linguaggio recettivo, espressivo, literacy e numeracy, attenzione sostenuta e altre funzioni cognitive superiori. **Socio-relazionali**: benessere socio-emotivo	Responsività, senso di autoefficacia e di competenza genitoriale	Contrasto all'insorgere precoce delle diseguaglianze

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La Cura della Lettura

Documento di indirizzo e indicazioni operative per la promozione della lettura condivisa in **Neonatologia e in Terapia Intensiva Neonatale (TIN)**

La mente è una sola. La sua creatività va coltivata in tutte le direzioni.

(Gianni Rodari)

I libri erano qualcosa di speciale, qualcosa di davvero speciale.
Leggevo molte pagine ad alta voce e mi piaceva il suono delle parole, il loro linguaggio.

(Bob Dylan)

La voce della vita in me non può raggiungere l'orecchio della vita in te;
parliamoci, tuttavia, per non sentirci soli.

(Kahlil Gibran)

Il documento è stato approvato dalla Società italiana di Medicina Perinatale (SIMP), dal gruppo Care SIN, Associazione Vivere ONLUS, SIN

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Introduzione:

I nati pretermine sono a rischio di neurosviluppo atipico, non solo per gli aspetti motori e sensoriali, ma anche per quelli cognitivi, comportamentali e sociali. Tale rischio è tanto maggiore quanto più il neonato è pretermine (in particolare se < 32 settimane di età gestazionale), ma numericamente la quota maggiore di neonati pretermine (circa il 75%) è rappresentata dai late-preterm (tra 34 e 36 settimane di età gestazionale).
Alla base delle anomalie del neurosviluppo sta la bassa età gestazionale di per sé, ma vi contribuiscono anche fattori ambientali e relazionali. È ben noto, infatti, come l'esposizione precoce all'ambiente extrauterino, le procedure stressanti e dolorose e la separazione dalla madre, impattino fortemente sulla maturazione cerebrale. In questo periodo di elevata vulnerabilità cerebrale, la ***developmental care***, personalizzata e centrata sulla famiglia ha come scopo cardine la neuroprotezione del cervello non solo mediante la riduzione dello stress del piccolo, ma soprattutto promuovendo il suo sviluppo e la relazione con i genitori. Nello specifico, è stato dimostrato che i neonati pretermine sono particolarmente **a rischio per i disturbi del linguaggio**. Ciò è dovuto alla brevità dell'esposizione temporale in utero al linguaggio umano e ad un inadeguato e stressante ambiente uditivo in TIN; inoltre, si verifica una **riduzione del linguaggio diretto** al neonato, sia in termini quantitativi, sia per una alterata modalità di messaggi verbali a minor contenuto relazionale, determinata dalla rotazione degli operatori-caregivers del reparto, rispetto ai neonati accuditi in ambiente famigliare.
Questi elementi sono di fondamentale rilevanza per lo sviluppo della parola e delle prime attitudini necessarie per sviluppare a distanza le abilità di lettura e non solo; vengono di conseguenza coinvolte le abilità attentive e cognitive.
Per limitare le distorsioni nello sviluppo neurocomportamentale nei bambini ricoverati in TIN è quindi **cruciale sia ridurre il rumore eccessivo ambientale, sia aumentare l'esposizione a suoni dotati di significato** e specificatamente **rivolti al piccolo, nel rispetto dei suoi segnali comportamentali**. (Filippa 2017)

I RISCHI DEL NEONATO PRETERMINE PER I DISTURBI DELL'UDITO E I RITARDI DEL LINGUAGGIO (ROR. 2021)

I bambini pretermine sono soggetti particolarmente a rischio per i disturbi dell'udito e per i deficit e/o ritardi di sviluppo del linguaggio (Lahav 2014; Lasky 2009; McMahon 2012; Hall 2000), in quanto:

- il funzionamento del sistema uditivo inizia precocemente, come dimostrato dalle reazioni vegetative e motorie al suono registrate da esperimenti in utero, presenti fin dalle 23-24 settimane gestazionali; si verifica quindi un continuo abbassamento della soglia uditiva con il procedere della maturazione fetale, con una progressiva capacità di discriminazione tonale a partire dalle 30 settimane.

- Il neonato, quindi, è presto in grado di distinguere, attraverso l'intonazione e la prosodia, la voce materna: un canale privilegiato di relazione che viene bruscamente interrotto dalla nascita pretermine, da ripristinare precocemente per limitare il disorientamento da input ambientali eccessivi e caotici.

- L'eccessiva stimolazione uditiva è inoltre potenziata da una scarsa modulazione dei sistemi efferenti inibitori, che maturano successivamente a quelli afferenti eccitatori, e che aggravano la sospensione della funzione di filtro esercitata dal grembo materno.

- Il neonato pretermine passa dall'ambiente uterino, in cui è esposto a suoni a bassa frequenza/vocalizzazioni trasmessi attraverso il mezzo fluido e attenuati dal tessuto materno, a quello della **TIN**, caratterizzato da **suoni ad alta frequenza**, **intensi** e **non attenuati**, che **raramente** si mantengono costantemente **sotto ai 45 dB** (livelli di 60-80 dB possono interferire con lo sviluppo dell'udito);
- alcuni studi suggeriscono che, a causa del rumore dato dalla commistione di voci umane e di rumori elettronici dell'ambiente, **solo il 2-5% dei suoni presenti in TIN** corrispondono a **linguaggio identificabile** dal neonato, per di più in genere **non diretto** specificatamente a lui.

I BENEFICI DELLA LETTURA IN NEONATOLOGIA E IN TERAPIA INTENSIVA NEONATALE

Gli studi che evidenziano l'importanza dell'esposizione al linguaggio diretto al neonato (Caskey, 2011; Caskey 2014; Ferjan Ramírez 2019; Ferjan Ramírez 2020; Provenzi 2018; Scala 2018; Saliba 2018) dimostrano che:

- l'esposizione alle parole umane in TIN:
  - **aumenta i vocalizzi** e pertanto una presenza genitoriale più assidua è associata ad una maggior vocalizzazione neonatale (i neonati iniziano ad emettere suoni **già a partire dalla 32ª settimana** di gestazione)
  - **aumenta la stabilità neurovegetativa neonatale** in termini di frequenza cardiaca e respiratoria, saturazione d'ossigeno; sono segnalati inoltre miglioramenti della tolleranza alimentare
- la voce genitoriale consente ai nati pretermine di sviluppare più rapidamente il linguaggio:
  - il **numero di parole/ora** udite alla **32ª e 36ª settimana** di età gestazionale corretta correla positivamente con gli **score Bayley III di sviluppo del linguaggio a 7 e 18 mesi di vita**;
  - con l'uso del "**maternese**" (diverso dalla conversazione tra adulti per la differente intonazione, prosodia e pronuncia delle vocali), i bambini mostrano un **aumento dell'attitudine a parlare e un miglioramento dello sviluppo del linguaggio**.

La **lettura ad alta voce** si rivela quindi una **sicura strategia di intervento linguistico in Neonatologia e in TIN** (Filippa 2017; Filippa 2020; Filippa 2021; Lester 2014). Pertanto, l'indicazione ai genitori sull'importanza di parlare con il loro neonato, **nel rispetto dei suoi segnali comportamentali**, dovrebbe essere fornita precocemente e continuativamente durante la degenza in reparto, e proseguire a casa.

PROPOSTA DI INDICAZIONI OPERATIVE

Come iniziare e sostenere il programma di lettura in TIN e in generale ai neonati

In rapporto alle condizioni cliniche del neonato si può **offrire alla famiglia il primo libro, spiegando** ai genitori l'**importanza della loro presenza accanto al bambino** e della possibilità di utilizzare anche la loro voce tramite la lettura o il canto, o semplicemente parlando al loro piccolo, sin dai primi momenti, cogliendone i segnali comportamentali.

Il rinforzo costante di questa buona pratica dovrà avvenire con il coinvolgimento dell'intera equipe: tutti i professionisti possono contribuire alla buona riuscita dell'intervento anche **parlando e cantando a basso volume durante lo svolgimento delle procedure** sanitarie di routine, **incoraggiando e facilitando** la lettura e il racconto da parte di genitori e contemporaneamente **guidando** i genitori **all'interpretazione dei segnali** forniti dal bambino (con l'osservazione condivisa ed eventuali strumenti scritti come " Il neonato ci parla": Artese, Blanchi 2009).

Idealmente la lettura effettuata dal genitore al neonato dovrebbe essere **quotidiana** (se possibile un nuovo libro al mese, ancor meglio ogni 2 settimane), consentendo in questo modo il riconoscimento precoce della voce del genitore, forte aggancio relazionale assieme agli altri input sensoriali provenienti dal contatto fisico, sensazioni olfattive e vestibolari che arricchiscono il messaggio uditivo.

La lettura condivisa: aiutare i genitori a capire i segnali comportamentali

(Artese, Blanchi 2009 "Il neonato ci parla"; Colombo "Con Ragione e sentimento")

L'equipe assistenziale può aiutare i genitori ad **imparare ad osservare, riconoscere ed interpretare i segnali del proprio neonato**, supportandoli nel valutare quando è un momento opportuno per la lettura. I segnali che indicano che il bambino può essere pronto all'interazione sono: battito cardiaco e respiro regolari, colorito stabile, posizione flessa e raccolta, movimenti armonici, postura e tono rilassati, occhi aperti, aspetto attivo, mani vicino alla faccia. Viceversa, sono segnali suggestivi dell'opportunità di riprovare in un'altra occasione: cambiamenti nella frequenza cardiaca, respiratoria o nel colorito, frequente estensione delle braccia e delle gambe, agitazione, pianto, tentativi del bambino di distogliere lo sguardo, dimenarsi e inarcarsi (vedi tabella *I segnali di benessere o di stress* in Colombo G. "Con Ragione e sentimento"). Il momento ideale per la lettura è quando il neonato è sveglio e tranquillo: questo però può accadere per brevi momenti in TIN, quindi, soprattutto a età gestazionali molto basse, è possibile leggere dolcemente al piccolo anche durante il sonno, senza l'intenzione di svegliarlo, ma di accompagnarlo delicatamente rispettando e proteggendo il sonno. Un momento adatto può essere durante la *kangaroo care* o quando il bambino è in braccio.

I segnali di benessere o di stress

I segnali di benessere o di stress che il neonato pretermine ci mostra attraverso il suo comportamento devono guidare l'approccio di tutti gli operatori della TIN (medici, infermiere, fisioterapista, psicologo, personale ausiliario, consulenti...): un approccio che costituisce la base del lavoro clinico.

Comportamenti indicanti stress rispetto allo stimolo: tutti i comportamenti ampiamente in estensione, poco modulati.	**Comportamenti indicanti autoregolazione rispetto allo stimolo:** tutti i comportamenti ampiamente in flessione e ben modulati.

In particolare, leggiamo i segnali di stress e i segnali di autoregolazione

Segnali di stress

- respiro irregolare, lento o veloce e pause tra un respiro e l'altro
- colorito pallido, marezzato rosso, grigiastro o cianotico
- tremori, startle
- segni viscerali: rigurgito, conato, singhiozzo, borborigmi, boccheggiamento
- flaccidità di braccia, gambe e tronco
- frequenti movimenti in estensione di braccia e gambe
- frequenti contorsioni del corpo e inarcamenti
- frequente protrusione della lingua, perdita di tono al volto, frequenti smorfie
- apertura a ventaglio delle dita, brusca abduzione delle braccia, congelamento in estensione delle braccia, congelamento in estensione delle gambe
- agitazione (pianto), frequenti sbadigli, starnuti, smorfie, occhi galleggianti

Segnali di autoregolazione

- respiro regolare e modulato, assenza di pause
- colorito roseo (rosa-pallido nei prematuri)
- stabilità viscerale
- tono muscolare mantenuto e ben modulato
- movimenti dolci delle braccia, delle gambe e del tronco
- capacità di mantenere una flessione modulata delle braccia raccolte verso il corpo e gambe che cercano con successo il bordo del nido e vi si appoggiano
- ricerca della suzione e suzione
- contatto mano-mano e piede-piede
- portarsi la mano/le mani alla bocca, afferrare ed aggrapparsi
- tutti gli stati comportamentali modulati, ad eccezione del pianto prolungato ed intenso
- espressione aperta/attiva del viso

Tabella 1. Tratto da *"Con ragione e sentimento - le cure neonatali a sostegno dello sviluppo"*.

La lettura condivisa: sostenere la buona pratica nel follow up del neonato pretermine o ad alto rischio neuro evolutivo

La buona pratica della lettura inserita in Neonatologia e in TIN può essere proseguita anche a casa, dopo le dimissioni: i libri possono accompagnare il bambino nel suo processo di sviluppo. Lo sviluppo del linguaggio e poi delle competenze per la lettura è sostenuto da esperienze ambientali favorenti, dalla frequente lettura interattiva in famiglia e da una buona disponibilità di libri. Inoltre, la lettura condivisa offre al genitore e al bambino piacevoli momenti di relazione e vicinanza, quindi favorisce lo stare insieme e l'apprendimento.
Medici, terapisti e altre figure presenti in follow up, in aggiunta al pediatra di famiglia, possono guidare i genitori sulle modalità più efficaci di lettura condivisa nelle diverse età. (Manetti 2011; Indicazioni Follow Up 2015-SIN; Alushaj, Tamburlini).
La lettura dialogica è una modalità di lettura praticata da un adulto con un bambino piccolo, sotto forma di dialogo interattivo. L'adulto, utilizzando anche canali comunicativi non verbali mediante l'uso di gesti, mimica e suoni onomatopeici, sollecita il bambino nell'indicare un personaggio o un oggetto presente nel libro con domande che offrano la possibilità di una risposta da parte del piccolo. Questa modalità stimola così il bambino a partecipare alla lettura condivisa di un libro, espandendone le risposte e mettendo in relazione la storia con l'esperienza del bambino, facendolo diventare il narratore della storia.
Nella lettura dialogica lo stile di lettura dei genitori deve avere 4 caratteristiche fondamentali nelle quali il genitore:

1. propone delle richieste al bambino stimolandolo a dare un nome agli oggetti del libro o a parlare della storia
2. considera la sua risposta
3. espande la sua risposta
4. ripete l'affermazione del bambino arricchendola con nuovi spunti.

Anche la scelta del libro è strategica: un libro che si legge per la prima volta, un libro alfabetico o con fotografie favorisce una sillabazione, la definizione di una parola nuova o risposte alla richiesta di un feedback positivo (Panza 2015).

Come promuovere la lettura in famiglia: messaggi e suggerimenti per i genitori (ROR. 2021)

› Il tuo bambino ama la tua voce e la conosce già, fin dalla nascita.

› Parla, leggi e canta dolcemente a tuo figlio il più frequentemente possibile, facendoti guidare dai suoi segnali comportamentali: sono azioni semplici, ma che possono aiutare il suo cervello e favorire lo sviluppo del linguaggio.

› Parla nella lingua che usi di più a casa: è la cosa migliore ed è già familiare.

› La lettura è un buon modo per aumentare il numero di parole che il tuo bambino sente, perché la lingua letteraria è più ricca di quella quotidiana.

› Puoi leggere ciò che ti interessa: un libro o un giornale di tuo gradimento, oppure un libro per l'infanzia.

› Il tuo bambino potrebbe rispondere all'ascolto della tua voce rilassandosi, facendo piccoli rumori mentre parli o forse semplicemente addormentandosi! Potresti non notare nulla, ma non scoraggiarti: per lui sentire la tua voce è comunque utile.

› Quando il tuo neonato è molto piccolo, può dormire per la maggior parte del tempo: anche quando riposa rilassato e tranquillo può essere un momento per la lettura, senza l'intenzione di svegliarlo, ma di accompagnarlo dolcemente nel suo sonno. Quando avrà qualche settimana in più, potrai vederlo un poco più sveglio e tranquillo: questo è un buon momento per interagire.

› Se puoi tienilo a marsupio o in braccio, ma va bene leggere per lui anche attraverso gli oblò dell'incubatrice o mentre si trova nella culla, vicino al suo viso.

› A volte può sembrare sciocco cantare dolcemente o leggere ad alta voce, ma il tuo bambino ama ascoltarti! La lettura è un buon modo per sentirti vicino a tuo figlio e per contribuire in modo unico alle sue cure: può diventare un'abitudine durante il periodo in Terapia Intensiva Neonatale e continuare una volta tornati insieme a casa.

› Non è necessario leggere un intero libro o passare molto tempo a leggere al tuo bambino: anche brevi periodi creeranno infatti forti connessioni nel suo cervello.

ASPETTI DI CUI TENERE CONTO NELL'UTILIZZO DI LIBRI E MATERIALI

La scelta dei libri

È importante leggere/cantare/parlare al bambino in modo dolce, cadenzato, con ritmo: questo aspetto è ancora più importante del contenuto. Se il genitore è pronto, può essere incoraggiato a leggere ad alta voce un testo di suo interesse, anche se la lettura di **un libro per l'infanzia** può rivelarsi più agevole per il genitore e fornire un ponte ideale verso il futuro atteso col proprio bambino.

Tra la vasta selezione di libri proposti vi potranno essere:

- libri con immagini di grandi dimensioni
- volumi cartonati
- libri più estesi, con più parole
- libri che stimolino i genitori a creare racconti basati sulle immagini
- libri che si possano cantare ai bambini
- libri di filastrocche, di rime
- idealmente, almeno un libro nella lingua madre o preferita dalla famiglia
- libri portati da casa, compatibilmente con le regole del reparto.

Fattori facilitanti la riuscita del programma di lettura durante la degenza

- Presenza in reparto di una biblioteca con libri di qualità e possibilmente in più lingue, catalogati per il genitore, per il neonato, per i fratelli e/o le sorelle.
- Dono del libro oppure, laddove non ce ne siano le possibilità, prevedere la presenza del libro in un kit di accoglienza della famiglia alla nascita, che verrà restituito alla fine della degenza.
- Individuazione di uno/due professionisti responsabili del progetto che possano essere trainanti, di riferimento, di sensibilizzazione verso il resto dell'équipe e con i genitori.
- Prevedere momenti formativi specifici relativi al "progetto lettura", per tutta l'équipe assistenziale.
- Presenza di volontari Nati per Leggere o di altre associazioni per i gruppi di lettura con i genitori e con i bambini.
- Esposizione in reparto di poster, disponibilità di brochure che presentino, illustrino e motivino il progetto ai genitori.

Messaggi chiave

In Neonatologia la Developmental Care, personalizzata e centrata sulla famiglia ha come scopo cardine la neuroprotezione del cervello mediante la riduzione dello stress, la promozione dello sviluppo e la cura della relazione con i genitori.

È riconosciuta la centralità delle cure offerte dai genitori.

I neonati pretermine sono particolarmente a rischio per i disturbi del linguaggio e dello sviluppo neurocomportamentale, per cui è fondamentale ridurre il rumore eccessivo ambientale ed aumentare l'esposizione a suoni dotati di significato rivolti al piccolo.

La lettura ad alta voce si rivela una sicura strategia di intervento linguistico in Neonatologia e in TIN. L'indicazione ai genitori sull'importanza di parlare, leggere e cantare con il loro neonato, nel rispetto dei suoi segnali comportamentali, dovrebbe essere fornita precocemente e continuativamente durante la degenza in reparto, e proseguire a casa.

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La Cura della Lettura

Documento di indirizzo e indicazioni operative per la promozione della lettura condivisa in **oncoematologia pediatrica**

In un ospedale di vetro possono essere eseguite riparazioni,
ma non si può certamente essere guariti.

(Ernst Jünger)

I am convinced that humanization begins
by considering the patient not as an
anonymous person, a number, a guinea-pig,
but as a human being, by trying to become his friend,
to take an interest in his problems.

(Allison Ballandras)

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Documento realizzato a cura del gruppo "oncoematologia pediatrica" del progetto Cepell *La cura della lettura*:
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Introduzione:

L'umanizzazione delle cure è da alcuni decenni al centro del dibattito ospedaliero: il paziente non si trova più relegato in un ruolo secondario di spettatore e corpo malato che sottostà a delle cure, ma si trova invece al centro degli sforzi del personale e dell'istituzione volti a permettergli di non perdere nulla della sua identità, della sua personalità e della sua storia in conseguenza di un ricovero ospedaliero più o meno lungo.
In questo senso, la pratica della lettura dialogica in ospedale assume tutto il suo particolare rilevo, perché diretta al paziente per intero, alla sua psiche come al suo soma, al suo ambiente come alla sua individualità, ai suoi gusti come alla sua storia e inoltre la lettura, in ospedale e non, e soprattutto quella effettuata dai genitori, è fortemente consigliata per i neonati e i bambini (Council on early childhood 2014; Brunelli, Manetti 2009; Panza, Davoli 2011).
Nelle branche pediatriche, ma non solo, siamo tutti al lavoro per sviluppare un sempre maggiore interesse per il paziente e la sua famiglia, interesse sincero che permetta un adattamento all'ambiente ospedaliero il più naturale possibile.

I BENEFICI DELLA LETTURA IN ONCOEMATOLOGIA PEDIATRICA

Esistono alcune evidenze, rintracciabili nella letteratura internazionale sui benefici possibili della lettura in ambiente ospedaliero, e più specificamente in oncoematologia pediatrica. Se la biblioterapia appare essere un vero e proprio metodo terapeutico focalizzato alla risoluzione di uno specifico problema, la lettura dialogica è invece parte integrante del trattamento relazionale di cura ospedaliero, che prevede cure mediche, psicologiche e sociali (Riordan, Wilson 1989).
Buoni risultati nella limitazione e nella cura dell'ansia nei bambini oncologici, sulla percezione del proprio funzionamento interpersonale, sulla sintomatologia depressiva, sull'adattamento alle cure e lo sviluppo di nuove strategie di *coping*, sono stati riportati in letteratura riguardo bambini ospedalizzati e in cura per malattia oncologica (Schneider 2012; Schneider, Peterson 2015; Malibiran, Taliman, Amer 2018; DeVries et al, 2019; Jones, Evans, Barfield 2021).

"It is hypothesized that reading a children's book that describes what a character undergoes when he or she has cancer, along with coping strategies employed, will improve a child's subjective perception of functioning and decrease their perceived emotional distress" (Schneider 2012).

La lettura dialogica che vede protagonisti i bambini, i genitori e gli operatori, acquisisce così, nel campo delle cure mediche, il valore di ausilio interdisciplinare (Losada 2020). Rappresenta un momento ludico che agisce in maniera sensibile sulla modulazione del vissuto di malattia e delle emozioni negative (Nascimento, Rosenberg 2007), sulle paure e sull'angoscia, nonché sulla cura del dialogo - tra le parti di sé (sana e malata) e tra se stessi e gli altri - che rischia per via della diagnosi stessa di essere interrotto spesso per sempre (Bernardino, Elliott, Neto 2012). In letteratura sono già riportate inoltre evidenze rispetto all'utilità del lavoro biblioterapico (quindi focalizzato a ridimensionare l'ansia e l'angoscia dovute al ricovero) con i fratelli dei bambini malati (DeVries, Sunden 2019), che in oncoematologia pediatrica sono da alcuni anni al centro dell'attenzione dei clinici e degli operatori in genere. Il lavoro con i libri, di lettura e commento insieme agli adulti, professionisti, genitori ma anche tra pari, agisce infatti in maniera sensibile nel contrastare i possibili vissuti abbandonici e la sintomatologia ansioso-depressiva che i fratelli possono sviluppare a causa del ruolo improvvisamente subordinato che sono costretti a vivere in conseguenza della malattia del familiare.

Infine, la lettura dei libri ai propri figli, soprattutto in caso di ricovero ospedaliero e per malattia grave, rappresenta un ausilio importante anche per l'identità e la figura degli stessi genitori, messa continuamente alla prova di fronte ai bambini - e ai loro stessi occhi - in conseguenza della delega quasi totale che sono costretti ad accordare a medici e operatori sanitari per via delle terapie necessarie.

Nei percorsi di cura dei quali ci occupiamo, nei quali si rischia di perdere finanche la propria identità,

oscurata dal nome ingombrante della malattia e delle terapie, e la propria strada, mascherata spesso da pregiudizi difficili da estirpare, si affacciano bisogni specifici ed esigenze particolari, che vedono al centro la necessità di non perdere nulla della propria vita passata insieme al bisogno di non sciupare e vedere confermati i sogni coltivati per i propri figli e l'idea di un futuro comunque possibile anche per loro.
In questo senso, attraverso i libri, la lettura e il commento degli albi illustrati, nonché l'interpretazione che possono dare delle storie in essi descritte, mamma e papà possono riprendere in mano la propria autonomia e capacità relazionale di ascolto e comprensione, e custodire allo stesso tempo la loro identità di genitori, di educatori e compagni di avventure dei propri bambini (Fosson, Husband 1984).
Vi è inoltre la necessità di mettere un limite e ostacolare il vissuto di passività che rischia di impadronirsi delle esistenze di quanti subiscono una diagnosi di malattia oncologica in età pediatrica e dei loro familiari, e la lettura guidata, l'appoggio di un'altra storia, diversa ma simile alla propria per note di esperienza vissuta, può rappresentare uno degli ausili nella ripresa del proprio, personale discorso sulla e nella propria vita.
Condividere quindi i libri e le loro storie in un reparto di Oncoematologia Pediatrica è quindi un segnale innanzitutto di speranza per il futuro, per ciò che è stato scritto e detto e ciò che ancora deve esserlo. Speranza declinata attivamente, come abbiamo visto, che investe tutti gli attori della lotta alla malattia, ovvero i bambini, i genitori e i fratelli, insieme agli operatori.

ESPERIENZE SIGNIFICATIVE SVOLTE DA ALTRI GRUPPI IN ITALIA E ALL'ESTERO

Esperienze sulla promozione della lettura in oncoematologia in Italia

La rete AIEOP, che conta attualmente 52 centri in tutta Italia, ha sviluppato al proprio interno una buona attenzione al ruolo della lettura nel percorso di cura dei bambini e dei ragazzi, soprattutto in virtù di diverse sistematiche donazioni di libri che hanno in questi anni arricchito le librerie di praticamente tutti i centri AIEOP e delle pediatrie, permettendo ai servizi ospedalieri di dotarsi di angoli lettura e vere e proprie biblioteche di reparto, dedicate ai ragazzi ma aperte anche alla lettura dei genitori e dei caregivers in generale.
Se sono note esperienze ed occasioni di formazione in medicina narrativa, in oncologia (Napolitano Valditara 2016) non ci sono, al momento attuale, notizie di esperienze significative e quindi non disponiamo attualmente di dati di letteratura circa progetti, esperienze organizzate e ricerche riguardo la lettura nei servizi di oncoematologia pediatrica italiani, campo che è stato sino a questo momento lasciato alla buona volontà dei singoli operatori dei centri della rete nazionale. Diffusa soprattutto nel campo delle cure per i pazienti adulti, spesso la lettura è stata utilizzata dalle associazioni di volontariato quale attività di intrattenimento ludico per i bambini e le famiglie in attesa dei risultati in Day Hospital (DH) o durante le terapie ambulatoriali (ad esempio *Molte Voci Molti Libri*, Roma - moltevocitantilibri.it) e gli scriventi hanno organizzato insieme a dei gruppi di attori e di scrittori alcune esperienze di laboratorio di lettura guidata e condivisa (grazie alla partecipazione, ad esempio, del Salento Book Festival 2018) con i bambini impegnati nelle mattinate in ambulatorio e DH.
Gli insegnanti della Scuola in Ospedale utilizzano inoltre albi illustrati scelti con cura fra quelli esistenti per leggere ad alta voce ai bambini ricoverati, letture che coinvolgono bambini, genitori e che hanno ricaduta anche su fratelli e sorelle perché spesso i libri vengono prestati o regalati per essere riletti dai genitori, a volte portati a casa per essere condivisi proprio con fratelli e sorelle ed essere letti dai genitori stessi in un clima familiare.

Esperienze di promozione della lettura in oncoematologia all'estero

Per quanto riguarda le esperienze svolte all'estero, abbiamo rintracciato una buona quantità di articoli scientifici riguardanti ricerche svolte in setting ospedalieri, che testimoniano, come riportato in precedenza, dei buoni risultati della biblioterapia in ospedale. Gli studi e le esperienze riguardanti la lettura in ospedale e l'oncoematologia pediatrica non sono però così numerosi rispetto a quelli riguardo l'applicazione della stessa all'età adulta; in ogni caso, negli ultimi anni si vanno accumulando prove scientifiche e buone revisioni della letteratura (Babarro Vélez, Lacalle Prieto 2018; Malibiran, Tariman 2019).
L'ospedale pediatrico St. Jude di Londra, ad esempio, ha all'interno del proprio sito una rubrica nella quale, oltre a sottolineare l'importanza della lettura per i bambini e i neonati, si propone ai genitori una lista di titoli da leggere insieme ai propri figli in sala d'attesa e in degenza (www.stjude.org/).
L'Ospedale Pediatrico di Boston (www.childrenshospital.org/patient-resources/your-visit/preparing-your-child-for-their-stay), propone ai genitori una nutrita lista di libri per i bambini dai 2 ai 12 anni che attendono di essere ricoverati, in modo da permettergli di familiarizzare con l'ambiente dello specifico ospedale, ma anche in generale con la vita di degenza. La lettura con i genitori è consigliata, allo stesso tempo e insieme al disegno e al gioco, per i bambini che tornano a casa dopo un periodo di degenza.
L'attenzione ai libri, e in senso lato alla relazione tra paziente e genitore e paziente e operatore, appare far parte di una indicazione generale alla lettura dialogica in ospedale pediatrico, ai benefici della stessa e al coinvolgimento dei genitori nel lavoro di lettura e commento dei testi. Non abbiamo comunque trovato indicazioni specifiche per la lettura in oncoematologia pediatrica.

PROPOSTA DI INDICAZIONI OPERATIVE

La lettura condivisa quando il bambino è nei servizi

Quando il bambino è ricoverato nelle stanze di degenza, dovrebbe trovarsi al centro di un racconto pensato per lui e ogni volta confermato dagli operatori che entrano nella sua stanza, in quello che diventa il suo mondo, spesso per lunghi periodi di tempo. I ricoveri delle oncoematologie pediatriche delineano un percorso di cure che spesso appare quasi infinito, senza soluzione di continuità tra un ingresso e l'altro, ma che, proprio per questo, deve poter essere costellato e ridefinito ogni volta da una narrazione che permetta ai bambini e ai familiari di riconoscere e riconoscersi in un percorso, in un ambiente e negli operatori cui sono affidati.
In questo senso vi è la forte necessità che gli operatori tutti siano informati dei ricoveri programmati in modo da preparare e personalizzare i propri interventi, tenendo conto dell'importanza della lettura in atto o programmata. È necessario quindi siano formati in maniera adeguata rispetto ai titoli che si offrono in reparto come supporto alle cure e alle famiglie; c'è inoltre da tenere in considerazione il fattore ambientale, ovvero la cura della stanza, come vedremo più avanti, e la cura dei diversi percorsi di cronicità.
Quando in regime di DH, i bambini devono poter essere seguiti durante le mattinate e i pomeriggi di terapie e controlli allo stesso modo che nella situazione di degenza. Pur non potendo adeguare in maniera completa l'ambiente delle camere del DH, gli operatori impegnati nell'assistenza dovrebbero essere formati allo stesso modo dei colleghi del reparto di degenza, e quindi conoscere il testo in lettura in quel momento e saper sostenere un dialogo sul 'viaggio' del bambino e della famiglia.
In questo senso, perché sia possibile garantire una continuità immaginativa e fantastica al bambino (e alla famiglia) che passa dalle cure di degenza a quelle del DH, è opportuno pensare a un registro delle letture in corso, i cui dati possano essere affiancati a quelli clinici e possano far sì che il bambino si senta accolto nel nuovo ambiente di cure.
Allo stesso tempo, è opportuno pensare a delle specifiche letture da poter intraprendere insieme ai bambini e alle famiglie quando termina la parte delle cure esclusivamente in regime di ricovero e possono quindi iniziare quelle in regime di DH, controlli e follow-up. In questo senso, l'accompagnamento verso un ritorno alla vita fuori dall'ospedale passa anche attraverso i libri, che spesso parlano di rinascita, riscoperta, riacquisizioni e ripartenze.

La lettura condivisa in famiglia

In nome della continuità assistenziale, che si fa in questo senso continuità esistenziale, il bambino e la sua famiglia devono poter essere seguiti anche dal punto di vista della pratica della lettura quando tornano dalla degenza al proprio domicilio. Grazie al supporto e alla collaborazione dei genitori, che segnaleranno i testi in lettura a casa e porteranno avanti, guidati dagli operatori, la lettura condivisa con i figli dei testi indicati e di nuovi lavori, sarà possibile non perdere di vista il bambino dal punto di vista del percorso di lettura. Non meno importante la figura del Pediatra di libera scelta, che potrà seguire l'andamento globale della situazione clinica e relazionale del bambino, nonché commentare con lui e i genitori le letture in atto, facendo così da ponte tra territorio, abitazione della famiglia e i colleghi ospedalieri. Ogni passaggio in ospedale rappresenterà così un momento per fare il punto sul personale tragitto di cura della lettura, tra abitazione e Pediatria, sulle storie che si sono attraversate e quelle ancora da attraversare.

La lettura condivisa a scuola o altri servizi educativi e scolastici

Sempre in nome della continuità esistenziale e di cura, anche la scuola può rappresentare un ausilio alla lettura e alla condivisione del percorso di cura della lettura. I dirigenti scolastici e le maestre dovranno essere contattati e messi a giorno del percorso del bambino e della famiglia (in questo senso i genitori rappresentano, almeno in un primo momento, la *longa manus* comunicativa dell'ospedale). La Scuola in Ospedale (SIO) gioca qui un ruolo fondamentale: alla SIO spetta infatti il compito di mantenere il collegamento proficuo e continuo con la scuola e la classe di appartenenza, con i compagni e gli insegnanti. Gli operatori, o i volontari adeguatamente formati, potranno quindi raggiungere la classe del bambino interessato per discutere con i maestri e realizzare degli incontri di lettura nei quali il bambino potrà avere il ruolo, insieme alle proprie maestre e all'operatore stesso, di lettore e commentatore primo della storia in lettura o che ha letto (si può pensare quindi ad una staffetta di piccoli lettori). Il bambino passerà così dal rischio di perdere amici e classe per le lunghe soste ospedaliere, alla possibilità di riprendere un ruolo centrale nella vita della classe, un ruolo attivo e propositivo. In questo modo, sempre in maniera leggera e restando sul testo, si riuscirà a fare cultura dei percorsi di vita, di quelli di cura e dell'avventura che può essere ed è la vita.

ASPETTI DI CUI TENERE CONTO NELL'UTILIZZO DI LIBRI E MATERIALI

È auspicabile scegliere i libri adatti ai bambini impegnati nelle cure ospedaliere, in particolare tra quelli che narrano viaggi e partenze, avventure e percorsi da compiere insieme a genitori o amici.
Il vissuto di passività del ricovero viene così ad essere contrastato grazie alla lettura delle vicende che coinvolgono eroi e supereroi, piccoli animali e loro famiglie, bambini, fratellini e genitori, tutti coinvolti in viaggi e prove di coraggio, percorsi non semplici ma comunque possibili.
Non è a nostro parere necessario, infatti, leggere dei testi che ricordino o affrontino direttamente il problema per cui il bambino e la famiglia (protagonisti, animali ecc.) si trovano ricoverati.
Ciò che è importante affrontare è l'esperienza stessa dell'essere malati, del ricovero, dell'isolamento e delle cure, nel tentativo di renderla parte di un percorso di cure condiviso, evitando così che si trasformi in una parentesi patologica, sospesa di tempo e spazio, un luogo e un tempo insensato o invece fin troppo ricco di particolari traumatici che potrebbero provocare una eccessiva reazione di difesa e quindi un ritiro del bambino di fronte ad una frustrazione valutata e sentita come non affrontabile.
I volontari insieme agli operatori, rivestono un ruolo fondamentale nel permettere al bambino di percorrere la sua strada nel miglior modo possibile. Volontari, infermieri e OSS, possono essere la sponda fonda-

mentale, dopo i genitori, nel permettere al bambino di tenere il segno della sua storia, nel tenere ovvero sempre accesa e rispondente la propria parte ludica, la lettura fantastica della propria vicenda personale, sempre intonata al libro in quel momento in lettura.

In questo senso, come detto, volontari e operatori, docenti della Scuola in Ospedale, dovranno essere informati della letteratura utilizzata e dovranno conoscere titoli e trama dei testi scelti per accompagnare i ragazzi nel loro viaggio di cura.

NUOVE MODALITÀ ASSISTENZIALI E DI CURA DA SVOLGERE CON GENITORI E FAMILIARI, OPERATORI SANITARI E I BAMBINI NELLA PROMOZIONE DELLA LETTURA

Permettere e sostenere il viaggio

La scelta dei libri da leggere ai propri figli, e ai propri pazienti, è un compito difficile e delicato (Deitcher, Aram, Adar 2017). Se nei paesi anglosassoni, dove vige maggiormente l'orientamento comportamentista in psicologia, la biblioterapia, specificamente utilizzata per diminuire la sintomatologia ansiosa negli adulti, bambini e ragazzi malati, approfitta soprattutto di testi educativi che trattano direttamente l'argomento, manualisticamente o biograficamente, anche attraverso la vita di personaggi reali o di fantasia[1], nella nostra idea, che origina dalla frequentazione prolungata della stessa modalità, i libri dovrebbero invece avvicinare gentilmente i ragazzi all'oggetto, creando piacevolezza e dando così loro la possibilità di identificarsi con i protagonisti delle storie senza provare l'angoscia del proprio diretto coinvolgimento nello stesso problema trattato nel testo. In questo senso, ci permettiamo di parafrasare Bruno Bettelheim (1977), le fiabe e i racconti altri dall'esperienza personale, quelli quindi che non implicano il diretto coinvolgimento del soggetto, autorizzano l'accostamento di contenuti ed emozioni altrimenti difficili da raggiungere e mentalizzare, permettendo così di elaborarli ed esercitarsi in *absentia*[2].

I bambini dovrebbero avere la possibilità, ovvero, di identificarsi con gli attori delle storie avendo sempre la possibilità di scansarsi, di mettersi da parte con facilità in caso di eccessivo coinvolgimento, perché più liberi da legami tra la propria personale vicenda e quella invece raccontata.

Ci spieghiamo con un esempio: se il momento (la settimana, le settimane o il mese) del ricovero è caratterizzato da specifiche coordinate esistenziali (come ad esempio un senso di passività molto accentuato, di ansia e di angoscia elevate, di spazio coartato ecc.), allora ciò che il libro consigliato dovrebbe presentare è una storia illustrata che abbia al proprio interno le stesse coordinate esistenziali, nelle quali il lettore possa riconoscersi gentilmente, senza che ciò causi alcuna 'irritazione'.

Il testo consigliato non deve essere per forza il racconto della malattia o del corpo, o addirittura della stessa esperienza passata da qualcun altro, ma deve permettere al giovane paziente o al bambino - nonché al genitore e al fratello - di immedesimarsi senza troppo timore nel personaggio del libro che affronta le stesse emozioni o similari situazioni, assimilabili per tempo, spazio, rapporto con gli altri e corpo vissuto.

Questa la nostra idea: quando qualcuno ci permette di rientrare attraverso le sue parole e i suoi gesti o sguardi nella nostra esistenza, pensiamo qui alla fascia di età tra i due e i sei anni (e a quella adolescenziale, magari con l'utilizzo dei romanzi veri e propri), quelle parole e quei gesti aprono a una nuova epifania, una rinascita autentica che può essere anche dolorosa ma che permette però di non sentirsi più soli. Il ritrovare parole e immagini per raccontarsi e per essere raccontati, con cui riconoscere e in cui riconoscersi, rappresenta un prezioso momento di rottura con la solitudine, indispensabile squarcio nell'isolamento esistenziale cui spesso le malattie conducono.

La nostra idea è quindi quella di fornire un kit lettera-

1 *"Currently, literature provided to adult patients is more often intended to educate them than to address their emotional needs"* (McMillen, Pehrsson 2004).

2 *"It is hypothesized that reading a children's book that describes what a character undergoes when he or she has cancer, along with coping strategies employed, will improve a child's subjective perception of functioning and decrease their perceived emotional distress"* (Schneider 2012, 7).

rio (una scialuppa) di sopravvivenza emotivo-mentale ai bambini che principiano il loro percorso di cura, nonché ai genitori che li accompagnano, attraverso la donazione al momento del primo ricovero, e quindi anche in occasione dei successivi ricoveri, di un kit composto da uno o più libri illustrati, quaderno, matita e gomma da cancellare, album da disegno e colori, cartoncini colorati.
Si potrebbe proporre anche di ambientare in qualche modo la stanza prima del ricovero con poster alle pareti, oggetti, giochi legati alla storia raccontata dal libro stesso, in modo da rendere ancora più suggestivo e inteso il racconto e più accogliente la stanza del ricovero pensata appositamente per quel bambino o quella bambina, anche in considerazione delle sue preferenze (a Trieste, ad esempio, grazie alla preziosa collaborazione con l'Associazione #IoTifoSveva, l'ambientazione della stanza è diventata una prassi per i lunghi ricoveri).

Il ruolo degli operatori

Il libro illustrato presente nel kit (possiamo pensare a una decina di titoli, ad esempio) dovrebbe essere stato letto e discusso in gruppo dagli operatori tutti, impegnati nell'assistenza ai ragazzi e alle loro famiglie, così che sia possibile per loro discuterne con il ragazzo o il bambino all'interno della stanza di ricovero o in ludoteca.
In questo senso la cura letteraria sarà cura ambientale, cura di gruppo, cura atmosferica e del percorso, cura condivisa da tutti e quindi sentita in maniera corale e per questo più efficace nel ridefinire e discutere le coordinate vissute proprie e caratteristiche dei difficili momenti che si affrontano nel periodo delle cure. Proprio come il coro delle tragedie greche, la partecipazione condivisa alla lettura, permetterà all'eroe di non sentirsi solo, di sapersi accompagnato nel viaggio, nel percorso e nelle difficoltà che, come ogni eroe che si rispetti, non potrà non incontrare.

ESPERIENZE DI CONDIVISIONE CON SOGGETTI ESTERNI E PROPOSTE DI PARTNERSHIP

Esperienza di condivisione sono possibili e certamente raccomandate.

Territorio: collaborazione con biblioteche e librai

La consulenza e i suggerimenti di bibliotecari e librai risulta essere molto preziosa per lo sviluppo e l'ampliamento delle conoscenze sui titoli, sui classici antichi e le novità nei cataloghi.
Biblioteche e librerie possono, per altro, rappresentare "contenitori territoriali" per gli interventi di lettura condivisa per i piccoli pazienti dimessi, fratelli e genitori, luoghi di ritrovo e partecipazione, apertura e informazione. Sul cosiddetto "territorio" si potrà sviluppare, quando possibile in alternativa e in momenti diversi rispetto all'ospedale, come tra l'altro già si fa per NpL, una rete di lettura e lettori, in ascolto delle specifiche necessità della popolazione alla quale ci rivolgiamo. Sarà in questo senso possibile sviluppare anche all'esterno dell'ospedale una diversa cultura dell'empatia e della condivisione, attraverso ovvero la conoscenza diretta degli operatori che si sposteranno sul territorio per incontrare i cittadini e quindi grazie alla lettura condivisa delle stesse storie di viaggio e avventura che si utilizzano in ospedale.

Associazioni di volontariato

Le associazioni di volontariato, da sempre ben presenti sulla scena della oncoematologia pediatrica, possono svolgere un ruolo molto importante in reparto come in DH, con l'organizzazione di incontri in cui si svolgono letture condivise dei testi consigliati dall'équipe.

Quotidiani locali

La collaborazione con i quotidiani locali è parte fondamentale di una buona comunicazione con il territorio, per tenere alta l'attenzione sul problema della malattia in età pediatrica e inoltre per pubblicizzare le attività collaterali da tenersi fuori dalle mura dell'ospedale. Si possono pensare a numerose modalità di collaborazione, tra cui, ad esempio, una rubrica fissa di recensioni dei libri utilizzati nel Servizio, a cura di genitori o operatori, che tenga alta l'attenzione sulle attività di lettura in ospedale e che possa così fare cultura e preparare a manifestazioni aperte al pubblico.

Nidi e scuole

Possono essere realizzati facilmente, con il contributo e la collaborazione dei dirigenti scolastici, delle educatrici e delle maestre, dei concorsi/eventi per i bambini delle Scuole dell'Infanzia e Primarie, che potrebbero essere coinvolti ad esempio nella scelta di nuovi titoli di viaggio da utilizzare in ospedale, nella realizzazione di video recensioni, di audiolibri realizzati dagli stessi bambini (Casares Jr., Binkley 2020, per quanto riguarda l'ambito della Salute Mentale), dedicati ai piccoli pazienti che ascolterebbero dalla voce di un proprio coetaneo la lettura del testo scelto.

Parole chiave

Lettura in oncoematologia pediatrica

La pratica della lettura dialogica può essere parte integrante delle cure ospedaliere per i bambini e i genitori in cura presso i Servizi di Oncoematologia Pediatrica. Il lavoro con i libri, di lettura e commento, con adulti di riferimento dei bambini, professionisti, genitori, docenti della Scuola in ospedale, Pediatri di Libera Scelta, ma anche tra pari, agisce infatti in maniera sensibile nel fornire una narrazione condivisa e meno angosciante di quanto sta avvenendo, contrastando allo stesso tempo i possibili vissuti abbandonici e la sintomatologia ansioso depressiva che può svilupparsi a causa del vissuto di passività che pervade i piccoli pazienti e le loro famiglie, fratelli compresi.

Genitori

La lettura dei libri ai propri figli fin da piccoli, ancora di più se effettuata nel caso di regime di degenza, rappresenta un ausilio importante per l'identità e la figura degli stessi genitori. La lettura e il commento dei testi e delle immagini, favorirà la ripresa di un ruolo attivo nel rapporto e di un sentimento di partecipazione diretta alla vicenda dei propri figli.

Lettura e percorsi di cura

Dal momento del ricovero e sino al ritorno a casa, comprendendo i rientri in DH, il bambino dovrebbe trovarsi al centro di un racconto pensato per lui, che segua e permetta il viaggio attraverso i diversi ambienti e i differenti personaggi delle cure.
È auspicabile scegliere i libri adatti ai bambini impegnati nelle cure onco-ematologiche, cure che possono durare anche alcuni anni, in particolare tra quelli che narrano di viaggi e partenze, avventure e percorsi da compiere insieme a genitori o amici. È importante affrontare l'esperienza stessa della malattia, ma si deve poterlo fare da una prospettiva indiretta.

Per una cura integrata ambientale

Ai bambini che principiano il loro percorso di cura, potrebbe essere donato un libro o un kit di lettura al momento del primo ricovero (e in occasione dei successivi), un kit composto da uno o più libri illustrati, quaderno, matita e gomma da cancellare, album da disegno e colori, cartoncini colorati. Il testo rappresenterebbe così la linea di senso e narrazione da raccontare e discutere, disegnare e sognare, durante il ricovero.
Gli operatori dovrebbero quindi aver letto e dibattuto in gruppo i libri presenti nei kit, così che sia possibile per loro discuterne con il bambino e i genitori durante la degenza.
In questo senso la cura letteraria sarà anche cura ambientale e cura di gruppo.

Territorio

La consulenza e i suggerimenti di bibliotecari e librai, insieme alla partecipazione delle Associazioni di Genitori, degli Istituti Scolastici, dei quotidiani locali e delle Società Scientifiche, nonché dei Pediatri, risulta essere molto preziosa per lo sviluppo e l'ampliamento delle conoscenze sui titoli, per il coinvolgimento delle classi dei bambini ricoverati, per migliorare la comunicazione e aumentare la sensibilizzazione sulle problematiche pediatriche e la cura della lettura, nonché per avviare progetti di ricerca ulteriori sulla pratica della lettura dialogica negli ambienti sanitari, e specificamente in Oncoematologia Pediatrica.

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La Cura della Lettura

Documento di indirizzo e indicazioni operative per la promozione della lettura condivisa nei **disturbi del neurosviluppo**

Leggimi subito, leggimi forte
Dimmi ogni nome che apre le porte
Chiama ogni cosa, così il mondo viene
Leggimi tutto, leggimi bene
Dimmi la rosa, dammi la rima
Leggimi in prosa, leggimi prima.

(Bruno Tognolini)

Documento realizzato a cura del gruppo "disturbi del neurosiluppo" del progetto Cepell *La cura della lettura*.

Introduzione: benefici ed evidenze specifiche

Come ormai è ampiamente noto ai più, leggere ad alta voce ai bambini sin dai primissimi giorni di vita, rappresenta una buona pratica educativa che promuove competenze linguistiche e scolastiche negli anni successivi. Numerosi sono a tutt'oggi gli studi che analizzano lo sviluppo delle funzioni linguistiche, attentive ed esecutive in famiglie in cui viene praticata la lettura condivisa.

Ancora povera, invece, risulta la letteratura riguardante questa pratica nelle famiglie in cui sono presenti uno o più bambini con disturbi del neurosviluppo. A dire il vero, fino a non troppo tempo fa, leggere ai bambini disabili era una pratica poco diffusa, non trovando, fra le proposte editoriali, materiali ritenuti fruibili. Una recente revisione sistematica Cochrane (Reichow et al 2019) ha analizzato le abilità di lettura in bambini e adolescenti con disabilità intellettiva (DI). Storicamente si riteneva che bambini con DI non potessero imparare a leggere, e che quindi l'istruzione alla lettura non fosse appropriata. Tuttavia in seguito, le prospettive di arricchimento intellettivo e sociale di queste persone sono drasticamente cambiate. Negli studi riportati che hanno coinvolto 352 bambini e adolescenti, si è rilevato come l'istruzione alla lettura incrementasse la consapevolezza fonologica, e le abilità di lettura e di linguaggio oltre che indicare un miglioramento nelle abilità di decodifica e nella fluenza della lettura orale.

L'approccio alla lettura nella disabilità intellettiva presenta alcune sfide, ad esempio nelle premesse della metanalisi Cochrane (Reichow et al 2019) si citano essenzialmente due approcci. Il primo è la cosiddetta lettura funzionale, dove al soggetto vengono insegnate parole intere che sono acquisite come forma di parola e memorizzate globalmente, spesso in associazione a immagini. In questo modo si insegnano parole significative solitamente legate all'esperienza pratica e ai bisogni primari. L'altro metodo fonetico-fonologico è invece basato sull'acquisizione dei suoni della lingua, ed è simile a quanto viene fatto in genere nell'apprendimento della lettura nel resto della popolazione. La novità introdotta da questa analisi riguarda quindi la proposta di una istruzione formale della lettura in bambini con disabilità intellettiva, simile a quella data ai pari, fino a pochi anni fa ritenuta inefficace.

Un aiuto ci è arrivato anche dalla tecnologia che ha portato grandi vantaggi nell'accesso alle risorse librarie: gli audiolibri, gli inbook, i lettori mp3, le applicazioni per smartphone e tablet hanno permesso a chi presenta disturbi del neurosviluppo, dai deficit visivi alle disabilità cognitive, passando da disturbi del linguaggio o dell'apprendimento a quadri di funzionamento atipico, di trovare e ritrovare il piacere della lettura.

Alcune evidenze (Mucchetti 2013; Stephenson 2009) hanno ormai dimostrato che l'utilizzo di ausili aumentativi alternativi, quali ad esempio libri modificati (con supporti visivi, con simboli, con oggetti tridimensionali, con testi semplificati) offre la possibilità di agganciare i bambini nonostante le specifiche difficoltà, agevolando così l'accesso alla lettura e alla comunicazione di questi bambini, e aumentando, in particolare, la loro capacità di comprendere storie e il loro coinvolgimento con i pari nella condivisione della lettura.

Altre ricerche (Binger, Kent-Walsh & King 2017; Boyle et al 2021), convergono sull'importanza della lettura come momento di condivisione e interazione con adulti e pari. Nei loro studi sull'incremento della competenza linguistico-simbolica nei bambini con bisogni comunicativi complessi, gli autori sottolineano in particolare, gli effetti positivi di una lettura "dialogica", che consente cioè al bambino di intervenire, domandare, commentare e ricondurre la narrazione alle proprie esperienze, sullo sviluppo linguistico sia in termini di aumento del vocabolario, che della comprensione linguistica.

In quest'ambito si colloca lo sviluppo dei cosiddetti Inbook che prendono avvio dalla comunicazione aumentativa (CAA). Quest'ultima, inizialmente sviluppata con una forte attenzione all'aspetto espressivo e come modalità comunicativa per le disabilità motorie, ha permesso di riconoscere l'importanza del supporto alla comprensione e alla consapevolezza spaziale e temporale, per stare nei contesti sociali, iniziando dai più semplici, per potersi poi spostare anche verso quelli più complessi.

Tra gli strumenti proposti dalla CAA, venivano proposti testi costruiti sull'esperienza del bambino o

adattati da testi editi esistenti. Questi libri in simboli inizialmente presentavano un testo solo parzialmente espresso in simboli, ritenendo in questo modo di facilitare "un'introduzione graduale della complessità". Con il tempo e la collaborazione con le famiglie, gli operatori e gli insegnanti, si è reso sempre più evidente che solo una traduzione completa avrebbe permesso narrazioni emotivamente e lessicalmente piene.

Attualmente si trovano diversi approcci alla CAA, che ne hanno messo a fuoco specificità e applicazioni diverse. In particolare, un bivio importante si apre sulla scelta di considerare i simboli prevalentemente come supporto visivo o come base per lo sviluppo di una lingua vera e propria. Il secondo paradigma viene considerato maggiormente adatto a provare a rispondere ai bisogni, ai desideri e ai diritti delle persone con disabilità di accedere a quel piano importantissimo della cultura che sta nei libri. La letteratura scientifica, pur con le criticità rispetto a un contesto specifico come la CAA, conferma l'importanza dell'esposizione a una rappresentazione ricca anche nelle illustrazioni e nei dettagli (Binger, Light 2008).

ESPERIENZE SIGNIFICATIVE SVOLTE DA ALTRI GRUPPI IN ITALIA E ALL'ESTERO

Esperienze in Italia

La nascita dei "libri in simboli" si presenta come una specificità italiana, sostanzialmente assente in altri Paesi, fino ad ora.

Nelle unità operative di neuropsichiatria dell'infanzia e dell'adolescenza (UONPIA) si è partiti dai libri su misura, il cui il contenuto viene adattato agli interessi, alle capacità, alla situazione in cui il bambino si trova. I libri su misura vengono personalizzati, costruiti intorno a un'esperienza emotivamente importante o ad interessi specifici. L'argomento ha un elevato livello motivazionale per il bambino, e spesso è il primo aggancio possibile in particolare per bambini molto piccoli che presentano una disabilità complessa, a cui possono associarsi gravi difficoltà nella comprensione linguistica. Possono anche essere creati libri in simboli partendo da libri già editi, adattando il contenuto, per quanto riguarda sia gli aspetti linguistici che la struttura narrativa, per renderli più vicini all'esperienza e alle possibilità del bambino. Questi libri "su misura" permettono di esporre a un linguaggio più ricco e strutturato, in cui si gioca con le ripetizioni e con le emozioni come spesso accade in molti libri dedicati ai bambini. I libri in simboli possono essere utilizzati in famiglia fin da piccoli ed è importante leggerli insieme ai bambini con una disabilità complessa anche a scuola, offrendo una adeguata formazione agli insegnanti.

A partire da queste basi avviene la transizione dal libro su misura a quello che nel Centro Sovrazonale di Comunicazione Aumentativa di Milano e Verdello (CSCA) viene definito inbook, poi ripreso e messo a punto in collaborazione con l'Università Bicocca di Milano e Ca' Foscari di Venezia. Caratteristiche fondanti sono il rispetto per il registro narrativo originale e la traduzione completa in simboli. Il modello inbook è curato dal Centro Studi Inbook (csinbook.eu), che ne è garante della coerenza e dello sviluppo.

Esperienze all'Estero

I vantaggi della lettura condivisa sono conosciuti, nell'ambito del modello bioecologico di Bronfenbrenner, come fattore trainante dello sviluppo del linguaggio orale (Grolig 2020). La lettura condivisa è stata utilizzata nei disturbi del neurosviluppo per stimolare l'ampliamento del vocabolario. In una esperienza riportata si è affrontato il concetto di lettura condivisa come fattore protettivo. Nell'ipotesi che la presenza di alleli sensibilizzanti nel circuito dopaminergico e serotoninergico possa portare un fattore di rischio in ambienti deprivati, Jimenez e collaboratori hanno svolto uno studio longitudinale (Jimenez et al

2019) basandosi su una coorte di neonati afferenti a 20 ospedali delle maggiori città statunitensi, e hanno reclutato e analizzato un campione di 1772 bambini. La proposta era data alle famiglie con istruzioni rispetto alla lettura condivisa, sono stati somministrati questionari e interviste sulle condizioni socioeconomiche e le abitudini alla lettura, proposti a 1, 3, 5, 9, e 15 anni e valutazioni dello sviluppo e del vocabolario recettivo con il test PPVT Peabody, a 3, 5 e 9 anni. A 9 anni veniva anche raccolto un campione di saliva per il dosaggio degli alleli sensibilizzanti. Le analisi dei campioni hanno messo in luce un beneficio della lettura condivisa. In particolare, dove si rilevava la presenza di uno degli alleli nel genoma dei bambini, si osservava che questo influenzava l'associazione fra lettura condivisa e vocabolario recettivo, ovvero, mentre in assenza di lettura condivisa i bambini con l'allele mostravano minore abilità di vocabolario ai tre anni, nel campione in cui c'era l'allele e si faceva la lettura, il vocabolario aumentava nel tempo, rendendolo pari ai bambini che non presentavano l'allele e che non mostravano le difficoltà iniziali.

In un recente studio randomizzato controllato, (Weisleder et al 2019) hanno cercato di caratterizzare il meccanismo con cui la lettura condivisa può diminuire i comportamenti esternalizzanti di bambini a 36 mesi. In questo studio si ipotizzava che i meccanismi sono da collegare sia ai processi associati all'investimento da parte dei genitori - e in particolare la loro disponibilità economica per provvedere ad una stimolazione cognitiva - che ai processi associati alle vie dello stress determinato dalla situazione di ristrettezza, e in particolare al funzionamento psicosociale delle madri. Per testare queste ipotesi, i ricercatori hanno utilizzato il VIP (Video Interaction Project) realizzato nell'ambito dei progetti Reach Out and Read (ROR) ovvero una serie di materiali messi a punto dalla rete di pediatri che attraverso la promozione della lettura e del gioco riducevano i comportamenti esternalizzanti. Hanno reclutato 362 diadi madre-figlio, appartenenti a famiglie a basso reddito e hanno testo una serie di variabili a 6 e 36 mesi. Fra le variabili rilevanti dello studio si evidenzia l'importanza di un avvio precoce della lettura condivisa e del gioco, prima dei 6 mesi, e un intervento sostenuto nel tempo come mediatore principale dell'effetto voluto, ovvero il calo dei sintomi esternalizzanti a 36 mesi.

PROPOSTA DI INDICAZIONI OPERATIVE

La lettura condivisa quando il bambino è nei servizi (in sala d'attesa o in terapia)

Nel nostro servizio (Casa di cura "Villa Immacolata" S. Martino al Cimino) i bambini sono in trattamento per il tempo della terapia individuale e hanno un tempo di attesa variabile che dipende dalle routine familiari. Nella progettazione di questo intervento abbiamo immaginato una sala d'attesa che inviti alla lettura attraverso la proposta di libri messi a disposizione dal progetto *La cura della lettura*. L'esempio delle famiglie in cui è già presente una cultura della lettura condivisa potrebbe trainare le altre, e portare ad una diminuzione del ricorso ad altri espedienti per passare il tempo (telefonino, consumo di merendine, o attività motoria incontrollata).

La pandemia e le conseguenti direttive per evitare il contagio hanno messo a dura prova questa idea di condivisione, e pertanto l'intera area dedicata all'attesa dei bambini è stata di fatto contingentata con spazi limitati e tempi di attesa dettati dalle regole generali di accesso alla struttura. Nonostante questo, il progetto è andato avanti e si attende un alleggerimento delle misure di sicurezza per renderlo più efficace.

La sala d'attesa può essere identificata come momento di condivisione, scambio e mediazione.

L'esperienza di lettura per le famiglie straniere

In una indagine del 2017, si riporta che l'8,3% della popolazione residente in Italia è straniera (dati ISTAT) e il 10% dei bambini nelle scuole italiane apprendono l'italiano come seconda lingua (dati MIUR). Nella nostra realtà che corrisponde alla media degli ambulatori di neuropsichiatria infantile, il 20% dei pazienti con disturbi del neurosviluppo proviene da famiglie in cui uno o entrambi i genitori sono stranieri.

L'interazione con bambini in condizioni di disabilità è complessa, soprattutto se a bassa efficienza del canale comunicativo-linguistico. Per i genitori con madrelingua straniera le difficoltà dunque aumentano. Fino a non molto tempo fa, si suggeriva ai genitori stranieri di evitare l'uso della propria lingua madre nella convinzione che questo facilitasse l'acquisizione della seconda lingua. Nel tempo si è visto che invece è vantaggioso che i genitori continuino l'utilizzo della lingua madre, sia per fornire il supporto emotivo relazionale dato dal linguaggio che si usa con il bambino, sia per gettare le basi di una corretta morfosintassi e successiva alfabetizzazione in L2. Nel bambino con difficoltà nell'area comunicativo-linguistica acquistano particolare valore le modalità condivise di lettura. Si tratta infatti di una attività che può facilitare anche il genitore che nell'acquisizione di più competenze lessicali e morfosintattiche, queste ultime tipicamente più ridotte in chi apprende una seconda lingua da adulto. Pertanto, oltre ai vantaggi emotivo relazionali derivanti dall'attività condivisa, si creano vantaggi linguistici sia per il bambino che per il genitore. Risulta quindi importante dare un esempio, e aiutare il genitore a familiarizzare con il materiale, che dovrà essere costruito insieme, se si tratta ad esempio di Inbook, oppure selezionato insieme sulla base dei livelli di competenza del bambino.

Il CSCA in collaborazione con l'IRCCS Istituto di ricerche farmacologiche Mario Negri, ha portato avanti due ricerche che hanno coinvolto scuole dell'infanzia della città di Milano e della provincia di Mantova, da cui emerge che l'esposizione alla lettura degli Inbook fornisce supporto a livello linguistico, soprattutto per gli studenti che si trovano in una situazione di maggiore svantaggio, in particolare per quanto riguarda gli aspetti morfologici. Inoltre, ci sono evidenze di un positivo effetto di supporto alla pragmatica che, come è noto, ha un forte impatto sulle relazioni sociali, in particolare per i bambini bilingui. A fianco alla lettura di Inbook, ci sentiamo comunque di raccomandare fin da piccoli l'uso dei libri tradizionali per l'infanzia, degli albi illustrati senza parole che facilitano la lettura dialogica in qualsiasi lingua e anche, e forse soprattutto, la lettura di libri realizzati appositamente per bambini con bisogni educativi speciali.

I lenti lettori e i bambini con dislessia

Le proposte per i lenti lettori e i bambini con dislessia coinvolgono la vasta gamma di offerte che provengono da case editrici che hanno optato per l'utilizzo di caratteri ad alta leggibilità per una lettura più autonoma dedicata in particolare ai bambini in età scolare, con struttura semplificata nella morfosintassi ma non nel contenuto. Questi libri possono essere letti insieme al genitore o ad un coetaneo, ed è possibile utilizzare anche l'audiolibro man mano che il grado di autonomia aumenta.

Anche nell'ambito dei Disturbi Specifici dell'Apprendimento, infatti, le evidenze vanno nella stessa direzione di quanto esposto finora rispetto a disturbi più profondi della comunicazione e della relazione. Alcuni studiosi (Powers et al 2016) hanno eseguito un elegante studio in cui si cercava in due popolazioni di bambini prescolari la correlazione fra l'esposizione ad ambienti in cui è consuetudine dedicarsi ad attività di dialogo e lettura a voce alta - prassi conosciute anche sotto il termine di Home Literacy Environment - e le attività neurali cerebrali. Nel gruppo di bambini a sviluppo tipico e senza rischio per dislessia, si è osservata una influenza delle attività HLE nelle regioni generalmente collegate allo sviluppo delle abilità fonologiche, mentre nei bambini a rischio di sviluppare dislessia, per presenza di familiarità, si è osservata una minore attivazione in queste regioni, ma l'insorgere di attivazioni in altre regioni, che evidentemente attivano circuiti di compenso. Come ha scritto Maryanne Wolf (Wolf 2012) ritorna l'importanza di un'esposizione precoce alla lettura nell'acquisizione di competenze di letto-scrittura. Per la Wolf si individuano tre fattori fondamentali, da ricercare nell'ambiente educativo, che influenzano l'apprendimento linguistico e più in generale, lo sviluppo del cervello durante il processo di lettura: oltre al sostegno alla genitorialità, soprattutto nei confronti di coloro che vivono condizioni di deprivazione linguistica e culturale, gli altri due fattori riguardano rispettivamente la possibilità di avere a disposizione libri e l'esposizione ad ambienti in cui sia consuetudine dedicarsi ad attività di dialogo e lettura a voce alta fin da piccoli.

ASPETTI DI CUI TENERE CONTO NELL'UTILIZZO DI LIBRI E MATERIALI

Dalla nostra esperienza lavorativa e familiare, e dalla lettura condivisa con i figli e con i bambini dell'ambulatorio di Villa Immacolata, non ci sentiamo di consigliare particolari adattamenti alla lettura per bambini con disturbi del neurosviluppo. I consigli sono gli stessi per tutti: scegliere i libri con cura, seguendo la "**zona di sviluppo prossimale**" del bambino che abbiamo di fronte, ascoltando i loro interessi, e cercando costantemente di ampliarli.

Un occhio di riguardo è bene averlo per le **illustrazioni**, che dovrebbero essere chiare e comprensibili a "colpo d'occhio". Per iniziare, sono preferibili quei libri che prevedono una sola immagine per pagina, soggetto delle semplici frasi che dovrebbero comporre il libro, per facilitare la comprensione e l'associazione immagine-vocabolo. Si procede aumentando la complessità di immagini e struttura sintattica, seguendo lo sviluppo e l'interesse del bambino.

Per la lettura dei libri Inbook è bona prassi svolgere incontri con i genitori, utilizzando lo spazio terapia e facendo rimanere il genitore in stanza per illustrare le modalità di approccio alla lettura. La lettura avviene attraverso il modeling: i simboli vengono indicati uno ad uno, facendo attenzione a non coprire con il dito né l'immagine né la parola, mantenendo velocità e ritmo della narrazione. All'ascolto si accompagna così la presenza del simbolo associato alla parola letta e chi ascolta può seguire più facilmente il testo.

Da non sottovalutare la **posizione da assumere durante la lettura**. Soprattutto con quei bambini che presentano un deficit nell'attenzione sociale, può essere utile prediligere la lettura posizionandosi di fronte al bambino, alla sua altezza, con il libro al centro.

Come per la lettura con qualsiasi bambino, è fondamentale la **scelta di tempi e luoghi**. È importante prediligere momenti in cui il bambino è calmo e sereno, e non impegnato in altre attività per lui interessanti. Un'idea può essere quella di utilizzare il libro per promuovere e favorire la routine dell'addormentamento.

È probabile che il tempo dedicato alla lettura sia inizialmente molto breve, potrebbe succedere che il primo scoglio da superare sia quello di fermare l'attenzione tra una pagina e l'altra. Alcuni bambini sembrano più affascinati dal girare le pagine che dall'osservare insieme le figure. È importante, in questi casi, mantenere il controllo del libro, permettendo al bambino di girare la pagina dopo aver osservato l'immagine, magari anche per breve tempo, da aumentare gradualmente, rispettando i tempi del piccolo lettore.

Per i bambini con sviluppo atipico, che possono presentare un sovraccarico sensoriale, è necessario porre particolare attenzione nella **scelta di colori e materiali dell'ambiente dove si legge**. In questi casi è consigliabile l'utilizzo di colori neutri, non troppo accesi, e la possibilità di variare facilmente il materiale di eventuali tappetini o cuscini, in base alla preferenza dei bambini.

Un requisito fondamentale affinché la lettura diventi un momento di piacevole condivisione per tutti i bambini è l'individuazione di un angolo tranquillo e "morbido", in un momento in cui il bambino appare orientato verso di noi e non "distratto" da altri interessi.

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La Cura della Lettura

Documento di indirizzo e indicazioni operative per la promozione della lettura condivisa **in modo integrato tra servizi sanitari, educativi, culturali e sociali**

La collaborazione rende più agevole il portare a compimento le cose e la condivisione può sopperire a eventuali carenze individuali. La tendenza alla collaborazione è inscritta nei nostri geni, ma non deve rimanere confinata a comportamenti di routine; ha bisogno di essere sviluppata e approfondita.

(R. Sennet)

Credo che l'evoluzione della nostra specie riguardi la nostra coscienza e i nostri valori. Ripercorrendo la nostra storia, riconosciamo l'apparire di momenti di consapevolezza, di persone - possiamo chiamarle santi, maestri yoga, illuminati - che hanno saputo rinunciare a una coscienza di tipo egocentrico e materialista, per scegliere un comportamento di compassione, comprensione e amore, nel quale non c'è posto per l'egocentrismo, lo sfruttamento dell'ambiente, il profitto o il guadagno individuale.
Credo che sia questa la direzione che dobbiamo seguire.

(P. Russel)

Documento realizzato a cura del Gruppo "Integrazione" attivato per il progetto Cepell "*La cura della lettura*":
Anna Pedrotti (Dipartimento salute e politiche sociali, Provincia autonoma di Trento), Michela Perolini e Alessia Ferrario (U.O.D Promozione Salute - U.O.S Servizi Territoriali/ATS Brianza).

Introduzione: la promozione della lettura in eta' 0-6 in modo integrato tra servizi

In un determinato territorio gli interventi di promozione della lettura 0-6 potrebbero essere avviati a partire "dal basso" (es.:associazioni, operatori, ...) oppure "dall'alto" (es: istituzioni...), possono essere iniziative piccole e limitate nel tempo oppure progettualità più complesse e articolate, possono rientrare nell'ambito di programmi nazionali noti e consolidati come ad esempio Nati per Leggere (NpL) o meno.

Qualsiasi sia la tipologia degli interventi, a partire dall'interesse di uno o più soggetti di un territorio che si pongono l'obiettivo di promuovere iniziative per la lettura precoce, riteniamo che dovrebbero essere presi in considerazione alcuni elementi di carattere generale:

- **l'equità**: significa offrire a tutti i bambini e le loro famiglie pari opportunità di migliorare e preservare la propria salute, in virtù di un accesso equo e giusto alle risorse per la salute e la propria crescita;
- **la centralità** del bambino e delle famiglie: significa porre al centro il bambino e i suoi genitori, nel loro contesto di vita e comunità di riferimento, e progettare iniziative patendo dal loro punto di vista (non da quello dei servizi);
- **l'intersettorialità**: significa considerare e coinvolgere fin dall'inizio tutti i potenziali interlocutori del territorio di riferimento che lavorano per e con le famiglie e che possono lavorare in maniera sinergica rispetto all'obiettivo, assicurando risultati migliori e duraturi nel tempo;
- **il metodo di lavoro**: significa porre attenzione a elaborare il progetto, definendolo in modo condiviso, prevedendo obiettivi, azioni, responsabilità, ecc.;
- **la sostenibilità**: considerare azioni sostenibili in grado di mantenere i propri vantaggi per le comunità e le popolazioni, oltre alla loro fase iniziale di implementazione, quindi che possono continuare ad essere realizzate, tenendo conto dei limiti dati dai finanziamenti, dalle competenze, dalle infrastrutture, dalle risorse naturali e dalla partecipazione da parte dei portatori di interesse;
- **l'efficacia**: ossia la capacità di un progetto di raggiungere gli obiettivi fissati e di apportare cambiamenti in termini di promozione alla salute, integrandosi al contesto ambientale e cercando di raggiungere il miglior risultato possibile in una determinata situazione;
- **la valutazione di impatto**: considerare se e come il progetto abbia raggiunto i risultati prefissati in termine di cambiamenti, nelle peculiarità e nelle capacità personali, e/o nelle azioni e nelle norme sociali, e/o nelle prassi organizzative e nelle politiche pubbliche, attribuibili all'attività di promozione della salute.

ESPERIENZE SIGNIFICATIVE NELLA PROVINCIA DI TRENTO, DI MONZA E DELLA BRIANZA

Facendo riferimento ad iniziative realizzate nei nostri contesti, presentiamo brevemente, e a titolo di esempio, alcuni progetti di promozione della lettura 0-6 che vedono sviluppata la rete territoriale e che interessano i servizi educativi per la prima infanzia, i reparti ospedalieri di neonatologia e pediatria, i consultori, i centri vaccinali, i pediatri di famiglia, le biblioteche, i musei, le associazioni del terzo settore, i comuni, le istituzioni e molti altri servizi dedicati alle famiglie.

Servizi educativi per la prima infanzia

Il Comune di Monza, dopo aver conosciuto il programma in un'iniziativa proposta da ATS, nel 2019 ha formato tutte le educatrici dei 7 servizi nido comunali, un Tempo per le Famiglie e una Scuola dell'Infanzia, raggiungendo 120 educatrici. Estremamente rilevante la ricaduta formativa sull'attività degli asili nido che hanno rivisto il proprio approccio alla lettura, riconoscendone l'importanza; le educatrici hanno potuto focalizzare le proprie modalità di lettura e acquisire nuovi strumenti mettendo all'attenzione la fascia d'età 0-1 anno. Interessante anche l'apertura del nido verso l'esterno attraverso il BIBLIONIDO, quando il nido apre al territorio con percorsi dedicati alla lettura.

I servizi educativi per la prima infanzia del Comune di Trento (nidi d'infanzia e servizi integrativi 0-3) da quasi vent'anni collaborano con la Biblioteca comunale per la promozione della lettura, organizzando visite nella biblioteca con i bambini e i genitori, oppure momenti di lettura da parte dei bibliotecari nei servizi. Le educatrici invitano i genitori a leggere anche a casa, promuovono attivamente il programma NpL diffondendo materiali informativi e curando l'acquisto dei libri secondo la bibliografia consigliata. Dal 2020 è stata offerto a tutte le educatrici il corso base sulle buone pratiche per lo sviluppo precoce (Corso Early Childhood Development del Centro per la Salute del Bambino) e alcune di loro hanno frequentato il corso multiprofessionale Nati per Leggere e Nati per la Musica (NpLM), a seguito del quale alcuni servizi hanno avviato ulteriori progetti specifici, anche rivolti al personale (es. dono del libro alle neomamme).

Reparti ospedalieri di Neonatologia e Pediatria

Il progetto del **Presidio Nati per Leggere presso l'Ospedale di Desio** ha preso forma all'inizio di maggio 2018 con la realizzazione di un angolo in corrispondenza del box infermiere, predisponendo un pannello raffigurante bimbi e libri e appendendo un ramo con delle frasi che riguardano la lettura. Sono state predisposte due bacheche dove i genitori possono trovare indicazioni su come avvicinarsi a questa esperienza e sui riferimenti per approfondire le informazioni di NpL in assenza di personale dedicato. Considerata la molteplicità di utenti stranieri, il box è dotato anche di pieghevoli informativi appositamente preparati da NpL per i genitori in varie lingue (italiano, albanese, arabo, cinese, croato, francese, inglese, romeno, serbo, sloveno, spagnolo, russo e tedesco).
Si sta cercando di coinvolgere e motivare anche il personale medico e infermieristico nell'utilizzo dei libri da proporre ai bambini durante le visite, sensibilizzando i genitori nell'utilizzo anche a casa.

ASST Brianza ha una consolidata collaborazione con la biblioteca per cui alle neo-mamme che hanno partecipato al corso di preparazione al parto viene proposto un incontro in biblioteca alla presenza anche dell'ostetrica. Spazi allestiti per la lettura sono presenti nei **reparti di Pediatria e di Ostetricia dell'ospedale di Vimercate**. La lettura viene proposta anche nel reparto di **Patologia Neonatale** come veicolo relazionale tra il neonato e i genitori nel momento della marsupio-terapia: il personale invita i genitori a parlare con il proprio bambino per creare la continuità dalla vita intrauterina dopo la nascita. I genitori possono raccontare, recitare una filastrocca e cantare, oltre ovviamente a toccare e accarezzare il proprio bambino. Nei reparti sono stati allestiti spazi dedicati alla lettura ove è presente materiale NpL a disposizione dei genitori. Grazie al progetto "Aiutaci a crescere, regalaci un libro" con Giunti editore, l'ospedale di Vimercate ha iniziato dal gennaio 2020 a donare un libro a tutti i nuovi nati e alla dimissione dal reparto di pediatria, accompagnato da un segnalibro descrittivo del progetto NpL.

Nella sala di aspetto del **Pronto soccorso pediatrico e presso gli ambulatori dell'Ospedale di Trento** e il **Reparto di Pediatria dell'ospedale di Rovereto dell'Azienda provinciale per i servizi sanitari della Provincia di Trento (Apss)** con i volontari NpL sono stati organizzati incontri di lettura per i bambini in attesa della visita o ricoverati, coinvolgendo i genitori e diffondendo materiali informativi sul programma NpL. Una maestra della **scuola** presente presso il reparto di Pediatria di Trento ha partecipato alla formazione multiprofessionale NpLM e si occupa della gestione dei libri a disposizione dei bambini ricoverati. Due operatori della **Terapia Intensiva Neonatale di**

Trento hanno partecipato recentemente alla formazione multiprofessionale NpLM e stanno coinvolgendo/informando altri colleghi sui benefici e sulla pratica della lettura, in un ambiente sonoro adeguato alle caratteristiche del neonato pretermine o ricoverato. Gli operatori suggeriscono ai genitori di portare un libro che leggevano al bimbo durante la gravidanza e di cantare a bassa voce ninne-nanne e filastrocche che fanno parte del loro bagaglio culturale, canzoncine che evocano ricordi ed emozioni piacevoli. L'associazione **Amici della Neonatologia Trentina** offre in dono a tutti i genitori dei bambini ricoverati in TIN un libro NpL e un CD NpM con materiali informativi per i genitori, favorendo la pratica della lettura e l'esperienza musicale già durante il ricovero. In futuro è previsto l'allestimento di una piccola biblioteca per i genitori dei bambini ricoverati.

Consultori, Centri vaccinali e Pediatri di famiglia

Il programma NpL è attualmente proposto in fase sperimentale dai **consultori di ASST Lecco, Monza e Brianza** durante i corsi di preparazione alla nascita ed è consolidato nel dopo parto nei gruppi mamma-bambino. Le attività NpL presso i consultori si svolgono durante gli incontri di preparazione alla nascita o di massaggio infantile e sono condotte insieme dal personale del consultorio e dai bibliotecari. Nel corso della sperimentazione si è passati da dedicare uno spazio durante uno degli incontri ad uno specifico incontro dedicato solo a NpL in cui viene presentato il programma e le sue finalità, cercando di sensibilizzare i genitori sull'importanza ed i benefici della lettura precoce. Vengono distribuiti pieghevoli e segnalibri con piccole bibliografie e indicazioni per la scelta del libro in base all'età del bambino, che vengono poi integrati in base alle curiosità e domande dei partecipanti. Vengono mostrati albi illustrati selezionati da NpL, volontari e bibliotecari, di cui un paio vengono letti al gruppo per poter dare consigli pratici sul come leggere ad alta voce. A fine incontro si presenta l'attività NpL che si svolge nelle biblioteche della zona, invitando adulti e bambini a scoprire gli spazi, le iniziative, le competenze del personale e i servizi messi a disposizione dal sistema bibliotecario e dalle singole sedi.

I consultori della Azienda provinciale per i servizi sanitari della Provincia di Trento offrono ai futuri genitori e famiglie incontri anche on-line e diffondono materiali informativi sulle buone pratiche per la salute materno-infantile, compresa la pratica della lettura. Le ostetriche, in rete con altri soggetti del territorio (bibliotecari, musicisti, operatori dei punti nascita, gruppi di genitori, ecc.), supportano le iniziative e attività di promozione della lettura organizzate dalle realtà locali, informando e indirizzando i genitori.

Il Sistema bibliotecario e ASST Lecco in collaborazione con le associazioni Favolare e Libringiro ha inaugurato spazi NpL all'interno dei **Centri vaccinali di Lecco e Cernusco Lombardone**, dove passa quasi la totalità della popolazione e nei quali, nell'attesa precedente e successiva al vaccino, è possibile raggiungere famiglie che non frequentano le biblioteche. Gli spazi sono allestiti con materiale informativo, libri tratti dalle bibliografie NpL e un raccoglitore contenente una breve spiegazione sui benefici della lettura in età precoce, la presentazione di alcuni libri NpL e consigli di lettura. Sulle pareti sono affisse alcune copertine di libri NpL e un calendario bimestrale delle iniziative NpL delle biblioteche e dei consultori del territorio.

Il Dipartimento di Cure Primarie di ATS Brianza attraverso un'indagine ha raccolto i dati dei pediatri che già conoscono il programma NpL e di quelli che sono interessati a conoscerlo. Durante un Convegno dedicato ai pediatri di famiglia è stato presentato il programma NpL ed è stato distribuito un Kit composto da libri, locandine e segnalibri da esporre nel proprio studio. È stato consigliato di proporre ai genitori la lettura attraverso la visione dei libri adatti nelle visite del bilancio di salute.

Alcuni **pediatri di famiglia della Provincia di Trento** hanno frequentato il corso multiprofessionale NpLM e promuovono attivamente il programma NpL e NpM in occasione dei bilanci di salute, anche con attività di lettura presso il proprio ambulatorio, in collaborazione con i volontari NpL locali. Altri pediatri di famiglia promuovono il programma con la diffusione di materiali informativi ai genitori.

Biblioteche e Musei

Il **Sistema Bibliotecario Trentino**, oltre a supportare attività specifiche NpL nelle biblioteche afferenti tramite bibliotecari e volontari formati, cura e diffonde la bibliografia e le mostre bibliografiche NpL e organizza eventi rivolti alla popolazione e agli operatori, promuovendo il programma nell'ambito del coordinamento provinciale NpL anche in occasione di eventi locali con diversi soggetti del territorio (es. **Festival dell'Economia, Giornata internazionale del rifugiato**,...).
Presso il **Museo della Scienza di Trento (MUSE) "Amico dei bambini e degli adolescenti"**, lo spazio Maxi-Ooh è dedicato ai bambini di 0-5 anni insieme ai loro genitori/adulti accompagnatori e permette di scoprire, capire, osservare, provare diverse esperienze sensoriali. Nello spazio sono a disposizione libri della bibliografia NpL. Al MUSE vengono organizzati anche incontri con i genitori (**"Parliamo di bimbi"**) su diversi argomenti, proposti all'interno di reti di collaborazioni tra diversi soggetti educativi, sanitari, ecc. della città che si occupano di bambini e famiglie. Tra gli incontri, vi sono anche quelli dedicati alla lettura e musica e condivise in famiglia, condotti dai referenti provinciali NpL NpM insieme ai volontari. Lo stesso Muse, in collaborazione con i pediatri, ha organizzato in passato incontri di informazione per i genitori e di formazione per i futuri educatori specifici su tutte le buone pratiche per lo sviluppo precoce dei bambini, comprese a la lettura e musica. Tale attività sono attualmente sospese a causa della pandemia.

Sul territorio di ATS **Brianza, il Sistema Bibliotecario del Territorio Lecchese e quelli di Brianza Biblioteche e Cubinrete**, oltre alle programmate letture per le diverse fasce di età consolidate da tempo, l'impegno si è concentrato sul rafforzamento della collaborazione con ASST Lecco-Monza-Brianza. Sono proseguiti gli incontri di presentazione del programma NpL e letture negli ospedali di Lecco, Merate, Desio e Vimercate e nei 35 consultori familiari presenti sul territorio a cura dei bibliotecari e dei volontari lettori.
I Sistemi bibliotecari sono intervenuti ad un incontro, uno per Provincia, organizzato da ATS Brianza e rivolto a operatori delle realtà educative 0-3 anni per presentare le proprie attività e le collaborazioni con le realtà territoriali costruite nel corso degli anni.

Associazioni e Terzo settore:

La collaborazione con le associazioni del territorio è una scelta importante perché permette di potenziare il lavoro realizzato dai sistemi sanitari e educativi e raggiunge la popolazione con canali diversi, più diretti ed immediati.
Le **Associazioni "Volta la pagina", "Favolare" e "Libri in giro" delle Province di Monza, Brianza e Lecco**, nate da iniziative di genitori sensibili, sono una importante ricchezza per il territorio perché agiscono durante eventi, anche in spazi informali e con modalità immediate avvicinano genitori e bambini sui temi della lettura precoce. I volontari dell'**Abio** agiscono direttamente all'interno dei reparti ospedalieri.

Alcune Associazioni che aderiscono alla **Rete "Piccoli intrecci" del Comune di Trento** (coordinate da **Punto Famiglie - Associazione A.M.A.**) organizzano e promuovono insieme attività con i bambini e i genitori, comprese attività di lettura 0-6 (es. Progetto **"Spazi per crescere"**, Progetto **"Istruzione a naviganti"**) progettate e realizzate in collaborazione con i servizi educativi, le biblioteche e altre realtà territoriali e il coordinamento provinciale NpLM. La attività sono state proposte anche nei parchi pubblici, all'aperto. Alcuni operatori hanno partecipato alla formazione multiprofessionale NpLM.
Il progetto **"Il valore della lettura e della musica in famiglia"** promosso dall'**Associazione culturale Le Arti** in **Val di Non e Piana Rotaliana in Provincia di Trento** prevede un'ampia collaborazione tra enti locali, biblioteche, scuole musicali, servizi sanitari e musei. Sensibilizza e informa genitori e operatori sul valore della lettura e della musica in famiglia secondo i programmi NpL e NpM, diffonde lettura e musica fin dalla gravidanza e nei primi anni di vita come buone pratiche di sviluppo integrate, promuove la conoscenza e l'accesso ai servizi culturali del territorio. Il progetto prevede anche: incontri pre-parto con i futuri genitori dedicati alla lettura e musica in famiglia; l'invito da parte dei pediatri di libera scelta in occasione del bilancio di salute a visitare la biblioteca più vicina per ritirare un libro in dono per il proprio bambino; interventi di volontari NpL e NpM presso le sale di aspetto degli ambulatori nei giorni dedicati ai bilanci di salute; laboratori di lettura e musica nelle biblioteche, al museo, nei parchi pubblici.

Comuni e Istituzioni

Alcuni Comuni della Provincia di Trento offrono il dono del libro e materiali informativi su NpL in occasione dell'iscrizione del neonato all'anagrafe.
ATS Brianza ha costituito un tavolo interistituzionale sui temi della salute del bambino ove è inserita la promozione e diffusione del programma NpL. Sulla base delle indicazioni del protocollo Regionale del 2016, ATS Brianza ogni anno ha dedicato risorse economiche della Promozione Salute per formare operatori e volontari che operano nei diversi contesti sanitari educativi e sociali. Agli enti aderenti è stato fornito un kit composto da libri, segnalibri, brochure anche in lingua straniera, locandine e guida per i genitori per sostenere l'avvio dell'attività.

È possibile attingere alle esperienze di altre realtà nazionali confrontandosi con i referenti territoriali NpL ed è possibile fare riferimento al sito per il Premio nazionale NpL (www.natiperleggere.it/premio-nazionale-npl.html).

PROPOSTA DI INDICAZIONI OPERATIVE

Sulla base del confronto delle nostre esperienze (**ATS Brianza e Provincia di Trento, nell'ambito del programma Nati per Leggere**), di seguito proponiamo una traccia di alcune **azioni/modalità di lavoro** che riteniamo siano efficaci per promuovere e sostenere la pratica della lettura precoce in famiglia in un territorio definito, sviluppando la rete e l'integrazione tra i servizi.

a) Definire i ruoli: individuare chi ha il mandato (se previsto), definire chi promuove il progetto/le attività/l'iniziativa (ente capofila), chi lo coordina (coordinamento), considerando che un progetto di promozione della lettura può essere più o meno complesso e articolato nel tempo (avviato dalle istituzioni amministrative, sanitarie, culturali, ecc., ma anche da singole associazioni, comuni, biblioteche, pediatri, ecc.)

b) Analizzare il contesto territoriale di riferimento e le attività che sono già in essere (da parte del coordinamento): individuare quali sono i soggetti da coinvolgere nel proprio contesto territoriale, considerando e valorizzando i soggetti che già promuovono iniziative/attività di lettura per bambini e famiglie a diverso titolo e ruolo e coloro che potrebbero essere potenzialmente coinvolti (in quanto operano a stretto contatto con i bambini e con le famiglie).

I settori da considerare sono i seguenti:

- culturale: biblioteche, musei, librerie, scuole musicali, ecc.
- educativo: nidi e scuole dell'infanzia
- sanitario: consultori, pediatri di famiglia, ospedali, servizi vaccinali, ecc.
- sociale: servizi e cooperative sociali e terzo settore
- volontariato anche presso le strutture sanitarie
- associazioni e gruppi di famiglie/genitori
- enti locali (comuni, ...)

c) Creare un gruppo di lavoro intersettoriale (da parte del coordinamento locale) che sia rappresentativo delle diverse realtà contattate e che hanno manifestato interesse a promuovere la lettura precoce in famiglia, garantendo un approccio multidimensionale alla tematica, condividendo paradigmi diversi nel rispetto delle reciproche competenze e considerando anche il coinvolgimento istituzionale.
La costituzione di un gruppo di lavoro che condivide fin dall'inizio un processo sinergico è favorevole alla realizzazione delle azioni e può essere elemento funzionale a garantire il raggiungimento dell'obiettivo con interventi differenziati ma con un'unica visione.

d) Definire il progetto (da parte del gruppo di lavoro): analizzare le attività già in essere nel territorio (risultati, punti di forza e criticità...), definire gli obiettivi, individuare e definire le azioni (comprensive di responsabilità e cronoprogramma), prevedere come monitorane l'implementazione, considerando anche l'inserimento del progetto nella programmazione sanitaria, culturale, ecc. (budget, ecc.). Ulteriori elementi da tener presente:

- le risorse necessarie (anche economiche)
- il possibile aggancio con altri programmi, progetti e buone pratiche di promozione dello sviluppo

del bambino (Nurturing Care for Early Childhood Development)
- la comunicazione sulle attività previste (incontri, eventi, ecc) e i materiali informativi (pieghevoli, video, locandine ecc.); prevedere diverse modalità (contatti, social, ecc) tramite i soggetti del gruppo di lavoro e siti specifici, con materiali condivisi; inserire i riferimenti per contatti e informazioni; dare visibilità alla rete (loghi dei soggetti coinvolti).

e) Organizzare un "evento lancio" del progetto rivolto agli operatori e alla comunità (da parte di coordinamento e gruppo di lavoro): un "evento lancio" di promozione della progettualità può essere una modalità per creare raccordi sul territorio con soggetti sensibili che già intervengono a livello locale con azioni che possono integrarsi tra loro; un laboratorio e/o un focus group può favorire l'emersione di peculiarità, di esperienze e di obiettivi a cui poter tendere.

f) Supportare le attività previste dal progetto: organizzare incontri operativi nei territori insieme alle diverse realtà coinvolte per conoscersi e far conoscere le azioni in atto; rilevare i bisogni, dare contatti e riferimenti (es. per reperire i libri attingendo a bibliografie validate tramite le biblioteche) che possono essere utili in ogni servizio.

g) Rilevare le conoscenze e competenze in essere nelle diverse realtà interessate dal progetto ed eventualmente organizzare la formazione (coordinamento e gruppo di lavoro): organizzare preferibilmente corsi multiprofessionali, rivolti ad operatori sanitari, educativi, culturali, sociali,...), con l'obiettivo non solo di sviluppare le conoscenze e competenze sui benefici della lettura precoce e sulla modalità per favorirla, ma anche di favorire l'incontro tra diversi soggetti (la frequenza di un corso multiprofessionale può creare i presupposti per sviluppare reti territoriali rappresentative dei diversi settori che condividano azioni e iniziative).
Nell'offerta informativa/formativa, considerare anche di organizzare corsi specifici per volontari che sono a contatto con bambini e genitori, nei diversi contesti. Gli stessi operatori possono contribuire a individuare volontari che operano nei diversi contesti (es. volontari Abio in ospedale).

h) Monitorare lo stato avanzamento del progetto (coordinamento e gruppo di lavoro), analizzando risultati ed eventuali criticità, e valutarne l'impatto, anche con strumenti previsti dai programmi di intervento o dalle Sorveglianze, se su scala regionale/provinciale (es. Sorveglianza Bambini 0-2 anni).

Indicazioni operative e progetti dedicate alle comunità straniere

Il Progetto **Mamma Lingua: storie per tutti, nessuno escluso** dell'Associazione italiana biblioteche ha come partner la **Biblioteca di Ala in provincia di Trento**. Il progetto si rivolge alla fascia di bambini 0-6 anni delle più numerose **comunità straniere** del nostro paese considerando che il riconoscimento delle diverse lingue d'origine e delle diverse situazioni di bilinguismo costituiscono il modo più efficace per favorire l'apprendimento dell'italiano e migliorare l'integrazione delle famiglie straniere. Sono stati realizzati supporti visivi (manifesto, sito web, breve video pubblicitario d'impatto realizzato da uno dei migliori studi creativi di storytelling in Italia) che saranno distribuite nelle biblioteche. Il gruppo di lavoro nazionale ha lavorato all'aggiornamento della bibliografia Mamma Lingua con l'aggiunta di libri per bambini in filippino/tagalog, hindi, tamil, urdu, portoghese, russo, tedesco, e ha curato la formazione di operatori e volontari sui benefici della lettura precoce e il sostegno del bilinguismo, oltre all'attività di supporto e stimolo ad organizzare attività di sostegno alla genitorialità tramite la condivisione dei libri con i bambini dal primo anno di vita. I libri multilingue sono consegnati ai partner territoriali in una valigia insieme al lettore ottico PENpal di Mantra Lingua. Utilizzando i libri si organizzano incontri sul territorio con l'intenzione di poter convogliare le giuste energie verso gli obiettivi del progetto.
All'interno delle **attività consultoriali di ASST Brianza** sono stati organizzati incontri con mamme straniere. In alcuni casi si è riusciti ad avere la presenza di un mediatore culturale. Alle mamme è stato chiesto di cantare o recitare filastrocche in lingua madre.
Sul **territorio monzese** le operatrici di **Spazio Colore**, un servizio gratuito offerto dalla Caritas Decanale di Monza alle donne straniere, hanno inserito nelle attività proposte quella della lettura. Donne provenienti da paesi differenti si ritrovano per chiacchierare, discutere di attualità e dare libero sfogo alla creatività con i laboratori artistici. È da qui che spesso mogli, ragazze e mamme straniere muovono i primi passi verso l'integrazione.

ARCHIVIO DELLE LEGGI, DEI PROGRAMMI REGIONALI E DEI PROTOCOLLI D'INTESA

In questa sezione elenchiamo una raccolta delle leggi e dei protocolli d'intesa relativi alla promozione e il sostegno della lettura sul territorio italiano. Cliccando sulla relativa legge è possibile visualizzarne il testo.

Legge nazionale numero 15 del 13 febbraio 2020
www.senato.it/4800?newsletter_item=8401&newsletter_numero=701#

Regione Marche: legge regionale 15 del 22 aprile 2020
www.consiglio.marche.it/banche_dati_e_documentazione/leggi/dettaglio.php?idl=2150

Regione Calabria: legge regionale 464 del 26 settembre 2019
www.consiglioregionale.calabria.it/upload/istruttoria/P.l.%20464%20X.pdf

Regione Puglia: legge regionale 40 del 12 dicembre 2013
trasparenza.regione.puglia.it/sites/default/files/provvedimento_amministrativo/45301_40_12-12-2013_L_40_12_12_2013.pdf

Regione Campania: legge regionale 15 del 24 giugno 2020
regione.campania.it/normativa/item.php?7b7fec2087f982d694b26f0cc9f850d6=8bb42a78e7ad30e-87769a5cfe7ec5f52&pgCode=G19I231R1887&id_doc_type=1&id_tema=22&refresh=on

Regione Lazio: legge regionale 16 del 21 ottobre 2008
www.consiglio.regione.lazio.it/consiglio-regionale/?vw=leggiregionalidettaglio&id=9122&sv=vigente

Protocollo d'intesa Regione Lombardia, Centro per la Salute del Bambino e Unicef:
www.promozionesalute.regione.lombardia.it/wps/wcm/connect/071960a0-c257-472e-89e3-c759a-174e2f5/schema+prot_rev_UNICEF_CSB_def.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPA-CE-071960a0-c257-472e-89e3-c759a174e2f5-mjmEvXO

Protocollo d'intesa Provincia Sondrio Ats della Montagna Asst Valtellina e Alto Lario:
www.asst-val.it/documents/3191802/8898696/Delibera_379+%287%29.pdf/09ceadb8-35be-832d-de31-99de7f666a2a

Protocollo d'intesa ASST e Comune di Lecco:
www.sistemasudovestbresciano.it/npl2/ASSTLeccoComunediLecco.pdf

Considerazioni

Il percorso che ha condotto all'elaborazione di questo documento di indirizzo relativo alla promozione della lettura in modo integrato tra servizi sanitari, educativi, culturali e sociali, ci ha permesso di conoscerci e di confrontarci, arricchendoci reciprocamente di idee per migliorare le iniziative 0-6 che entrambe le realtà stanno portando avanti nel proprio territorio.
Nel documento abbiamo sintetizzato alcune azioni a supporto dello sviluppo della rete territoriale per la promozione della lettura ricavate dalle nostre esperienze e contestualizzate alle nostre realtà. Si tratta di azioni certamente non esaustive, ma che ci auguriamo possano essere utili e fornire spunti operativi anche ad altre realtà per realizzare iniziative collaborative di promozione della lettura per e con i bambini e le famiglie.

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://www.adhd.marionegri.it/index.php/newsletter/iscrizione-newsletter

link per potersi cancellare dalla mailing list:
http://adhd.marionegri.it/index.php/newsletter/cancellazione-newsletter

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

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