Cerebral palsy research news

Monday 25 July 2022

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Interventions and Management

1. Assisting hand use and self-care bimanual performance of children with unilateral spastic cerebral palsy
Marina B Brandão, Wendy J Coster, Priscilla R P Figueiredo, Maíra F Amaral, Andrew M Gordon, Marisa C Mancini

Dev Med Child Neurol. 2022 Jul 22. doi: 10.1111/dmcn.15362. Online ahead of print.

Aim: To examine the relationship between assisting hand use in bimanual activities and children's self-care activities and task performance. Method: We retrospectively analysed daily functioning (Pediatric Evaluation of Disability Inventory [PEDI]) and bimanual performance (Assisting Hand Assessment [AHA]) data from the assessment of 112 children (mean age: 8 years 10 months [SD 2 years 1 month], range 3 years 7 months-17 years 4 months; 66 males, 46 females) with unilateral spastic cerebral palsy (CP). We used Rasch analysis to examine the relationship between individual item scores from the AHA and the self-care items (functional skills, caregiver assistance) from the PEDI. Results: Most self-care functional skills and caregiver-assisted tasks were located on the middle of the unidimensional continuum. These items showed similar levels of difficulty as the items from the AHA related to the effective coordination of two hands, appropriate pace, and use of the assisting hand to stabilize and release objects, as well as variations in arm movements. Interpretation: The distribution of the PEDI self-care and AHA items along the unidimensional continuum illustrates the relationship between assisting hand use and self-care bimanual performance. Interpretation of the items' locations on the hierarchical unidimensional continuum may be helpful to therapists' clinical reasoning and suggest intervention goals to improve the hand function and daily functioning of children with unilateral spastic CP. Such an application needs further investigation.

PMID: 35866562

2. Predictors of postoperative systemic inflammatory response syndrome after scoliosis surgery in adolescents with cerebral palsy: A retrospective analysis
Kesavan Sadacharam, Zhaoping He, Maureen F Edelson, Kimberly McMahon, Catherine Madurski, B Randall Brenn

N Am Spine Soc J. 2022 Jun 11;11:100135. doi: 10.1016/j.xnsj.2022.100135. eCollection 2022 Sep.

Background: Systemic inflammatory response syndrome (SIRS) is known to complicate postsurgical intensive care patients. We noticed that roughly half children with cerebral palsy who undergo posterior spinal fusion (PSF) for neuromuscular scoliosis developed SIRS in the intensive care unit. There is a paucity of literature detailing the impact of intraoperative causes of postoperative SIRS and downstream consequences in these patients. Study purpose was to understand the factors associated with SIRS in children who undergo PSF for neuromuscular scoliosis. Methods: This retrospective, case control study included children who underwent PSF for neuromuscular scoliosis. Patients with idiopathic scoliosis, osteogenesis imperfecta, and tracheotomy were excluded. Subjects were divided into two study groups based on the diagnosis of SIRS in the intensive care unit. Descriptive statistical analysis was used to identify factors associated with SIRS; a regression analysis

was used to further evaluate the independent and significant influence of these factors. Results: There was no significant difference in the demographic and other preoperative variables. However, total blood products (ml/kg) administered was significantly higher among the SIRS group compared with the non-SIRS group (54.4±41.0 vs 34.1±21.5 P <0.034). Percent of patients remaining intubated was greater in the SIRS group compared with the non-SIRS group (44.1% vs 7.0%, P < 0.001). The regression model revealed that the odds to develop SIRS in patients who were not extubated were 7.467-fold higher (CI: 1.534-36.347) compared with those who were extubated (p=0.013). Conclusions: The incidence of SIRS is significantly higher among the patients who were not extubated at the end of PSF surgery. Further prospective studies are needed to look at the factors that impede the ability to extubate these patients at the end of surgery.

PMID: 35846346

3. Efficacy of Rehabilitation Therapy and Pharmacotherapy on Children with Cerebral Palsy: A Meta-Analysis
Qiuying Hou, Liang Li

Meta-Analysis Comput Math Methods Med. 2022 Jul 9;2022:6465060. doi: 10.1155/2022/6465060. eCollection 2022.

Background: Cerebral palsy (CP) has a serious impact on children's multiple motor functions and life behavior. Rehabilitation therapy or pharmacotherapy alone has been proven to have a good effect on patients' strength and gait. However, the efficacy of rehabilitation combined with pharmacotherapy for CP in children needs to be further explored. This study is aimed at assessing the effectiveness of this combined method on life function and social behavior in children with CP. Methods: PubMed, China National Knowledge Infrastructure, WanFang Data, EMBASE, and Web of Science databases were searched for all kinds of literature related to the treatment of pediatric CP published between 2000 and 2021. Basic information and experimental data from the literature were screened and extracted, and a meta-analysis was performed using Stata 16. Results: A total of 605 studies were retrieved, and finally, 10 studies involving 805 pediatric patients were included in the analysis. The analysis results showed that rehabilitation combined with pharmacotherapy could improve the treatment effective rate in children with CP compared with the control group using either alone (RR = 1.184, 95% CI (1.102, 1.273), P < 0.001). In addition, in terms of social behavior, the combined therapy could significantly improve activities of daily living (SMD = 2.94, 95% CI (1.66, 4.22), P < 0.001), motor ability (SMD = 1.86, 95% CI (0.75, 2.96), P = 0.001), adaptability behavior (SMD = 2.82, 95% CI (0.45, 5.18), P = 0.019), language behavior (SMD = 3.08, 95% CI (0.95, 5.22), P = 0.005), social behavior (SMD = 3.78, 95% CI (2.22, 5.35), P < 0.001), and fine motor behavior (SMD = 3.52, 95% CI (1.17, 5.86), P = 0.003). Conclusion: The current study shows that rehabilitation combined with pharmacotherapy can effectively improve the recovery, quality of life, and social behavior of children with CP.

PMID: 35855834

4. Effects of music therapy on functional ability in people with cerebral palsy: a systematic review
Sohei Yanagiwara, Tsubasa Yasuda, Minami Koike, Takatsugu Okamoto, Kenta Ushida, Ryo Momosaki

J Rural Med. 2022 Jul;17(3):101-107. doi: 10.2185/jrm.2022-014. Epub 2022 Jul 1.

Objective: This review aimed to investigate the effects of music therapy on functional ability in people with cerebral palsy. Materials and Methods: An electronic search of the CENTRAL, MEDLINE, and EMBASE databases was conducted. Randomized controlled trials that examined the effects of music therapy in patients with cerebral palsy were included. Results: Eight trials were eligible for inclusion in this study. We found a low risk of bias in random sequence generation and allocation concealment in all trials. The risk of bias in blinding of the outcome assessment was low in all studies. We found that music therapy had a significant effect on the Gross Motor Function Measure score (standardized mean difference [SMD] -0.42), Functional Independence Measure for Children score (SMD 0.38), and Goal Attainment Scale score (SMD -1.43). Music therapy had no significant effect on any of the other items. Conclusion: There is limited evidence that music therapy improves gross motor function and activities of daily living in patients with cerebral palsy. However, this was insufficient to allow for generalizable conclusions. Further studies with larger sample sizes are required to confirm the effects of music therapy in this population.

PMID: 35847757

5. Dietary and nutritional interventions in children with cerebral palsy: A systematic literature review
Fernanda Rebelo, Isabela Rodrigues Mansur, Teresa Cristina Miglioli, Maria Dalva Baker Meio, Saint Clair Gomes Junior

PLoS One. 2022 Jul 22;17(7):e0271993. doi: 10.1371/journal.pone.0271993. eCollection 2022.

Background: Cerebral palsy is an extremely severe brain injury associated with multiple nutritional and clinical issues, such as underweight, gastroesophageal reflux, constipation, and nutrient deficiency. Evidence-based dietary and nutritional interventions may improve the quality of life of children with cerebral palsy. Aim: Systematically review randomized clinical trials evaluating nutritional and dietary interventions in the clinical, nutritional, and neurodevelopmental aspects of children with cerebral palsy. Methods: A search was performed in electronic databases (LILACS, Medline, Web of Science, Embase, Scopus, Cochrane Library, ClinicalTrials.gov, Brazilian Digital Library of Theses and Dissertations, ProQuest Dissertations and Theses Database, OpenGrey) using keywords. The search was firstly performed in May 2020 and updated on June 18th, 2021. Eligible studies were randomized clinical trials, that included children between 2 and 12 years old, and evaluated the effect of nutritional or dietetic interventions on clinical, nutritional or neurodevelopmental outcomes. Risk of bias was investigated using the RoB-2 tool. The study was registered on PROSPERO (CRD42020181284). Results: Fifteen studies were selected. Positive results included the use of whey-based or pectin-enriched enteral formulas for gastroesophageal reflux (n = 6); 25-hydroxy-vitamin D supplementation for hypovitaminosis D (n = 2); supplementation with lipid mixture or diet with high -density energy for improvements in anthropometric measures (n = 2); supplementation with probiotics, prebiotics, symbiotics or magnesium for constipation (n = 2); nutritional support system for gross motor function (n = 1); lactoferrin and iron hydroxide polymaltose for iron deficiency anemia (n = 1); and educational intervention to improve feeding skills (n = 1). The overall risk of bias was high for 60% of the studies, and some concerns were raised for the remaining 40%. Conclusion: Some promising dietary and nutritional interventions may promote important clinical improvements for patients with cerebral palsy. However, evidence is weak, as few clinical trials have been published with many methodological errors, leading to a high risk of bias.

PMID: 35867728

6. Impact and management of drooling in children with neurological disorders: an Italian Delphi consensus
Antonella Riva, Elisabetta Amadori, Maria Stella Vari, Alberto Spalice, Vincenzo Belcastro, Maurizio Viri, Donatella Capodiferro, Antonino Romeo, Alberto Verrotti, Delphi panel experts' group; Pasquale Striano

Ital J Pediatr. 2022 Jul 19;48(1):118. doi: 10.1186/s13052-022-01312-8.

Background: The rate of chronic drooling in children older than 4 years is 0.5%, but it rises to 60% in those with neurological disorders. Physical and psychosocial consequences lead to a reduction in the quality of Life (QoL) of affected patients; however, the problem remains under-recognized and under-treated. We conducted an Italian consensus through a modified Delphi survey to discuss the current treatment paradigm of drooling in pediatric patients with neurological disorders. Methods: After reviewing the literature, a board of 10 experts defined some statements to be administered to a multidisciplinary panel through an online encrypted platform. The answers to the questions were based on a 1-5 Likert scale (1 = strongly disagree; 5 = strongly agree). The scores were grouped into 1-2 (disagreement) and 4-5 (agreement), while 3 was discarded. The consensus was reached when the sum of the disagreement or agreement was ≥75%. Results: Fifteen statements covered three main topics, namely clinical manifestations and QoL, quantification of drooling, and treatment strategies. All statements reached consensus (≥75% agreement). The 55 Italian experts agreed that drooling should be assessed in all children with complex needs, having a major impact on the QoL. Attention should be paid to investigating posterior hypersalivation, which is often neglected but may lead to important clinical consequences. Given that the severity of drooling fluctuates over time, its management should be guided by the patients' current needs. Furthermore, the relative lack of validated and universal scales for drooling quantification limits the evaluation of the response to treatment. Finally, the shared therapeutic paradigm is progressive, with conservative treatments preceding the pharmacological ones and reserving surgery only for selected cases. Conclusion: This study demonstrates the pivotal importance of a multidisciplinary approach to the management of drooling. National experts agree that progressive treatment can reduce the incidence of complications, improve the QoL of patients and caregivers, and save healthcare resources. Finally, this study highlights how the therapeutic strategy should be reconsidered over time according to the available drugs on the market, the progression of symptoms, and the patients' needs.

PMID: 35854335

7. Pharmacoeconomic Review Report: Glycopyrrolate (Cuvposa): (Medexus Pharmaceuticals, Inc.) [Internet]
No authors listed

Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2020 Jul. CADTH Common Drug Reviews.

Glycopyrrolate oral solution (Cuvposa) is an anticholinergic drug indicated to reduce chronic severe drooling in patients three to 18 years of age with neurologic conditions (e.g., cerebral palsy [CP]). It is available in a 1 mg/5 mL concentration in 473 mL bottles at a submitted price of $625.00 per bottle, or $6.61 per mL. The recommended starting dose of glycopyrrolate is 0.02 mg/kg three times daily, titrated in increments of 0.02 mg/kg every five to seven days based on therapeutic response and adverse reactions. The maximum recommended dose is 0.1 mg/kg three times daily, not to exceed 1.5 to 3 mg per dose (see Table 11 for further details). For a 30 kg patient, depending on dose, the daily cost of glycopyrrolate at the submitted price may range from $11.98 to $59.46 (see Table 5).The sponsor submitted a cost-utility analysis comparing glycopyrrolate oral solution to no treatment in the indicated population from the perspective of a Canadian publicly funded health care system over a 24-week time horizon.

PMID: 35849658

8. The Multidisciplinary Guidelines for Diagnosis and Referral in Cerebral Visual Impairment
Frouke N Boonstra, Daniëlle G M Bosch, Christiaan J A Geldof, Catharina Stellingwerf, Giorgio Porro

Front Hum Neurosci. 2022 Jun 30;16:727565. doi: 10.3389/fnhum.2022.727565. eCollection 2022.

Introduction: Cerebral visual impairment (CVI) is an important cause of visual impairment in western countries. Perinatal hypoxic-ischemic damage is the most frequent cause of CVI but CVI can also be the result of a genetic disorder. The majority of children with CVI have cerebral palsy and/or developmental delay. Early diagnosis is crucial; however, there is a need for consensus on evidence based diagnostic tools and referral criteria. The aim of this study is to develop guidelines for diagnosis and referral in CVI according to the grade method. Patients and methods: We developed the guidelines according to the GRADE method 5 searches on CVI (children, developmental age ≤ 18 years) were performed in the databases Medline, Embase, and Psychinfo, each with a distinct topic. Results: Based on evidence articles were selected on five topics: 1. Medical history and CVI-questionnaires 23 (out of 1,007). 2. Ophthalmological and orthoptic assessment 37 (out of 816). 3. Neuropsychological assessment 5 (out of 716). 4. Neuroradiological evaluation and magnetic resonance imaging (MRI) 9 (out of 723). 5. Genetic assessment 5 (out of 458). Conclusion: In medical history taking, prematurity low birth weight and APGAR (Appearance, Pulse, Grimace, Activity, Respiration) Scores (<5) are important. Different questionnaires are advised for children under the age of 3 years, older children and for specific risk groups (extremely preterm). In ophthalmological examination, eye movements, specially saccades, accommodation, crowding, contrast sensitivity and visual fields should be evaluated. OCT can show objective signs of trans-synaptic degeneration and abnormalities in fixation and saccades can be measured with eye tracking. Screening of visual perceptive functioning is recommended and can be directive for further assessment. MRI findings in CVI in Cerebral Palsy can be structured in five groups: Brain maldevelopment, white and gray matter lesions, postnatal lesions and a normal MRI. In children with CVI and periventricular leukomalacia, brain lesion severity correlates with visual function impairment. A differentiation can be made between cortical and subcortical damage and related visual function impairment. Additional assessments (neurological or genetic) can be necessary to complete the diagnosis of CVI and/or to reveal the etiology.

PMID: 35845239

9. Opioid prescription patterns among adults with cerebral palsy and spina bifida
Mark D Peterson, Neil Kamdar, Heidi J Haapala, Chad Brummett, Edward A Hurvitz

Heliyon. 2022 Jul 8;8(7):e09918. doi: 10.1016/j.heliyon.2022.e09918. eCollection 2022 Jul.

Background: Pain is the most common symptom of cerebral palsy and spina bifida (CP/SB). The objective of this study was to compare the opioid prescription patterns for differing pain types and overlapping pain among adults living with and without CP/SB. Methods: Privately-insured beneficiaries were included if they had CP/SB (n = 22,647). Adults without CP/SB were also included as controls (n = 931,528). Oral morphine equivalents (OMEs) were calculated. A multivariable logistic regression

was used to analyze the association between CP/SB and OMEs, across the three pain categories: (1) no pain, (2) isolated pain, and (3) pain multimorbidity. Results: Adults living with CP/SB had a higher OME prescription pattern per year than adults without CP or SB (8,981.0 ± 5,183.0 vs. 4,549.1 ± 2,988.0), and for no pain (4,010.8 ± 828.1 vs. 1,623.53 ± 47.5), isolated pain (7,179.9 ± 378.8 vs. 3,531.0 ± 131.0), and pain multimorbidity (15,752.4 ± 1,395.5 vs. 8,492.9 ± 398.0) (all $p < 0.001$), and differences were to a clinically meaningful extent. Adjusted odds ratios (OR) for prescribed OMEs were higher for adults with CP/SB vs. control and (1) no pain (OR: 1.51; 95%CI: 1.46, 1.56), (2) isolated pain (OR: 1.48; 95%CI: 1.44, 1.52), and (3) pain multimorbidity (OR: 1.79; 95%CI: 1.72, 1.86). Conclusions: Adults with CP/SB obtain significantly higher prescription of OMEs than adults without CP/SB.

PMID: 35847615

10. Examining older adults with neuroatypical conditions for MCI/dementia: Barriers and recommendations of the Neuroatypical Conditions Expert Consultative Panel
Matthew P Janicki, James A Hendrix, Philip McCallion, and the Neuroatypical Conditions Expert Consultative Panel

Review Alzheimers Dement (Amst). 2022 Jul 8;14(1):e12335. doi: 10.1002/dad2.12335. eCollection 2022.

The Neuroatypical Conditions Expert Consultative Panel composed of numerous clinical and academic experts was convened to examine barriers to the examination of cognitive impairment in adults with a variety of neuroatypical conditions. Neuroatypical conditions affect normative intellectual development and function (such as intellectual disability and intellectual disability with conjoint psychiatric conditions), thought, moods, and cognition (such as severe mental illness), communication functions (such as the autism spectrum and hearing/vision impairments), and brain and motor function (such as cerebral palsy and acquired or traumatic brain injury). The panel concluded that current federal guidance for the assessment of cognitive impairment for mild cognitive impairment (MCI) or dementia does not sufficiently include information as to how to assess such adults. In addition, it concluded that adults with these conditions (1) challenge clinicians when attempting to discern current behavior and function from that which was pre-existing; (2) often have inherent comprehension and oral communication difficulties, motor task performance impediments, and difficulty with visuals; and (3) pose difficulties when assessed with standardized dementia measures and can benefit from the use of specialized instruments. The panel recommended that federal guidance be broadened to include adaptations of assessment practices to accommodate neuroatypical conditions; that educational packs be developed for clinicians about such conditions and on detecting and diagnosing MCI or dementia; and that research be expanded to produce more evidence-based information on both assessing adults with neuroatypical conditions for later-life adult cognitive diseases/disorders and planning post-diagnostic care.

PMID: 35845263

11. Novel treatment for hypotonic airway obstruction and severe obstructive sleep apnea using a nasopharyngeal airway device with 3D printing innovation
Allison R Powell, Sudharsan Srinivasan, Jennifer L Helman, Annie Dian-Ru Li, Louise M O'Brien, Albert Shih, Jeff S Plott, David A Zopf

J Clin Sleep Med. 2022 Jul 22. doi: 10.5664/jcsm.10202. Online ahead of print.

Study objectives: Pediatric obstructive sleep apnea (OSA) impacts child and familial well-being. Airway management in patients with hypotonic pharyngeal conditions is complex. Some patients may benefit from CPAP or BPAP, others may require further invasive measures for treatment. There is critical need for treatment alternatives for patients with pharyngeal hypotonia. Methods: This is a retrospective case series. Collaboratively with patients, families, biomedical engineers, and medical professionals, a long-term nasopharyngeal airway (NPA) was created to bypass upper airway obstruction. Two patients used a safety pin and tape attachment, and two patients used a novel 3D-printed, self-supporting nasal securement (ssNPA). All four patients had polysomnography before and during NPA use. Paired 1-tailed t-tests were conducted to compare apnea-hypopnea index (AHI), hypopnea index (HI), obstructive index (OI), and oxygen nadir. Results: Compared to baseline polysomnography, repeat polysomnography with the NPA in place demonstrated statistically significant improvement for AHI (75.8±36.6 to 8.9±2.9, p=0.03), HI (45.4±25.8 to 7.7±3.2, p=0.04), and SpO2 nadir (60.3±13.0% to 79.3±8.7%, p=0.01). The NPA had been used for over one year in three of the four children. Those using the safety pin and tape did report skin irritation due to adhesive required to keep device in place. Conclusions: Current management of severe upper airway obstruction and obstructive sleep apnea in hypotonic pharyngeal conditions requires a team-based approach to care. A long-term NPA device may be an alternative or temporizing option to CPAP, upper airway surgery, or tracheostomy in children with pharyngeal hypotonia and

severe OSA. Larger studies of this approach are underway to assess efficacy in a range of OSA severity in this population.

PMID: 35866230

12. Prioritizing indigenous health equity in health registers: an environmental scan of strategies for equitable ascertainment and quality data
Karen Wright, Aria Dehar, N Susan Stott, Anna Mackey, Alexandra Sorhage, Rachel Tapera, Sîan A Williams

Glob Health Res Policy. 2022 Jul 19;7(1):24. doi: 10.1186/s41256-022-00250-6.

Background: Cerebral palsy (CP) registers serve as instrumental tools to support development of care pathways, preventative strategies, and health gains. Such health gains, however, are not always universal, with Indigenous health inequities common. To support Indigenous health, health registers need complete, consistent, and high-quality data. The aim of this study was to identify perceived barriers to the ascertainment of Indigenous peoples on health registers and to collate strategies supporting comprehensive ascertainment and achievement of high-quality Indigenous data. Methods: Environmental scanning methods were utilized within a Kaupapa Māori theoretical framework, which aims to produce research that is transformational and supportive of Indigenous health gain. Knowledge and insights were obtained from CP registers in countries with Indigenous populations and complemented by information from health registers in Aotearoa New Zealand (NZ). Data collection methods included an online survey and scan of organizational websites. Data extraction focused on general information about the register, barriers to ascertainment, and strategies to support ascertainment and high data quality. Results: 52 registers were identified, 20 completed the survey and 19 included in the study (CP registers, n = 10, NZ health registers, n = 9). Web scan data were included for the other 32 registers (CP registers, n = 21, NZ health registers, n = 11). Indigenous health equity was identified in the visions and aims of only two health registers. Ethnicity data collection was identified in nearly three quarters of survey respondents and a limited number of organizational websites. Over half of survey respondents described system, health provider/service, or workforce barriers to ascertainment. Strategies were categorized into collaboration, health provider/service, workforce, and systems-levels. Indigenous-specific strategies were limited and focused on personal behaviour and access to registration. Conclusions: CP and other health registers can have a significant role in identifying and addressing Indigenous health inequities. However, this is not currently an overt priority for many registers in this study and few registers describe ascertainment and data quality strategies specific to Indigenous peoples. Significant opportunity exists for health registers to be accountable and to implement approaches to support Indigenous health equity, address structural determinants of inequities, and achieve health gain for all.

PMID: 35854338

13. Which is the Most Common Physiologic Type of Cerebral Palsy?
Mahesh Kamate, Mayank Detroja

Neurol India. 2022 May-Jun;70(3):1048-1051. doi: 10.4103/0028-3886.349640.

Introduction: Spastic cerebral palsy (CP) is the commonest physiological type according to literature which comes mainly from the developed countries where prematurity is a common cause for cerebral palsy. In developing countries like India, the leading causes of cerebral palsy are birth asphyxia, infections, and hyperbilirubinemia and, hence, the physiological type of CP is likely to be different. However, the data from our country is scant. Methods: 103 consecutive treatment-naive CP patients attending pediatric neurology clinic were evaluated in detail using an objective tool, hypertonia assessment tool (HAT) over a period of 6months. Based on the predominant tone, the cases were classified as spastic, dyskinetic, ataxic/hypotonic, and mixed. The type of cerebral palsy was correlated with perinatal details and neuroimaging findings. Results: Out of 103 children, the most common physiological type of CP seen was of dyskinetic type [54 (52.4%)], followed by spastic CP in 30 (29.1%) and mixed (dyskinetic+spastic) CP in 19 (18.4%) children. The most common cause for dyskinetic CP was perinatal asphyxia 33 (61%); for spastic CP was prematurity 17 (56.7%) and; for mixed CP, the main cause was perinatal asphyxia 12 (63.2%). The main neuroimaging finding in predominant dyskinetic CP was basal ganglia/thalamus involvement followed by pericentral and perirolandic gliosis, whereas in spastic CP, it was periventricular leucomalacia. In mixed CP, there was multicystic encephalomalacia. Conclusions: Dyskinetic CP either as predominant type or along with spasticity is the most common physiological type of CP in India and is due to birth-asphyxia, hyperbilirubinemia, hypoglycemia, and infections.

PMID: 35864637

14. Neurodevelopmental outcome of Italian preterm ELBW infants: an eleven years single center cohort
Camilla Caporali, Stefania Longo, Giovanna Tritto, Gianfranco Perotti, Camilla Pisoni, Cecilia Naboni, Barbara Gardella, Arsenio Spinillo, Federica Manzoni, Stefano Ghirardello, Renato Borgatti, Simona Orcesi, ELBWI Neurodevelopmental Follow-up Study Group

Ital J Pediatr. 2022 Jul 19;48(1):117. doi: 10.1186/s13052-022-01303-9.

Background: Preterm extremely low birth weight infants (ELBWi) are known to be at greater risk of developing neuropsychiatric diseases. Identifying early predictors of outcome is essential to refer patients for early intervention. Few studies have investigated neurodevelopmental outcomes in Italian ELBWi. This study aims to describe neurodevelopmental outcome at 24 months of corrected age in an eleven-year single-center cohort of Italian ELBWi and to identify early risk factors for adverse neurodevelopmental outcomes. Methods: All infants born with birth weight < 1000 g and admitted to the Neonatal Intensive Care Unit of the "Fondazione IRCCS Policlinico San Matteo" hospital in Pavia, Italy, from Jan 1, 2005 to Dec 31, 2015 were eligible for inclusion. At 24 months, Griffiths' Mental Developmental Scales Extended Revised (GMDS-ER) were administered. Neurodevelopmental outcome was classified as: normal, minor sequelae (minor neurological signs, General Quotient between 76 and 87), major sequelae (cerebral palsy; General Quotient ≤ 75; severe sensory impairment). Univariate and multivariate multinomial logistic regression models were performed to analyze the correlation between neonatal variables and neurodevelopmental outcome. Results: 176 ELBWi were enrolled (mean gestational age 26.52 weeks sd2.23; mean birthweight 777.45 g sd142.89). 67% showed a normal outcome at 24 months, 17% minor sequelae and 16% major sequelae (4.6% cerebral palsy on overall sample). The most frequent major sequela was cognitive impairment (8.52%). In the entire sample the median score on the Hearing-Speech subscale was lower than the median scores recorded on the other subscales and showed a significantly weaker correlation to each of the other subscales of the GMDS-ER. Severely abnormal cUS findings (RRR 10.22 p 0.043) and bronchopulmonary dysplasia (RRR 4.36 p 0.008) were independent risk factors for major sequelae and bronchopulmonary dysplasia for minor sequelae (RRR 3.00 p 0.018) on multivariate multinomial logistic regression. Conclusions: This study showed an improvement in ELBWI survival rate without neurodevelopmental impairment at 24 months compared to previously reported international cohorts. Cognitive impairment was the most frequent major sequela. Median scores on GMDS-ER showed a peculiar developmental profile characterized by a selective deficit in the language domain. Severely abnormal cUS findings and bronchopulmonary dysplasia were confirmed as independent risk factors for major sequelae.

PMID: 35854369

15. [Functional characterization of patients with cerebral palsy living in the Magallanes region and the Chilean Antarctic][Article in Spanish]
Patricio Barria Aburto, Vanessa Barria Ruiz, Matías Castillo Aguilar, Rolando Aguilar Cárdenas, Asterio Andrade Gallardo, Cristian Núñez-Espinosa

Observational Study Andes Pediatr. 2022 Jun;93(3):361-370. doi: 10.32641/andespediatr.v93i3.3636.

Objective: To functionally characterize patients with Cerebral Palsy (CP) living in the Magallanes Re gion and the Chilean Antarctic. Patient and method: Descriptive-retrospective observational study of patients with cerebral palsy, registered in the Outpatient Rehabilitation Program of the Corporación de Rehabilitación Club de Leones Cruz del Sur de Punta Arenas between 1986 and 2018. Patients with CP were clinically categorized and then functionally characterized according to gross motor skills (GMFCS), manual ability (MACS), feeding ability (EDACS), and communication function (CFCS). Results: 106 patients were included. Regarding the clinical classification, the most common type of CP was bilateral spastic paralysis, with the highest percentage of functional involvement in each of the evaluated areas, followed by unilateral spastic paralysis, while cases of dystonic CP and other non-classifiable types presented were less frequent. According to the clinical subclassification, spastic diplegia was more frequent, especially affecting manual and communication skills level I compared with hemiplegia, while cases of mixed and unclassifiable quadriplegia were less frequent with greater overall involvement of level I feeding skills. Conclusion: The observed results of CP in the Magalla nes Region and the Chilean Antarctic are similar to studies available in the literature. The complete evaluation and classification of patients with CP enable a better understanding of the pathology for future studies.

PMID: 35857007

16. ASXL3 De Novo Variant-Related Neurodevelopmental Disorder Presenting as Dystonic Cerebral Palsy
Jana Švantnerová, Michal Minár, Silvia Radová, Miriam Kolníková, Peter Vlkovič, Michael Zech

Neuropediatrics. 2022 Jul 21. doi: 10.1055/s-0042-1750721. Online ahead of print.

ASXL3 loss-of-function variants represent a well-established cause of Bainbridge-Ropers syndrome, a syndromic neurodevelopmental disorder with intellectual and motor disabilities. Although a recent large-scale genomics-based study has suggested an association between ASXL3 variation and cerebral palsy, there have been no detailed case descriptions. We report, here, a female individual with a de novo pathogenic c.1210C > T, p.Gln404* nonsense variant in ASXL3, identified within the frame of an ongoing research project applying trio whole-exome sequencing to the diagnosis of dystonic cerebral palsy. The patient presented with a mixture of infantile-onset limb/trunk dystonic postures and secondarily evolving distal spastic contractures, in addition to more typical features of ASXL3-related diseases such as severe feeding issues, intellectual disability, speech impairment, and facial dysmorphic abnormalities. Our case study confirms a role for ASXL3 pathogenic variants in the etiology of cerebral-palsy phenotypes and indicates that dystonic features can be part of the clinical spectrum in Bainbridge-Ropers syndrome. ASXL3 should be added to target-gene lists used for molecular evaluation of cerebral palsy.

PMID: 35863334

17. Congenital Infection Influence on Early Brain Development Through the Gut-Brain Axis
Gregory W Kirschen, Snigdha Panda, Irina Burd

Review Front Neurosci. 2022 Jun 30;16:894955. doi: 10.3389/fnins.2022.894955. eCollection 2022.

The mechanisms by which various pathogens cause congenital infections have been studied extensively, aiding in the understanding of the detrimental effects these infections can have on fetal/neonatal neurological development. Recent studies have focused on the gut-brain axis as pivotal in neurodevelopment, with congenital infections causing substantial disruptions. There remains controversy surrounding the purported sterility of the placenta as well as concerns regarding the effects of exposure to antibiotics used during pregnancy on neonatal microbiome development and how early exposure to microbes or antibiotics can shape the gut-brain axis. Long-term neurodevelopmental consequences, such as autism spectrum disorder, attention deficit hyperactivity disorder, and cerebral palsy, may be attributable, in part, to early life infection and changes in the immature gut microbiome. The goal of this review is thus to critically evaluate the current evidence related to early life infection affecting neurodevelopment through the gut-brain axis.

PMID: 35844234

18. Relationship of caffeine regimen with osteopenia of prematurity in preterm neonates: a cohort retrospective study
Manoj Kumar, Amin Ali, Muhammad Azeem Khan, Sadia Sohail, Syed Muzafar Saleem, Midhat Khan, Fizzah Naz, Wasif Ahmed Khan, Muhammad Sohail Salat, Kashif Hussain, Gul Ambreen

BMC Pediatr. 2022 Jul 21;22(1):437. doi: 10.1186/s12887-022-03493-x.

Background: Caffeine is a routinely prescribed pharmacological active compound in neonatal intensive care units (NICU) for treating apnea of prematurity (AOP), which also decreases the risk of bronchopulmonary dysplasia and cerebral palsy in neonates. Caffeine-induced excessive calcium loss can promote the development of metabolic bone disease (MBD) in preterm neonates. This study aimed to evaluate the effect of the caffeine regimen on the development of osteopenia of prematurity (OOP), using serum alkaline phosphatase (serum-ALP) concentrations as a surrogate marker at the 4th week of life. Methods: This retrospective cohort study was conducted including neonates of < 32 weeks gestational age (GA) and birth weight < 1500 g, admitted to NICU from April-2017 to December-2018 and received caffeine therapy till 28 days of life for AOP. Based on serum-ALP levels, formed the high and low-ALP groups. Neonatal characteristics, caffeine regimen, risk factors for OOP, including duration of parenteral nutrition (PN), exposure to medicines associated with MBD, and intake of essential vitamins and minerals, were compared in both groups. Predictors of OOP were analyzed through logistic regression. Results: From the total of 268 participants, 52 (19%) developed OOP, mostly female (61.5%). In the high ALP group, the serum-ALP levels were significantly higher than in the low-ALP group (725.0 ± 143.8 vs 273.6 ± 55.0 units/L, $p < 0.001$). The high-ALP group received significantly ($p < 0.001$) higher daily and cumulative caffeine doses and were associated with a higher likelihood of

developing OOP in this study cohort [cumulative dose (mg) (AOR = 1.082 95% CI 1.011 to 1.157) and daily dose (mg/kg/day) (AOR = 2.892 95% CI 1.392 to 6.007)]. Smaller GA was found directly related to OOP. Among the other medical risk factors, phosphorus intake was significantly low in the high-ALP group. No, significant relationship between duration of PN and use of steroids and diuretics, and intake of vitamins and minerals were identified. Conclusion: The daily and cumulative doses of caffeine and smaller GA are associated with the development of OOP in this study cohort. Clinical randomized control studies are needed to validate the outcomes and determine the range of safest and most effective caffeine doses for treating AOP in preterm neonates.

PMID: 35864501

19. Diagnosis and Surgical Management of Neonatal Hydrocephalus
Jonathan Pindrik, Lauren Schulz, Annie Drapeau

Review Semin Pediatr Neurol. 2022 Jul;42:100969. doi: 10.1016/j.spen.2022.100969. Epub 2022 Apr 8.

Neonatal hydrocephalus represents an important pathological condition with significant impact on medical care and neurocognitive development. This condition requires early recognition, appropriate medical and surgical management, and long-term surveillance by clinicians and pediatric neurosurgeons. Common etiologies of neonatal and infant hydrocephalus include intraventricular hemorrhage related to prematurity with subsequent post-hemorrhagic hydrocephalus, myelomeningocele, and obstructive hydrocephalus due to aqueductal stenosis. Clinical markers of elevated intracranial pressure include rapid increases in head circumference across percentiles, elevation and firmness of the anterior fontanelle, splitting or splaying of cranial sutures, upgaze palsy, lethargy, frequent emesis, or episodic bradycardia (unrelated to other comorbidities). Complementing these clinical markers, imaging modalities used for the diagnosis of neonatal hydrocephalus include head ultrasonography, brain magnetic resonance imaging, and head computed tomography in urgent or emergent situations. Following diagnosis, temporizing measures may be employed prior to definitive treatment and include ventricular access device or ventriculo-subgaleal shunt insertion. Definitive surgical management involves permanent cerebrospinal fluid (CSF) diversion via CSF shunt insertion, or endoscopic third ventriculostomy with or without choroid plexus cauterization. Surgical decision-making and approaches vary based on patient age, hydrocephalus etiology, neuroanatomy, imaging findings, and medical comorbidities. Indications, surgical techniques, and clinical outcomes of these procedures continue to evolve and elicit significant attention in the research environment. In this review we describe the epidemiology, pathophysiology, clinical markers, imaging findings, early management, definitive surgical management, and clinical outcomes of pediatric patients with neonatal hydrocephalus.

PMID: 35868728

20. Causal factors affecting gross motor function in children diagnosed with cerebral palsy
Bruce A MacWilliams, Sarada Prasad, Amy L Shuckra, Michael H Schwartz

PLoS One. 2022 Jul 18;17(7):e0270121. doi: 10.1371/journal.pone.0270121. eCollection 2022.

Background: Cerebral palsy (CP) is a complex neuromuscular condition that may negatively influence gross motor function. Children diagnosed with CP often exhibit spasticity, weakness, reduced motor control, contracture, and bony malalignment. Despite many previous association studies, the causal impact of these impairments on motor function is unknown. Aim: In this study, we proposed a causal model which estimated the effects of common impairments on motor function in children with spastic CP as measured by the 66-item Gross Motor Function Measure (GMFM-66). We estimated both direct and total effect sizes of all included variables using linear regression based on covariate adjustment sets implied by the minimally sufficient adjustment sets. In addition, we estimated bivariate effect sizes of all measures for comparison. Method: We retrospectively evaluated 300 consecutive subjects with spastic cerebral palsy who underwent routine clinical gait analysis. Model data included standard information collected during this analysis. Results: The largest causal effect sizes, as measured by standardized regression coefficients, were found for selective voluntary motor control and dynamic motor control, followed by strength, then gait deviations. In contrast, common treatment targets, such as spasticity and orthopedic deformity, had relatively small effects. Effect sizes estimated from bivariate models, which cannot appropriately adjust for other causal factors, substantially overestimated the total effect of spasticity, strength, and orthopedic deformity. Interpretation: Understanding the effects of impairments on gross motor function will allow clinicians to direct treatments at those impairments with the greatest potential to influence gross motor function and provide realistic expectations of the anticipated changes.

PMID: 35849563

21. Gabapentin as Add-on Therapy to Trihexyphenidyl in Children with Dyskinetic Cerebral Palsy: A Randomized, Controlled Trial
Sonu Kumar, Jaya Shankar Kaushik, Savita Verma, Surekha Dabla

Indian J Pediatr. 2022 Jul 22. doi: 10.1007/s12098-022-04265-2. Online ahead of print.

Objective: To compare the efficacy of gabapentin as add-on therapy to trihexyphenidyl in the treatment of children with dyskinetic cerebral palsy (CP). Methods: An open-labelled, randomized, controlled trial was conducted among children aged 3-9 y with dyskinetic CP [Gross Motor Functional Classification System (GMFCS) 4-5]. Participants were assigned into two groups: gabapentin with trihexyphenidyl (n = 30) and trihexyphenidyl alone (n = 30). Dyskinesia Impairment Scale (DIS), Dystonia Severity Assessment Plan (DSAP), and International Classification of Functioning, Disability, and Health-Children and Youth Version (ICF-CY) were measured at baseline, 4 and 12 wk. Results: There was significant reduction in baseline dystonia in both the groups (DIS: $p < 0.001$; DSAP: $p = 0.007$; ICF-CY: $p < 0.001$) but when data were compared between the groups, there was no significant difference in the severity of dystonia at 4 wk and at 12 wk (DIS: $p = 0.09$; DSAP: $p = 0.49$; ICF-CY: $p = 0.25$). Constipation was the commonest side effect observed in both the groups [3 (11.5%) vs. 4 (14.3%)]. Conclusion: Trihexyphenidyl alone is as effective as combination of gabapentin with trihexyphenidyl in decreasing the severity of dystonia at 12 wk. Hence, there is no added benefit of gabapentin as add-on therapy for dystonia among children with dyskinetic CP. Trial registration: CTRI/2019/04/018603.

PMID: 35867274

22. 5-year fracture risk among children with cerebral palsy
Daniel G Whitney

Pediatr Res. 2022 Jul 19. doi: 10.1038/s41390-022-02207-4. Online ahead of print.

Background: Epidemiologic evidence documenting fracture risk as children with cerebral palsy (CP) age throughout growth is lacking to inform on when to implement fracture prevention strategies. The objective was to characterize the 5-year risk of fractures by each year of age among <1-13 year olds with CP and effects by patient-level factors. Methods: This retrospective cohort study used commercial administrative claims from 01/01/2001 to 12/31/2018 from children <1-13 years old with ≥5 years of insurance enrollment. Fractures were examined during the 5-year follow-up. For the CP cohort, the association between 5-year fracture rate and patient-level factors was assessed using Cox regression. Results: Children with (n = 5559) vs. without (n = 2.3 million) CP had a higher 5-year fracture risk at the vertebral column, hip, and lower extremities at almost each year of age, but lower 5-year fracture risk at the upper extremities after 6 years old (all $P < 0.05$). Among children with CP, the 5-year fracture rate was elevated for co-occurring neurological conditions and non-ambulatory status at the vertebral column, hip, and lower extremities (hazard ratio [HR] range, 1.44-2.39), and higher for males at the upper extremities (HR = 1.29) (all $P < 0.05$). Conclusions: This study provides novel epidemiologic evidence of 5-year fracture risk for each year of age for children with CP. Impact: This study provides novel epidemiologic evidence of 5-year fracture risk for each year of age across important developmental stages for children with vs. without cerebral palsy (CP). Children with vs. without CP were more likely to fracture at the vertebral column, hip, lower extremities, and humerus and less likely to fracture at the forearm and hands. The age-related 5-year fracture risk was associated with clinically relevant patient-level factors, but in different ways by fracture region. Study findings may be used to enhance clinical detection of at-risk children and strategize when to implement fracture prevention efforts for children with CP.

PMID: 35854092

23. Gross Motor Function Measure (GMFM-66 & GMFM-88) User's Manual, 3rd Edition, Book Review
Anna Te Velde, Catherine Morgan

Pediatr Phys Ther. 2022 Jan 1;34(1):88-89. doi: 10.1097/PEP.0000000000000858. Epub 2021 Dec 6.

No abstract available

PMID: 35853040

24. An investigation of the psychometric properties of the Turkish adaptation of the activity limitations in cerebral palsy questionnaire
Merve Kınık, Ilknur Naz

Disabil Rehabil. 2022 Jul 22;1-7. doi: 10.1080/09638288.2022.2099586. Online ahead of print.

Purpose: To translate the ACTIVLIM-CP questionnaire, developed to assess global activity performance in children with Cerebral Palsy (CP), into Turkish and to investigate its psychometric properties. Methods: Eighty-nine children with CP, aged between 2 and 18 years (mean age: 10.08 ± 4.94 years), were included in the study. Internal consistency was measured by Cronbach's alpha and test-retest reliability was assessed using intraclass correlation coefficient (ICC). Convergent validity was evaluated through the pattern of correlations between the ACTIVLIM-CP with PEDI, ABILOCO-Kids, ABILHAND-Kids, and Wee-FIM scores. Known-group comparisons were made according to epilepsy existence and ambulation level measured by Gross Motor Function Classification System (GMFCS). Results: Internal consistency was excellent (Cronbach's $\alpha = 0.990$), and the ICC for the test-retest reliability was 0.990. There was a very strong correlation between ACTIVLIM-CP and ABILHAND-Kids ($r = 0.946$), WeeFIM ($r = 0.900$), PEDI Functional Skills and Caregiver Assistance scores ($r = 0.954$, $r = 0.937$, respectively), and ABILOCO-Kids ($r = 0.817$) ($p < 0.001$) score. ACTIVLIM-CP score was lower in children with epilepsy ($p = 0.001$) and in the high-level group according to GMFCS ($p < 0.001$). Conclusion: The Turkish adaptation of ACTIVLIM-CP is a valid and reliable scale for measuring activity limitations in children with CP and is compatible with other scales evaluating activity limitations. Clinical trial number: NCT05184244. IMPLICATIONS FOR REHABILITATION: Activity limitation measurements are crucial and necessary to determine the global activity performance of children with CP. ACTIVLIM-CP was translated and culturally adapted to Turkish and showed good psychometric properties. ACTIVLIM-CP is a valid and reliable tool to evaluate activity performance in children with CP.

PMID: 35866563

25. How clinicians can provide support during the transition to adulthood for young people with cerebral palsy: A parent and healthcare worker's perspective
Lynne Fogel

Dev Med Child Neurol. 2022 Jul 20. doi: 10.1111/dmcn.15342. Online ahead of print.

No abstract available

PMID: 35856632

Prevention and Cure

26. Protective Effects of Interleukin-1 Blockade on Group B Streptococcus-Induced Chorioamnionitis and Subsequent Neurobehavioral Impairments of the Offspring
Taghreed A Ayash, Seline Y Vancolen, Mariela Segura, Marie-Julie Allard, Guillaume Sebire

Front Endocrinol (Lausanne). 2022 Jul 1;13:833121. doi: 10.3389/fendo.2022.833121. eCollection 2022.

Group B Streptococcus (GBS) is one of the most common bacteria isolated in human chorioamnionitis. Placental infection due to GBS is a major risk factor for fetal organ injuries, preterm birth, perinatal morbidity and mortality, and life-long multiorgan morbidities. Preclinical and clinical studies have shown that GBS-induced infection drives polymorphonuclear (PMN) cell infiltration within the placenta, the hallmark of human chorioamnionitis. In preclinical and clinical studies, the upregulation of interleukin(IL)-1β in the placenta and maternal/fetal blood was associated with a high risk of neurodevelopmental impairments in the progeny. We hypothesized that targeted IL-1 blockade administered to the dam alleviates GBS-induced chorioamnionitis and the downstream fetal inflammatory response syndrome (FIRS). IL-1 receptor antagonist (IL-1Ra) improved the gestational weight gain of GBS-infected dams and did not worsen the infectious manifestations. IL-1Ra reduced the IL-1β titer in the maternal sera of GBS-infected dams. IL-1Ra decreased the levels of IL-1β, IL-6, chemokine (C-X-C motif) ligand 1 (CXCL1), and polymorphonuclear (PMN) infiltration in GBS-infected placenta. IL-1Ra treatment reduced the IL-1β titer in the fetal sera of GBS-exposed fetuses. IL-1 blockade also alleviated GBS-induced FIRS and subsequent neurobehavioral impairments of the offspring without worsening the outcome of GBS infection. Altogether, these results showed that IL-1 plays a key role in the physiopathology of live GBS-induced chorioamnionitis and consequent neurobehavioral impairments.

PMID: 35846278