Cerebral Palsy ALLIANCE

Cerebral palsy research news

Monday 18 September 2023

Cerebral Palsy Alliance is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at cerebralpalsy.org.au/our-research

Professor Nadia Badawi AM
CP Alliance Chair of Cerebral Palsy Research

Subscribe to CP Research News

Interventions and Management

1. Effect of intrathoracic oscillations on pulmonary functions in children with cerebral palsy

Mahmood D Al-Mendalawi

J Taibah Univ Med Sci. 2023 Aug 30;18(6):1509-1510. doi: 10.1016/j.jtumed.2023.08.003. eCollection 2023 Dec.

No abstract available

PMID: 37693821

2. Risk Factors for Failure of Calcaneal Lengthening Osteotomy in Children and Adolescents With Planovalgus Foot Deformity: A Retrospective Study

Joe Mehanna, Abir Massaad, Ayman Assi, Joe Rassi, Alexis Atallah, Ismat Ghanem

Cureus. 2023 Aug 8;15(8):e43157. doi: 10.7759/cureus.43157. eCollection 2023 Aug.

Introduction: The calcaneal lengthening procedure (CLP) is a well-known surgical technique used for the correction of symptomatic planovalgus foot deformities. Literature shows a significant rate of relapse and undercorrection of the foot post-operatively. Factors determining the failure or success of CLP are still not well understood. The purpose of this retrospective study was to assess the most significant factors related to the failure of this procedure. Methods: A case-control retrospective study was conducted on 50 patients (80 feet) aged 12.4±2.5 years who underwent CLP. A clinical (demographic parameters, etiology, Gross Motor Function Classification System (GMFCS) level) and radiological evaluation were assessed preoperatively and repeated postoperatively at 56.5±32.5 months. Two methods of osteotomy bone fixation were studied: K-wires vs. eight-plate. Standing anteroposterior (AP) and lateral (L) radiographs were done, and the following radiographic parameters were measured: calcaneocuboid (CC) joint subluxation classified into normal, moderate, and severe (L); AP and L talo-first metatarsal (T1MT) angle; AP talonavicular (TN) coverage angle; AP and L talocalcaneal (TC) angle; calcaneal pitch (CP) angle; and L talo-horizontal (TH) angle. Mosca's criteria were used for clinical and radiological assessments. The association between demographic data, clinical and radiological results, and the variation between preoperative and postoperative angles were studied. The main risk factors affecting clinical results and CC joint subluxation were investigated (logistic regression and analysis of covariance (ANCOVA)). Results: Satisfactory clinical results were associated with satisfactory radiological ones on Mosca's criteria ($p<0.001$). The use of an eight-plate for osteotomy fixation gave better results than K-wires (79% vs. 59%). Radiological angles were improved in both techniques postoperatively (increase of CP and L-TC and decrease of AP-T1MT, AP-TC, AP-TN, and L-T1MT, all $p<0.05$). Non-satisfactory clinical results were associated with a high GMFCS level, a low preoperative AP-TN coverage angle, and a low preoperative CP angle ($R2=0.45$). Both a young age and a low CP angle preoperatively were associated with CC subluxation ($R2=0.31$). Conclusion: The neurological status and the severity of the planovalgus foot deformity preoperatively were the main risk factors affecting clinical outcomes after CLP. However, young age and the severity of the deformity preoperatively were the main risk factors behind CC joint subluxation affecting CLP outcomes.

PMID: 37692710

3. A case series on the effect of dynamic neoprene orthosis on lower limb kinematic variables in children with cerebral palsy

Sedigheh Sadat Mirbagheri, Mahmood Bahramizadeh, Gholamreza Aminian, Hamid Dalvand, Farzam Farahmand, Mohsen Vahedi

J Pediatr Rehabil Med. 2023 Sep 1. doi: 10.3233/PRM-200806. Online ahead of print.

Purpose: This study examined the effects of a dynamic neoprene orthosis on kinematic variables of gait in children with spastic bilateral cerebral palsy (CP). Methods: Five children (whose median age was 9.6 years and who ranged in age from six to 12) with spastic bilateral CP and flexed knee at levels I-III of the Gross Motor Function Classification System were examined using kinematic gait analysis in three different conditions: 1) with dynamic neoprene orthosis; 2) without dynamic neoprene orthosis (immediate effect); and 3) without orthosis after six weeks of intervention. Results: The comparison between condition one (with dynamic neoprene orthosis) and condition two (without dynamic neoprene orthosis) demonstrated the existence of improvements in minimum hip and knee flexion variables. Moreover, the results indicated that the improvements remained constant in several key gait variables after six weeks. Conclusion: The results varied from subject to subject, and there were signs of improvement in some of the subjects. Therefore, it was not possible to draw conclusions at a group level. Nonetheless, a number of individuals may benefit from this type of orthosis.

PMID: 37694316

4. Evidence for gait improvement with robotic-assisted gait training of children with cerebral palsy remains uncertain

Mátyás Vezér, Orsolya Gresits, Marie Anne Engh, Laszlo Szabó, Zsolt Molnar, Peter Hegyi, Tamás Terebessy

Review Gait Posture. 2023 Sep 1;107:8-16. doi: 10.1016/j.gaitpost.2023.08.016. Online ahead of print.

Background: Cerebral palsy (CP) is a group of neuromotor diseases that develops as a result of damage to the developing central nervous system during the perinatal period. The condition is usually accompanied by musculoskeletal problems resulting in movement disorders. Gait improvement therefore, is an important part of its treatment. Roboticassisted gait training (RAGT) is a new potential rehabilitation tool for CP patients, however there is no clear evidence for the effectiveness of this method. Research question: Can robotic-assisted gait training improve walking function in children with CP? Methods: A systematic search was performed in five databases: MEDLINE (via PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), Embase, Scopus, and Web of Science. Eligible studies were randomized controlled trials (RCT) with CP patients under the age of 18. Gross motor function and kinematic gait parameters of patients were the main outcomes. Two authors determined the risk of bias of the RCTs independently using the revised Risk of Bias 2 (ROB 2) tool. Mean Differences (MDs) along with their 95% Confidence Interval (CI) were calculated when at least three studies were present for an outcome, subgroup analysis was performed based on the treatment of the control group. Results: Of the 7363 screened articles, 13 papers met our inclusion criteria and among them, 7 studies could be used in our meta-analyses. The results related to RAGT suggest nonsignificant improvement in standing and walking function (Gross Motor Function Measure D, E), moreover changes in gait speed, step length, and in cadence were also only comparable to controls. Significance: The results indicate that there is a trend in some gait parameters where the improvement was higher in the intervention group than in control group. The therapeutic effect of RAGT was probably not superior to physiotherapy combined with treadmill training.

PMID: 37703782

5. Early cerebral palsy motor therapies research: Hope springs and science matters

Nathalie L Maitre

Dev Med Child Neurol. 2023 Sep 11. doi: 10.1111/dmcn.15752. Online ahead of print.

No abstract available

PMID: 37697819

6. Effects of a 12 week community-based high-level mobility programme on sustained participation in physical activity by adolescents with cerebral palsy: a single subject research design study

Gaela Kilgour, Ngaire Susan Stott, Michael Steele, Brooke Adair, Amy Hogan, Christine Imms

Disabil Rehabil. 2023 Sep 15;1-11. doi: 10.1080/09638288.2023.2256225. Online ahead of print.

Purpose: To assess if a high-level mobility programme (HLMP) can promote sustained participation in physical activity by

adolescents with cerebral palsy. Methods: Eight adolescents with cerebral palsy, Gross Motor Function Classification System levels I-II, 11-16 years, participated in 24 community-based group HLMP sessions across 12 weeks. Participants set attendance, involvement, and physical performance goals, completed activity diaries over 58 weeks and undertook physical capacity tests. Measures of activity frequency and diversity (attendance) and involvement level were collected weekly across baseline (4-6 weeks), intervention (12 weeks), and nine months follow-up (including Covid lockdown). Results: Median attendance was 23 of 24 HLMP sessions. Attendance goal/s attainment was highest during COVID lockdown. Involvement goals were consistently attained throughout all phases. Physical performance goal/s attainment was highest during intervention phase but reduced during nine months follow-up. Frequency of participation in physical activities varied greatly across study phases (range 0-33 episodes/week) with stable variety of activities and generally high 'involvement.' During the intervention, seven participants improved physical capacity and six maintained, or increased, the gains six months later. Conclusion: Most participants improved physical capacity post-intervention but only some had sustained attendance and involvement in physical activity, highlighting the complexity of physical activity participation.

PMID: 37712610

7. Short- to Long-Term Effects of Virtual Reality on Motor Skill Learning in Children With Cerebral Palsy: Systematic Review and Meta-Analysis

Seyma Kilcioglu, Benoît Schiltz, Rodrigo Araneda, Yannick Bleyenheuft

Review JMIR Serious Games. 2023 Sep 12;11:e42067. doi: 10.2196/42067.

Background: Many studies have started integrating virtual reality (VR) into neurorehabilitation for children with cerebral palsy (CP). The results of the effects of VR on motor skill learning, including the short- to long-term results of relevant studies, must be pooled in a generic framework. Objective: This systematic review and meta-analysis aimed to investigate the short- to long-term effects of therapies including VR on motor skill learning in children with CP. Methods: Two examiners followed the inclusion and exclusion criteria of the "Participant, Intervention, Control, and Outcome" framework. Randomized controlled trials (RCTs) and non-RCTs were considered if they compared VR-included interventions with control groups on motor functions and daily life activities in children with CP. PubMed, ScienceDirect, Embase, and IEEE Xplore databases were searched. The modified Downs and Black assessment was used to assess the methodological quality of the included studies. Meta-analyses and subgroup analyses for RCTs were conducted whenever possible. Results: A total of 7 RCTs, 2 non-RCTs, and 258 children with CP were included. The priority focus of 78% (7/9) of the studies was upper limb functions. There was a significant short-term effect of adding VR to conventional therapies on upper limb functions when compared with conventional therapies (P=.04; standardized mean difference [SMD]=0.39, 95% CI 0.01-0.76). The overall medium- to long-term effects showed a trend toward favoring the VR group, although the difference was not statistically significant (P=.06; SMD=0.37, 95% CI -0.02 to 0.77). For balance (P=.06; SMD=1.04, 95% CI -0.04 to 2.12), gross motor functions (P=.30; SMD=2.85, 95% CI -2.57 to 8.28), and daily life activities outcomes (P=.21; SMD=0.29, 95% CI -0.16 to 0.74), the overall effect in the short term also showed a trend toward favoring the VR group, but these results were not statistically significant. Conclusions: VR seems to have additional benefits for motor skill learning in children with CP. Studies with follow-up outcomes of VR training focusing on balance and gross motor functions in patients with CP were quite limited. Future research on balance and gross motor function outcomes should target particularly long-term results of therapies including VR on motor skill learning. Trial registration: PROSPERO International Prospective Register of Systematic Reviews CRD42021227734; https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021227734.

PMID: 37698895

8. A Patient with Cerebral Palsy Presents for Evaluation of Third Molar Pain

Alicia Risner-Bauman, Miriam R Robbins

Review Dent Clin North Am. 2023 Oct;67(4):577-579. doi: 10.1016/j.cden.2023.05.023. Epub 2023 Jun 20.

Cerebral palsy (CP) is a developmental disorder caused by brain trauma in utero or within the first few days of life, although symptoms may not develop until early infancy. Each of the 4 types of CP has its own signs and symptoms and can present unique challenges to accessing and providing dental care. Providers may be reluctant to treat these individuals due to uncontrolled body movements, primitive reflexes, varying mental capabilities, seizures, visual and hearing impairments, dysphagia, and dysarthria.

PMID: 37714598

9. Cost-effectiveness analysis of robot-assisted gait training in patients with bilateral spastic cerebral palsy

Stanislava Klobucká, Robert Klobucký, Katarína Valovičová, Pavol Šiarnik, Branislav Kollár

Cost Eff Resour Alloc. 2023 Sep 11;21(1):60. doi: 10.1186/s12962-023-00475-3.

Background: To date, there have been no published studies evaluating the cost-effectiveness of robot-assisted gait training (RAGT) in adolescent and adult patients with cerebral palsy (CP). The study´s aim was to analyse the cost-effectiveness of RAGT versus conventional kinesiotherapy (CON) from the health care provider's perspective. Methods: We expressed the cost-effectiveness of RAGT in the Lokomat® system after analysing the costs and effects of RAGT and conventional therapy through the Incremental Cost-Effectiveness Ratio (ICER) based on a bicentric randomized controlled study, in which we demonstrated that the intensive RAGT regimen is more effective than conventional therapy in terms of improvements in gross motor functions in adolescent and adult patients with bilateral spastic CP. Results: According to the calculated ICER ratio for Lokomat®, an additional improvement per unit of effect (1% in GMFM), compared to conventional therapy, results in an average cost increase of EUR70.38 per patient in a therapeutic block consisting of 20 TUs (Therapeutic Units). Conclusion: However, from the comprehensive analysis of the results and evaluation of the long-term effects, it follows that RAGT applied in adolescent and adult patients with bilateral spastic CP is not only more effective in terms of evaluation of monitored clinical parameters, but in the long term it is also more cost-effective compared to conventional therapy.

PMID: 37697377

10. Evaluating Camera Mouse as a computer access system for augmentative and alternative communication in cerebral palsy: a case study

Lauren E MacLellan, Cara E Stepp, Susan K Fager, Michelle Mentis, Alyssa R Boucher, Defne Abur, Gabriel J Cler

Assist Technol. 2023 Sep 12;1-7. doi: 10.1080/10400435.2023.2242893. Online ahead of print.

Camera Mouse is a freely available software program that visually tracks the movement of facial features to allow individuals with motor impairments to control a computer mouse. The goal of this case study was to provide an evaluation of Camera Mouse as a computer access method as part of a multiple modality communication system for an individual with cerebral palsy. The participant was asked to reproduce sentences and respond to ethical dilemmas for language sampling. Tasks were completed using natural speech and an AAC solution consisting of Camera Mouse paired with an orthographic selection interface and speech synthesis. The participant completed a questionnaire for satisfaction with the introduced assistive technology. Camera Mouse resulted in higher intelligibility than natural speech, while natural speech had a higher rate. She used more complex language with her natural speech. The participant rated Camera Mouse as at least 3/5 on all measures, including 5/5 on weight and safety. The results of this case study suggest Camera Mouse is a promising computer access system for communication supported by the participant's satisfaction rating, expressive language, and synthesized speech production capabilities.

PMID: 37699111

11. Improving Health-Related Quality of Life in Middle-Age Children with Cerebral Palsy Following Selective Percutaneous Myofascial Lengthening and Functional Physiotherapy [Article in English, Spanish]

Vasileios C Skoutelis, Anastasios D Kanellopoulos, Stamatis Vrettos, Zacharias Dimitriadis, Argirios Dinopoulos, Panayiotis J Papagelopoulos, Vasileios A Kontogeorgakos

Rev Esp Cir Ortop Traumatol. 2023 Sep 7;S1888-4415(23)00190-X. doi: 10.1016/j.recot.2023.08.018. Online ahead of print.

Introduction and objectives: Children with cerebral palsy (CP) experience decreased health-related quality of life (HRQOL). This study aimed to assess the HRQOL of children with CP before versus after a combined program of minimally invasive selective percutaneous myofascial lengthening (SPML) and functional physiotherapy. Material and methods: A single-group pre-posttest design was used. Twenty-six middle childhood children with spastic CP, aged 5-7 years, with Gross Motor Function Classification System levels II-IV underwent SPML surgery and 9 months of postoperative functional strength training therapy. The proxy version of the DISABKIDS-Smiley questionnaire was completed by one parent of each child. Dependent t-tests were used to compare mean pre- and post-measurement scores. Results: After the 9-month intervention, the children with CP had significantly higher quality of life scores (mean difference, 11.06 ± 9.05; 95% confidence interval [CI], 7.40-14.71; $p < 0.001$). Conclusions: This study demonstrated that children with CP had better HRQOL after a combined program of minimally invasive SPML surgery and functional physiotherapy (ACTRN12618001535268).

PMID: 37689354

12. [Neurological consequences of prematurity] [Article in Spanish]

Alfredo Cerisola, Federico Baltar

Review Medicina (B Aires). 2023 Sep;83 Suppl 4:18-24.

Premature births are an important health indicator for a country. These children have a higher risk of mortality and morbidity. The main brain injuries in preterm infants include white matter injuries, intracranial hemorrhages, and cerebellar injuries. These injuries can be detected through brain ultrasound and magnetic resonance imaging (MRI), with MRI being the most sensitive technique. Perinatal brain injuries may have long-term consequences on the neurodevelopment of preterm infants, with an increased risk of cerebral palsy, cognitive, behavioral, sensory, and learning disorders, among others. It is key to implement prevention strategies and early intervention to reduce the negative consequences of brain injuries associated with prematurity. Key words: prematurity, periventricular leukomalacia, intracranial hemorrhage, neurodevelopmental disorders, cerebral palsy.

PMID: 37714118

13. Neonatal seizures: Etiologies, clinical characteristics, and radiological features: A cross-sectional study

Mohammed Almuqbil, Yousof Alrumayyan, Shahad Alattas, Duaa Baarmah, Waleed AlTuwaijri, Ahmed AlRumayyan, Mohammed Tala AlRifai, Asma Al Madhi, Hassan Al-Shehri, Saif Alsaif

Medicine (Baltimore). 2023 Sep 15;102(37):e35185. doi: 10.1097/MD.0000000000035185.

Seizures are a common clinical indication of central nervous system damage or abnormality in neonates. We aimed to identify the etiologies, clinical characteristics, and radiological features of neonatal seizures. This is a cross-sectional, retrospective, descriptive study using data obtained from the neonatal intensive care unit in King Abdulaziz Medical City (KAMC), a governmental, academic tertiary hospital in Riyadh, Saudi Arabia. The population of interest were neonates diagnosed with a neonatal seizure at KAMC between April 2015 and March 2019. A total of 61 patients with neonatal seizures were included in the study. The most common etiology was hypoxic-ischemic encephalopathy (43%). A total of 32 patients were full-term (52.5%). Around one-fifth of the study sample (21.3%) had a family history of neonatal seizures. Around 43.0% of the patients had epilepsy episodes. More than half of the patients (57.0%) were on one anti-seizure medication. Patients were followed up after 1 year, they had multiple comorbidities, including developmental delay, epilepsy, and cerebral palsy. Developmental delay was identified in 62.3% of the patients. A total of 19 patients have passed away (31%). Neonatal seizures are a common manifestation of neurologic disorders in neonates and are associated with high morbidity and mortality. Therefore, early identification of seizure etiology and proper management may help to improve the outcome.

PMID: 37713864

14. Long-chain omega-3 polyunsaturated fatty acids are reduced in neonates with substantial brain injury undergoing therapeutic hypothermia after hypoxic-ischemic encephalopathy

Simon C Dyall, Isabell Nessel, Jennine A Sharpe, Ping K Yip, Adina T Michael-Titus, Divyen K Shah

Front Neurol. 2023 Aug 30;14:1231743. doi: 10.3389/fneur.2023.1231743. eCollection 2023.

Hypoxic-ischemic encephalopathy (HIE) is a major cause of neonatal morbidity and mortality. Although therapeutic hypothermia is an effective treatment, substantial chronic neurological impairment often persists. The long-chain omega-3 polyunsaturated fatty acids (PUFAs), docosahexaenoic (DHA) and eicosapentaenoic (EPA) acids, offer therapeutic potential in the post-acute phase. To understand how PUFAs are affected by HIE and therapeutic hypothermia we quantified for the first time the effects of HIE and therapeutic hypothermia on blood PUFA levels and lipid peroxidation. In a cross-sectional approach, blood samples from newborns with moderate to severe HIE, who underwent therapeutic hypothermia (sHIE group) were compared to samples from newborns with mild HIE, who did not receive therapeutic hypothermia, and controls. The sHIE group was stratified into cerebral MRI predictive of good (n = 10), or poor outcomes (n = 10; nine developed cerebral palsy). Cell pellets were analyzed for fatty acid content, and plasma for lipid peroxidation products, thiobarbituric acid reactive substances and 4-hydroxy-2-nonenal. Omega-3 Index (% DHA + EPA) was similar between control and HIE groups; however, with therapeutic hypothermia there were significantly lower levels in poor vs. good prognosis sHIE groups. Estimated Δ-6 desaturase activity was significantly lower in sHIE compared to mild HIE and control groups, and linoleic acid significantly increased in the sHIE group with good prognosis. Reduced long-chain omega-3 PUFAs was associated with poor outcome after HIE and therapeutic hypothermia, potentially due to decreased biosynthesis and tissue incorporation. We speculate a potential role for long-chain omega-3 PUFA interventions in addition to existing treatments to improve neurologic outcomes in sHIE.

PMID: 37712085

15. Constructing validity evidence from a pilot key-features assessment of clinical decision-making in cerebral palsy diagnosis: application of Kane's validity framework to implementation evaluations

L M McNamara, K M Scott, R N Boyd, E A Farmer, A E Webb, I E Novak

BMC Med Educ. 2023 Sep 14;23(1):668. doi: 10.1186/s12909-023-04631-4.

Background: Physician decision-making skills training is a priority to improve adoption of the cerebral palsy (CP) clinical guideline and, through this, lower the age of CP diagnosis. Clinical guideline implementation aims to improve physician practice, but evaluating meaningful change is complex. Limitations in the validity evidence of evaluation instruments impact the evidence base. Validity frameworks, such as Kane's, enable a targeted process to gather evidence for instrument scores, congruent to context and purpose. Yet, application of argument-based methodology to implementation validation is rare. Key-features examination methodology has established validity evidence supporting its use to measure decision-making skills, with potential to predict performance. We aimed to apply Kane's framework to evaluate a pilot key-features examination on physician decision-making in early CP diagnosis. Methods: Following Kane's framework, we evaluated evidence across inferences of scoring, generalisation, extrapolation and implications in a study design describing the development and pilot of a CP diagnosis key-features examination for practising physicians. If found to be valid, we proposed to use the key-feature scores as an outcome measure of decision-making post education intervention to expedite CP diagnosis and to correlate with real-world performance data to predict physician practice. Results: Supporting evidence for acceptance of scoring inferences was achieved through examination development with an expert group (n = 10) and pilot results (n = 10): (1) high internal consistency (0.82); (2) acceptable mean item-discrimination (0.34); and (3) acceptable reliability of examination scorers (95.2% congruence). Decreased physician acceptance of examination time (70%) was identified as a threat and prioritised in case reduction processes. Partial acceptance of generalisation, extrapolation and implications inferences were defensible with: (1) accumulated development evidence following established key-features methodology; (2) high pilot acceptance for authenticity (90%); and (3) plausibility of assumptions of score correlation with population register data. Conclusions: Kane's approach is beneficial for prioritising sources of validity evidence alongside the iterative development of a key-features examination in the CP field. The validity argument supports scoring assumptions and use of scores as an outcome measure of physician decision-making for CP guideline education implementation interventions. Scoring evidence provides the foundation to direct future studies exploring association of key-feature scores with real-world performance.

PMID: 37710200

16. The assessment and management of voiding dysfunction in adults living with cerebral palsy

Matthew Playfair, Sean Elliott, Blayne Welk

World J Urol. 2023 Sep 14. doi: 10.1007/s00345-023-04603-9. Online ahead of print.

Purpose: Improvements in life expectancy have resulted in an increasing number of adults with cerebral palsy, of which over a third will have neurogenic lower urinary tract dysfunction (NLUTD). This review explores urinary dysfunction in adults with cerebral palsy. Methods: Relevant literature on NLUTD in adults with cerebral palsy was identified using an unrestricted search of PubMed. Results: Urinary incontinence is the most common complaint, often accompanied by frequency and urgency. Special consideration should be given to women and in those with worse motor or cognitive dysfunction as they have been shown to have more severe urologic symptoms. NLUTD can have significant morbidity and impact quality of life. Hospital admission, urinary tract infections, and hydronephrosis are common urologic complications, with poor urinary function associated with decreased quality of life (QOL). Neurogenic detrusor overactivity is the most common urodynamic abnormality, with elevated detrusor leak point pressure and reduced bladder capacity. Detrusor sphincter dyssynergy is present in some patients and maybe secondary to generalized spasticity or incomplete upper motor neuron injury. Elevated bladder capacity is also present in a portion of patients, and becomes particularly relevant in adults as a result of increased spasticity of the urinary sphincter. Conservative management like functional toileting strategies, medications, and incontinence aids are successful in most patients. Medical management with anticholinergics is well described, and frequently the only intervention required, particularly in children. Intermittent clean catheterization has mixed results with this population, as its efficacy is limited by pelvic spasticity and patient factors. Surgical intervention, while often successful, should be restricted to select patients, as it is associated with significant morbidity in this population. Conclusion: Management of NLUTD in adults with CP involves conservative management, medications, and in rare cases surgical intervention.

PMID: 37710012

17. Childhood-onset epilepsy in patients with dyskinetic cerebral palsy caused by basal ganglia and thalamic lesions

Shizuka Nishimoto, Yukihiro Kitai, Satori Hirai, Mika Hirotsune, Naomi Okuyama, Shodo Hirano, Yukiko Mogami, Hiroshi Arai

Eur J Paediatr Neurol. 2023 Sep 7;47:41-46. doi: 10.1016/j.ejpn.2023.09.006. Online ahead of print.

Objective: To elucidate the incidence and outcomes of childhood-onset epilepsy and associated factors in term-born patients with basal ganglia and thalamic lesion (BGTL)-induced dyskinetic cerebral palsy (DCP) caused by perinatal hypoxic-ischemic encephalopathy (HIE). Methods: We studied 104 term-born patients with BGTL-induced DCP (63 males and 41 females, aged 2-22 years) to investigate the incidence of epilepsy and the factors related to its development. We used multivariate analysis to assess perinatal factors, gross motor function, and the extent of brain lesions. We also investigated the seizure onset, clinical course, and electroencephalography (EEG) characteristics. Results: The cumulative epilepsy incidence was 36%. Multiple logistic regression analysis revealed that deep white matter lesions were the only independent risk factor for epilepsy. The confirmed seizure types included epileptic spasms (ES, n = 13), myoclonic seizures (MS, n = 6), and focal-onset seizures (FS, n = 24). Only patients with deep white matter lesions exhibited ES or MS. The symptoms of FS resembled those of self-limited epilepsy with centrotemporal spikes; however, only half of the patients reached remission by the time of investigation, and four patients had more than one seizure per month despite appropriate drug therapy. Focal spikes in the peri-rolandic area were detected not only in patients with FS but also in half of the patients without epilepsy. Conclusions: One-third of term-born patients with BGTL-induced DCP caused by perinatal HIE develop epilepsy, and deep white matter lesions increase the likelihood of epilepsy. Preparation for early-onset ES, MS, and subsequent FS is beneficial.

PMID: 37708783

18. Calcification of the pump pouch in patients receiving ITB therapy: A rare complication affecting refill procedure - Analysis of two cases

Marco Pavanello, Anna Ronchetti, Ida Barretta, Paolo Moretti, Gianluca Piatelli

Clin Neurol Neurosurg. 2023 Aug 23;233:107949. doi: 10.1016/j.clineuro.2023.107949. Online ahead of print.

Background: Intrathecal baclofen therapy (ITB) is an effective treatment for reducing spasticity but can be associated with various complications, including infection and implant malfunction. Methods: This retrospective cohort study analyzed refill reports, complications, and functional outcomes in 40 consecutive patients with intractable spasticity or dystonia undergoing ITB. Results: Among the 40 patients, 8 experienced complications, including two cases of calcification of the baclofen pump pouch and surrounding tissue, a rare complication not extensively described in the literature. Discussion: Calcification, in addition to port access difficulties, could lead to drug delivery failure. We hypothesize that calcification may result from microtrauma or needlestick injury to the subcutaneous tissue and muscle fascia. The length of time the pump stays in the pocket could also contribute to favoring this phenomenon. Conclusion: As the number of patients receiving ITB increases, physicians must be aware of potential life-threatening complications. The risk of pouch calcification should be further investigated and considered in managing patients undergoing ITB, as it could significantly impact patient care.

PMID: 37703618

19. Neurodevelopmental and behavioral outcomes of very preterm infants: latent profile analysis in the Environmental influences on Child Health Outcomes (ECHO) Program

Marie Camerota, Elisabeth C McGowan, Judy Aschner, Annemarie Stroustrup, T Michael O'Shea, Julie A Hofheimer, Robert M Joseph, Rashelle Musci, Genevieve Taylor, Brian S Carter, Jennifer Check, Lynne M Dansereau, Semsa Gogcu, Jennifer B Helderman, Charles R Neal, Steven L Pastyrnak, Lynne M Smith, Carmen J Marsit, Barry M Lester; program collaborators for Environmental influences on Child Health Outcomes

Pediatr Res. 2023 Sep 12. doi: 10.1038/s41390-023-02814-9. Online ahead of print.

Background: Very preterm infants are at high risk for neurodevelopmental impairments. We used a child-centered approach (latent profile analysis [LPA]) to describe 2-year neurobehavioral profiles for very preterm infants based on cognitive, motor, and behavioral outcomes. We hypothesized that distinct outcome profiles would differ in the severity and co-occurrence of neurodevelopmental and behavioral impairment. Methods: We studied children born <33 weeks' gestation from the Environmental influences on Child Health Outcomes Program with at least one neurobehavioral assessment at age 2 (Bayley Scales of Infant and Toddler Development, Child Behavior Checklist, Modified Checklist for Autism in Toddlers, cerebral palsy diagnosis). We applied LPA to identify subgroups of children with different patterns of outcomes. Results: In 2036 children (52% male; 48% female), we found four distinct neurobehavioral profiles. Most children (~85%) were categorized into one of two profiles characterized by no/mild neurodevelopmental delay and a low prevalence of behavioral problems. Fewer children (~15%) fell into one of two profiles characterized by severe neurodevelopmental impairments. One profile consisted of children (5%) with co-occurring neurodevelopmental impairment and behavioral problems. Conclusion: Child-centered approaches provide a comprehensive, parsimonious description of neurodevelopment following preterm birth and can be useful for clinical and research purposes. Impact: Most research on outcomes for children born very preterm have reported rates of impairment in single domains. Child-centered approaches describe profiles of children with unique combinations of cognitive, motor, and behavioral strengths and weaknesses. We capitalized on data from the nationwide Environmental influences on Child Health Outcomes Program to examine these profiles in a large sample of children born <33 weeks gestational age. We found four distinct neurobehavioral profiles consisting of different combinations of cognitive, motor, and behavioral characteristics. This information could aid in the development of clinical interventions that target different profiles

of children with unique developmental needs.

PMID: 37700161

20. An eHealth Program for Insomnia in Children With Neurodevelopmental Disorders (Better Nights, Better Days): Protocol for an Economic Evaluation of a Randomized Controlled Trial

Xiao Yang Jia, Pantelis Andreou, Cary Brown, Evelyn Constantin, Roger Godbout, Ana Hanlon-Dearman, Osman Ipsiroglu, Graham Reid, Sarah Shea, Isabel M Smith, Jennifer D Zwicker, Shelly K Weiss, Penny Corkum

JMIR Res Protoc. 2023 Sep 12;12:e46735. doi: 10.2196/46735.

Background: Children with neurodevelopmental disorders have a high risk of sleep disturbances, with insomnia being the most common sleep disorder (ie, chronic and frequent difficulties with going and staying asleep). Insomnia adversely affects the well-being of these children and their caregivers. Pediatric sleep experts recommend behavioral interventions as the first-line treatment option for children. Better Nights, Better Days for Children with Neurodevelopmental Disorders (BNBD-NDD) is a 5-session eHealth behavioral intervention delivered to parents to improve outcomes (eg, Pediatric Quality of Life Inventory [PedsQL]) for their children (ages 4-12 years) with insomnia and who have a diagnosis of mild to moderate attention-deficit/hyperactivity disorder, autism spectrum disorder, cerebral palsy, or fetal alcohol spectrum disorder. If cost-effective, BNBD-NDD can be a scalable intervention that provides value to an underserved population. Objective: This protocol outlines an economic evaluation conducted alongside the BNBD-NDD randomized controlled trial (RCT) that aims to assess its costs, efficacy, and cost-effectiveness compared to usual care. Methods: The BNBD-NDD RCT evaluates the impacts of the intervention on children's sleep and quality of life, as well as parents' daytime functioning and psychosocial health. Parent participants were randomized to the BNBD-NDD treatment or to usual care. The economic evaluation assesses outcomes at baseline and 8 months later, which include the PedsQL as the primary measure. Quality of life outcomes facilitate the comparison of competing interventions across different populations and medical conditions. Cost items include the BNBD-NDD intervention and parent-reported usage of private and publicly funded resources for their children's insomnia. The economic evaluation involves a reference case cost-effectiveness analysis to examine the incremental cost of BNBD-NDD per units gained in the PedsQL from the family payer perspective and a cost-consequence analysis from a societal perspective. These analyses will be conducted over an 8-month time horizon. Results: Research funding was obtained from the Kids Brain Health Network in 2015. Ethics were approved by the IWK Health Research Ethics Board and the University of Calgary Conjoint Health Research Ethics Board in January 2019 and June 2022, respectively. The BNBD-NDD RCT data collection commenced in June 2019 and ended in April 2022. The RCT data are currently being analyzed, and data relevant to the economic analysis will be analyzed concurrently. Conclusions: To our knowledge, this will be the first economic evaluation of an eHealth intervention for insomnia in children with neurodevelopmental disorders. This evaluation's findings can inform users and stakeholders regarding the costs and benefits of BNBD-NDD. Trial registration: ClinicalTrial.gov NCT02694003; https://clinicaltrials.gov/study/NCT02694003.

PMID: 37698915

21. Correlating Quantitative MRI-based Apparent Diffusion Coefficient Metrics with 24-month Neurodevelopmental Outcomes in Neonates from the HEAL Trial

Evan Calabrese, Yvonne Wu, Aaron Wolfe Scheffler, Jessica L Wisnowski, Robert C McKinstry, Amit Mathur, Hannah C Glass, Bryan A Comstock, Patrick J Heagerty, Shivani Gillon, Sandra E Juul, Christopher P Hess, Yi Li

Radiology. 2023 Sep;308(3):e223262. doi: 10.1148/radiol.223262.

Background Multiple qualitative scoring systems have been created to capture the imaging severity of hypoxic ischemic brain injury. Purpose To evaluate quantitative volumes of acute brain injury at MRI in neonates with hypoxic ischemic brain injury and correlate these findings with 24-month neurodevelopmental outcomes and qualitative brain injury scoring by radiologists. Materials and Methods In this secondary analysis, brain diffusion-weighted MRI data from neonates in the High-dose Erythropoietin for Asphyxia and Encephalopathy trial, which recruited participants between January 2017 and October 2019, were analyzed. Volume of acute brain injury, defined as brain with apparent diffusion coefficient (ADC) less than 800 × 10-6 mm2/sec, was automatically computed across the whole brain and within the thalami and white matter. Outcomes of death and neurodevelopmental impairment (NDI) were recorded at 24-month follow-up. Associations between the presence and volume (in milliliters) of acute brain injury with 24-month outcomes were evaluated using multiple logistic regression. The correlation between quantitative acute brain injury volume and qualitative MRI scores was assessed using the Kendall tau-b test. Results A total of 416 neonates had available MRI data (mean gestational age, 39.1 weeks ± 1.4 [SD]; 235 male) and 113 (27%) showed evidence of acute brain injury at MRI. Of the 387 participants with 24-month follow-up data, 185 (48%) died or had any NDI. Volume of acute injury greater than 1 mL (odds ratio [OR], 13.9 [95% CI: 5.93, 32.45]; P < .001) and presence of any acute injury in the brain (OR, 4.5 [95% CI: 2.6, 7.8]; P < .001) were associated with increased odds of death or any NDI. Quantitative whole-brain acute injury volume was strongly associated with radiologists' qualitative scoring of diffusion-weighted images (Kendall tau-b = 0.56; P < .001). Conclusion Automated quantitative volume of brain injury is associated with death, moderate to severe NDI, and cerebral palsy in neonates with hypoxic ischemic encephalopathy and correlated well with qualitative MRI

scoring of acute brain injury. Clinical trial registration no. NCT02811263 © RSNA, 2023 Supplemental material is available for this article. See also the editorial by Huisman in this issue.

PMID: 37698478

22. Caregivers' experiences of having a child with cerebral palsy. A meta-synthesis

Maggie Dumsile Dlamini, Ying-Ju Chang, Tram Thi Bich Nguyen

Review J Pediatr Nurs. 2023 Sep 8;73:157-168. doi: 10.1016/j.pedn.2023.08.026. Online ahead of print.

Aim: To synthesize qualitative research findings of caregiver experiences and challenges in caring for and raising a child with cerebral palsy. Design: A systematic review and meta-synthesis. Methods: Four electronic databases: CINAHL, Embase, OVID Medline, and Cochrane, were systematically searched for qualitative research papers published before December 2022. Two independent reviewers assessed eligibility and further appraised the quality of methodology using the Critical Appraisal Skills Program (CASP) tool for qualitative research. A content thematic analysis approach was used to synthesize the qualitative research findings, construct core subthemes, and synthesize themes. Results: Sixty-seven findings were extracted from the 12 included studies. The findings were grouped into eleven sub-themes and then into five synthesized themes. The synthesized themes are 1. Need for convenient healthcare facilities, therapeutic services, and accessible public places, 2. Need for healthcare information and financial aid, 3. Psychological, and physical constraints, 4. Societal rejection and stigma, and 5. Overwhelming caring burden. Conclusion: Caregivers face many challenges in adjusting their lifestyles to meet the needs of the child with cerebral palsy. Some adjustments reported included giving up full-time jobs and businesses to be full-time caregivers, giving up leisure activities, and confinement to one place.

PMID: 37690430

Prevention and Cure

23. Prevention of fetal brain injury in category II tracings

Masahiro Nakao, Michael G Ross, Shoichi Magawa, Satoshi Toyokawa, Kiyotake Ichizuka, Naohiro Kanayama, Shoji Satoh, Nanako Tamiya, Akihito Nakai, Keiya Fujimori, Tsugio Maeda, Akira Oka, Hideaki Suzuki, Mitsutoshi Iwashita, Tomoaki Ikeda

Acta Obstet Gynecol Scand. 2023 Sep 11. doi: 10.1111/aogs.14675. Online ahead of print.

Introduction: With category II fetal heart rate tracings, the preferred timing of interventions to prevent fetal hypoxic brain damage while limiting operative interventions remains unclear. We aimed to estimate fetal extracellular base deficit (BDecf) during labor with category II tracings to quantify the timing of potential interventions to prevent severe fetal metabolic acidemia. Material and methods: A longitudinal study was conducted using the database of the Recurrence Prevention Committee, Japan Obstetric Compensation System for Cerebral Palsy, including infants with severe cerebral palsy born at ≥34 weeks' gestation between 2009 and 2014. Cases included those presumed to have an intrapartum onset of hypoxic-ischemic insult based on the fetal heart rate pattern evolution from reassuring to an abnormal pattern during delivery, in association with category II tracings marked by recurrent decelerations and an umbilical arterial BDecf ≥ 12 mEq/L. BDecf changes during labor were estimated based on stages of labor and the frequency/severity of fetal heart rate decelerations using the algorithm of Ross and Gala. The times from the onset of recurrent decelerations to BDecf 8 and 12 mEq/L (Decels-to-BD8, Decels-to-BD12) and to delivery were determined. Cases were divided into two groups (rapid and slow progression) based upon the rate of progression of acidosis from onset of decelerations to BDecf 12 mEq/L, determined by a finite-mixture model. Results: The median Decels-to-BD8 (28 vs. 144 min, $p < 0.01$) and Decels-to-BD12 (46 vs. 177 min, $p < 0.01$) times were significantly shorter in the rapid versus slow progression. In rapid progression cases, physicians' decisions to deliver the fetus occurred at ~BDecf 8 mEq/L, whereas the "decisions" did not occur until BDecf reached 12 mEq/L in slow progression cases. Conclusions: Fetal BDecf reached 12 mEq/L within 1 h of recurrent fetal heart rate decelerations in the rapid progression group and within 3 h in the slow progression group. These findings suggest that cases with category II tracings marked by recurrent decelerations (i.e., slow progression) may benefit from operative intervention if persisting for longer than 2 h. In contrast, cases with sudden bradycardia (i.e., rapid progression) represent a challenge to prevent severe acidosis and hypoxic brain injury due to the limited time opportunity for emergent delivery.

PMID: 37697658

24. Systemic administration of clinical-grade multilineage-differentiating stress-enduring cells ameliorates hypoxic-ischemic brain injury in neonatal rats

Kazuto Ueda, Yoshiaki Sato, Shinobu Shimizu, Toshihiko Suzuki, Atsuto Onoda, Ryosuke Miura, Shoji Go, Haruka Mimatsu, Yuma Kitase, Yuta Yamashita, Keiichi Irie, Masahiro Tsuji, Kenichi Mishima, Masaaki Mizuno, Yoshiyuki Takahashi, Mari Dezawa, Masahiro Hayakawa

Sci Rep. 2023 Sep 11;13(1):14958. doi: 10.1038/s41598-023-41026-3.

Multilineage-differentiating stress-enduring (Muse) cells are endogenous reparative pluripotent stem cells present in the bone marrow, peripheral blood, and organ connective tissues. We assessed the homing and therapeutic effects of systemically administered nafimestrocel, a clinical-grade human Muse cell-based product, without immunosuppressants in a neonatal hypoxic-ischemic (HI) rat model. HI injury was induced on postnatal day 7 (P7) and was confirmed by T2-weighted magnetic resonance imaging on P10. HI rats received a single dose nafimestrocel (1 × 106 cells/body) or Hank's balanced salt solution (vehicle group) intravenously at either three days (on P10; M3 group) or seven days (on P14; M7 group) after HI insult. Radioisotope experiment demonstrated the homing of chromium-51-labeled nafimestrocel to the both cerebral hemispheres. The cylinder test (M3 and M7 groups) and open-field test (M7 group) showed significant amelioration of paralysis and hyperactivity at five weeks of age compared with those in the vehicle group. Nafimestrocel did not cause adverse events such as death or pathological changes in the lung at ten weeks in the both groups. Nafimestrocel attenuated the production of tumor necrosis factor-α and inducible nitric oxide synthase from activated cultured microglia in vitro. These results demonstrate the potential therapeutic benefits and safety of nafimestrocel.

PMID: 37696826

25. Quality improvement interventions to increase the uptake of magnesium sulphate in preterm deliveries for the prevention of cerebral palsy (PReCePT study): a cluster randomised controlled trial

Hannah B Edwards, Maria Theresa Redaniel, Carlos Sillero-Rejon, Christalla Pithara-McKeown, Ruta Margelyte, Tracey Stone, Tim J Peters, William Hollingworth, Hugh McLeod, Pippa Craggs, Elizabeth M Hill, Sabi Redwood, Emma Treloar, Jenny L Donovan, Brent C Opmeer, Karen Luyt

BJOG. 2023 Sep 10. doi: 10.1111/1471-0528.17651. Online ahead of print.

Objective: To compare two quality improvement (QI) interventions to improve antenatal magnesium sulphate (MgSO4) uptake in preterm births for the prevention of cerebral palsy. Design: Unblinded cluster randomised controlled trial. Setting: Academic Health Sciences Network, England, 2018. Sample: Maternity units with ≥10 preterm deliveries annually and MgSO4 uptake of ≤70%; 40 (27 NPP, 13 enhanced support) were included (randomisation stratified by MgSO4 uptake). Methods: The National PReCePT Programme (NPP) gave maternity units QI materials (clinical guidance, training), regional support, and midwife backfill funding. Enhanced support units received this plus extra backfill funding and unit-level QI coaching. Main outcome measures: MgSO4 uptake was compared using routine data and multivariable linear regression. Net monetary benefit was estimated, based on implementation costs, lifetime quality-adjusted life-years and societal costs. The implementation process was assessed through qualitative interviews. Results: MgSO4 uptake increased in all units, with no evidence of any difference between groups (0.84 percentage points lower uptake in the enhanced group, 95% CI -5.03 to 3.35). The probability of enhanced support being cost-effective was <30%. NPP midwives gave more than their funded hours for implementation. Units varied in their support needs. Enhanced support units reported better understanding, engagement and perinatal teamwork. Conclusions: PReCePT improved MgSO4 uptake in all maternity units. Enhanced support did not further improve uptake but may improve teamwork, and more accurately represented the time needed for implementation. Targeted enhanced support, sustainability of improvements and the possible indirect benefits of stronger teamwork associated with enhanced support should be explored further.

PMID: 37691262