# Cerebral palsy research news

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CP Alliance Chair of Cerebral Palsy Research

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## Interventions and Management

**1. Construct Validity of the Both Hands Assessment Using Wrist-Worn Accelerometers**

Andrea Burgess, Stina Oftedal, Roslyn N Boyd, Sarah Reedman, Stewart G Trost, Robert S Ware, Leanne Sakzewski

Phys Occup Ther Pediatr. 2023 May 14;1-14. doi: 10.1080/01942638.2023.2207635. Online ahead of print.

Aim: The aim of this study was to evaluate the construct validity of the Both Hands Assessment (BoHA) using activity of the upper limbs as detected by accelerometry in children with bilateral cerebral palsy (CP). Methods: Observational study of children with CP (n = 44, n = 27 boys, aged 9.1 ± 1.6 years; Manual Ability Classification Scale I: n = 15, II: n = 22, III: n = 7) completing a BoHA assessment while wearing a triaxial accelerometer on each wrist. BoHA Each-Hand sub-scores, BoHA percentage difference between hands, BoHA Units, mean activity for each hand, mean activity asymmetry index and total mean activity were calculated. Linear regressions were used to analyze associations between measures. Results: There were significant, positive associations between BoHA Units and total mean activity (B = 0.86, 95%CI: 0.32, 1.40), BoHA Percentage difference between hands and mean activity asymmetry index (B = 0.95, 95%CI: 0.75,1.15), and BoHA Each-Hand sub-score and mean activity for the non-dominant hand (B = 1.71, 95%CI: 1.16, 2.28), but not the dominant hand (B = 0.50, 95%CI: -0.45, 1.45). Conclusions: This study provides further evidence for the construct validity of the BoHA as a measure of upper limb performance. Wearable wrist sensors such as accelerometers capture and quantify gross upper limb movement in children with CP but cannot measure fine finger movements captured by the BoHA.

PMID: 37183420

**2. The association between isometric strength and cognitive function in adults with cerebral palsy**

Patricia C Heyn, Alex Tagawa, Zhaoxing Pan, Timothy Reistetter, Ted Kheng Siang Ng, Meredith Lewis, James J Carollo

Front Med (Lausanne). 2023 Apr 26;10:1080022. doi: 10.3389/fmed.2023.1080022. eCollection 2023.

Background: The literature supports quantifying the maximum force/tension generated by one's forearm muscles such as the hand grip strength (HGS) to screen for physical and cognitive frailty in older adults. Thus, we postulate that individuals with cerebral palsy (CP), who are at higher risk for premature aging, could benefit from tools that objectively measure muscle strength as a functional biomarker to detect frailty and cognitive decline. This study assesses the clinical relevancy of the former and quantifies isometric muscle strength to determine its association with cognitive function in adults with CP. Methods: Ambulatory adults with CP were identified from a patient registry and were enrolled into this study. Peak rate of force development (RFD) and maximum voluntary isometric contraction of the quadriceps were measured using a commercial isokinetic machine, while HGS was collected with a clinical dynamometer. Dominant and non-dominant side were identified. Standardized cognitive assessments, including the Wechsler Memory and Adult Intelligence Scales IV, Short Test of Mental Status, and the Patient-Reported Outcomes Measurement Information System (PROMIS®) were used to evaluate cognitive function. Results: A total of 57 participants (32 females; mean age 24.3 [SD 5.3]; GMFCS levels I-IV) were included in the analysis. Although dominant and non-dominant RFD and HGS measures were associated with cognitive function, non-dominant peak RFD showed the strongest associations with cognitive function. Conclusion: RFD capacity may reflect age-related neural and physical health and could be a better health indicator than HGS in the CP population.

PMID: 37181370

**3. Intrathecal baclofen therapy does not prevent hip displacement in children with cerebral palsy**

Jason J Howard, M Wade Shrader

Dev Med Child Neurol. 2023 May 20. doi: 10.1111/dmcn.15641. Online ahead of print.

No abstract available

PMID: 37208917

**4. Reducing spasticity does not prevent hip displacement in cerebral palsy**

Kerr Graham, Erich Rutz, Pam Thomason, Kate Willoughby

Dev Med Child Neurol. 2023 May 20. doi: 10.1111/dmcn.15613. Online ahead of print.

No abstract available

PMID: 37208916

**5. The use of botulinum toxin and intrathecal baclofen in hip dysplasia in cerebral palsy**

Mark Gormley

Dev Med Child Neurol. 2023 May 20. doi: 10.1111/dmcn.15642. Online ahead of print.

No abstract available

PMID 37208907

**6. [Solidarity with children and people with disabilities? : An economic analysis of reconstructive hip interventions in pediatric orthopedics]**

Katharina Susanne Gather, Sébastien Hagmann, Simone Gantz, Tobias Renkawitz

Orthopadie (Heidelb). 2023 May 17. doi: 10.1007/s00132-023-04381-7. Online ahead of print.
[Article in German]

Background: Brain damage in childhood can be caused cerebral palsy (CP) or be due to other diseases. Disturbance of muscle tone results in consecutive development of hip subluxation. Hip reconstructive surgery can significantly improve the mobility and quality of care of children. However, the DRG for surgical care of these conditions has been increasingly devalued. In Germany, this has already led to a reduction of pediatric orthopedics departments, accompanied by an important risk of insufficient treatment options for children and people with disabilities. Method: The aim of this retrospective study was an economic analysis of pediatric orthopedic interventions using the example of neurogenic hip decentration. For this purpose, the revenue-cost situation in patients with CP or other causes of brain damage was evaluated at a maximum care hospital in the period of 2019-2021. Results: The entire analysis period showed a deficit. The non-CP-group showed the most important deficit. In CP-patients, however, the plus decreased each year and resulted in a deficit in 2021. Conclusion: While the distinction between cerebral palsy and other forms of brain damage in children is usually not relevant for treatment, it is evident that the non-CP group is massively underfinanced. Overall, the negative economic balance of pediatric orthopedics in the field of neurogenic hip reconstruction is clearly revealed. In the current interpretation of the DRG system, children with disabilities cannot be offered cost-effective care at a maximum-care university center.

PMID: 37195420

**7. Kindy Moves: the feasibility of an intensive interdisciplinary programme on goal and motor outcomes for preschool-aged children with neurodisabilities requiring daily equipment and physical assistance**

Matthew Haddon, Loren West, Catherine Elliott, Corrin Walmsley, Jane Valentine, Natasha Bear, Dayna Pool; Healthy Strides Research Advisory Council

Randomized Controlled Trial BMJ Open. 2023 May 11;13(5):e068816. doi: 10.1136/bmjopen-2022-068816.

Objectives: To determine the feasibility of an intensive interdisciplinary programme in improving goal and motor outcomes for preschool-aged children with non-progressive neurodisabilities. The primary hypothesis was that the intervention would be feasible. Design: A single group feasibility study. Setting: An Australian paediatric community therapy provider. Participants: Forty children were recruited. Inclusion criteria were age 2-5 years with a non-progressive neurodisability, Gross Motor Function Classification System (GMFCS) levels III-V or equivalent, and goals relating to mobility, communication and upper limb function. Exclusion criteria included orthopaedic surgery in the past 6 months, unstable hip subluxation, uncontrolled seizure disorder or treadmill training in the past month. Intervention: A goal-directed programme of three 2-hour sessions per week for 4 weeks (24 hours total). This consisted of treadmill and overground walking, communication practice, and upper limb tasks tailored by an interdisciplinary team. Primary and secondary outcome measures: Limited-efficacy measures from preintervention (T1) to postintervention (T2) and 4-week follow-up (T3) included the Goal Attainment Scaling (GAS), Canadian Occupational Performance Measure (COPM), Gross Motor Function Measure (GMFM-66) and 10-Metre Walk Test (10MWT). Acceptability, demand, implementation and practicality were also explored. Results: There were improvements at T2 compared with T1 for all limited-efficacy measures. The GAS improved at T2 (mean difference (MD) 27.7, 95% CI 25.8 to 29.5) as well as COPM performance (MD 3.2, 95% CI 2.8 to 3.6) and satisfaction (MD 3.3, 95% CI 2.8 to 3.8). The GMFM-66 (MD 2.3, 95% CI 1.0 to 3.5) and 10MWT (median difference -2.3, 95% CI -28.8 to 0.0) improved at T2. Almost all improvements were maintained at T3. Other feasibility components were also demonstrated. There were no adverse events. Conclusions: An intensive interdisciplinary programme is feasible in improving goal and motor outcomes for preschool children with neurodisabilities (GMFCS III-V or equivalent). A randomised controlled trial is warranted to establish efficacy.

PMID: 37169503

**8. Reliability and validity of a mobile application for femoral anteversion measurement in adult patients**

Joon Woo Lee, Minjoon Oh, Mi Na Choi, Seung Yeol Lee

J Orthop Surg Res. 2023 May 19;18(1):372. doi: 10.1186/s13018-023-03853-y.

Background: Femoral torsion is primarily measured by computed tomography (CT), which has cost and radiation exposure concerns. Recently, femoral anteversion measurement by a simple radiograph-based mobile application was developed for patients with cerebral palsy. This study aimed to validate the use of a mobile application that can reconstruct a three-dimensional model of the femur from conventional radiographs for adults. Methods: Medical records of 76 patients undergoing conventional femur anteroposterior/lateral radiography and femur CT were reviewed. To measure femoral anteversion on the reconstructed 3-dimensional images from both the mobile application and CT, we drew a line which connects the posterior margins of each femoral condyle and another line which passes through the center of the femoral head and the midpoint of the femoral neck. After the reliability test, a single examiner measured femoral anteversion on the mobile application and CT. Pearson's correlation analysis was used to assess the correlation between anteversion on the mobile application and CT. Results: Femoral anteversion measured on both CT and the mobile application showed excellent reliability (intraclass correlation coefficients: 0.808-0.910). The correlation coefficient between femoral anteversion measured using CT and the mobile application was 0.933 ($p < 0.001$). The correlation of femoral anteversion between CT and the mobile application was relatively higher in the absence of metallic implants (correlation coefficient: 0.963, $p < 0.001$) than in the presence of metallic implants (correlation coefficient: 0.878, $p < 0.001$). Conclusions: Using two simple radiographs, the mobile application showed excellent validity and reliability for femoral anteversion measurement in adults as compared to CT. With the high accessibility and cost-effectiveness of this mobile application, femoral torsion measurement might be easily performed with simple radiography in clinical settings in the near future.

PMID: 37208695

**9. Unsupervised machine learning effectively clusters pediatric spastic cerebral palsy patients for determination of optimal responders to selective dorsal rhizotomy**

Xiaobin Hou, Yanyun Yan, Qijia Zhan, Junlu Wang, Bo Xiao, Wenbin Jiang

Sci Rep. 2023 May 19;13(1):8095. doi: 10.1038/s41598-023-35021-x.

Selective dorsal rhizotomy (SDR) can reduce the spasticity in patients with spastic cerebral palsy (SCP) and thus improve the motor function in these patients, but different levels of improvement in motor function were observed among patients after SDR. The aim of the present study was to subgroup patients and to predict the possible outcome of SDR based on the pre-operational parameters. A hundred and thirty-five pediatric patients diagnosed with SCP who underwent SDR from January 2015 to January 2021 were retrospectively reviewed. Spasticity of lower limbs, the number of target muscles, motor functions, and other clinical parameters were used as input variables for unsupervised machine learning to cluster all included patients. The postoperative motor function change is used to assess the clinical significance of clustering. After the SDR procedure, the spasticity of muscles in all patients was reduced significantly, and the motor function was promoted significantly at the follow-up duration. All patients were categorized into three subgroups by both hierarchical and K-means clustering methods. The three subgroups showed significantly different clinical characteristics except for the age at surgery, and the post-operational motor function change at the last follow-up in these three clusters was different. Three subgroups clustered by two methods could be

identified as "best responders", "good responders" and "moderate responders" based on the increasement of motor function after SDR. Clustering results achieved by hierarchical and K-means algorithms showed high consistency in subgrouping the whole group of patients. These results indicated that SDR could relieve the spasticity and promote the motor function of patients with SCP. Unsupervised machine learning methods can effectively and accurately cluster patients into different subgroups suffering from SCP based on pre-operative characteristics. Machine learning can be used for the determination of optimal responders for SDR surgery.

PMID: 37208393

**10. Collagenase treatment decreases muscle stiffness in cerebral palsy: A preclinical ex vivo biomechanical analysis of hip adductor muscle fiber bundles**

Jason J Howard, Venus Joumaa, Karyn G Robinson, Stephanie K Lee, Robert E Akins, Faizan Syed, M Wade Shrader, James S Huntley, H Kerr Graham, Timothy Leonard, Walter Herzog

Dev Med Child Neurol. 2023 May 17. doi: 10.1111/dmcn.15637. Online ahead of print.

Aim: To determine the dose-response relationship of collagenase Clostridium histolyticum (CCH) on collagen content and the change in muscle fiber bundle stiffness after ex vivo treatment of adductor longus biopsies with CCH in children with cerebral palsy (CP). Method: Biopsy samples of adductor longus from children with CP (classified in Gross Motor Function Classification System levels IV and V) were treated with 0 U/mL, 200 U/mL, 350 U/mL, or 500 U/mL CCH; percentage collagen reduction was measured to determine the dose-response. Peak and steady-state stresses were determined at 1%, 2.5%, 5%, and 7.5% strain increments; Young's modulus was calculated. Results: Eleven patients were enrolled (nine males, two females, mean age at surgery 6 years 5 months; range: 2-16 years). A linear CCH dose-response relationship was determined. Peak and steady-state stress generation increased linearly at 5.9/2.3mN/mm2 , 12.4/5.3mN/mm2 , 22.2/9.7mN/mm2 , and 33.3/15.5mN/mm2 at each percentage strain increment respectively. After CCH treatment, peak and steady-state stress generation decreased to 3.2/1.2mN/mm2 , 6.5/2.9mN/mm2 , 12.2/5.7mN/mm2 , and 15.4/7.7mN/mm2 respectively ($p < 0.004$). Young's modulus decreased from 205 kPa to 100 kPa after CCH ($p = 0.003$). Steady-state Young's elastic modulus decreased from median (IQR) 205.4 (118.5) to 100.3 (64.0) after CCH treatment ($p = 0.003$). Interpretation: This preclinical ex vivo study provides proof of concept for the use of collagenase to decrease muscle stiffness in individuals with CP.

PMID: 37198748

**11. Developmental motor problems and health-related quality of life in 5-year-old children born extremely preterm: A European cohort study**

Adrien M Aubert, Raquel Costa, Samantha Johnson, Ulrika Ådén, Véronique Pierrat, Marina Cuttini, Mairi Männamaa, Iemke Sarrechia, Jo Lebeer, Arno F Van Heijst, Rolf F Maier, Mariane Sentenac, Jennifer Zeitlin; SHIPS research group

Dev Med Child Neurol. 2023 May 14. doi: 10.1111/dmcn.15632. Online ahead of print.

Aim: To measure the association between cerebral palsy (CP) and non-CP-related movement difficulties and health-related quality of life (HRQoL) among 5-year-old children born extremely preterm (<28 weeks gestational age). Method: We included 5-year-old children from a multi-country, population-based cohort of children born extremely preterm in 2011 to 2012 in 11 European countries (n = 1021). Children without CP were classified using the Movement Assessment Battery for Children, Second Edition as having significant movement difficulties (≤5th centile of standardized norms) or being at risk of movement difficulties (6th-15th centile). Parents reported on a clinical CP diagnosis and HRQoL using the Pediatric Quality of Life Inventory. Associations were assessed using linear and quantile regressions. Results: Compared to children without movement difficulties, children at risk of movement difficulties, with significant movement difficulties, and CP had lower adjusted HRQoL total scores (β [95% confidence interval] = -5.0 [-7.7 to -2.3], -9.1 [-12.0 to -6.1], and - 26.1 [-31.0 to -21.2]). Quantile regression analyses showed similar decreases in HRQoL for all children with CP, whereas for children with non-CP-related movement difficulties, reductions in HRQoL were more pronounced at lower centiles. Interpretation: CP and non-CP-related movement difficulties were associated with lower HRQoL, even for children with less severe difficulties. Heterogeneous associations for non-CP-related movement difficulties raise questions for research about mitigating and protective factors.

PMID: 37179525

**12. Assessment of Five-Foot Plantar Morphological Pressure Points of Children with Cerebral Palsy Using or Not Dynamic Ankle Foot Orthosis**

Senem Guner, Serap Alsancak, Enver Güven, Ali Koray Özgün

Children (Basel). 2023 Apr 13;10(4):722. doi: 10.3390/children10040722.

People with spastic cerebral palsy (CP) often experience a decline in gait function and flexion. The children's posture and hip strategy, which leads to knee flexion, predisposes these children to increased contact area in the medial foot region. This study investigated the use of DAFO (dynamic ankle-foot orthosis) prescribed to patients with cerebral palsy (CP) to determine the plantar pressure distribution with orthosis use. Eight children with spastic CP (age 4-12 years) were classified as Gross Motor Function Classification System (GMFCS) levels I-II with a maximum spasticity level of 3 in their ankle muscles according to the Modified Ashworth Scale. We assessed the plantar distribution by using eight WalkinSense sensors in each trial and exported data from the proprietary software (WalkinSense version 0.96, Tomorrow Options Microelectronics, S.A.). The plantar pressure distribution was conducted under two conditions: only shoes and DAFO with shoes. The activation percentages for sensor number 1 under the 1st metatarsal and sensor number 4 under the lateral edge of the heel were significantly different under the DAFO condition. The 1-point sensor activation percentage significantly decreased, while the 4 -point sensor activation percentage increased during DAFO walking. According to our study findings, there was an increase in pressure distribution in the lateral part of the foot during the stance phase in DAFO. DAFO improved the gait cycle and influenced the plantar foot pressure in children with mild cerebral palsy.

PMID: 37189971

**13. Differences in kinetic characteristics during countermovement jump of football players with cerebral palsy according to impairment profiles**

Matías Henríquez , Rafael Sabido, David Barbado, Alba Rolda, Jose L L Elvira, Javier Yanci, Raúl Reina

Front Physiol. 2023 Apr 26;14:1121652. doi: 10.3389/fphys.2023.1121652. eCollection 2023.

Objectives: The purpose of this study was 1) to determine and compare kinetic parameters during the realization of a countermovement jump (CMJ) between footballers with cerebral palsy (CP) and non-impaired footballers, and 2) to analyze the differences in this action between different players' impairment profiles and a group of non-impaired footballers. Methods: This study involved 154 participants comprising 121 male footballers with CP from 11 national teams and 33 male non-impaired football players recruited as the control group (CG). The footballers with CP were described according to the different impairment profiles (bilateral spasticity = 10; athetosis or ataxia = 16; unilateral spasticity = 77; minimum impairment = 18). All participants performed three CMJs on a force platform to record kinetic parameters during the test. Results: The group of para-footballers presented significantly lower values than the CG in the jump height ($p < 0.01$, $d = -1.28$), peak power ($p < 0.01$, $d = -0.84$), and the net concentric impulse ($p < 0.01$, $d = -0.86$). Concerning the pairwise comparisons between CP profiles and the CG, significant differences were found for the bilateral spasticity, athetosis or ataxia, and unilateral spasticity subgroups compared to the non-impaired players for jump height ($p < 0.01$; $d = -1.31$ to $-2.61$), power output ($p < 0.05$; $d = -0.77$ to $-1.66$), and concentric impulse of the CMJ ($p < 0.01$; $d = -0.86$ to $-1.97$). When comparing the minimum impairment subgroup with the CG, only significant differences were found for jump height ($p = 0.036$; $d = -0.82$). Footballers with minimum impairment presented higher jumping height ($p = 0.002$; $d = -1.32$) and concentric impulse ($p = 0.029$; $d = -1.08$) compared to those with bilateral spasticity. Also, the unilateral spasticity subgroup reports a higher jump height performance than the bilateral group ($p = 0.012$; $d = -1.12$). Conclusion: These results suggest that the variables related to power production during the concentric phase of the jump are crucial for the performance differences between groups with and without impairment. This study provides a more comprehensive understanding of kinetic variables that would differentiate CP and non-impaired footballers. However, more studies are necessary to clarify which parameters better differentiate among different profiles of CP. The findings could help to prescribe effective physical training programs and support the classifier's decision-making for class allocation in this para-sport.

PMID: 37179834

**14. Effectiveness of a Telecare Physical Therapy Program in Improving Functionality in Children and Adolescents with Cerebral Palsy: A Cases Study**

Isabel Rodríguez-Costa, Vanesa Abuín-Porras, Paula Terán-García, Andrea Férez-Sopeña, Victoria Calvo-Fuente, Concepción Soto-Vidal, Soraya Pacheco-da-Costa

Children (Basel). 2023 Mar 31;10(4):663. doi: 10.3390/children10040663.

Cerebral palsy (CP) is the most common physical disability in childhood and results in motor impairment that is often associated with other disorders. The aim of this study was to assess whether a telecare intervention consisting of Action Observation Therapy with a family-center approach produces improvements in functionality in children and adolescents with CP. Seven girls with CP ages between 6 and 17 participated in this case series study that lasted 12 weeks: 6 weeks of telecare program with a total of six sessions; and a follow-up period of 6 weeks. The outcome variables were Gross Motor Function (Spanish version of the Gross Motor Function Measure), balance (Spanish version of the Pediatric Balance Scale), walking endurance (6-min walk test) and walking speed (10-m walk test). The variables were measured before starting the study, after 6 weeks of intervention and after the 6-week follow-up period. Results showed statistically significant improvements in gross motor function ($p = 0.02$) after the intervention. After the follow-up period, gross motor function remained statistically significant ($p = 0.02$), as well as balance ($p = 0.04$) and walking endurance ($p = 0.02$). These results show that a telecare

program has been beneficial in improving functionality with enhancements in gross motor function, balance and endurance in children and adolescents with CP that will facilitate participation.

PMID: 37189912

**15. Validation of the Pediatric Quality of Life Inventory 3.0 Cerebral Palsy Module (Parent Form) for use in Türkiye**

Sehim Kutlay, Birkan Sonel Tu, Melek Sezgin, Atilla Halil Elhan, Derya Gökmen, Alan Tennant, Ayşe Adile Küçükdeveci

Turk J Phys Med Rehabil. 2022 Nov 24;69(1):52-60. doi: 10.5606/tftrd.2023.11462. eCollection 2023 Mar.

Objectives: This study was planned to test the reliability and validity of the Turkish version of the Pediatric Quality of Life Inventory (PedsQL) 3.0 cerebral palsy (CP) module (parent form) in children with CP. Patients and methods: In the validation study conducted between June 2007 and June 2009, 511 children (299 normal children, 212 children with CP) were assessed by the seven scales of PedsQL [daily activities (DA), school activities (SA), movement and balance (MB), pain and hurt (PH), fatigue (F), eating activities (EA), and speech and communication (SC)]. Reliability was tested by internal consistency and person separation index (PSI); internal construct validity by Rasch analysis and external construct validity by correlation with the Gross Motor Function Classification System (GMFCS) and Functional Independence Measure for Children (WeeFIM). Results: Only 13 children with CP completed the inventory by themselves and thus were excluded. Consequently, 199 children with CP (113 males, 86 females; mean age: 7.3±4.2 years; range, 2 to 18 years) and 299 normal children (169 males, 130 females; mean age: 9.4±4.0 years; range, 2 to 17 years) were included in the final analysis. Reliabilities of the seven scales of the PedsQL 3.0 CP module were adequate, with Cronbach's alphas between 0.66 and 0.96 and the PSI between 0.672 and 0.943 for the CP group. In Rasch analysis, for each scale, items showing disordered thresholds were rescored; then testlets were created to overcome local dependency. Internal construct validity of the unidimensional seven scales was good with the mean item fit of -0.107±1.149, 0.119±0.818, 0.232±1.069, -0.442±0.672, 0.221±0.554, -0.091±0.606, and -0.333±1.476 for DA, SA, MB, PH, F, EA, and SC, respectively. There was no differential item functioning. External construct validity of the instrument was confirmed by expected moderate to high correlations with WeeFIM and GMFCS (Spearman's r=0.35-0.89). Conclusion: Turkish version of the PedsQL 3.0 CP module is reliable, valid, and available for use in clinical setting to evaluate health-related quality of life of children with CP.

PMID: 37201004

**16. Outcomes in children after mild neonatal hypoxic ischaemic encephalopathy: A population-based cohort study**

A E Törn, S Hesselman, K Johansen, J Ågren, A-K Wikström, M Jonsson

BJOG. 2023 May 18. doi: 10.1111/1471-0528.17533. Online ahead of print.

Objective: To investigate whether mild neonatal hypoxic ischaemic encephalopathy (HIE) in term born infants is associated with cerebral palsy, epilepsy, mental retardation and death up to 6 years of age. Design: Population-based cohort study. Setting: Sweden, 2009-2015. Population: Live term born infants without congenital malformations or chromosomal abnormalities (n = 505 075). Methods: Birth and health data were retrieved from Swedish national health and quality registers. Mild HIE was identified by diagnosis in either the Swedish Medical Birth Register or the Swedish Neonatal Quality Register. Cox proportional hazards regression was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). Main outcome measures: A composite of the outcomes cerebral palsy, epilepsy, mental retardation and death up to 6 years of age. Results: Median follow-up time was 3.3 years after birth. Of 414 infants diagnosed with mild HIE, 17 were classified according to the composite outcome and incidence rates were 12.6 and 2.9 per 1000 child-years in infants with and without HIE respectively. Infants with mild HIE was four times as likely to be diagnosed with the composite outcome (HR 4.42, 95% CI 2.75-7.12) compared with infants without HIE. When analysed separately, associations were found with cerebral palsy (HR 21.50, 95% CI 9.59-48.19) and death (HR 19.10, 95% CI 7.90-46.21). HRs remained essentially unchanged after adjustment for covariates. Conclusions: Mild neonatal HIE was associated with neurological morbidity and mortality in childhood. Challenges include identifying infants who may develop morbidity and how to prevent adverse outcomes.

PMID: 37199188

**17. Incidence and risk factors for care-related pain in children with physical disabilities**

Amandine Dubois, Caroline Hall, Emmanuelle Courtois-Communier, Arnaud Brasseur, Marine Cacioppo, Sylvain Brochard

Eur J Phys Rehabil Med. 2023 May 15. doi: 10.23736/S1973-9087.23.07726-2. Online ahead of print.

Background: The daily life of children with a physical disability is organized around interventions and care, which is coordinated by a multidisciplinary team. Little is known about the incidence of care-related pain in pediatric rehabilitation centers and health facilities for children. Aim: To determine the incidence and intensity of care-related pain in children with

physical disabilities, identify risk factors for pain and practices used to prevent care-related pain in pediatric rehabilitation centers and health facilities for children in France. Design: Non-interventional observational study. Setting: Sixteen pediatric rehabilitation and special education centers in 4 departments of Brittany (France). Population: A number of 280 children with physical disabilities randomly selected (mean age: 12±4 years). Predominant medical diagnosis was nervous system diseases (68%; e.g., cerebral palsy 33%). Methods: The FLACC-r scale was used to evaluate pain during each care activity or intervention that required physical contact with the child for five consecutive days and one night. Results: The recorded interventions were 7689. Pain was induced by 6% of physical acts, and 48% of children experienced at least one painful act during the study period. Acts that were more frequently associated with pain and had the highest pain intensity were standing frame use, feeding, gentle mobilizations and bladder catheterization. Age, level of dependency and type of act were all risk factors for care-related pain ($P<0.01$). Pain prevention was used for only 26.5% of acts. Conclusions: Care-related pain is frequent and under-recognized in pediatric rehabilitation and health facilities for children. All acts that involve direct physical contact can cause pain. Young and severely dependent children are most at risk of pain. Clinical rehabilitation impact: All professionals who are involved in the care of children with a physical disability and significant limitations in activity and participation must be aware of the issue of pain and that pain can be induced by even the most routine physical act. The management of care-related pain requires a benefit-risk analysis, a prevention and pain assessment, and a family-professional partnership. A multidimensional approach is needed for more individualized pain management and to evaluate the impact of pain on children's participation.

PMID: 37184414

**18. Social determinants of health for children with cerebral palsy and their families**

Katarina Ostojic, Isra Karem, Simon P Paget, Alison Berg, Betty-Jean Dee-Price, Raghu Lingam, Russell C Dale, Valsamma Eapen, Sue Woolfenden; EPIC-CP Group

Review Dev Med Child Neurol. 2023 May 14. doi: 10.1111/dmcn.15640. Online ahead of print.

Social determinants of health (SDH) influence health and social outcomes in positive and negative ways. Understanding the impact of SDH on children with cerebral palsy (CP) is essential to improve health equity, optimize health outcomes, and support children with CP and their families to thrive in society. In this narrative review, we summarize the landscape of SDH impacting children with CP and their families worldwide. In high-income countries, children from poorer neighbourhoods are more likely to have severe comorbidities, present with spastic bilateral CP, and report lower frequency of participation in community activities. In low- and middle-income countries, socioeconomic disadvantage is associated with increased risk of malnutrition, living in poorer housing conditions, not having access to proper sanitation, and living below the poverty line. Low maternal education is associated with increased likelihood of the child with CP experiencing increased severity of gross motor and bimanual functioning challenges, and poorer academic performance. Lower parental education is also associated with reduced child autonomy. On the other hand, higher parental income is a protective factor, associated with greater diversity of participation in day-to-day activities. A better physical environment and better social support are associated with higher participation in daily activities. Clinicians, researchers, and the community should be aware of these key challenges and opportunities. Then adopt a range of approaches that target adverse SDH/social needs and foster positive SDH in the clinical setting.

PMID: 37179527

**19. Follow-up of Kangaroo Mother Care programmes in the last 28 years: results from a cohort of 57 154 low-birth-weight infants in Colombia**

Nathalie Charpak, Adriana Montealegre-Pomar

BMJ Glob Health. 2023 May;8(5):e011192. doi: 10.1136/bmjgh-2022-011192.

Background: Kangaroo Mother Care (KMC) is an evidence-based intervention focused on premature and low-birth-weight (LBW) infants. In different healthcare systems, outpatient KMC programmes (KMCPs) have been pioneers in the follow-up of these high-risk newborns.Here, we describe an overview analysis performed in an unprecedented data set comprising Colombian infants and spanning 28 years. Methods: Cohort study of 57 154 infants discharged home in kangaroo position (KP) for follow-up in four KMCPs between 1993 and 2021. Results: At birth and at hospital discharge to a KMCP, median gestational age and weight were 34.5 and 36 weeks, 2000 g and 2200 g, respectively. Chronological age at admission was 8 days. Over time, anthropometric measures at birth and somatic growth during follow-up improved; on the other hand, percentages of mechanical ventilation, intraventricular haemorrhage and need for intensive care decreased as neuropsychomotor, sensory disorders and bronchopulmonary dysplasia incidence at 40 weeks. Risk of cerebral palsy and teenage mothers' frequency was higher in the poorest population. Early home discharge in KP in less than 72 hours was possible in 19% of the cohort. During the COVID-19 pandemic, we observed a more than twofold increase in exclusive breast feeding at 6 months and a reduction in readmission rates. Conclusion: This study provides a general overview of KMCPs follow-up during the last 28 years within the Colombian healthcare system. These descriptive analyses have allowed us to structure KMC as an evidence-based method. KMCPs allow close monitoring with regular feedback about preterm or LBW

infants' perinatal care, quality of care over time and health status during their first year of life. Monitoring these outcomes is challenging but guarantees access to high-risk infants' care with equity.

PMID: 37208122

**20. Paroxysmal Nonepileptic Events in Children With Epilepsy and Cerebral Palsy**

Monica S Cooper, Michael C Fahey, Charuta Dagia, Dinah Reddihough, Susan M Reid, Mark T Mackay

J Child Neurol. 2023 May 18;8830738231176055. doi: 10.1177/08830738231176055. Online ahead of print.

To determine the frequency of paroxysmal nonepileptic events in children with cerebral palsy due to brain injury who have epilepsy and to describe the factors associated with paroxysmal nonepileptic events. Methods: Retrospective, population-based study of children from the Victorian CP Register born 1999-2006. Neuroimaging, medical records, electroencephalograms (EEG), and EEG requests were analyzed. Results: Of the included 256 children, 87 had epilepsy. EEGs (with video correlation) were available for 82 of 87. Eighteen (18/82, 22%) had epileptic events captured on EEG. Twenty-one (21/82, 26%) had paroxysmal nonepileptic events captured on EEG. The majority (13/18, 77%) of children with epileptic events also had paroxysmal nonepileptic events captured. Ten parents and carers continued to report events as epileptic despite there being no ictal EEG correlate for specific events on multiple EEGs. There were no clear associations to identify which children would have ongoing paroxysmal nonepileptic events reported. Conclusions: Paroxysmal nonepileptic events were captured on EEG in one-fourth of children from this cerebral palsy cohort with epilepsy and available EEG. Half the parents and carers reported previously identified paroxysmal nonepileptic events as epileptic on subsequent EEGs, highlighting the need for clearer counseling so that parents better understand seizure semiology in children with EEG-proven paroxysmal nonepileptic events.

PMID: 37203178

**21. Spontaneous movements as a prognostic tool of neurodevelopmental outcomes in preterm infants: a narrative review**

Hyun Iee Shin, Myung Woo Park, Woo Hyung Lee

Clin Exp Pediatr. 2023 May 16. doi: 10.3345/cep.2022.01235. Online ahead of print.

An estimated 15 million infants are born each year prematurely. Although the survival rate of preterm infants has increased with advances in perinatal and neonatal care, many of them still suffer from various complications. Since improving neurodevelopmental outcomes of preterm births are a crucial topic of interest, accurate evaluations should be preceded for the detection of high-risk infants for cerebral palsy. General movements are spontaneous movements involving the whole body as the expression of neural activity and can be an excellent biomarker of neural dysfunction caused by brain impairment in preterm infants. The predictive value of general movements with respect to cerebral palsy increases with continuous observation. Automated approaches for general movements based on machine learning can help to overcome the limited utilization of assessment tools due to their qualitative or semi-quantitative nature and high dependency on the skills and experience of the assessors. This review will cover each of these topics, from the summarization of normal and abnormal general movements to the recent advance of automatic approaches based on infantile spontaneous movements.
PMID: 37202346

**22. The impact of the COVID-19 pandemic on children with disabilities and their parents or caregivers**

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Turk J Phys Med Rehabil. 2023 Jan 1;69(1):75-82. doi: 10.5606/tftrd.2023.10193. eCollection 2023 Mar.

Objectives: The study aimed to determine the impact of the pandemic on parents/caregivers and children with neurologic disabilities. Patients and methods: This multi-center cross-sectional study was conducted with 309 parents/caregivers (57 males, 252 females) and their 309 children (198 males, 111 females) with disabilities between July 5, 2020, and August 30, 2020. The parents/caregivers were able to answer the questions and had internet access. The survey included questions on the utilization of educational and health care services (whether they could obtain medicine, orthosis, botulinum toxin injection, or rehabilitation) during the pandemic. A Likert scale was used to evaluate the effect of the specific health domains, including mobility, spasticity, contractures, speech, communication, eating, academic, and emotional status. The Fear of COVID-19 Scale was used to assess fear of COVID-19. Results: Among the children, 247 needed to visit their physician during the pandemic; however, 94% (n=233) of them could not attend their physician appointment or therapy sessions. The restricted life during the first wave of the pandemic in Türkiye had negatively affected 75% of the children with disabilities and 62% of their parents. From the perspective of the parents/caregivers, mobility, spasticity, and joint range of motion of the children were affected. Forty-four children required repeated injections of botulinum toxin; however, 91% could not be administered. The Fear of COVID-19 Scale scores were significantly higher in the parents who could not bring their children to the routine

physician visit (p=0.041). Conclusion: During the pandemic, access to physical therapy sessions was disrupted in children with neurological disabilities, and this may have harmful consequences on the functional status of children.

PMID: 37201002

**23. Early neurodevelopmental outcomes of extreme preterm infants exposed to paracetamol: a retrospective cohort study**

Bella Zhong, Kenneth Tan, Abdul Razak, Vathana Sackett, Catherine Machipisa, Lindsay Zhou, Samira Samiee-Zafarghandy, Arvind Sehga, Rod W Hunt, Pramod Pharande, Atul Malhotra

Pediatr Res. 2023 May 17;1-6. doi: 10.1038/s41390-023-02649-4. Online ahead of print.

Background: Paracetamol is commonly used for analgesia and patent ductus arteriosus (PDA) treatment in preterm infants. We aimed to evaluate early neurodevelopmental outcomes of extreme preterm infants exposed to paracetamol during their neonatal admission. Methods: This retrospective cohort study included surviving infants born at <29 weeks gestation, or with a birth weight of <1000 grams. Neurodevelopmental outcomes studied were early cerebral palsy (CP) or high risk of CP diagnosis, Hammersmith Infant Neurological Examination (HINE) score and Prechtl General Movement Assessment (GMA) at 3-4 months corrected age. Results: Two hundred and forty-two infants were included, of which 123 were exposed to paracetamol. After adjusting for birth weight, sex and chronic lung disease, there were no significant associations between paracetamol exposure and early CP or high risk of CP diagnosis (aOR 1.46, 95% CI 0.61, 3.5), abnormal or absent GMA (aOR 0.82, 95% CI 0.37, 1.79) or HINE score (adjusted β -0.19, 95% CI -2.39, 2.01). Subgroup analysis stratifying paracetamol exposure into <180 mg/kg or ≥180 mg/kg cumulative dose found that neither had significant effects on outcomes. Conclusions: In this cohort of extreme preterm infants, no significant association was found between exposure to paracetamol during the neonatal admission and adverse early neurodevelopment. Impact: Paracetamol is commonly used in the neonatal period for analgesia and patent ductus arteriosus treatment in preterm infants, although prenatal paracetamol use has been associated with adverse neurodevelopmental outcomes. Exposure to paracetamol during the neonatal admission was not associated with adverse early neurodevelopment at 3-4 months corrected age in this cohort of extreme preterm infants. The findings from this observational study is consistent with the small body of literature supporting the lack of association between neonatal paracetamol exposure and adverse neurodevelopmental outcomes in preterm infants.

PMID: 37198403

**24. Participation measures that evaluate attendance and involvement for young people aged 15 to 25 years with cerebral palsy: a systematic review**

Jacinta R Quartermaine, Tanya A Rose, Megan L Auld, Leanne M Johnston

Disabil Rehabil. 2023 May 17;1-17. doi: 10.1080/09638288.2023.2207042. Online ahead of print.

Purpose: To identify participation-focused measures used for young people with cerebral palsy (CP), evaluate their psychometric evidence, and map item content to the International Classification of Functioning, Disability, and Health (ICF), and family of Participation-Related Constructs (fPRC) frameworks. Methods: Four databases (PubMed, Embase, Web of Science, CINAHL) were searched for papers that involved young people with CP aged 15 to 25 years and reported original data from a participation measure. Each measure was examined for validity, reliability, responsiveness (using the COSMIN checklist), clinical utility, the inclusion of accessible design features, self- and/or proxy-report from people with communication support needs, and item content according to ICF and fPRC. Results: Of 895 papers, 80 were included for review. From these, 26 measures were identified. Seven measures (27 papers/resources) were participation-focused, capable of producing a score for participation Attendance and/or Involvement. Of these, all measured Attendance (n = 7) but fewer than half measured Involvement (n = 3). Few included studies (37%) reported including some self-report of people with communication support needs. Conclusions: Participation measures for young people with CP are evolving but require more: (i) emphasis on measurement of involvement; (ii) investigation of psychometric properties; and (iii) adaptation to enable self-report by young people with communication support needs.IMPLICATIONS FOR REHABILITATIONIdentifies seven participation-focused measures which are available for young people with cerebral palsy, all seven measure Attendance and three measure Involvement.Provides a decision-making tool to assist clinicians and researchers with the selection of participation-focused measures for young people with cerebral palsy.Recommends that more accessible self-report measures are needed which capture age-appropriate participation of young people with cerebral palsy.

PMID: 37195908

**25. Genome-wide analysis of transcription factors in hippocampal tissue of cerebral palsy rats after acupuncture treatment**

Yu Zhou, Naerbuli Bahetibieke, Lina Fang, Yang Wu, Miao Wang, Xianglai Niu, Binfang Zeng, Guang Zhou

Am J Transl Res. 2023 Apr 15;15(4):2622-2633. eCollection 2023.

Background: Acupuncture has been shown to be effective in treating cerebral palsy (CP), reducing muscle tension, and improving motor function. However, macro-screening of key gene sets and gene-causal interaction networks for their therapeutic mechanisms have not been studied. Methods: Applying high-throughput sequencing technology, this research discussed differentially expressed mRNAs and differential alternative splicing pre-mRNAs at the transcriptome level in rats with CP treated with acupuncture and moxibustion, and analyzed the regulatory mechanisms of these differentially expressed genes (DEGs) in CP. Changes in the levels of transcripts and alternative splicing in the hippocampi of CP rats after acupuncture treatment were analyzed. Global genes that were differentially expressed and alternative splicing events (ASEs) and regulated ASEs (RASEs) in acupuncture treatment of CP rats were analyzed. Results: The RNA-seq data of acupuncture-treated rat hippocampi revealed 198 DEGs, 125 of which were related to CP, and the transcriptional regulation of RNA polymerase II was up-regulated; moreover, there were 1168 significantly different ASEs associated with CP and transcriptional regulation. There were 14 overlapping gene expression changes in transcription factors (TFs) and DEGs. Conclusions: This study found that 14 TFs were differentially expressed and a large number of TFs underwent differential alternative splicing. It is speculated that these TFs and the translated proteins of the two different transcripts produced by the differential alternative splicing of these TFs may play corresponding functions in acupuncture treatment of young rats with CP by modulating the differential expression of their target mRNAs.

PMID: 37193171

**26. A Semi-Supervised Graph Convolutional Network for Early Prediction of Motor Abnormalities in Very Preterm Infants**

Hailong Li, Zhiyuan Li, Kevin Du, Yu Zhu, Nehal A Parikh, Lili He

Diagnostics (Basel). 2023 Apr 21;13(8):1508. doi: 10.3390/diagnostics13081508.

Approximately 32-42% of very preterm infants develop minor motor abnormalities. Earlier diagnosis soon after birth is urgently needed because the first two years of life represent a critical window of opportunity for early neuroplasticity in infants. In this study, we developed a semi-supervised graph convolutional network (GCN) model that is able to simultaneously learn the neuroimaging features of subjects and consider the pairwise similarity between them. The semi-supervised GCN model also allows us to combine labeled data with additional unlabeled data to facilitate model training. We conducted our experiments on a multisite regional cohort of 224 preterm infants (119 labeled subjects and 105 unlabeled subjects) who were born at 32 weeks or earlier from the Cincinnati Infant Neurodevelopment Early Prediction Study. A weighted loss function was applied to mitigate the impact of an imbalanced positive:negative (~1:2) subject ratio in our cohort. With only labeled data, our GCN model achieved an accuracy of 66.4% and an AUC of 0.67 in the early prediction of motor abnormalities, outperforming prior supervised learning models. By taking advantage of additional unlabeled data, the GCN model had significantly better accuracy (68.0%, $p = 0.016$) and a higher AUC (0.69, $p = 0.029$). This pilot work suggests that the semi-supervised GCN model can be utilized to aid early prediction of neurodevelopmental deficits in preterm infants.

PMID: 37189608

**27. Eating and Drinking Ability Classification System to detect aspiration risk in children with cerebral palsy: a validation study**

Ksenia M Bykova, Ulrike Frank, Gay L Girolami

Eur J Pediatr. 2023 May 15;1-9. doi: 10.1007/s00431-023-04998-y. Online ahead of print.

This prospective study has two aims. The first aim is to assess the concurrent validity of the Eating and Drinking Ability Classification System (EDACS) as a means of identifying aspiration risk in children with cerebral palsy by using the Pediatric version of the Eating Assessment Tool (PEDI-EAT-10) as the reference test. The second aim is to investigate the relationship between the aspiration and non-aspiration groups using both the EDACS and the PEDI-EAT-10. Data were collected and analyzed from the EDACS and PEDI-EAT-10 using a convenience sample of 131 children with cerebral palsy and feeding problems (77 males, 54 females; median age 4.4 years [IQR 2.5 years]). Risk of aspiration was identified in 118 individuals using the PEDI-EAT-10 scores of ≥ 5 points. The EDACS proved to be a valid tool in identifying aspiration risk in children who are classified in EDACS levels III-V. There was a significant correlation between the EDACS and PEDI-EAT-10 ($r_s = 0.597$, $p < 0.001$). The EDACS had 78% (95% CI = 71-86%) sensitivity and 92% (95% CI = 88-97%) specificity in identifying aspiration risk a positive predictive value of 0.99, a negative predictive value of 0.32, a positive likelihood ratio of 9.75, and a negative likelihood ratio of 0.24. Conclusion: The EDACS is a useful clinical tool to identify aspiration risk in children with cerebral palsy. Children in EDACS levels III to V are at risk of aspiration. As time permits, we recommend the use of both tools, the EDACS and the PEDI-EAT-10, when making decisions regarding referral for an instrumented swallowing study. What is Known: • Approximately 50% of children with cerebral palsy have dysphagia. • The Eating and Drinking Ability Classification System (EDACS) can be used to classify eating and drinking efficiency and safety in children with cerebral palsy. What is New: • Based on ROC analysis, EDACS demonstrates sensitivity of 78% and specificity of 92% in clinical

identification of aspiration risk. • The combined use of the EDACS and the Pediatric version of the Eating Assessment Tool is recommended to make decisions about referral for an instrumented swallow study.

PMID: 37184644

**28. The Experience of Living through the Transition from Adolescence to Adulthood for Young People with Cerebral Palsy**

Paul Boyle, Kathleen T Galvin, Pirjo Vuoskoski, Graham Stew

Occup Ther Health Care. 2023 May 15;1-20. doi: 10.1080/07380577.2023.2211669. Online ahead of print.

This study explored the lived experience of transition from adolescence to adulthood for young people with cerebral palsy to inform occupational therapy practitioners as to what might promote positive life opportunities. A phenomenological methodology was used with six participants, aged 18 to 25 years with cerebral palsy. The findings are presented in the form of hermeneutic stories and three themes: The storm of uncertainty; time, space and the body, Capsizing in a world of others and, Securing anchorage; being heard and understood. Recommendations include service integration across health, social care and education based on partnership and provision of coordinators.

PMID: 37184443

**29. Niemann-Pick type C disease: Case report and review of the literature**

Chang Liu, Jiamin Li, Tao Xu, Min Song, Haiyan Luo

Case Reports Neuro Endocrinol Lett. 2023 Apr 30;44(2):101-104. Online ahead of print.

Niemann-Pick type C (NPC) disease is an autosomal recessive disease of lysosomal lipid storage disorder caused by mutations in either the NPC1 (95%) or the NPC2 (5%) gene. We report a case of a 23-year-old woman who initially showed ataxia, altered gait and tremor. She subsequently developed cognitive decline and psychiatric symptoms. She had asphyxia at birth and was diagnosed as hypoxic-ischemic encephalopathy and cerebral palsy before. The chest computed tomography (CT) incidentally showed splenomegaly. Brain magnetic resonance imaging (MRI) showed no significant abnormalities. Genetic analysis revealed compound heterozygous mutations of NPC1. The clinical picture of NPC can be markedly variable, so comprehensive clinical evaluation, neurological examination and laboratory test are quite important for the diagnosis of NPC.

PMID: 37182232

**30. Late-Onset Seizure Disorder in Adult Cerebral Palsy Associated With COVID-19 Infection**

Caroline S McCauley, Vivian Li, Steven Kobrin

Case Reports Cureus. 2023 Apr 11;15(4):e37438. doi: 10.7759/cureus.37438. eCollection 2023 Apr.

COVID-19 can affect many organ systems, including the CNS, with symptoms of altered mental status and seizures. We present a case of a 30-year-old man with cerebral palsy who developed seizures after a COVID-19 infection. Admission labs were remarkable for hypernatremia, and elevated creatine kinase, and troponin levels as well as creatinine above baseline. MRI was performed demonstrating a small, evolving acute/subacute abnormality in the midline splenium of the corpus callosum. An EEG showed moderate to severe abnormalities with low-voltage delta waves. The patient was treated with medication and advised to follow up with a neurologist. One month later, no residual CT abnormality corresponding to the previously reported lesion in the midline splenium of the corpus callosum was observed. Although epilepsy is a common finding in patients with cerebral palsy, the complete lack of seizure activity throughout this patient's early life, coupled with previously unremarkable brain imaging, further supports our claim that his recent onset of seizures was directly related to COVID-19. This case highlights the possibility of new seizures in patients with pre-existing neurological conditions after COVID-19 infection and emphasizes the need for more research.

PMID: 37181998

**31. Severity and duration of dysglycemia and brain injury among patients with neonatal encephalopathy**

Daphne Kamino, Elysa Widjaja, Rollin Brant, Linh G Ly, Eva Mamak, Vann Chau, Aideen M Moore, Tricia Williams, Emily W Y Tam

EClinicalMedicine. 2023 Mar 23;58:101914. doi: 10.1016/j.eclinm.2023.101914. eCollection 2023 Apr.

Background: Evidence is needed to inform thresholds for glycemic management in neonatal encephalopathy (NE). We investigated how severity and duration of dysglycemia relate to brain injury after NE. Methods: A prospective cohort of 108 neonates ≥36 weeks gestational age with NE were enrolled between August 2014 and November 2019 at the Hospital for Sick Children, in Toronto, Canada. Participants underwent continuous glucose monitoring for 72 h, MRI at day 4 of life, and follow-up at 18 months. Receiver operating characteristic curves were used to assess the predictive value of glucose measures (minimum and maximum glucose, sequential 1 mmol/L glucose thresholds) during the first 72 h of life (HOL) for each brain injury pattern (basal ganglia, watershed, focal infarct, posterior-predominant). Linear and logistic regression analyses were used to assess the relationship between abnormal glycemia and 18-month outcomes (Bayley-III composite scores, Child Behavior Checklist [CBCL] T-scores, neuromotor score, cerebral palsy [CP], death), adjusting for brain injury severity. Findings: Of 108 neonates enrolled, 102 (94%) had an MRI. Maximum glucose during the first 48 HOL best predicted basal ganglia (AUC = 0.811) and watershed (AUC = 0.858) injury. Minimum glucose was not predictive of brain injury (AUC <0.509). Ninety-one (89%) infants underwent follow-up assessments at 19.0 ± 1.7 months. A glucose threshold of >10.1 mmol/L during the first 48 HOL was associated with 5.8-point higher CBCL Internalizing Composite T-score (P = 0.029), 0.3-point worse neuromotor score (P = 0.035), 8.6-fold higher odds for CP diagnosis (P = 0.014). While the glucose threshold of >10.1 mmol/L during the first 48 HOL was associated with higher odds of the composite outcome of severe disability or death (OR 3.0, 95% CI 1.0-8.4, P = 0.042), it was not associated with the composite outcome of moderate-to-severe disability or death (OR 0.9, 95% CI 0.4-2.2, P = 0.801). All associations with outcome lost significance after adjusting for brain injury severity. Interpretation: Maximum glucose concentration in the first 48 HOL is predictive of brain injury after NE. Further trials are needed to assess if protocols to control maximum glucose concentrations improve outcomes after NE.

PMID: 37181414

**32. Recent developments in muscle synergy analysis in young people with neurodevelopmental diseases: A Systematic Review**

Giulia Beltrame, Alessandro Scano, Giorgia Marino, Andrea Peccati, Lorenzo Molinari Tosatti, Nicola Portinaro

Review Front Bioeng Biotechnol. 2023 Apr 27;11:1145937. doi: 10.3389/fbioe.2023.1145937. eCollection 2023.

The central nervous system simplifies motor control by sending motor commands activating groups of muscles, known as synergies. Physiological locomotion can be described as a coordinated recruitment of four to five muscle synergies. The first studies on muscle synergies in patients affected by neurological diseases were on stroke survivors. They showed that synergies can be used as biomarkers for motor impairment as they vary in patients with respect to healthy people. Likewise, muscle synergy analysis has been applied to developmental diseases (DD). The need for a comprehensive view of the present findings is crucial for comparing results achieved so far and promote future directions in the field. In the present review, we screened three scientific databases and selected thirty-six papers investigating muscle synergies extracted from locomotion in children affected by DD. Thirty-one articles investigate how cerebral palsy (CP) influences motor control, the currently exploited method in studying motor control in CP and finally the effects of treatments in these patients in terms of synergies and biomechanics; two articles investigate how muscle synergies vary in Duchenne muscular dystrophy (DMD), and three other articles assess other developmental pathologies, such as chronic and acute neuropathic pain. For CP, most of the studies demonstrate that the number of synergies is lower and that the synergy composition varies in the affected children with respect to normal controls. Still, the predictability of treatment's effects and the etiology of muscle synergy variation are open questions, as it has been reported that treatments minimally modify synergies, even if they improve biomechanics. The application of different algorithms in extracting synergies might bring about more subtle differences. Considering DMD, no correlation was found between non-neural muscle weakness and muscle modules' variation, while in chronic pain a decreased number of synergies was observed as a possible consequence of plastic adaptations. Even if the potential of the synergistic approach for clinical and rehabilitation practices is recognized, there is not full consensus on protocols nor widely accepted guidelines for the systematic clinical adoption of the method in DD. We critically commented on the current findings, on the methodological issues and the relative open points, and on the clinical impact of muscle synergies in neurodevelopmental diseases to fill the gap for applying the method in clinical practice.

PMID: 37180039

**33. Spontaneous resolution of post-hemorrhagic ventricular dilatation in preterm newborns and neurodevelopment**

Emilie Groulx-Boivin, Mariane Paquette, May Khairy, Marc Beltempo, Roy Dudley, Amaryllis Ferrand, Mireille Guillot, Victoria Bizgu, Jarred Garfinkle

Pediatr Res. 2023 May 13. doi: 10.1038/s41390-023-02647-6. Online ahead of print.

Background: We investigated the temporal evolution of post-hemorrhagic ventricular dilatation (PHVD) and compared neurodevelopmental impairments (NDI) in newborns with (Group 1) spontaneous resolution of PHVD, (Group 2) persistent PHVD without neurosurgical intervention, and (Group 3) progressive PHVD receiving neurosurgical intervention. Methods: A multicenter retrospective cohort study of newborns born at ≤34 weeks with PHVD (ventricular index [VI] >97th centile for gestational age and anterior horn width [AHW] >6 mm) from 2012 to 2020. Severe NDI was defined as global developmental

delay or cerebral palsy GMFCS III-V at 18 months. Results: Of 88 survivors with PHVD, 39% had a spontaneous resolution, 17% had persistent PHVD without intervention, and 44% had progressive PHVD receiving intervention. The median time between PHVD diagnosis and spontaneous resolution was 14.0 days (IQR 6.8-32.3) and between PHVD diagnosis and first neurosurgical intervention was 12.0 days (IQR 7.0-22.0). Group 1 had smaller median maximal VI (1.8, 3.4, 11.1 mm above p97; $p < 0.001$) and AHW (7.2, 10.8, 20.3 mm; $p < 0.001$) than Groups 2 and 3. Neurodevelopmental outcome data were available for 82% of survivors. Group 1 had reduced severe NDI compared to Group 3 (15% vs 66%; $p < 0.001$). Conclusion: Newborns with PHVD without spontaneous resolution are at higher risk for impairments despite neurosurgical interventions, which may be due to larger ventricular dilatation. Impact: The natural evolution of post-hemorrhagic ventricular dilatation (PHVD) and developmental implications of spontaneous resolution are not well established. In this study, approximately one in three newborns with PHVD experienced spontaneous resolution and this subset of newborns had reduced rates of neurodevelopmental impairments. More prominent ventricular dilatation was associated with reduced rates of spontaneous resolution and increased rates of severe neurodevelopmental impairment among newborns with PHVD. Understanding clinically relevant time points in the evolution of PHVD and predictors of spontaneous resolution may help inform the discussion around the optimal timing for intervention and allow for more precise prognostication in this population.

PMID: 37179437