Cerebral palsy research news

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Interventions and Management

1. Children With Bilateral Cerebral Palsy Exhibit Bimanual Asymmetric Motor Deficits and EEG Evidence of Dominant Sensorimotor Hemisphere Overreliance During Reaching

Connor Phillips, Julia Kline, Christopher J Stanley, Thomas C Bulea, Diane L Damiano

Neurorehabil Neural Repair. 2023 Aug 29;15459683231195044. doi: 10.1177/15459683231195044. Online ahead of print.

Background: Reaching is a fundamental motor skill often impaired in cerebral palsy (CP). Studies on manual function, intervention, and underlying brain mechanisms largely focus on unilateral CP. This first electroencephalography (EEG) evaluation of reaching exclusively in bilateral CP aims to quantify and relate brain activation patterns to bimanual deficits in this population. Methods: A total of 15 children with bilateral CP (13.4 ± 2.9 years) and 13 with typical development (TD: 14.3 ± 2.4 years) performed 45 reaches per hand while recording motion capture and EEG data. The Box and Blocks test was administered bilaterally. Cortical sources were identified using independent component analysis and clustered using k-means. Alpha (8-12 Hz) and beta (13-30 Hz) band event-related desynchronization (ERD) values were compared across groups and hands within clusters, between dominant and non-dominant sensorimotor clusters, and related to reach kinematics and the Box and Block test. Results: The group with CP demonstrated bimanual motor deficits with slower reaches, lower Box and Blocks scores, and stronger hand preference than in TD. Beta ERD, representing motor execution, was notably higher in the dominant sensorimotor cluster in CP compared to TD. Both groups demonstrated more contralateral than ipsilateral activity in both hands and clusters, with CP showing a less lateralized (more bilateral) alpha response. Higher brain activation was generally related to better function. Conclusion: Bimanual deficits in bilateral CP and related EEG differences warrant more clinical and research attention particularly earlier in life when greater potential for neural and functional recovery exists.

PMID: 37644730

2. Reliability of the Clinical Measurement of Upper and Lower Extremity Joint Motion in the Pediatric Population: A Systematic Review

Debra A Sala, Lori B Ragni

Review Phys Occup Ther Pediatr. 2023 Aug 29;1-29. doi: 10.1080/01942638.2023.2247072. Online ahead of print.

Aim: To examine intraobserver and interobserver reliability of the clinical measurement of pediatric joint motion of upper and lower extremities, based on participant condition and measurement technique. Methods: PubMed, CINAHL, and Web of Science were searched using combinations of children or adolescents, range of motion, and reliability. Reference lists and citations of reviewed studies were searched for additional publications. Results: Thirty-one studies of pediatric samples of developing typically, orthopedic injuries, athletes, cerebral palsy, and other diagnoses were reviewed. For techniques, measurements were made most frequently with a goniometer followed by visual estimation, inclinometer, smartphone apps, and specialized devices. The reliability of hip abduction measurements of participants with cerebral palsy was evaluated most often and varied widely for both intraobserver and interobserver. In general, goniometric results indicated greater reliability for upper than lower extremities and for intraobserver than interobserver. As the other techniques were each utilized in only a few studies, involving different participant conditions, joint motions and statistics, the analysis of their reliability was limited.

Conclusions: Intraobserver and interobserver reliability have not been established for pediatric joint motion measurements. Further research should include various joint motion measurements for different pediatric conditions using appropriate statistics. Results would provide important information for making clinical decisions.

PMID: 37644707

3. Does the Intrathecal Baclofen Dose Need to Be Changed after Spinal Fusion Surgery for Neuromuscular Scoliosis?

Kathryn M DeFoe, Jeremiah Atkinson, Jean Stansbury, Angela Sinner, Walter H Truong

Spine Surg Relat Res. 2023 Mar 13;7(4):385-389. doi: 10.22603/ssrr.2022-0230. eCollection 2023 Jul 27.

Introduction: Patients with cerebral palsy (CP) may receive intrathecal baclofen (ITB) to reduce muscle spasticity and dystonia. It can be challenging to identify the proper dose of ITB, and anecdotally these dosing needs may change after spinal fusion surgery. This study aimed to evaluate the need for changes in ITB dosing following a spinal fusion in pediatric neuromuscular scoliosis (NMS) patients and identify predisposing factors for those changes. Methods: This was a retrospective case-control study of NMS patients with an ITB pump who later received a spinal fusion surgery. Dosing changes and the indications for the changes were postoperatively noted. Demographics, preoperative factors, and surgical factors were evaluated for correlation with dosing changes. Results: A total of 49 patients were included in this study. Most had no change in ITB dose (71.4%), and others required a change that averaged about 10%. Male patients, those with larger pumps, and those that had a longer hospital stay were more likely to require a decrease in dose. Complications were similar between groups. Three catheters were revised during surgery: two continued on the same dose and one required an increase in dose after surgery. Conclusions: Spinal fusion after ITB pump placement is feasible and safe. Most patients did not require dosing changes after spine fusion; however, careful evaluation postoperatively remains prudent.

PMID: 37636147

4. Distal fusion level, complications, and reoperations in individuals with cerebral palsy undergoing surgery for scoliosis

I Green-Petersen, L Magnano, A Charalampidis, P Gerdhem

Eur Spine J. 2023 Sep 1. doi: 10.1007/s00586-023-07907-x. Online ahead of print.

Purpose: To compare radiological outcome, complications and reoperations in individuals with cerebral palsy and scoliosis fused to the fifth lumbar vertebra (L5), the sacrum, or the ilia. Methods: 208 individuals were identified in the national quality registry Swespine. Lowest level of fusion was L5 in 58, the sacrum in 92, and the ilia in 58 individuals. A subanalysis on 58 matched pairs operated to L5 or the pelvis (sacrum = 42, ilia = 16) with similar pelvic obliquity (± 5°) was performed. Results: The median (interquartile range) follow-up for the last radiograph was 1.7 (1.7) years and for reoperations 6.0 (5.9) years. Preoperatively, median Cobb angle of the major curve was 65° (23°) in the L5 group, 68° (28°) in the sacrum group, and 78° (25°) in the ilia group ($p = 0.006$). Preoperative median pelvic obliquity according to Maloney was 16° (19°), 21° (13°), and 27° (28°), respectively ($p = 0.004$). Immediate postoperative Cobb angles were 28° (18°), 28° (16°), and 32° (25°), respectively ($p = 0.11$). Immediate postoperative pelvic obliquity was 7° (10°), 7° (8°), and 8° (10°), respectively ($p = 0.28$). The median change in pelvic obliquity from the first to the last postoperative radiograph was - 5° (7°), - 3° (6°), - 3° (6°), respectively ($p = 0.55$). 7 (12%), 11 (12%), and 7 (12%) patients required at least one reoperation ($p = 1.0$), respectively. In the matched analysis, no significant differences in the radiological outcomes were found (all $p \geq 0.38$). Conclusions: Maintained curve and pelvic obliquity correction with no significant difference in complication and reoperation rates were found irrespective of distal fusion level.

PMID: 37656234

5. Muscle morphology and architecture of the medial gastrocnemius between typically developing children with different ancestral background

Fenna Walhain, Marlies Declerck, Ruby Chin A Fat, Lynn Bar-On, Anja Van Campenhout, Kaat Desloovere

J Anat. 2023 Aug 30. doi: 10.1111/joa.13945. Online ahead of print.

Muscle ultrasonography is frequently used to improve the understanding of musculoskeletal impairments in children with spastic cerebral palsy (SCP). So far, most studies on muscle morphology and architecture have included typically developing children and children with SCP with similar ancestry, being mainly Caucasian. Less is known about differences in muscle morphology between children with different ancestral backgrounds. Therefore, the aim of this study was to compare muscle morphology and architecture of the medial gastrocnemius in typically developing children with African, South Asian and Southeast Asian descent from Suriname. This explorative cohort study identified children as Maroon (Ghana, African descent), Hindustani (India, South Asian) or Javanese (Indonesia, Southeast Asian), aged 5-10 years. Using 3D freehand ultrasound with the subject prone, the following medial gastrocnemius parameters were defined: muscle tendon unit (MTU) length, muscle

belly length, tendon length, muscle volume, muscle thickness, anatomical cross-sectional area (ACSA), fascicle length, pennation angle, and physiological cross-sectional area (PCSA). In addition, differences between ancestral groups were assessed for the length of the MTU, muscle, tendon and fascicles in two passive stretch conditions corresponding to an externally applied joint torque of 1Nm and 4Nm. One-way ANOVA with post hoc t-tests were used to investigate differences between the ancestral groups. In total, 100 Hindustani (n = 34), Javanese (n = 34) and Maroon (n = 32) children were included. For statistical analyses, we matched the children by age, which resulted in groups of 25 children per ancestral group (n = 75). There were no differences found in MTU length, muscle belly length, ACSA, PCSA and muscle volume. Tendon length, fascicle length and pennation angle were different between ancestral groups. Compared to Javanese children, tendon length was longer ($p = 0.001$) and pennation angle ($p = 0.001$) was larger in Maroon children and fascicle length was shorter in both Maroon and Hindustani children ($p < 0.001$). While there was a difference found in MTU length at different conditions of passive stretch between ancestries, no differences were found in the muscle, tendon and fascicles. This is the first study that investigated macroscopic morphological and architectural parameters for the medial gastrocnemius in one extended cohort of typically developing children, stratified in three ancestral subgroups. The current results imply that ancestry-specific reference data for children are needed, especially for tendon length, fascicle length and pennation angle when investigating altered muscle morphology in neurological or neuromuscular pathologies, such as SCP. Future studies should report the ancestral background when describing muscle morphology and architecture of children and ancestral specifications should be included in normative databases.

PMID: 37646379

6. Mobility for individuals with cerebral palsy: Shifting the focus from method to independence

Ulrica Jonsson

Dev Med Child Neurol. 2023 Aug 30. doi: 10.1111/dmcn.15742. Online ahead of print.

No abstract available

PMID: 37649270

7. The efficacy of Equine Assisted Therapy intervention in gross motor function, performance, and spasticity in children with Cerebral Palsy

Alexandra N Stergiou, Sanna Mattila-Rautiainen, Dimitrios N Varvarousis, Meropi Tzoufi, Panagiota Plyta, Alexandros Beris, Avraam Ploumis

Front Vet Sci. 2023 Aug 15;10:1203481. doi: 10.3389/fvets.2023.1203481. eCollection 2023.

Purpose: To evaluate the efficacy of Equine Assisted Therapy in children with Cerebral Palsy, in terms of gross motor function, performance, and spasticity as well as whether this improvement can be maintained for 2 months after the end of the intervention. Methods: Children with Cerebral Palsy participated in this prospective cohort study. The study lasted for 28 weeks, of which the equine assisted therapy lasted 12 weeks taking place once a week for 30 min. Repeated measures within the subject design were used for the evaluation of each child's physical performance and mental capacity consisting of six measurements: Gross Motor Function Measure-88 (GMFM-88), Gross Motor Performance Measure (GMPM), Gross Motor Function Classification System (GMFCS), Modified Ashworth Scale (MAS) and Wechsler Intelligence Scale for Children (WISC III). Results: Statistically significant improvements were achieved for 31 children in Gross Motor Function Measure and all its subcategories ($p < 0.005$), also in total Gross Motor Performance Measure and all subcategories ($p < 0.005$). These Gross Motor Function Measure results remained consistent for 2 months after the last session of the intervention. Regarding spasticity, although an improving trend was seen, this was not found to be statistically significant. Conclusion and implications: Equine Assisted Therapy improves motor ability (qualitatively and quantitatively) in children with Cerebral Palsy, with clinical significance in gross motor function.

PMID: 37649564

8. Effect of Active Motor Learning Interventions on Gross Motor Function and Mobility in Children Aged 2 to 6 Years With Bilateral Cerebral Palsy: A Systematic Review and Meta-analysis

Kate L McLeod, Megan Thorley, Sarah E Reedman, Mark D Chatfield, Leanne Sakzewski

Pediatr Phys Ther. 2023 Sep 2. doi: 10.1097/PEP.0000000000001041. Online ahead of print.

Purpose: The purpose of this systematic review is to identify evidence-based interventions to promote active motor learning in children aged 2 to 6 years with bilateral cerebral palsy. Summary of key points: Seven randomized clinical trials of active motor learning interventions targeting gross motor function and mobility were included. Two studies compared context-focused therapy to child-focused therapy. Five studies compared active motor therapy to usual care. Context-focused therapy,

child-focused therapy, and active motor therapy were comparable to usual care to improve functional mobility and gross motor function. Conclusions and recommendations for clinical practice: There are limited active intervention studies targeting gross motor function for young children with bilateral cerebral palsy. The authors recommend consideration of the clinical good practice guidelines, dosage parameters, and improved reporting methods when implementing active motor learning interventions targeting gross motor function and mobility for children with cerebral palsy.

PMID: 37656984

9. Low skeletal muscle mass and liver fibrosis in children with cerebral palsy

Marie Mostue Naume, Marianne Hørby Jørgensen, Christina Engel Høi-Hansen, Maja Risager Nielsen, Alfred Peter Born, John Vissing, Lise Borgwardt, Dorte Marianne Rohde Stærk, Mette Cathrine Ørngreen

Eur J Pediatr. 2023 Sep 1. doi: 10.1007/s00431-023-05177-9. Online ahead of print.

The purpose of the study was to conduct a nutritional and metabolic assessment of children with cerebral palsy, including an investigation of liver status, body composition, and bone mineral density. In this cross-sectional study we included 22 children with cerebral palsy. By using ultrasound, transient elastography, dual x-ray absorptiometry (DXA) scan, blood samples, anthropometric measurements, and a three-day diet registration, the nutritional and metabolic status was evaluated. Liver fibrosis and steatosis were found in four patients (18.2%), all with severe motor impairments, low skeletal muscle mass, and epilepsy. All patients with liver involvement had normal liver-related blood samples. Decreased bone mineral density was found in 26.3%, and 91.0% had low skeletal muscle mass. Fat mass and muscle mass were significantly lower in the patients with severe motor impairments compared to the patients with less severe motor impairments. Within the children classified as 'underweight' or 'normal' according to body mass index, body fat determined by DXA scan was normal or high in 50% of these patients. Conclusions: This study is the first to report liver fibrosis and steatosis in children with cerebral palsy. Possible causes of liver fibrosis and/or steatosis are altered body composition with low skeletal muscle mass, decreased mobility and medical drug intake. Further investigations of liver involvement and risk factors are needed. What is known: • Children and adolescents with cerebral palsy are at risk of malnutrition and altered body composition, both of which can lead to fatty liver disease. • It is unknown whether children with cerebral palsy are at increased risk of metabolic disturbances such as fatty liver disease. What is new: • Altered body composition and low skeletal muscle mass, regardless of ambulation is present in 91% of the children with cerebral palsy. • Liver fibrosis and/or steatosis were found in 18.2% of the patients. Possible causes are altered body composition, decreased mobility and medical drug intake.

PMID: 37656239

10. Feasibility study on a longer side-alternating vibration therapy protocol (15 min per session) in children and adolescents with mild cerebral palsy

Alena Adaikina, José G B Derraik, Janene McMillan, Patricia Colle, Paul L Hofman, Silmara Gusso

Front Pediatr. 2023 Aug 15;11:1231068. doi: 10.3389/fped.2023.1231068. eCollection 2023.

Objective: Previous studies on side-alternating vibration therapy (sVT) have usually used a 9 min intervention protocol. We performed a feasibility study aimed at assessing the safety, acceptability, and potential effectiveness of a longer sVT protocol (15 min per session) in children and adolescents with cerebral palsy (CP). Methods: Fifteen participants aged 5.2-17.4 years (median = 12.4 years) with CP GMFCS level II underwent 20 weeks of sVT consisting of 15 min sessions 4 days/week. Participants were assessed at baseline and after the intervention period, including mobility (six-minute walk-test; 6MWT), body composition (whole-body dual-energy x-ray absorptiometry scans), and muscle function (force plate). Results: Adherence level to the 15 min VT protocol was 83% on average. There were no adverse events reported. After 20 weeks, there was some evidence for an increase in the walking distance covered in 6MWT (+43 m; $p = 0.0018$) and spine bone mineral density (+0.032 g/cm2; $p = 0.012$) compared to baseline. Conclusions: The 15 min sVT protocol is feasible and well tolerated. The results also suggest potential benefits of this protocol to mobility and bone health. Randomized controlled trials are needed to reliably ascertain the potential effectiveness of a longer sVT protocol on physical function and body composition in young people with CP.

PMID: 37650047

11. Defining, quantifying, and reporting intensity, dose, and dosage of neurorehabilitative interventions focusing on motor outcomes

Gaizka Goikoetxea-Sotelo, Hubertus J A van Hedel

Front Rehabil Sci. 2023 Aug 10;4:1139251. doi: 10.3389/fresc.2023.1139251. eCollection 2023.

Introduction: Determining the minimal amount of therapy needed for positive neurorehabilitative outcomes is important for

optimizing active treatment interventions to improve motor outcomes. However, there are various challenges when quantifying these relationships: first, several consensuses on the definition and usage of the terms intensity, dose, and dosage of motor interventions have been proposed, but there seems to be no agreement, and the terms are still used inconsistently. Second, randomized controlled trials frequently underreport items relevant to determining the intensity, dose, and dosage of the interventions. Third, there is no universal measure to quantify therapy intensity accurately. This "perspectives" paper aims to increase awareness of these topics among neurorehabilitation specialists. Defining quantifying and reporting: We searched the literature for definitions of intensity, dose, and dosage and adapted the ones we considered the most appropriate to fit the needs of neurorehabilitative interventions. Furthermore, we suggest refining the template for intervention description and replication (TIDieR) to enhance the reporting of randomized controlled trials. Finally, we performed a systematic literature search to provide a list of intensity measures and complemented these with some novel candidate measures. Discussion: The proposed definitions of intensity, dose, and dosage could improve the communication between neurorehabilitation specialists and the reporting of dose and dosage in interventional studies. Quantifying intensity is necessary to improve our understanding of the minimal intensity, dose, and dosage of therapy needed to improve motor outcomes in neurorehabilitation. We consider the lack of appropriate intensity measures a significant gap in knowledge requiring future research.

PMID: 37637933

12. Bruxism, parafunctional oral habits and oral motor problems in children with spastic cerebral palsy: A cross-sectional study

Aysenur Tuncer, Asiye Uzun, Abidin H Tuncer, Hazel C Guzel, Elif D Atılgan

J Oral Rehabil. 2023 Aug 28. doi: 10.1111/joor.13578. Online ahead of print.

Background: Individuals with spastic cerebral palsy are more predisposed to parafunctional oral activities and oral motor problems because of spasticity. Objectives: The aim of the study was to evaluate the relationship between the gross motor function classification system score (GMFCS), age, bruxism, parafunctional oral habits and oral motor problems in children with cerebral palsy. Methods: This cross-sectional study included 63 children with spastic cerebral palsy, aged 3-18 years, with developmental disabilities. The relationship between parentally reported bruxism, parafunctional oral activity rates, oral motor problems, and GMFCS was analysed. Results: The prevalence of bruxism was 52.4%, and the rate decreased as age increased. There was a greater likelihood of bruxism in individuals with tongue thrust (OR [95% CI] = 8.15 [1.4-47.3]) and swallowing problems (OR [95% CI] = 5.78 [1.3-24.68]). Conclusion: In children with spastic cerebral palsy, bruxism and the rate of parafunctional oral habits were high, thus affecting oral motor activities. A relationship was found between oral motor problems and increased GMFCS levels, but no relationship was found between bruxism and GMFCS levels. Children with spastic cerebral palsy who display tongue thrust or swallowing problems have an increased likelihood of presenting with bruxism.

PMID: 37641411

13. Cerebral palsy pain instruments: Recommended tools for clinical research studies by the National Institute of Neurological Disorders and Stroke Cerebral Palsy Common Data Elements project

Verónica Schiariti, Angela Shierk, Elaine E Stashinko, Theresa Sukal-Moulton, Robin S Feldman, Clara Aman, M Carolina Mendoza-Puccini, Joline E Brandenburg; National Institute of Neurological Disorders and Stroke Cerebral Palsy Common Data Elements Oversight Committee

Review Dev Med Child Neurol. 2023 Aug 31. doi: 10.1111/dmcn.15743. Online ahead of print.

Aim: This study describes the process of updating the cerebral palsy (CP) common data elements (CDEs), specifically identifying tools that capture the impact of chronic pain on children's functioning. Method: Through a partnership between the American Academy for Cerebral Palsy and Developmental Medicine and the National Institute of Neurological Disorders and Stroke (NINDS), the CP CDEs were developed as data standards for clinical research in neuroscience. Chronic pain was underrepresented in the NINDS CP CDEs version 1.0. A multi-step methodology was applied by an interdisciplinary professional team. Following an adapted CP chronic pain tools' rating system, and a review of psychometric properties, clinical utility, and compliance with inclusion/exclusion criteria, a set of recommended pain tools was posted online for external public comment in May 2022. Results: Fifteen chronic pain tools met inclusion criteria, representing constructs across all components of the International Classification of Functioning, Disability and Health. Interpretation: This paper describes the first condition-specific pain CDEs for a pediatric population. The proposed set of chronic pain tools complement and enhance the applicability of the existing pediatric CP CDEs. The novel CP CDE pain tools harmonize the assessment of chronic pain, addressing not only intensity of chronic pain, but also the functional impact of experiencing it in everyday activities.

PMID: 37650571

14. A high-performance neuroprosthesis for speech decoding and avatar control

Sean L Metzger, Kaylo T Littlejoh, Alexander B Silva, David A Moses, Margaret P Seaton, Ran Wang, Maximilian E Dougherty, Jessie R Liu, Peter Wu, Michael A Berger, Inga Zhuravlev, Adelyn Tu-Chan, Karunesh Ganguly, Gopala K Anumanchipalli, Edward F Chang

Nature. 2023 Aug;620(7976):1037-1046. doi: 10.1038/s41586-023-06443-4. Epub 2023 Aug 23.

Speech neuroprostheses have the potential to restore communication to people living with paralysis, but naturalistic speed and expressivity are elusive. Here we use high-density surface recordings of the speech cortex in a clinical-trial participant with severe limb and vocal paralysis to achieve high-performance real-time decoding across three complementary speech-related output modalities: text, speech audio and facial-avatar animation. We trained and evaluated deep-learning models using neural data collected as the participant attempted to silently speak sentences. For text, we demonstrate accurate and rapid large-vocabulary decoding with a median rate of 78 words per minute and median word error rate of 25%. For speech audio, we demonstrate intelligible and rapid speech synthesis and personalization to the participant's pre-injury voice. For facial-avatar animation, we demonstrate the control of virtual orofacial movements for speech and non-speech communicative gestures. The decoders reached high performance with less than two weeks of training. Our findings introduce a multimodal speech-neuroprosthetic approach that has substantial promise to restore full, embodied communication to people living with severe paralysis.

PMID: 37612505

15. Head Gesture Interface for Mouse Stick Users by AAGI

Ikushi Yoda, Kazuyuki Itoh, Tsuyoshi Nakayama

Stud Health Technol Inform. 2023 Aug 23;306:481-486. doi: 10.3233/SHTI230665.

We developed a gesture interface (AAGI) for individuals with motor dysfunction who cannot use standard interface switches. These users have cerebral palsy, quadriplegia, or traumatic brain injury and experience involuntary movement, spasticity, and so on. In this paper, we describe a disabled user who utilizes a mouth stick for laptop PC input in daily life. Our objective is to lower the burden on his body by using gestures. To this end, we developed a "home position" for the head that enables gestures to coexist with the mouse stick usage. The results of basic experiments with five healthy participants indicate that our system has reached the level where it can be applied to actual disabled persons. Finally, we applied the system to a user with cerebral palsy asked him to perform web browsing.

PMID: 37638952

16. Translation and cross-cultural adaptation of the functional mobility scale in children with cerebral palsy into Arabic

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Front Public Health. 2023 Aug 14;11:1199337. doi: 10.3389/fpubh.2023.1199337. eCollection 2023.

Introduction: Cerebral palsy (CP) is a lifelong disorder of posture and movement which often leads to a myriad of limitations in functional mobility. The Functional Mobility Scale (FMS) is a parent-report measure of functional mobility for children with CP at three different distances (5 m, 50 m, and 500 m). This is a cross-sectional study which sought to translate and culturally adapt the FMS into Arabic and to validate the translated version. Functional mobility for children and adolescents with CP in Saudi Arabia was examined. Methods: The translation methodology complied with the World Health Organization Disability Assessment Schedule 2.0 translation package. A total of 154 children with CP were recruited (mean age 8.16 ± 3.32 years). Parents were interviewed to rate the usual walking ability of their children on the Arabic FMS. The re-test assessment was done with 34 families. The mean time interval between the first and second sessions was 14.3 days (SD = 8.5), with a range of 6-37 days. Results: Concurrent validity was explored using Spearman's rank correlation coefficient between scores of the Arabic FMS with their corresponding score on the Gross Motor Function Classification System (GMFCS). Spearman's r values ranged between (-0.895 and -0.779), indicating strong to very strong correlations. The Test-retest reliability was examined using Cohen's weighted kappa, which showed almost perfect agreements. There was greater limitation for functional mobility at longer distances as 55.2% of children could not complete 500 meters (FMS score N). Overall, there was limited use of wheelchairs for all distances (ranging from 9.1% to 14.3%). Levels IV and V on the GMFCS had less variation in FMS scores and most of the children in these levels either did not complete the distances (no functional mobility at all distances) or used a wheelchair for mobility. Discussion: The Arabic FMS was shown to be a reliable and valid measure of functional mobility for children with CP in their environment based on the parental reports. Functional mobility varied at different distances and within each GMFCS level. The use of both the GMFCS and FMS when assessing children with CP is recommended.

PMID: 37645707

17. Growth and neurodevelopmental outcomes of preterm and low birth weight infants in rural Kenya: a cross-sectional study

Susanne P Martin-Herz, Phelgona Otieno, Grace M Laanoi, Vincent Moshi, Geofrey Olieng'o Okoth, Nicole Santos, Dilys Walker

BMJ Open. 2023 Aug 31;13(8):e064678. doi: 10.1136/bmjopen-2022-064678.

Objective: Data on long-term outcomes of preterm (PT) and low birth weight (LBW) infants in countries with high rates of neonatal mortality and childhood stunting are limited, especially from community settings. The current study sought to explore growth and neurodevelopmental outcomes of PT/LBW infants from a rural community-based setting of Kenya up to 18 months adjusted age. Design: Cross-sectional study. Setting: Migori County, Kenya. Participants: Three hundred and eighty-two PT/LBW infants (50.2% of those identified as eligible) from a cluster randomised control trial evaluating a package of facility-based intrapartum quality of care interventions for newborn survival consented for follow-up. Outcome measures: Caregiver interviews and infant health, growth and neurodevelopmental assessments were completed at 6, 12 or 18 months±2 weeks. Data included sociodemographic information, medical history, growth measurements and neurodevelopmental assessment using the Ten Questions Questionnaire, Malawi Developmental Assessment Tool and Hammersmith Infant Neurological Examination. Analyses were descriptive and univariate regression models. No alterations were made to planned data collection. Results: The final sample included 362 PT/LBW infants, of which 56.6% were moderate to late PT infants and 64.4% were LBW. Fewer than 2% of parents identified their child as currently malnourished, but direct measurement revealed higher proportions of stunting and underweight than in national demographic and health survey reports. Overall, 22.7% of caregivers expressed concern about their child's neurodevelopmental status. Neurodevelopmental delays were identified in 8.6% of infants based on one or more standardised tools, and 1.9% showed neurological findings indicative of cerebral palsy. Conclusions: Malnutrition and neurodevelopmental delays are common among PT/LBW infants in this setting. Close monitoring and access to early intervention programmes are needed to help these vulnerable infants thrive. Trial registration number: NCT03112018.

PMID: 37652593

18. Navigating the complexity of 18 motor disorder combinations in cerebral palsy

Saranda Bekteshi

Dev Med Child Neurol. 2023 Sep 2. doi: 10.1111/dmcn.15749. Online ahead of print.

No abstract available

PMID: 37658665

19. Tone management: An environmental scan of current management practices across Canada

My-An Tran, Madhura Thipse, Anne Tsampalieros, Richard Webster, Anna McCormick, Hana Alazem, Sunita Venkateswaran, Kevin Cheung, Kevin Smit, Albert Tu

Child Care Health Dev. 2023 Sep 1. doi: 10.1111/cch.13169. Online ahead of print.

Background: Currently, there are no standardized approaches to care or evaluation for tone dysfunction in Canada. The study authors hypothesize that there is significant practice variation across the country. This environmental scan is aimed to describe the current practice for management of paediatric patients with hypertonia across Canada. Methods: A web-based survey was developed by the authors with a multi-disciplinary approach and sent to representative paediatric rehabilitation sites in each province in Canada. Disciplines at the rehabilitation sites surveyed included all or some of the following disciplines: physiatry, neurology, neurosurgery, plastic surgery, orthopaedic surgery, physiotherapy and occupational therapy. All statistical analyses were performed using the R statistical software version 4.0. Fifteen rehabilitation sites were contacted, and 12 sites were used for the final analysis. Results: Cerebral palsy was found to be the most common diagnosis for tone dysfunction, with 58% of sites diagnosing greater than 20 new patients per year. In 67% of sites, patients were seen within a formal multidisciplinary clinic to manage hypertonia. All 12 sites utilized oral baclofen and gabapentin, and 92% of sites utilized trihexyphenidyl. Botulinum toxin injections were offered at 50% of sites. Upper and lower extremity surgical procedures were offered in 83% of the sites. Conclusion: The information gained from this study provides some insight into the current practice across Canada for children with hypertonia. This study may assist in the development of a national, standardized strategy to tone management, potentially facilitating more equitable access to care for patients.

PMID: 37658639

20. The Bobath Clinical Reasoning Framework: A systems science approach to the complexity of neurodevelopmental conditions, including cerebral palsy

Margaret J Mayston, Gillian M Saloojee, Sarah E Foley

Review Dev Med Child Neurol. 2023 Aug 31. doi: 10.1111/dmcn.15748. Online ahead of print.

The current recommended developmental Bobath practice within the Bobath Clinical Reasoning Framework (BCRF) can be conceptualized using the lens of systems science, thereby providing a holistic perspective on the interrelatedness and interconnectedness of the variables associated with childhood-onset disability. The BCRF is defined as an in-depth clinical reasoning framework that can be applied to help understand the relationships between the domains of the International Classification of Functioning, Disability and Health, how those domains can be influenced, and how they impact each other. The BCRF is a transdisciplinary observational system and practical reasoning approach that results in an intervention plan. This provides a holistic understanding of the complexity of situations associated with disorders such as cerebral palsy (CP) and the basis for the lifelong management and habilitation of people living with neurological disorders. The clinical reasoning used by the BCRF draws on the important contextual factors of the individual and their social environment, primarily the family unit. It is rooted in an understanding of the interrelationships between typical and atypical development, pathophysiology (sensorimotor, cognitive, behavioural), and neuroscience, and the impact of these body structure and function constructs on activity and participation. The systems science model integral to the BCRF is a useful way forward in understanding and responding to the complexity of CP, the overarching goal being to optimize the lived experience of any individual in any context.

PMID: 37653669

21. Safety, tolerability and feasibility of remotely-instructed home-based transcranial direct current stimulation in children with cerebral palsy

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No abstract available

PMID: 37652136

22. How do parents frame their engagement experience in early intervention? A grounded theory study

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Purpose: Parent and therapist engagement and partnership are critical in early intervention physiotherapy and occupational therapy for infants with cerebral palsy to improve outcomes. The main aim of this study was to understand how parents perceive their engagement experience in early intervention over time. Methods: Grounded theory methodology was used. Twenty parents of diverse backgrounds participated in 22 interviews (including some repeated longitudinally) to reflect on their engagement experience within the context of early intervention community services provided in the UK NHS. Results: The findings highlight how parents' perspectives of their engagement in EI change according to critical circumstances, including their preceding neonatal trauma, the at-risk CP label, firmer diagnosis of CP and their child's response to intervention. We theorise that this disrupted transition experience to parenthood becomes part of parental framing (or sense-making) of their engagement in EI. Overlapping frames of uncertainty, pursuit and transformation capture and explain nuances in parents' engagement patterns within EI over time. Conclusion: This theorising has implications for early intervention therapists in how they engage in the lives of families and partner with parents to support healthier parental transition, wellbeing and subsequent improved infant outcomes.

PMID: 37652081

23. The 'process of doing' in everyday occupations - a challenge for young adults with cerebral palsy

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Scand J Occup Ther. 2023 Aug 30;1-10. doi: 10.1080/11038128.2023.2251528. Online ahead of print.

Background: There is a lack of knowledge about how persons with cerebral palsy (CP) perceive their 'process of doing' while performing everyday occupations. As described in the Model of the Process of Doing (MPoD), performing an occupation is a

complex process consisting of six phases (generate idea, plan, initiate, enact, adjust, end) and time management.Aim: To collect the experiences of young adults with CP, classified at Manual Ability Classification System (MACS) level I or II, regarding how they perceive challenges in their occupational performance in relation to the different phases of the 'process of doing'.Method: Semi-structured interviews were performed with ten participants with CP aged 19-30 years, MACS level I or II. The interview material was related to the MPoD phases using directed content analysis.Results: The participants' descriptions of how they perceived their personal 'process of doing' showed problems in all MPoD phases. All participants experienced difficulties in one or more phases, but none had difficulties in all phases. Difficulties were more frequent in some phases than in others.Conclusion/Significance: To understand the complexity of doing everyday occupations in young adults with CP, there is a need to address all phases of the 'process of doing'.

PMID: 37647414

24. Biological and environmental factors may affect children's executive function through motor and sensorimotor development: Preterm birth and cerebral palsy

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Disruptive biological and environmental factors may undermine the development of children's motor and sensorimotor skills. Since the development of cognitive skills, including executive function, is grounded in early motor and sensorimotor experiences, early delays or impairments in motor and sensorimotor processing often trigger dynamic developmental cascades that lead to suboptimal executive function outcomes. The purpose of this perspective paper is to link early differences in motor/sensorimotor processing to the development of executive function in children born preterm or with cerebral palsy. Uncovering such links in clinical populations would improve our understanding of developmental pathways and key motor and sensorimotor skills that are antecedent and foundational for the development of executive function. This knowledge will allow the refinement of early interventions targeting motor and sensorimotor skills with the goal of proactively improving executive function outcomes in at-risk populations.

PMID: 37643499

25. Risk factors associated with traumatic dental injuries in individuals with special healthcare needs-A systematic review and meta-analysis

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Review Dent Traumatol. 2023 Aug 28. doi: 10.1111/edt.12882. Online ahead of print.

Background/aim: Individuals with special healthcare needs (SHCN) are more likely to sustain traumatic dental injuries (TDIs) due to distinct risk factors. The aim of this review was to assess various risk factors associated with TDIs in individuals with SHCN. Materials and methods: The protocol was designed according to the recommendations of the Cochrane-handbook, Joanna Briggs Institute, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and registered in PROSPERO (CRD42022357422). A comprehensive search was performed in PubMed, LILACS, Web of Science, EMBASE and Scopus using a pre-defined strategy without any limitation of language and year of publication. It was last updated on 25 April 2023. Studies addressing the TDIs in individuals with SHCN were included. Data extraction and analyses were performed, risk of bias (ROB) assessment was done using the Joanna Briggs Institute's critical appraisal tool, and a meta-analysis was performed using random-effects model. Results: A total of 21 studies were included in the review. They were categorized according to the target disease/condition: cerebral palsy (n = 5), ADHD and autism spectrum disorders (n = 5), visually impaired (n = 4), and multiple disorders (n = 7). The studies showed variability in the design and methods; however, 17 out of 21 studies showed moderate to low ROB. Increased overjet and lip incompetence were the main risk factors reported in the studies. The commonest injuries were observed to be enamel and enamel and dentine fractures. Conclusion: The overall pooled prevalence of TDI in individuals with special healthcare needs was 23.16% with 20.98% in males and 27.06% in females. Overjet >3 mm and inadequate lip coverage were found to be associated with a higher risk of TDI in all the categories of individuals with special healthcare needs except ADHD and ASD. Falls at home in cerebral palsy, falls while walking and self-harm in ADHD and ASD, falls at home and collision in visual impairment, and unspecified falls in multiple disorders could be identified as the most common cause of TDI.

PMID: 37638637

26. Bilateral globus pallidus interna deep brain stimulation in the treatment of mixed cerebral palsy in ataxia with dyskinesia: a case report

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Case Reports Front Neurol. 2023 Aug 10;14:1238292. doi: 10.3389/fneur.2023.1238292. eCollection 2023.

Background: Cerebral palsy (CP), a complex syndrome with multiple etiologies, is characterized by a range of movement disorders within the hypokinetic and hyperkinetic spectrum (dystonia or choreoathetosis). CP is often accompanied by neurological and psychiatric signs, such as spasticity, ataxia, and cognitive disorders. Although current treatment options for CP include pharmacological interventions, rehabilitation programs, and spasticity relief surgery, their effectiveness remains limited. Deep brain stimulation (DBS) has demonstrated significant effectiveness in managing dyskinesia; however, its potential therapeutic effect on CP remains determined. Methods: We present a case of a 44-year-old Asian female who was born as a twin with neonatal ischemic-hypoxic encephalopathy due to prolonged labor and delivery. She was diagnosed with CP at the age of 1 year. The patient exhibited delayed development compared to her peers and presented with various symptoms, including slurred speech, broad-based gait, horseshoe inversion of the right lower extremity, involuntary shaking of the upper extremities bilaterally, and hypotonia and showed no improvement with levodopa therapy. Two years ago, she developed progressive head tremors, which worsened during periods of tension and improved during sleep. As medical treatments proved ineffective and there were no contraindications to surgery, we performed bilateral globus pallidus interna DBS (GPi-DBS) to alleviate her motor dysfunction. Results: Following a 6-month follow-up, the patient demonstrated significant improvements in motor symptoms, including head and limb tremors and dystonia. In addition, significant improvement was observed in her overall psychological well-being, as evidenced by reduced anxiety and depression levels. Conclusion: DBS is an effective treatment for dyskinesia symptoms associated with CP in adults. Moreover, its effectiveness may continue to increase over time.

PMID: 37638197

27. Structure of brain grey and white matter in infants with spastic cerebral palsy and periventricular white matter injury

Chengxiang Liu, Ying Peng, Yanli Yang, Pengyu Li, Duoli Chen, Dingxin Nie, Heng Liu, Peng Liu

Dev Med Child Neurol. 2023 Aug 27. doi: 10.1111/dmcn.15739. Online ahead of print.

Aim: To investigate the possible covariation of grey matter volume (GMV) and white matter fractional anisotropy in infants with spastic cerebral palsy (CP) and periventricular white matter injury. Method: Thirty-nine infants with spastic CP and 25 typically developing controls underwent structural magnetic resonance imaging and diffusion tensor imaging. Multimodal canonical correlation analysis with joint independent component analysis were used to capture differences in GMV and fractional anisotropy between groups. Correlation analysis was performed between imaging findings and clinical features. Results: Infants with spastic CP showed one joint group-discriminating component (i.e. GMV-fractional anisotropy) associated with regions in the cortico-basal ganglia-thalamo-cortical loop and in the corpus callosum compared to typically developing controls and one modality-specific group-discriminating component (i.e. GMV). Significant negative correlations were found between loadings in certain regions and the motor function score in spastic CP. Interpretation: In infants with spastic CP, covarying GMV-fractional anisotropy and altered GMV in specific regions were implicated in motor dysfunction, which confirmed that simultaneous GMV and fractional anisotropy changes underly motor deficits, but might also extend to sensory, cognitive, or visual dysfunction. These findings also suggest that multimodal fusion analysis allows for a more comprehensive understanding of the relevance between grey and white matter structures and its crucial role in the neuropathological mechanisms of spastic CP.

PMID: 37635344

28. Brain Region Size Differences Associated With Dystonia in People With Cerebral Palsy Born Premature

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Pediatr Neurol. 2023 Jul 20;148:8-13. doi: 10.1016/j.pediatrneurol.2023.07.011. Online ahead of print.

Background: Dystonia in cerebral palsy (CP) is classically associated with deep gray matter injury at term gestation, but the patterns of injury associated with dystonia following premature birth are unclear. We examined whether there were brain regional size differences associated with dystonia in people with CP born premature. Methods: In this retrospective cohort study, we identified subjects with CP born premature (<37 weeks gestational age) seen at a tertiary care CP center between February 1, 2017, to February 1, 2021, who had T1-weighted brain magnetic resonance imaging (MRI) done between ages one and five years available in the clinical record. We measured the following on these brain MRI images per the 2013 Kidokoro criteria: interhemispheric distance, biparietal width, lateral ventricle diameter, transcerebellar diameter, deep gray matter area, and corpus callosum thickness. We then compared the sizes of these structures between those with and without dystonia correcting for gestational age at birth and gross motor functional ability (univariate general linear models). Results: Fifty-five subjects met the inclusion and exclusion criteria. Interhemispheric distance was significantly greater in those with dystonia, suggesting decreased cortical volume (P = 0.005). There was no significant difference in the other measured structures between those with and without dystonia, including deep gray matter area. Conclusions: Increased interhemispheric distance, not measures of deep gray matter size, correlate with the presence of dystonia in people with CP born premature.

PMID: 37633215

Prevention and Cure

29. Therapeutic Hypothermia for Hypoxic-Ischemic Brain Injury Is More Effective in Newborn Infants than in Older Patients: Review and Hypotheses

Andrew Whitelaw, Marianne Thoresen

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Posthypoxic therapeutic hypothermia has been tested in newborn infants, with seven randomized trials showing consistent evidence of reduction in death, cerebral palsy, and cognitive impairment at school age. In contrast, randomized trials of hypothermia after cardiac arrest in adults have not shown consistent evidence of lasting neurological protection. The apparently greater effectiveness of therapeutic hypothermia in newborns may be due to important biological and clinical differences. One such difference is that adults are heavily colonized with microbes, and many have active inflammatory processes at the time of arrest, but few newborns are heavily colonized or infected at the time of birth. Inflammation can interfere with hypothermia's neuroprotection. A second difference is that apoptosis is more commonly the pathway of neuronal death in newborns than in adults. Hypothermia inhibits apoptosis but not necrosis. Newborns have a larger endogenous supply of stem cells (which reduce apoptosis) than adults and this may favor regeneration and protection from hypothermia and regeneration. A third difference is that immature oligodendroglia are more sensitive to free radical attack then mature oligodendroglia. Hypothermia reduces free radical release. In addition, immature brain has increased N-methyl-D-aspartate receptor subunits compared with adults and hypothermia reduces excitotoxic amino acids. Adults suffering cardiac arrest often have comorbidities such as diabetes, hypertension, and atherosclerosis, which complicate recovery, but newborn infants rarely have comorbidities before asphyxia. Adult hypothermia treatment may have been too short as no trial has cooled for longer than 48 hours, some only 24 or 12 hours, but neonatal therapeutic hypothermia has routinely lasted 72 hours. We hypothesize that this combination of differences favors the effectiveness of therapeutic hypothermia in newborn infants compared with adults.

PMID: 37638830

30. Systemic corticosteroids for the prevention of bronchopulmonary dysplasia, a network meta-analysis

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Review Cochrane Database Syst Rev. 2023 Aug 31;8:CD013730. doi: 10.1002/14651858.CD013730.pub2.

Background: Despite considerable improvement in outcomes for preterm infants, rates of bronchopulmonary dysplasia (BPD) remain high, affecting an estimated 33% of very low birthweight infants, with corresponding long-term respiratory and neurosensory issues. Systemic corticosteroids can address the inflammation underlying BPD, but the optimal regimen for prevention of this disease, balancing of the benefits with the potentially meaningful risks of systemic corticosteroids, continues to be a medical quandary. Numerous studies have shown that systemic corticosteroids, particularly dexamethasone and hydrocortisone, effectively treat or prevent BPD. However, concerning short and long-term side effects have been reported and the optimal approach to corticosteroid treatment remains unclear. Objectives: To determine whether differences in efficacy and safety exist between high-dose dexamethasone, moderate-dose dexamethasone, low-dose dexamethasone, hydrocortisone, and placebo in the prevention of BPD, death, the composite outcome of death or BPD, and other relevant morbidities, in preterm infants through a network meta-analysis, generating both pairwise comparisons between all treatments and rankings of the treatments. Search methods: We searched the Cochrane Library for all systematic reviews of systemic corticosteroids for the prevention of BPD and searched for completed and ongoing studies in the following databases in January 2023: Cochrane Central Register of Controlled Trials, MEDLINE, Embase, and clinical trial databases. Selection criteria: We included randomized controlled trials (RCTs) in preterm infants (< 37 weeks' gestation) at risk for BPD that evaluated systemic corticosteroids (high-dose [≥ 4 mg/kg cumulative dose] dexamethasone, moderate-dose [≥ 2 to < 4 mg/kg] dexamethasone, low-dose [< 2 mg/kg] dexamethasone, or hydrocortisone) versus control or another systemic corticosteroid. Data collection and analysis: Our main information sources were the systematic reviews, with reference to the original manuscript only for data not included in these reviews. Teams of two paired review authors independently performed data extraction, with disagreements resolved by discussion. Data were entered into Review Manager 5 and exported to R software for network meta-analysis (NMA). NMA was performed using a frequentist model with random-effects. Two separate networks were constructed, one for early (< seven days) initiation of treatment and one for late (≥ seven days) treatment initiation, to reflect the different patient populations evaluated. We assessed the certainty of evidence derived from the NMA for our primary outcomes using principles of the GRADE framework modified for application to NMA. Main results: We included 59 studies, involving 6441 infants, in our analyses. Only six of the included studies provided direct comparisons between any of the treatment (dexamethasone or hydrocortisone) groups, forcing network comparisons between treatments to rely heavily on indirect evidence through

comparisons with placebo/no treatment groups. Thirty-one studies evaluated early corticosteroid treatment, 27 evaluated late corticosteroid treatment, and one study evaluated both early and late corticosteroid treatments. Early treatment (prior to seven days after birth): Benefits: NMA for early treatment showed only moderate-dose dexamethasone to decrease the risk of BPD at 36 weeks' postmenstrual age (PMA) compared with control (RR 0.56, 95% CI 0.39 to 0.80; moderate-certainty evidence), although the other dexamethasone dosing regimens may have similar effects compared with control (high-dose dexamethasone, RR 0.71, 95% CI 0.50 to 1.01; low-certainty evidence; low-dose dexamethasone, RR 0.83, 95% CI 0.67 to 1.03; low-certainty evidence). Other early treatment regimens may have little or no effect on the risk of death at 36 weeks' PMA. Only moderate-dose dexamethasone decreased the composite outcome of death or BPD at 36 weeks' PMA compared with control (RR 0.77, 95% CI 0.60 to 0.98; moderate-certainty evidence). Harms: Low-dose dexamethasone increased the risk for cerebral palsy (RR 1.92, 95% CI 1.12 to 3.28; moderate-certainty evidence) compared with control. Hydrocortisone may decrease the risk of major neurosensory disability versus low-dose dexamethasone (RR 0.65, 95% CI 0.41 to 1.01; low-certainty evidence). Late treatment (at seven days or later after birth): Benefits: NMA for late treatment showed high-dose dexamethasone to decrease the risk of BPD both versus hydrocortisone (RR 0.66, 95% CI 0.51 to 0.85; low-certainty evidence) and versus control (RR 0.72, CI 0.59 to 0.87; moderate-certainty evidence). The late treatment regimens evaluated may have little or no effect on the risk of death at 36 weeks' PMA. High-dose dexamethasone decreased risk for the composite outcome of death or BPD compared with all other treatments (control, RR 0.69, 95% CI 0.59 to 0.80, high-certainty evidence; hydrocortisone, RR 0.69, 95% CI 0.58 to 0.84, low-certainty evidence; low-dose dexamethasone, RR 0.73, 95% CI 0.60 to 0.88, low-certainty evidence; moderate-dose dexamethasone, RR 0.76, 95% CI 0.62 to 0.93, low-certainty evidence). Harms: No effect was observed for the outcomes of major neurosensory disability or cerebral palsy. The evidence for the primary outcomes was of overall low certainty, with notable deductions for imprecision and heterogeneity across the networks. Authors' conclusions: While early treatment with moderate-dose dexamethasone or late treatment with high-dose dexamethasone may lead to the best effects for survival without BPD, the certainty of the evidence is low. There is insufficient evidence to guide this therapy with regard to plausible adverse long-term outcomes. Further RCTs with direct comparisons between systemic corticosteroid treatments are needed to determine the optimal treatment approach, and these studies should be adequately powered to evaluate survival without major neurosensory disability.

PMID: 37650547

31. Periventricular Microglia Polarization and Morphological Changes Accompany NLRP3 Inflammasome-Mediated Neuroinflammation after Hypoxic-Ischemic White Matter Damage in Premature Rats

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White matter damage (WMD) is a primary cause of cerebral palsy and cognitive impairment in preterm infants, and no effective treatments are available. Microglia are a major component of the innate immune system. When activated, they form typical pro-inflammatory (M1) and anti-inflammatory (M2) phenotypes and regulate myelin development and synapse formation. Therefore, they may play a pivotal role in hypoxic-ischemic (HI) WMD. Herein, we investigated neural inflammation and long-term microglia phenotypic polarization in a neonatal rat model of hypoxia-ischemia-induced WMD and elucidated the underlying pathophysiological processes. We exposed 3-day-old (P3) Sprague-Dawley rats to hypoxia (8% oxygen) for 2.5 hr after unilateral common carotid artery ligation. The activation of NLRP3 inflammatory bodies, microglia M1/M2 polarization, myelination, and synaptic development in our model were monitored 7, 14, and 21 days after birth. In addition, the Morris water maze test was performed on postnatal Day 28. We confirmed myelination disturbance in the periventricular white matter, abnormal synaptic development, and behavioral changes in the periventricular area during the development of HI WMD. In addition, we found an association between the occurrence and development of HI WMD and activation of the NLRP3 inflammasome, microglial M1/M2 polarization, and the release of inflammatory factors. NLRP3 inhibition can play an anti-inflammatory role by inhibiting the differentiation of microglia into the M1 phenotype, thereby improving myelination and synapse formation. In conclusion, microglia are key mediators of the inflammatory response and exhibit continuous phenotypic polarization 7-21 days after HI-induced WMD. This finding can potentially lead to a new treatment regimen targeting the phenotypic polarization of microglia early after HI-induced brain injury.

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