

Cerebral palsy research news

Monday 30 May 2022

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

Professor Nadia Badawi AM CP Alliance Chair of Cerebral Palsy Research

Subscribe to CP Research News

Interventions and Management

1. An international survey mapping practice and barriers for upper-limb assessments in movement analysis Fraser Philp, Robert Freeman, Caroline Stewart

Gait Posture. 2022 May 20;96:93-101. doi: 10.1016/j.gaitpost.2022.05.018. Online ahead of print.

Background: Upper-limb movement analysis could improve our understanding of function, pathological mechanisms and inform rehabilitation and surgical decision-making. Despite the potential benefits, the use of clinical upper-limb motion analysis is not well established and it is not clear what the barriers to clinical motion analysis are. Research question: What is current practice for assessment of the upper-limb and what are the barriers currently limiting upper-limb motion analysis being routinely used in clinical practice? Methods: A web-based questionnaire was used to collect responses through international professional movement analysis society coordinators over an 18 month-period. Results: A total of 55 responses were received and 75% of laboratories performed some form of upper-limb assessment. In total 44% of laboratories performed upper-limb assessments for clinical purposes and only 33% did 3D-movement analysis. The most commonly seen patient groups were those with neurological injury e.g. cerebral palsy (adults and children) and normal controls for comparative purposes. Barriers to upper-limb motion analysis were the availability of standard reference tasks, protocols, software, funding and clinical need. Practice was variable with no universally identified approaches to upper-limb movement analysis. Differences in practice were also identified between laboratories accredited by the Clinical Movement Analysis Society of the UK and Ireland and other international professional societies and affiliate laboratories. Significance: These findings may be used to inform the development of practice standards and progress the use of clinical motion analysis in the upper-limb. This study provides a summary and describes current practice, potentially providing access to peer support and experience for laboratories with an identified clinical need looking to conduct upper-limb assessment. A national picture (UK and Ireland) for practice regarding upper-limb assessment in this sub-population is presented. We have laid out further work which is needed to establish standards of practice or consensus initiatives for enhancing clinical upper-limb motion analysis.

PMID: <u>35623317</u>

2. Pelvic fixation in surgical correction of neuromuscular scoliosis

Mazda Farshad, Sabrina Weber, José Miguel Spirig, Michael Betz, Samuel Haupt

N Am Spine Soc J. 2022 May 11;10:100123. doi: 10.1016/j.xnsj.2022.100123. eCollection 2022 Jun.

Background: Surgical correction of neuromuscular scoliosis can be associated with high complication rates, including such associated with pelvic fixation. Up to now it is debated whether and when to include the pelvis into the fusion construct. Therefore, we aimed to illuminate when pelvic fixation is beneficial in surgical correction of neuromuscular scoliosis. Methods: A prospective cohort of 49 patients (mean age 13 ± 3 y, 63% females, follow up 56 months, range 24-215) who

underwent correction of neuromuscular scoliosis including S1/the ileum (n = 18) or without (n = 31) pelvic fixation were included. The outcome was measured with analysis of radiological parameters, clinical improvement and complication/revision rates. Subgroup analysis was performed to find if non-ambulatory patients with gross motor function classification system (GMFCS) levels >III, with larger scoliotic curves (>60°) and moderate pelvic obliquities up to 35° benefit from pelvic fixation. Results: There was no significant difference in complications when comparing patients with (9 out of 18 patients, 50%) or without (9 out of 31 patients, 29%) fixation to the pelvis (p = .219). Wheelchair bound patients (GMFCS >III) with cobb angles greater than 60° and pelvic obliquity less than 35° (n = 20) revealed no differences in amount of clinical improvement of ambulation with (n = 9) or without (n = 11) pelvic fixation (p: n.s.). And even complication or revision rates where not different in those two groups. Conclusion: Pelvic fixation does not seem obligatory in wheelchair bound patients per definition. Even with pelvic obliquities up to 35° and large scoliotic curves >60°, avoiding pelvic fixation does not result in higher revision rate or worse clinical outcomes.

PMID: <u>35619626</u>

3. The influence of tone on proximal femoral and acetabular geometry in neuromuscular hip displacement: A comparison of cerebral palsy and spinal muscular atrophy

Armagan Can Ulusaloglu, Ali Asma, Kenneth J Rogers, Michael Wade Shrader, H Kerr Graham, Jason J Howard

J Child Orthop. 2022 Apr;16(2):121-127. doi: 10.1177/18632521221084184. Epub 2022 Apr 30.

Purpose: The aim of this article was to compare longitudinal changes in hip morphology in cerebral palsy (hypertonic) and spinal muscular atrophy (hypotonic) to examine the influence of muscle tone on development of hip displacement. Methods: Children with spinal muscular atrophy (Types I and II) and cerebral palsy (Gross Motor Function Classification System IV and V) with hip displacement (migration percentage >30%) were included. Head shaft angle, migration percentage, and acetabular index were measured at T1 (1-2.5 years), T2 (3-5 years), and T3 (6-8 years). Analysis of variance testing and linear regression were utilized. Results: Sixty patients (cerebral palsy, N = 41; spinal muscular atrophy, N = 19) were included. Hip displacement occurred earlier in spinal muscular atrophy (34 months) than cerebral palsy (49 months) (p = 0.003). Head shaft angle was high and did not change between T1, T2, and T3, but significant changes in migration percentage were found (cerebral palsy: 23%, 36%, 45% (p < 0.01) and spinal muscular atrophy: 37%, 57%, 61% (p = 0.02)). Migration percentage increased by age in cerebral palsy (r = 0.41, p < 0.001), but not in spinal muscular atrophy (r = 0.18, p = 0.09). Acetabular index increased with migration percentage (cerebral palsy: r = 0.41, p < 0.001; spinal muscular atrophy and cerebral palsy. Abnormal physeal alignment may be causally related to weakness of the hip abductor muscles rather than spasticity or muscle imbalance, resulting in coxa valga and secondary acetabular dysplasia. Level of evidence: III (case-control study).

PMID: <u>35620131</u>

4. Prevalence and treatment of hip displacement in children with cerebral palsy in Finland Ira Jeglinsky, Ann I Alriksson-Schmidt, Gunnar Hägglund, Matti Ahonen

J Child Orthop. 2022 Apr;16(2):128-135. doi: 10.1177/18632521221089439. Epub 2022 Apr 30.

Purpose: The aim was to study the prevalence of hip displacements, dislocations, and the hip surgeries performed in a Finnish cohort of children with cerebral palsy not followed up in a hip surveillance program and to compare these with previous studies performed in Northern European countries before and after the implementation of hip surveillance programs. Methods: A cross -sectional study. A cohort including 480 children with cerebral palsy, born during the period 2000-2018, not enrolled in a hip surveillance program. Migration percentages were recorded from hip radiographs, age at first hip surgery and type of surgery was extracted from medical records. In a separate analysis, the inclusion criteria were adapted to fit two studies analyzing hip dislocation and hip surgery in Sweden, Norway, and Scotland before and after the implementation of a hip surveillance program. Chi-square tests were used to assess differences in proportions between the groups. Results: In total, 286 children (60%) have had at least one hip radiograph. Of these, 10 (3.5%) developed hip dislocation, which is more than in children of countries with hip surveillance programs (Sweden 0.7%, Scotland 1.3%, p < 0.001). Initial surgery to prevent hip dislocation was performed at an older age (p < 0.001). Conclusion: Children with cerebral palsy in Finland not participating in a surveillance hip program were more likely to undergo hip surgery at an older age and to develop hip displacements and dislocations. The results support the effectiveness of surveillance programs to prevent hip dislocation in children with cerebral palsy. Level of evidence: III.

5. Anterior distal femoral hemiepiphysiodesis in children with cerebral palsy: Establishing surgical indications and techniques using the modified Delphi method and literature review

Benjamin J Shore, James McCarthy, M Wade Shrader, H Kerr Graham, Matthew Veerkamp, Erich Rutz, Henry Chambers, Jon R Davids, Unni Narayanan, Tom F Novacheck, Kristan Pierz, Thomas Dreher, Jason Rhodes, Jeffery Shilt, Tim Theologis, Anja Van Campenhout, Robert M Kay

J Child Orthop. 2022 Feb;16(1):65-74. doi: 10.1177/18632521221087529. Epub 2022 Apr 5.

Purpose: The purpose of this study was to develop consensus for the surgical indications of anterior distal femur hemiepiphysiodesis in children with cerebral palsy using expert surgeon opinion through a modified Delphi technique. Methods: The panel used a 5-level Likert-type scale to record agreement or disagreement with 27 statements regarding anterior distal femur hemiepiphysiodesis. Consensus was defined as at least 80% of responses being in the highest or lowest 2 of the Likert-type ratings. General agreement was defined as 60%-79% falling into the highest or lowest 2 ratings. Results: For anterior distal femur hemiepiphysiodesis, 27 statements were surveyed: consensus or general agreement among the panelists was achieved for 22 of 27 statements (22/27, 82%) and 5 statements had no agreement (5/27, 18%). There was general consensus that anterior distal femur hemiepiphysiodesis is indicated for ambulatory children with cerebral palsy, with at least 2 years growth remaining, and smaller (<30 degrees) knee flexion contractures and for minimally ambulatory children to aid in standing/transfers. Consensus was achieved regarding the importance of close radiographic follow-up after screw insertion to identify or prevent secondary deformity. There was general agreement that percutaneous screws are preferred over anterior plates due to the pain and irritation associated with plates. Finally, it was agreed that anterior distal femur hemiepiphysiodesis can be used to treat fixed knee flexion contractures in the setting of crouch gait, but other associated lever arm dysfunctions must be addressed by single-event multilevel surgery. Level of evidence: V.

PMID: 35615394

6. Finding consensus for hamstring surgery in ambulatory children with cerebral palsy using the Delphi method Robert M Kay, James McCarthy, Unni Narayanan, Jason Rhodes, Erich Rutz, Jeffery Shilt, Benjamin J Shore, Matthew Veerkamp, M Wade Shrader, Tim Theologis, Anja Van Campenhout, Kristan Pierz, Henry Chambers, Jon R Davids, Thomas Dreher, Tom F Novacheck, Kerr Graham

J Child Orthop. 2022 Feb;16(1):55-64. doi: 10.1177/18632521221080474. Epub 2022 Apr 5.

Purpose: There is marked variation in indications and techniques for hamstring surgery in children with cerebral palsy. There is particular uncertainty regarding the indications for hamstring transfer compared to traditional hamstring lengthening. The purpose of this study was for an international panel of experts to use the Delphi method to establish consensus indications for hamstring surgery in ambulatory children with cerebral palsy. Methods: The panel used a five-level Likert-type scale to record agreement or disagreement with statements regarding hamstring surgery, including surgical indications and techniques, post-operative care, and outcome measures. Consensus was defined as at least 80% of responses being in the highest or lowest two of the five Likert-type ratings. General agreement was defined as 60%-79% falling into the highest or lowest two ratings. There was no agreement if neither of these thresholds was reached. Results: The panel reached consensus or general agreement for 38 (84%) of 45 statements regarding hamstring surgery. The panel noted the importance of assessing pelvic tilt during gait when considering hamstring surgery, and also that lateral hamstring lengthening is rarely needed, particularly at the index surgery. They noted that repeat hamstring lengthening often has poor outcomes. The panel was divided regarding hamstring transfer surgery, with only half performing such surgery. Conclusion: The results of this study can help pediatric orthopedic surgeons optimize decision-making in their choice and practice of hamstring surgery for ambulatory children with cerebral palsy. This has the potential to reduce practice variation and significantly improve outcomes for ambulatory children with cerebral palsy. Level of evidence: level V.

PMID: 35615393

7. Assessment of foot alignment and function for ambulatory children with cerebral palsy: Results of a modified Delphi technique consensus study

Jon R Davids, Jeff Shilt, Robert Kay, Thomas Dreher, Benjamin J Shore, James McCarthy, Wade Shrader, Kerr Graham, Matthew Veerkamp, Unni Narayanan, Hank Chambers, Tom Novacheck, Jason Rhodes, Anja Van Campenhout, Kristan Pierz, Tim Theologis, Erich Rutz J Child Orthop. 2022 Apr;16(2):111-120. doi: 10.1177/18632521221084183. Epub 2022 Apr 30.

Purpose: The purpose of this study was to establish consensus for the assessment of foot alignment and function in ambulatory children with cerebral palsy, using expert surgeon's opinion through a modified Delphi technique. Methods: The panel used a five-level Likert-type scale to record agreement or disagreement with 33 statements regarding the assessment of foot alignment and function. Consensus was defined as at least 80% of responses being in the highest or lowest of two of the five Likert-type ratings. General agreement was defined as 60%-79% falling into the highest or lowest two ratings. There was no agreement if neither threshold was reached. Results: Consensus was achieved for 25 (76%) statements, general agreement for 4 (12%) statements, and lack of consensus for 4 (12%) of the statements. There was consensus that the functional anatomy of the foot is best understood by dividing the foot into three segments and two columns. Consensus was achieved concerning descriptors of foot segmental alignment for both static and dynamic assessment. There was consensus that radiographs of the foot should be weight-bearing. There was general agreement that foot deformity in children with cerebral palsy can be classified into three levels based on soft tissue imbalance and skeletal malalignment. Conclusion: The practices identified in this study can be used to establish best care guidelines, and the format used will be a template for future Delphi technique studies on clinical decision-making for the management of specific foot segmental malalignment patterns commonly seen in children with cerebral palsy. Level of evidence: V.

PMID: 35620124

8. Individual muscle force-energy rate is altered during crouch gait: A neuro-musculoskeletal evaluation Emiliano Pablo Ravera, Marcos José Crespo, Adam Rozumalski

J Biomech. 2022 May 17;139:111141. doi: 10.1016/j.jbiomech.2022.111141. Online ahead of print.

Children with pathological movement patterns like crouch gait present with excessive knee and hip flexion during stance phase due to multiple factors. A good treatment requires that the primary factor is reduced or eliminated to optimise the relationship between muscle energy expenditure and muscle force production during walking. In this way, neuro-musculoskeletal simulations are reliable tools to evaluate how individual muscles contribute to gait. However, previous studies have reported that changes in energy consumed per unit time have not correlated with crouch gait severity. In this study, EMG-informed musculoskeletal simulations combined with analytical approaches (which include altered muscle composition and morphology presented in children with CP) were used to evaluate individual muscle force, energy expenditure and their relationship in five typically developing children and eleven children with different degrees of crouch gait severity. In agreement with the literature, our results show an increase in Watts required per Newton of muscle force during walking in children with crouch gait when compared to unimpaired gait. This is true for all levels of crouch but does not correlate with severity. Hamstrings required more than three times the muscle energy per Newton of muscle force during crouch gait compared with unimpaired gait. Also, a different strategy in muscle force-energy rate of quadriceps and plantarflexors muscle groups was present in crouch gait. Finally, our results showed weakness in hamstrings and gastrocnemius with an increment in their muscle energy expenditures during moderate and severe crouch gait. This could suggest that well controlled strength training (i.e. personalised and designed to improve both the muscle strength and functional mobility) focused in these muscle groups could improve knee extension of these children by providing a more efficient plantarflexor-knee extension couple during stance phase (action of the ankle plantarflexor muscles to control the progress of the tibia over the foot and the knee kinetics) and more control of the distal limb at initial contact. However, strength training of hamstrings only could be better for children with mild crouch gait.

PMID: 35609492

9. Neurodevelopmental Therapy for Cerebral Palsy: A Meta-analysis

Anna Te Velde, Catherine Morgan, Megan Finch-Edmondson, Lynda McNamara, Maria McNamara, Madison Claire Badawy Paton, Emma Stanton, Annabel Webb, Nadia Badawi, Iona Novak

Pediatrics. 2022 May 24;e2021055061. doi: 10.1542/peds.2021-055061. Online ahead of print.

Background and objective: Bobath therapy, or neurodevelopmental therapy (NDT) is widely practiced despite evidence other interventions are more effective in cerebral palsy (CP). The objective is to determine the efficacy of NDT in children and infants with CP or high risk of CP. Methods: Cumulative Index to Nursing and Allied Health Literature, Cochrane Library, Embase, and Medline were searched through March 2021. Randomized controlled trials comparing NDT with any or no intervention were included. Meta-analysis was conducted with standardized mean differences calculated. Quality was assessed by using Cochrane Risk of Bias tool-2 and certainty by using Grading of Recommendations Assessment, Development, and Evaluation. Results: Of 667 records screened, 34 studies (in 35 publications, 1332 participants) met inclusion. Four meta-

analyses were conducted assessing motor function. We found no effect between NDT and control (pooled effect size 0.13 [-0.20 to 0.46]), a moderate effect favoring activity-based approaches (0.76 [0.12 to 1.40]) and body function and structures (0.77 [0.19 to 1.35]) over NDT and no effect between higher- and lower-dose NDT (0.32 [-0.11 to 0.75]). A strong recommendation against the use of NDT at any dose was made. Studies were not all Consolidated Standards of Reporting Trials-compliant. NDT versus activity-based comparator had considerable heterogeneity (I2 = 80%) reflecting varied measures. Conclusions: We found that activity-based and body structure and function interventions are more effective than NDT for improving motor function, NDT is no more effective than control, and higher-dose NDT is not more effective than lower-dose. Deimplementation of NDT in CP is required.

PMID: 35607928

10. Comparison of the Physical Response During Official Matches and Small-Sided Games in International Cerebral Palsy Footballers: Implications for Evidence-Based Classification Javier Yanci, Daniel Castillo, Aitor Iturricastillo, Matías Henríquez, Alba Roldan, Raúl Reina

Adapt Phys Activ Q. 2022 May 23;1-15. doi: 10.1123/apaq.2021-0206. Online ahead of print.

This study aimed to analyze whether there are differences and associations in the physical responses in international-level cerebral palsy footballers between official matches and 2v2 small-sided games (2v2-SSG). One hundred seventy international cerebral palsy footballers participated in this study during three international championships. The physical responses of mean and maximum velocities, total distance, distance covered at different intensities, short-term actions, and player load were collected during 2v2-SSG and the real competition. The mean velocity, total distance, jogging, medium- and high-intensity distances, the number of moderate/high accelerations, decelerations, and player load were relatively higher in the 2v2-SSG than in the official matches. Even though the 2v2-SSG could become an appropriate drill to include during the classification process, due to the differences between a 2v2-SSG and the official competition, it is necessary to deepen the scientific knowledge for developing observation methods during real competition to strengthen the relationships between eligible impairments and activity limitation.

PMID: 35606092

11. Epidemiology and risk factors for sleep disturbances in children and youth with cerebral palsy: An ICF-based approach

Aletheia Zh Chia, Yi Hua Tan, Tong Hong Yeo, Oon Hoe Teoh, Zhi Min Ng

Sleep Med. 2022 May 13;96:93-98. doi: 10.1016/j.sleep.2022.04.021. Online ahead of print.

OBJECTIVES AND BACKGROUND: Children with cerebral palsy are at risk for sleep disorders, and there is a complex relationship between sleep and physical, environmental and functional factors in such children. The WHO International Classification of Functioning, Disability and Health model serves as a universal framework for describing and organizing functioning and disability. This study aimed to describe sleep disturbances in Singaporean children and youth with cerebral palsy, and develop a holistic framework for evaluating risk factors and potential management strategies for poor sleep. Methods: A cross-sectional analysis was conducted on 151 children and youth in a nationwide registry for cerebral palsy. The WHO International Classification of Functioning, Disability and Health for Cerebral Palsy Questionnaire was used to identify sleep disturbances. Risk factors analyzed were age, gender, ethnic background, financial assistance, the dominant motor feature of cerebral palsy, functional status, and comorbidities such as active epilepsy, hearing and visual impairments, generalized pain, muscle tone and involuntary contractions. Results: 46% had difficulty with sleep, with similar proportions having difficulty with amount, onset, maintenance and quality of sleep. On multivariate regression analysis, higher functional gross motor impairment as indicated by a GMFCS level of V (adjusted OR 4.24; 95% CI 1.09-19.0) and difficulty with involuntary contractions (aOR 2.80; 1.20-6.71) were significant factors for sleep difficulties. Conclusion: An ICF-based framework was useful in identifying possible contributory factors and strategies for managing poor sleep. Further studies with objective sleep measures would allow for better characterization of sleep disturbances in children and youth with cerebral palsy, and guide management.

PMID: <u>35617716</u>

12. A novel investigation of eye-gaze as an access method for children with dyskinetic cerebral palsy Kristine Stadskleiv

Dev Med Child Neurol. 2022 May 21. doi: 10.1111/dmcn.15269. Online ahead of print.

PMID: 35598090

13. Effect of standing frames used in real life on bone remodeling in non-walking children with cerebral palsy V Barbier, V Goëb, C Klein, S Fritot, R Mentaverri, J Sobhy Danial, P Fardellone, L Le Monnier

Osteoporos Int. 2022 May 26. doi: 10.1007/s00198-022-06436-5. Online ahead of print.

Children with severe cerebral palsy are prone to low bone mineral density. No clear recommendation exists for an optimal use of standing frame to enhance bone health in this context. Used in real life, this study suggests for the first time that standing practice improved bone mineralization by limiting bone resorption. Introduction: To compare the bone health of children with severe cerebral palsy who use a static standing frame in real life to that of children who do not. Methods: A total of 24 children with severe cerebral palsy GMFCS IV & V were included in the study and were divided into two groups: 13 were using a passive standing frame and 11 were not. We performed a single center retrospective cross-sectional study comparing the two groups using dual X-ray absorptiometry data and tests on biological samples, including bone remodeling factors. Results: Total body (less head) bone mineral content was significantly higher in children who used a standing frame for an average of 30 min/ day. This was confirmed in the lumbar spine. Although the total body bone mineral density (less head and proximal femur) densitometric data were not significantly higher, a positive trend favored the use of a standing frame in the children. Bone resorptive factors (CTX) were higher in the non-standing-frame group, whereas there was no difference among osteoformation factors. No difference in fracture history was found. Conclusions: We show that non-ambulant children with cerebral palsy who use a static standing frame in real life have better bone health, with lower bone resorption, than children who do not. Further studies are needed to determine how standing practice could impact bone mineralization over time in real life and to explore more bone remodeling factors.

PMID: 35614237

14. In the Driver's Seat: A Randomized, Crossover Clinical Trial Protocol Comparing Home and Community Use of the Permobil Explorer Mini and a Modified Ride-On Car by Children With Cerebral Palsy Heather A Feldner, Samuel W Logan, Lisa K Kenyon

Phys Ther. 2022 May 23;pzac062. doi: 10.1093/ptj/pzac062. Online ahead of print.

Objective: The aims of this study are twofold: (1) to evaluate a powered mobility intervention to promote developmental, activity, and participation outcomes of young children aged 12 to 36 months who have cerebral palsy (CP); and (2) to compare the use patterns (frequency, duration, environment) of 2 different powered mobility options. Methods: This study is a multisite, mixed-methods, doubly counterbalanced, randomized, crossover clinical trial, where intervention A is the Permobil Explorer Mini and intervention B is a modified ride-on toy car. The study will take place in rural and urban home and community settings surrounding 3 sites (Washington, Oregon, and Michigan). There will be 24 child-caregiver dyads in the study (8 dyads per site). Primary outcome measures include the Bayley Scale of Infant and Toddler Development, the Youth and Children's Participation and Environment Measure, the Assessment for Learning Power mobility use, automated device use tracking logs, caregiver semistructured interviews, and the Acceptability, Feasibility, and Intervention Appropriateness Measures. Secondary measures include the Child Engagement in Daily Life and caregiver diaries. Impact: The use of powered mobility devices for young children with cerebral palsy has gained traction, with evidence that the use of powered mobility at young ages complements (rather than detracts from) other interventions focused on more traditional mobility skills such as crawling and walking. However, research is limited, and often comprised of low-level evidence. Given the clearance of the first powered mobility device for infants, the Permobil Explorer Mini, and the recent popularity of modified ride-on toy cars as 1 alternative for powered mobility for young children with disabilities, this study will contribute to rigorous examination of the developmental outcomes, use patterns, and caregiver perceptions of these novel devices.

PMID: 35607923

15. Protocol for the Birth Asphyxia in African Newborns (Baby BRAiN) Study: a Neonatal Encephalopathy Feasibility Cohort Study

Carol Nanyunja, Samantha Sadoo, Ivan Mambule, Sean R Mathieson, Moffat Nyirenda, Emily L Webb, J Mugalu, Nicola J Robertson, A Nabawanuka, Guillaume Gilbert, J Bwambale, Kathryn Martinello, Alan Bainbridge, Samson Lubowa, Latha Srinivasan, H Ssebombo, Cathy Morgan, Cornelia Hagmann, Frances M Cowan, Kirsty Le Doare, Pia Wintermark, Michael Kawooya, Geraldine B Boylan, Annettee Nakimuli, Cally J Tann

Gates Open Res. 2022 Mar 3;6:10. doi: 10.12688/gatesopenres.13557.1. eCollection 2022.

BACKGROUND: Neonatal encephalopathy (NE) is a leading cause of child mortality worldwide and contributes substantially to stillbirths and long-term disability. Ninety-nine percent of deaths from NE occur in low-and-middle-income countries (LMICs). Whilst therapeutic hypothermia significantly improves outcomes in high-income countries, its safety and effectiveness in diverse LMIC contexts remains debated. Important differences in the aetiology, nature and timing of neonatal brain injury likely influence the effectiveness of postnatal interventions, including therapeutic hypothermia. METHODS: This is a prospective pilot feasibility cohort study of neonates with NE conducted at Kawempe National Referral Hospital, Kampala, Uganda. Neurological investigations include continuous video electroencephalography (EEG) (days 1-4), serial cranial ultrasound imaging, and neonatal brain Magnetic Resonance Imaging and Spectroscopy (MRI/MRS) (day 10-14). Neurodevelopmental follow-up will be continued to 18-24 months of age including Prechtl's Assessment of General Movements, Bayley Scales of Infant Development, and a formal scored neurological examination. The primary outcome will be death and moderate-severe neurodevelopmental impairment at 18-24 months. Findings will be used to inform explorative science and larger trials, aiming to develop urgently needed neuroprotective and neurorestorative interventions for NE applicable for use in diverse settings. DISCUSSION: The primary aims of the study are to assess the feasibility of establishing a facility-based cohort of children with NE in Uganda, to enhance our understanding of NE in a low-resource sub-Saharan African setting and provide infrastructure to conduct high-quality research on neuroprotective/ neurorestorative strategies to reduce death and disability from NE. Specific objectives are to establish a NE cohort, in order to 1) investigate the clinical course, aetiology, nature and timing of perinatal brain injury; 2) describe electrographic activity and quantify seizure burden and the relationship with adverse outcomes, and; 3) develop capacity for neonatal brain MRI/S and examine associations with early neurodevelopmental outcomes.

PMID: 35614965

16. The Risk Factors of Cerebral Palsy among the Children Attending a Children's Hospital Tulashi Adhikari Mishra, Sarala Shrestha, Bina Prajapati Manandhar, Pratima Sharma

J Nepal Health Res Counc. 2022 Mar 13;19(4):778-783. doi: 10.33314/jnhrc.v19i04.3808.

Background: Cerebral Palsy is a disorder of movement and posture caused by nonprogressive abnormal brain function. It is a lifelong condition and one of the most common causes of physical disability in children. The objective of this study was to find out the risk factors associated with cerebral palsy among children. Methods: A case control study was carried out among 330 children where cases and controls were taken in the ratio of 1:2. Cases included children diagnosed with cerebral palsy and attending neurological out-patient department of a Children's Hospital in Kathmandu, Nepal and control included children not having cerebral palsy and attending medical out-patient department of the same hospital for other medical problems. The data were collected from November 29, 2017 to May 20, 2018 by using a pretested interview schedule. The findings were analyzed using frequency, percentage, mean, standard deviation and chi square test and odds ratio. Results: Findings revealed that about one-fourth (24.5%) cases were diagnosed to have CP within one year of age. In terms of sex majority (63.6%) of the cases were male and majority were the first born children. Findings also revealed that infection during pregnancy (OR:2.9, CI: 1.1-7.5), family history of cerebral palsy (OR:5.6, CI: 1.4-21.8), instrumental delivery (OR: 10.9, CI:2.3-50.6), not crying immediately after birth (OR: 17.3, CI: 8.6-34.6), were significantly associated with cerebral palsy. Conclusions: Most of the identified risk factors are preventable and controllable through proper antenatal and skilled intranatal care. Thus, every pregnant woman should receive proper care during pregnancy as well as during delivery for the prevention of the identified risk factors.

PMID: 35615837

17. Orthopedic surgical procedures in 3,305 children and young adults with cerebral palsy: a register-based cohort study

Anna Telléus, Nikolaos Kiapekos, Johan Von Heideken, Philippe Wagner, Eva Broström, Gunnar Hägglund, Per Åstrand

Acta Orthop. 2022 May 23;93:472-477. doi: 10.2340/17453674.2022.2583.

Background and purpose: Few reports have described the panorama of orthopedic surgeries that children with cerebral palsy (CP) undergo. We analyzed the risk of a first surgery, and describe the frequency of orthopedic surgeries in terms of age, sex, anatomical location, and Gross Motor Function Classification System (GMFCS) level in children and young adults with CP. Patients and methods: This was a register-based cohort study of 3,305 individuals followed until 2-25 years of age. We used data from 2 national Swedish registers: the CPUP CP surveillance program and the Swedish National Patient Register. Kaplan-Meier survival curves were calculated to describe the risk of undergoing a first orthopedic surgery, related to age. Results: We included data for 3,311 orthopedic operations in 1,717 surgical sessions. The percentage of children operated on before age 15 years increased from 22% (95% CI 19-26) for GMFCS level I to 70% (CI 64-75) for level V. Ankle and foot surgery was predominant as first surgery for GMFCS I-II, and hip and femur surgery for GMFCS IV-V. Spinal surgery occurred almost exclusively for GMFCS IV-V. Descriptive data showed repeated surgical sessions to be frequent for higher GMFCS levels. Interpretation: The risk of having a first orthopedic surgical treatment increased with increasing GMFCS level and was initiated at younger age in children with higher GMFCS level.

PMID: 35611478

18. RNAseq of amniotic fluid cell-free RNA: a discovery phase study of the pathophysiology of congenital cytomegalovirus infection

Lisa Hui, Luc DE Catte, Sally Beard, Jovana Maksimovic, Neeta L Vora, Alicia Oshlack, Susan P Walker, Natalie J Hannan

Am J Obstet Gynecol. 2022 May 21;S0002-9378(22)00386-6. doi: 10.1016/j.ajog.2022.05.035. Online ahead of print.

Background: Congenital cytomegalovirus (cCMV) is the most common perinatal infection and a significant cause of sensorineural hearing loss, cerebral palsy and neurodevelopmental disability. There is a paucity of human gene expression studies examining the pathophysiology of CMV infection. Objectives: The aim of this study was to perform a whole transcriptomic assessment of amniotic fluid from pregnancies with live fetuses to identify differentially-expressed genes and enriched Gene Ontology categories associated with cCMV infection. Study design: Amniotic fluid supernatant was prospectively collected from pregnant women undergoing amniocentesis for suspected cCMV due to first trimester maternal primary infection or ultrasound features suggestive of fetal infection. Women who had received therapy to prevent fetal infection were excluded. cCMV was diagnosed via viral PCR of amniotic fluid; CMV-infected fetuses were paired with noninfected controls, matched for gestational age and fetal sex. Paired-end RNA sequencing was performed on amniotic fluid cell-free RNA with the Novaseq6000 at a depth of 30 million reads/sample. Following quality control and filtering, reads were mapped to the human genome and counts summarised across genes. Differentially expressed genes were identified using two approaches: voomWithQualityWeights in conjunction with limma and RUVSeq with edgeR. Genes with a false discovery rate (FDR) < 0.05 were considered statistically significant. Differential exon usage was analysed using DEXSeq. Functional analysis was performed using Gene Set Enrichment Analysis and Ingenuity Pathway Analysis. Manual curation of differentially regulated genes was also performed. Results: Amniotic fluid samples were collected from 50 women; 16 (32%) had cCMV confirmed by PCR. After excluding 3 samples without matched controls, 13 CMV-infected samples collected at 18-23 weeks and 13 CMV-negative gestation matched controls were submitted for RNA sequencing and analysis (total n=26). Ten of the 13 pregnancies with CMV-infected fetuses had amniocentesis due to serological evidence of maternal primary infection with normal fetal ultrasound, and three had amniocentesis due to ultrasound abnormality suggestive of CMV infection. Four CMV-infected pregnancies ended in termination (n=3) or fetal death (n=1), and 9 resulted in live births. Pregnancy outcomes were available on 11 of the 13 CMV-negative controls; all resulted in live births of clinically-well infants. Differential gene expression analysis revealed 309 up-regulated and 32 down-regulated genes in the CMV-infected group compared with the CMV-negative group. Gene set enrichment analysis showed significant enrichment of multiple Gene Ontology categories involving the innate immune response to viral infection and interferon signalling. Of the 32 significantly down-regulated genes, 8 were known to be involved in neurodevelopment and preferentially expressed by the brain. Six specific cellular restriction factors involved in host defence to CMV infection were upregulated in the CMV-infected group. Ingenuity Pathway Analysis predicted activation of pathways involved in 'progressive neurological disease', and 'inflammatory neurological disease'. Conclusions: In this next generation sequencing study, we reveal new insights into the pathophysiology of cCMV infection. These data on the upregulation of the intraamniotic innate immune response to CMV infection and the dysregulation of neurodevelopmental genes may inform future approaches to developing prognostic markers and assessing fetal responses to in utero therapy.

PMID: 35609640

19. Where words are powerless to express: Use of music in paediatric neurology

Anna K Szewczyk, Krystyna Mitosek-Szewczyk, Ewa Dworzańska

Review J Pediatr Rehabil Med. 2022 May 16. doi: 10.3233/PRM-200802. Online ahead of print.

Music is an art form that strongly affects people and can elicit many different emotions at the same time, including happiness, anxiety, sadness, and even ecstasy. What is it about music that causes such a strong reaction from each of us? Music engages many senses, which in turn can produce a multiplicity of responses and help create more extensive neuronal connections, as well as influence behaviour through structural and functional changes in the brain. Music-based interventions as a therapeutic tool in rehabilitation are becoming more common. It is said that the impact of music on the human body is positive. However, what impact does music have on the young nervous system, especially the affected one? This review presents the advantages and disadvantages of the use of music in paediatric neurology to treat dyslexia, cerebral palsy, and stroke, among others. Potential negative impacts such as musicogenic epilepsy and hallucinations will be discussed.

PMID: 35599509

20. [Modern application possibilities hopanthenic acid (Pantocalcin) in treatment diseases of the nervous system in children] [Article in Russian]

S A Nemkova

Zh Nevrol Psikhiatr Im S S Korsakova. 2022;122(5):69-77. doi: 10.17116/jnevro202212205169.

The review analyzes the current possibilities of using hopanthenic acid (Pantocalcin) in the treatment of diseases of the nervous system in children (perinatal CNS lesions, developmental delays, cerebral palsy, ADHD, tics, enuresis, cognitive and neurotic disorders), taking into account modern standards and clinical recommendations. The results of numerous studies demonstrate that Pantocalcin is a highly effective and safe drug in the treatment of diseases of the nervous system in children with complex neurometabolic, neuroprotective, neurotrophic properties.

PMID: 35611903

21. Co-development of the ENVISAGE-Families programme for parents of children with disabilities: Reflections on a parent-researcher partnership

Kinga Pozniak, Andrea Cross, Rose Babic, Vicki Cavalieros, Rachel Martens, Peter Rosenbaum, Christine Imms, Monika Novak-Pavlic, Abha Balram, Debra Hughes, Bridget O'Connor, Laura Miller

Aust Occup Ther J. 2022 May 22. doi: 10.1111/1440-1630.12811. Online ahead of print.

Introduction: In childhood disability research, the involvement of families is essential for optimal outcomes for all participants. ENVISAGE (ENabling VISions And Growing Expectations)-Families is a programme comprising five online workshops for parents of children with neurodevelopmental disorders. The workshops aim to introduce parents to strengths-based perspectives on health and development. The research is based on an integrated Knowledge Translation (iKT) approach, in which knowledge users are involved throughout the research process. This article is co-authored by the ENVISAGE health service researchers (N = 9) and parent partners (N = 3) to describe the process through which we co-developed and implemented the workshops. Methods: Collaborative auto-ethnography methods, based on a combination of interviews, qualitative surveys, and discussions held to complete the Guidance for Reporting Involvement of Patients and Public-2 tool, were used to describe the co-design process, the benefits gained, and lessons learned. Findings: Parents (n = 118) were involved in developing and implementing the ENVISAGE workshops across the different phases, as partners, collaborators, or participants. Three parents were involved as investigators throughout. We identify seven key ingredients that we believe are necessary for a successful parent-researcher working relationship: (i) consistent communication; (ii) clear roles and expectations; (iii) onboarding and feedback; (iv) flexibility; (v) understanding; (vi) self-reflection; and (vii) funding. Conclusion: Patient and family engagement in research is a rapidly growing area of scholarship with new knowledge and tools added every year. As our team embarks on new collaborative studies, we incorporate this knowledge as well as the practical experience we gain from working together.

PMID: <u>35599379</u>