

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

Professor Nadia Badawi AM

Macquarie Group Foundation Chair of Cerebral Palsy

[Subscribe to CP Research News](#)

Interventions and Management

1. How Do Complications Within the First 30 Days After Spinal Deformity Surgery in Children With Cerebral Palsy Affect Length of Stay?

Annabel Dekker, Haemish A Crawford, N Susan Stott

Clin Orthop Relat Res. 2020 May 6. doi: 10.1097/CORR.0000000000001290. Online ahead of print.

Background: Surgery for spinal deformity in patients with cerebral palsy is reported to have high perioperative complication rates. However, minor complications are not generally reported and the influence of the varied severity of complications on length of stay is not known. Understanding the risk factors for both minor and major perioperative complications and their effect on length of stay is important information for clinicians who seek to improve care for this group of children. **Questions/purposes:** (1) What is the prevalence of postoperative complications in the first 30 days after surgery for spinal deformity in a New Zealand national cohort of children with cerebral palsy using the Clavien-Dindo classification? (2) What are the patient and operative predictive risk factors for minor and major perioperative complications? (3) What is the effect of year of operation on risk of minor and major perioperative complications? (4) What is the effect of perioperative complications on length of stay? **Methods:** We conducted a retrospective cohort study, identifying all children in New Zealand with a confirmed diagnosis of cerebral palsy who had surgery for a spinal deformity from January 1997 to January 2018. Two hundred-three patients with cerebral palsy (102 boys) were surgically treated for a spinal deformity, at a mean age of 14 ± 3 years, at one of three centers in New Zealand. Six children had Gross Motor Function Classification System Level II or III, 66 had Gross Motor Function Classification System Level IV, and 131 had Gross Motor Function Classification System Level V. Thirty-day perioperative complications were extracted from the patients' health records and classified according to the Clavien-Dindo system. Univariate and multivariate analyses were performed to identify patient and operative risk factors for complications, and the effect on length of stay. **Results:** In all, 85% of patients experienced at least one perioperative complication. There were 300 Clavien-Dindo Grade I complications in 141 patients, 156 Clavien-Dindo Grade II complications in 102 patients, 25 Clavien-Dindo Grade III complications in 22 patients, 29 Clavien-Dindo Grade IV complications in 28 patients, and one Clavien-Dindo Grade V complication (death; 0.5%). Univariate analysis showed that multiple independent factors, Gross Motor Function Classification System Level V ability (odds ratio 2.13 [95% confidence interval 1.15 to 3.95]; $p = 0.02$), seizure disorder (OR 2.27 [95% CI 1.20 to 4.32]; $p < 0.01$), preoperative Cobb angle of greater than 70° (OR 2.40 [95% CI 1.20 to 4.78]; $p < 0.01$), and anterior approach to surgery (OR 3.29 [95% CI 1.21 to 8.90]; $p = 0.02$), were associated with Grade I complications but, of these factors, only the presence of a seizure disorder (OR 2.27 [95% CI 1.20 to 4.32]; $p < 0.01$) was associated with Grade I complications on multivariate analysis. Previous recurrent respiratory infections predicted an increased risk of Clavien-Dindo Grade II complications (OR 3.6 [95% CI 1.81 to 7.0]; $p = 0.03$). The presence of a feeding gastrostomy was associated with an increased risk of Clavien-Dindo Grade IV complications (OR 2.6 [95% CI 1.19 to 5.87]; $p = 0.02$). The year of operation did not influence the frequency of any grade of complication, but the presence of any complication led to an increased length of stay. **Conclusion:** Overall, 85% of patients with cerebral palsy had at least one complication after spinal deformity surgery and 25% had major complications (Grades III, IV, and V), with proportionate increases in the postoperative length of stay. Patient-specific factors aid in the identification of complication risk. Level of evidence: Level II, prognostic study.

PMID: [32398555](https://pubmed.ncbi.nlm.nih.gov/32398555/)

2. Tibial Rotation Outcomes Following Hamstring Lengthening as Part of Single Event Multilevel Surgery in Children With Cerebral Palsy

A Marron, R O'Sullivan, E Kelly, D Kiernan

Gait Posture. 2020 May 1;79:126-132. doi: 10.1016/j.gaitpost.2020.04.026. Online ahead of print.

Background: Hamstring lengthening remains the most common surgical procedure in the treatment of crouch gait for children with cerebral palsy (CP). While sagittal plane knee kinematics have been shown to improve post-surgery, the effects on transverse plane kinematics have not been reported. Given the differing actions of the medial and lateral hamstring muscles there is potential for change in tibial rotation post hamstring lengthening. Research question: What is the effect of medial only versus combined medial and lateral hamstring lengthening on tibial rotation during gait in children with CP? Methods: A retrospective analysis of children with a diagnosis of CP who underwent a hamstring lengthening procedure. These children were divided into 2 groups: G1 (n = 18) had isolated medial hamstring lengthening while G2 (n = 30) had combined medial and lateral hamstring lengthening. A matched non-surgical control group (n = 15) was also included. Kinematic data were analysed pre and post-operatively. Pre-operative to post-operative outcomes for G1 and G2, a comparison at baseline for both groups and the difference in outcomes between the groups were analysed. Baseline to follow-up outcomes for the control group were also analysed. Results: External tibial rotation increased significantly within groups (G1: -10° , $p < 0.01$; G2: -11° , $p < 0.001$, control: -7.7 , $p < 0.01$), with no significant difference in the change between the intervention groups. Foot progression angles became more external in both intervention groups (G1: -15° , $p < 0.001$; G2: -15° , $p < 0.0001$) and did not change in the control group. Significance: Results demonstrated similar increases in external tibial rotation, regardless of whether an isolated medial or combined medial and lateral surgery was performed. The control group demonstrated a similar change in external tibial rotation suggesting that hamstring lengthening surgery does not contribute to increased external tibial rotation in children with CP compared to what would be expected due to natural progression.

PMID: [32408035](#)

3. A Prospective Assessment of the Progression of Flexed-Knee Gait Over Repeated Gait Analyses in the Absence of Surgical Intervention in Bilateral Cerebral Palsy

Rory O'Sullivan, Helen P French, Frances Horgan

Gait Posture. 2020 May 1;79:133-138. doi: 10.1016/j.gaitpost.2020.04.021. Online ahead of print.

Background: Flexed-knee gait is a common pattern associated with cerebral palsy (CP). It leads to excessive forces on the knee and is thought to contribute to pain and deformity. While studies have shown improvements in mid-stance knee flexion following surgery there remains a lack of prospective data on the progression of flexed-knee gait in the absence of surgery. Research question: Does knee flexion progress over repeated assessments in the absence of surgery in a prospectively assessed cohort with CP? Methods: Inclusion criteria were a diagnosis of bilateral CP, knee flexion at mid-stance $>19^\circ$ and no surgery within one year of the first gait analysis. Gait analysis was carried out at six-month intervals (minimum of three and maximum of six assessments). The progression of knee flexion over repeated analyses was assessed. The association between changes in knee flexion between assessments and gender, age, GMFCS level, change in ankle dorsiflexion, change in height and change in weight was examined. Results: Forty-eight participants met the initial inclusion criteria and 32 (GMFCS I = 11, II = 17, III = 4) completed the minimum three assessments. Of the 32 included participants, 21 participants (66%) demonstrated decreased knee flexion at mid-stance (mean decrease $6.6^\circ \pm 3.4^\circ$; range 2.0° - 13.0°) and 11 participants (34%) demonstrated increased knee flexion at mid-stance (mean increase $10.4^\circ \pm 7.1^\circ$; range 2.0° - 20.0°) at one-year follow-up. Eighteen (56%) then demonstrated an overall decrease (mean $7.4^\circ \pm 5.1^\circ$) in knee flexion between the first and last assessment with last follow-up at 1-2 years (n = 3), 2-3 years (n = 3) and 3-4 years (n = 12). The majority of participants (78%) demonstrated episodes of both increasing and decreasing Knee flexion between individual assessments and further analysis found that age was associated with this inter-assessment variability in knee flexion. Significance: Flexed-knee gait is not always progressive in bilateral CP and demonstrated variability associated with age.

PMID: [32408036](#)

4. An Unsupervised Data-Driven Model to Classify Gait Patterns in Children With Cerebral Palsy

Julie Choisine, Nicolas Fourier, Geoffrey Handsfield, Nada Signal, Denise Taylor, Nichola Wilson, Susan Stott, Thor F Besier

J Clin Med. 2020 May 12;9(5):E1432. doi: 10.3390/jcm9051432.

Ankle and foot orthoses are commonly prescribed to children with cerebral palsy (CP). It is unclear whether 3D gait analysis (3DGA) provides sufficient and reliable information for clinicians to be consistent when prescribing orthoses. Data-driven modeling can probe such questions by revealing non-intuitive relationships between variables such as 3DGA parameters and gait outcomes of orthoses use. The purpose of this study was to (1) develop a data-driven model to classify children with CP according to their gait biomechanics and (2) identify relationships between orthotics types and gait patterns. 3DGA data were acquired from walking trials of 25 typically developed children and 98 children with CP with additional prescribed orthoses. An unsupervised self-organizing map followed by k-means clustering was developed to group different gait patterns based on children's 3DGA. Model inputs were gait variable scores (GVs) extracted from the gait profile score, measuring root mean square differences from TD children's gait cycle. The model identified five pathological gait patterns with statistical differences in GV scores. Only 43% of children improved their gait pattern when wearing an orthosis. Orthotics prescriptions were variable even in children with similar gait patterns. This study suggests that quantitative data-driven approaches may provide more clarity and specificity to support orthotics prescription.

PMID: [32408489](#)

5. Analysis of Orthopedic Surgical Procedures in Children With Cerebral Palsy

Ignacio Rehbein, Viviana Teske, Ignacio Pagano, Alejandro Cúneo, María Elena Pérez, Johan von Heideken

World J Orthop. 2020 Apr 18;11(4):222-231. doi: 10.5312/wjo.v11.i4.222.

Background: Orthopedic surgery in children with cerebral palsy (CP) aims to improve function and prevent deformities. Each child's condition in CP is unique and many co-variables influence surgical decision-making including a patient's age and their functional level. Little is known about the frequency of different types of orthopedic surgery in children with CP who have varied functional levels, particularly in countries from Latin America. Aim: To assess the type of orthopedic surgical procedures in relation to age and gross motor function in children with CP. Methods: This retrospective study included all children with CP (n = 245) treated with elective orthopedic surgery at a Uruguayan university hospital between October 2010 and May 2016 identified from a surgical database. Eighteen children (7%) were lost to follow-up due to missing medical charts. Demographics, gross motor function classification (GMFCS), and orthopedic surgeries were obtained from the medical records of 227 children. Chi-squared tests and analysis of variance were used to assess the frequency of surgery, accounting for GMFCS levels. Mean age for soft tissue vs bone surgery was compared with the independent samples t-test. Results: A total of 711 surgical procedures were performed between 1998 and 2016. On average, children had 3.1 surgical procedures and the mean age at first surgery was 8.0 years. There were no significant differences in age at first surgery among GMFCS levels (P = 0.47). The most common procedures were lower leg soft tissue surgery (n = 189, 27%), hip tenotomy (n = 135, 19%), and hamstring tenotomy (n = 104, 14%). For children with GMFCS level I, the mean number of surgeries per child [1.8 (range 1-9)] differed significantly at P < 0.05 in children with GMFCS levels II [3.2 (1-12)], III [3.2 (1-8)], IV [3.3 (1-13)], and V [3.6 (1-11)]. Within II, III, IV, and V, there was no significant difference in mean number of surgeries per child when comparing across the groups. The proportion of soft tissue surgery vs bone surgery was higher in GMFCS levels I-III (80%-85%) compared to levels IV (68%) and V (55%) (P < 0.05). Conclusion: The frequency of surgical procedures per child did not increase with higher GMFCS level after level I. However, the proportion of bone surgery was higher in GMFCS levels IV-V compared to I-III.

PMID: [32405471](#)

6. Effectiveness of Therapeutic Footwear for Children: A Systematic Review

Matthew Hill, Aoife Healy, Nachiappan Chockalingam

Review J Foot Ankle Res. 2020 May 13;13(1):23. doi: 10.1186/s13047-020-00390-3.

Background: It is estimated that 2% of the global childhood population is living with some form of mobility impairment. Although footwear interventions are proposed to aid ambulation, there appears to be a paucity in the understanding of the effects of therapeutic footwear. This review aims to explore the effectiveness of footwear as an intervention for mobility impairment in children. Methods: A systematic search of MEDLINE, CINAHL, PubMed, SPORTdiscus and Scopus databases were performed. Studies which focused on children with some form of mobility impairment, age of 9 months to 18 years,

therapeutic footwear that allowed walking, and outcome measures that had explored biomechanical or skeletal geometry or psychosocial aspects were included in this review. Modified Downs and Black quality assessment index of randomised and non-randomised studies were used to assess the methodologies of included papers. Results: Out of 5003 articles sourced, 13 met the inclusion criteria for this review. These were grouped into two titled "corrective and "functional" based on the types of footwear used for intervention. Studies within the corrective footwear group included participants aged 11 months to 5 years with moderate congenital talipes equino varus or mobile pes planus. While using skeletal geometry as an outcome, there was a limited fair quality (level II) evidence that corrective footwear has no significant effect on the development of pes planus but may assist in the reduction of deformity in congenital talipes equino varus. The functional footwear group included participants aged 3 to 17 years, predominantly with mobile pes planus or cerebral palsy. Based on biomechanical measures as an outcome, there was a limited fair quality (level III) evidence that functional footwear alters biomechanical parameters in mobile pes planus (spatiotemporal) and cerebral palsy (spatiotemporal, kinematic). Although psychosocial outcomes were considered within two studies, the analysis was limited. Conclusion: Only a limited number of studies have explored the effects of therapeutic footwear and only in a narrow range of mobility impairments. Further high-quality research is required to improve the evidence base for the effectiveness of therapeutic footwear. This should include a wide range of mobility impairments and should focus both on physical and psychosocial outcomes.

PMID: [32404124](#)

7. Guided Growth for Ankle Valgus Deformity: The Challenges of Hardware Removal

David E Westberry, Ashley M Carpenter, Jonathan T Thomas, George D Graham, Erin Pichiotino, Lauren C Hyer

J Pediatr Orthop. 2020 May 8. doi: 10.1097/BPO.0000000000001583. Online ahead of print.

Background: Ankle valgus deformity is associated with conditions such as clubfoot, cerebral palsy, and myelodysplasia. Guided growth strategies using a transphyseal screw provide effective correction of ankle valgus deformity. When correction occurs before skeletal maturity, screw removal is required to prevent overcorrection in the coronal plane. In this study, we reviewed the outcomes of guided growth procedures for correction of ankle valgus and related difficulty with hardware extraction. Methods: A retrospective review of patients with ankle valgus managed with transphyseal screw placement was performed. Clinical and radiographic data, including the lateral distal tibial angle (LDTA), type of screw placed, and time to correction was recorded. At hardware removal, we reviewed elements associated with difficult extraction defined as requiring the use of specialized screw removal/extraction sets or inability to remove the entirety of the screw. Results: One hundred nineteen patients (189 extremities) with a mean age of 11.7 years at time of screw placement met study inclusion criteria. Following correction of the valgus deformity, hardware removal occurred at an average of 18.4 months after placement of the screw. Preoperatively, the mean LDTA for the entire cohort was 81.3 degrees, and was corrected to a mean LDTA of 91.1 degrees. Complicated hardware removal occurred in 69 (37%) extremities. These 69 extremities had hardware in place an average of 1.8 years compared with an average of 1.4 years in extremities without difficult extraction ($P < 0.01$). Six (9%) screws were unable to be removed in their entirety. Rebound valgus deformity occurred in 5 extremities (3%). Conclusions: Extraction of transphyseal screws in the correction of ankle valgus can be problematic. Specialized instrumentation was required in approximately one third of cases. Longevity of screw placement may be a factor that affects the ease of extraction. Additional exposure, access to specialized instrumentation, and additional operative time may be required for extraction. Level of evidence: Level IV-case series.

PMID: [32398628](#)

8. Motor Skill Training May Restore Impaired Corticospinal Tract Fibers in Children With Cerebral Palsy

Yannick Bleyenheuft, Laurence Dricot, Daniela Ebner-Karestinos, Julie Paradis, Geoffroy Saussez, Anne Renders, Anne De Volder, Rodrigo Araneda, Andrew M Gordon, Kathleen M Friel

Neurorehabil Neural Repair. 2020 May 14;1545968320918841. doi: 10.1177/1545968320918841. Online ahead of print.

Background. In children with unilateral cerebral palsy (UCP), the fibers of the corticospinal tract (CST) emerging from the lesioned hemisphere are damaged following the initial brain injury. The extent to which the integrity of these fibers is restorable with training is unknown. Objective. To assess changes in CST integrity in children with UCP following Hand-and-Arm-Bimanual-Intensive-Therapy-Including-Lower-Extremity (HABIT-ILE) compared to a control group. Methods. Forty-four children with UCP participated in this study. Integrity of the CSTs was measured using diffusion tensor imaging before and after 2 weeks of HABIT-ILE (treatment group, $n = 23$) or 2 weeks apart without intensive treatment (control group, $n =$

18). Fractional anisotropy (FA) and mean diffusivity (MD) were the endpoints for assessing the integrity of CST. Results. As highlighted in our whole tract analysis, the FA of the CST originating from the nonlesioned and lesioned hemispheres increased significantly after therapy in the treatment group compared to the control group (group * test session interaction: $P < .001$ and $P = .049$, respectively). A decrease in MD was also observed in the CST emerging from the nonlesioned and lesioned hemispheres (group * time interaction: both $P < .001$). In addition, changes in manual ability correlated with changes in FA in both CSTs ($r = 0.463$, $P = .024$; $r = 0.643$, $P < .001$) and changes in MD in CST emerging from nonlesioned hemisphere ($r = -0.662$, $P < .001$). Conclusions. HABIT-ILE improves FA/MD in the CST and hand function of children with UCP, suggesting that CST fibers retain a capacity for functional restoration. This finding supports the application of intensive motor skill training in clinical practice for the benefit of numerous patients.

PMID: [32407247](#)

9. Single-event Multilevel Surgery, but Not Botulinum Toxin Injections Normalize Joint Loading in Cerebral Palsy Patients

S Van Rossom, H Kainz, M Wesseling, E Papageorgiou, F De Groote, A Van Campenhout, G Molenaers, K Desloovere 8, I Jonkers

Clin Biomech (Bristol, Avon). 2020 May 1;76:105025. doi: 10.1016/j.clinbiomech.2020.105025. Online ahead of print.

Background: Many patients with cerebral palsy present a pathologic gait pattern, which presumably induces aberrant musculoskeletal loading that interferes with natural bone growth, causing bone deformations on the long term. Botulinum toxin interventions and single-event multilevel surgeries are used to restore the gait pattern, assuming that a normal gait pattern restores musculoskeletal loading and thus prevents further bone deformation. However, it is unknown if these interventions are able to restore musculoskeletal loading. Hence, we investigated the impact of botulinum toxin injections and single-event multilevel surgery on musculoskeletal loading. Methods: Gait data collected in 93 children with bilateral cerebral palsy, which included pre- and post multi-level botulinum toxin (49 children) and single-event multilevel surgery (44 children) assessments, and 15 typically developing children were retrospectively processed using a musculoskeletal modelling workflow to calculate joint angles, moments, muscle and joint contact force magnitudes and orientations. Differences from the typically developing waveform were expressed by a root-mean square difference were compared using paired t-tests for each intervention separately ($\alpha < 0.05$). Findings: Botulinum toxin induced significant changes in the joint angles, but did not improve the muscle and joint contact forces. Single-event multilevel surgery induced significant kinematic and kinetic changes, which were associated with improved muscle and joint contact forces. Interpretation: The present results indicate that botulinum toxin injections were not able to restore normal gait kinematics nor musculoskeletal loading, whereas single-event multilevel surgery did successfully restore both. Therefore, single-event multilevel surgery might be protective against the re-occurrence of bone deformation on the longer term.

PMID: [32402900](#)

10. Assistive Products and Childhood Neurodisability: A Retrospective Study on Factors Associated With Aids/Orthoses Prescription

Carla Assenza, Denise Cacciatore, Mattia Manica, Marco Iosa, Calogero Foti, Tiziana Gobbetti, Stefano Paolucci, Daniela Morelli

Eur J Phys Rehabil Med. 2020 May 14. doi: 10.23736/S1973-9087.20.06224-3. Online ahead of print.

Background: Children affected by pathologies causing neurodisability go through motor, cognitive, sensory and other limitations. The selection of assistive products can influence their level of independence and quality of life. Aim: The present study investigated the possibility to assess the equipment needs of children with neurodisabilities, based on their clinical characteristics. Design: A Retrospective Observational study. Setting: Outpatients. Population: Inclusion criteria: diagnosis of cerebral palsy or genetic/chromosomal/syndromic disorders, age range 0-18 years, intelligence quotient evaluation, medical history of positive or negative presence of epilepsy and of communication disorders, admission at our neurorehabilitation service between 2007 and 2017, and registration of all equipment prescribed to each child. Methods: In 192 children (111 males, 57.81%) we evaluated the relationship between several independent variables (diagnosis, sex, Gross Motor Function Classification System level, intelligence quotient, history of epilepsy and communication disorders) and equipment prescription by means of logistic regression models. Results: Our data showed significant correlation between the Gross Motor Function Classification System level and the equipment prescribed. A history of seizures was negatively correlated with walker

prescriptions (the log odds of prescription decreases by -2.156 CI: -4.16 - -0.65) and positively with those of stroller (the log odds increases by 1.427 CI: 0.22 - 2.69). Stroller and knee-ankle-foot orthoses and hip-knee-ankle-foot orthoses prescriptions were negatively correlated with the cerebral palsy diagnosis. The prescription of foot orthoses was positively correlated with mental retardation (the log odds increases by 0.358 CI: 0.12 - 0.61). A negative correlation between communication disorders and the prescription of ankle-foot orthoses and communication/learning devices was also found (the log odds decreases by -0.833 CI -1.66 - -0.01). Conclusions: Several clinical characteristics correlate with specific equipment needs. Clinical rehabilitation impact: The definition of the clinical characteristics with a potential predicting value, may facilitate the task of physician on choosing what is more appropriate to prescribe, as well as the authorizing office responsible for evaluating the appropriateness of prescriptions. Furthermore, it could be possible to foresee the care needs in terms of type and number of aids / orthoses and to guarantee every disabled child the possibility to take advantage of the same opportunities.

PMID: [32406225](#)

11. Deep Brain Stimulation Reduces Pain in Children With Dystonia, Including in Dyskinetic Cerebral Palsy

Sarah Perides, Jean-Pierre Lin, Geraldine Lee, Hortensia Gimeno, Daniel E Lumsden, Keyoumars Ashkan, Richard Selway, Margaret Kaminska

Dev Med Child Neurol. 2020 May 9. doi: 10.1111/dmcn.14555. Online ahead of print.

Aim: To establish the prevalence of dystonic pain in children and their response to deep brain stimulation (DBS). **Method:** Dystonic pain was assessed in a cohort of 140 children, 71 males and 69 females, median age 11 years 11 months (range 3y-19y 1mo), undergoing DBS in our centre over a period of 10 years. The cohort was divided into aetiological dystonia groups: 1a, inherited; 1b, hereditary; 2, acquired; and 3, idiopathic. Motor responses were measured with the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS). **Results:** Dystonic pain was identified in 63 (45%) patients, 38% of whom had a diagnosis of cerebral palsy (CP). Dystonic pain improved in 90% of children and in all aetiological subgroups 1 year after DBS, while the BFMDRS motor score improved in 70%. Statistically significant improvement ($p < 0.01$) was noted for the whole cohort on the Numerical Pain Rating Scale ($n=27$), Paediatric Pain Profile ($n=17$), and Caregivers Priorities and Child Health Index of Life with Disabilities questionnaire ($n=48$). There was reduction of pain severity, frequency, and analgesia requirement. Findings were similar for the whole cohort and aetiological subgroups other than the inherited hereditary group where the improvement did not reach statistical significance. **Interpretation:** Dystonic pain is frequent in children with dystonia, including those with CP, who undergo DBS; this can be an important, realizable goal of surgery irrespective of aetiology. We encourage the use of multimodal approach in pain research to reduce the risk of bias.

PMID: [32386250](#)

12. Effect of Pain on Mood Affective Disorders in Adults With Cerebral Palsy

Daniel G Whitney, Sarah Bell, Daniel Whibley, Wilma M A Van der Slot, Edward A Hurvitz, Heidi J Haapala, Mark D Peterson, Seth A Warschausky

Dev Med Child Neurol. 2020 May 10. doi: 10.1111/dmcn.14559. Online ahead of print.

Aim: To determine if pain is associated with 12-month incidence of mood affective disorders (MAD) in adults with cerebral palsy (CP). **Method:** Data from Optum Clinformatics® Data Mart (2013-2016) were used for this retrospective cohort study. Diagnostic codes were used to identify adults (≥ 18 y) with CP, incident cases of MAD, and covariates (other neurodevelopmental conditions, sleep disorders, arthritis). Pain (any type, location) was identified between 1st October 2014 and 30th September 2015. The pain group was divided into new or consistent pain if they had a history of pain (i.e. consistent) in the 12 months before their first pain claim date. Crude incidence rates of MAD (expressed per 100 person-years) were estimated. Cox regression was used to estimate hazard ratio (95% confidence interval [CI]) of MAD after adjusting for covariates. **Results:** Adults that had new pain ($n=859$; incidence rate=15.5) or consistent pain ($n=1303$; incidence rate=17.9) had greater crude incidence rate of MAD compared to adults without pain ($n=3726$; incidence rate=5.9). The elevated rate of MAD remained after adjusting for covariates, for new pain (hazard ratio=2.4; 95% CI=1.9-3.0) and consistent pain (hazard ratio=2.1; 95% CI=1.7-2.7). **Interpretation:** Pain is associated with greater incidence of MAD in adults with CP. This association remained after accounting for potential confounding factors. **What this paper adds:** Pain was associated with higher 12-month incidence of mood affective disorders (MAD). The 12-month MAD incidence was similar between new and consistent pain groups. The MAD incidence remained higher adjusting for neurodevelopmental comorbidities, sleep disorders, and arthritis.

PMID: [32388867](#)

13. ASSESSMENT OF NUTRITIONAL STATUS AND FREQUENCY OF COMPLICATIONS ASSOCIATED TO FEEDING IN PATIENTS WITH SPASTIC QUADRIPLEGIC CEREBRAL PALSY [Article in Portuguese, English]

Kamilla Tavares de Sousa, Gabrielle Bemfica Ferreira, Amanda Torido Santos, Quintiliano Siqueira Schroden Nomelini, Luciana Oliveira de Almeida Minussi, Érica Rodrigues Mariano de Almeida Rezende, Isabella Lopes Nonato

Rev Paul Pediatr. 2020;38:e2018410. doi: 10.1590/1984-0462/2020/38/2018410. Epub 2020 May 11.

Objective: To correlate the nutritional status with variables associated to the type of diet and feeding route of children and adolescents with spastic quadriplegic cerebral palsy (CP). **Methods:** This cross-sectional study included 28 patients aged ≤ 13 years old who presented a diagnosis of spastic quadriplegic CP and were followed by the nutrition team of the Outpatient Clinic for Special Patients of Hospital de Clínicas de Uberlândia - Universidade Federal de Uberlândia (HC-UFU), between July/2016 and January/2017. Consent forms were signed by the legal guardians. The nutritional status was evaluated and data on dietary complications food route and type of diet were collected. For the description of data, average and median values were used. Correlation was tested with Spearman's index. Significance was set at $p < 0.05$. **Results:** 75% of patients used alternative feeding routes (nasogastric, catheter or gastrostomy), 57% were eutrophic. The most frequent complications were oropharyngeal dysphagia, reflux and intestinal constipation. No correlation was found between the occurrence of complications and the nutritional status. There was a positive correlation between the diet received and the patient's nutritional status (0.48; $p = 0.01$), i.e. individuals with adequate caloric and macronutrients intake had a better nutritional status. **Conclusions:** The results reinforce the need for continued nutritional guidance for the children's parents/caregivers, as well as the choice of an adequate route of feeding to each child by the multi-professional team, in order to contribute to improved nutritional status and adequate dietary intake.

PMID: [32401853](#)

14. BMI Change Following Spinal Fusion for Neuromuscular Scoliosis Surgery

Keith D Baldwin, Patrick J Cahill, Paul D Sponseller, Mark F Abel, David A Spiegel, John M Flynn, Josh M Pahys, Harms Study Group Investigators

Spine Deform. 2020 May 11. doi: 10.1007/s43390-020-00109-1. Online ahead of print.

Objectives: We hypothesize that a post-operative weight gain will result in patients who are underweight prior to surgery. Cachexia and low body mass index is common among children with cerebral palsy (CP). Many interventions are undertaken to assist the child in nourishment and to obtain a more normal body mass. Additionally, scoliosis is common among children with CP. In our practice we have noted weight gain post operatively in severely underweight children after spinal fusion. **Methods:** We underwent a retrospective review of a CP cohort from a multicenter prospective registry. Percentiles on the CP specific growth chart for which each child belonged were plotted based on the patients' age, weight, gender, GMFCS level, and tube feeding status. We then assessed percentile change in patients between pre-op visit, 1 year, 2 years and for those with available data, 5 years follow up visits. Patients with under two years of follow up, patients with GMFCS III and below, and patients without weight data were excluded. **Results:** We identified a total of 211 potentially eligible patients from a multicenter prospective registry. 109 had complete 2 years data to analyze and 37 patients had full 5 years data to analyze. We found that patients under the 50th percentile pre-operatively increased their percentile on the CP growth chart for weight 12.1 percentiles (95% CI 6.7, 17.5 p value < 0.001) whereas patients that began at the 50th percentile or above on average lost 2.2 percentiles (95% CI -6.8, 2.3) though the change was not statistically significant (p value 0.330). These changes appeared stable at 5 years. Although regression analysis showed that Cobb correction and pelvic obliquity correction, and hyperlordosis were not independent predictors of the change, we noted that patients with residual curves after surgery of 40° or more experienced 13.3 percentile less weight gain than those with better corrections. **Conclusions:** Patients with CP are at risk for cachexia, malnutrition, reflux and other GI disorders. Data presented here suggests that corrective spinal surgery may improve weight percentile in patients who start out at 50th percentile and lower. Patients with 40° or greater of residual scoliosis may benefit less from spinal fusion than those with a better correction. Level of evidence: II; Prognostic retrospective cohort study.

PMID: [32394323](#)

15. The Effects of Traditional Massage on Spasticity of Children With Cerebral Palsy: A Randomized Controlled Trial
Qamar Mahmood, Shaista Habibullah, Muhammad Naveed Babur

J Pak Med Assoc. 2020 May;70(5):809-814. doi: 10.5455/JPMA.24442.

Objective: To examine the effects of traditional massage on spasticity of children with cerebral palsy. **Methods:** The randomised control trial was conducted at the National Institute of Rehabilitation Medicine, Islamabad, Pakistan, from September 2016 to August 2018, and comprised children with spastic cerebral palsy aged 2-10 years who were randomly allocated to control and intervention groups. Both the groups received routine physical therapy once daily, five times a week for three months. The intervention group additionally received traditional massage. Spasticity was evaluated using the Modified Ashworth Scale at baseline, and after 6th and 12th weeks of intervention. Data analysed using SPSS 20. **Results:** Of the 86 subjects enrolled, 75(87.2%) completed the study; 37(49.3%) in the control group with a mean age of 6.81 ± 2.31 years, and 38(50.6%) in the intervention group with a mean age of 7.05 ± 2.47 years. There were 25(68%) boys among the controls and 22(58%) in the intervention group. There was no statistically significant difference in baseline scores between the groups ($p > 0.05$). At 6th week, reduction in scores was statistically significant in the right upper limb ($p < 0.05$), and in the right lower limb ($p < 0.05$) after the 12th week. **Conclusions:** Traditional massage was found to have significant effect on the right side compared to the routine physical therapy for reduction of spasticity in children with cerebral palsy.

PMID: [32400732](#)

16. The Value of a Short Practical Training Course for Newly Qualified Therapists Working With Children With Cerebral Palsy in South Africa

Takondwa C Bakuwa, Sonti Pilusa, Gillian Saloojee

Afr J Disabil. 2020 Apr 21;9:610. doi: 10.4102/ajod.v9i0.610. eCollection 2020.

Background: Cerebral palsy (CP) is the most common and most complex disabling disorder in children. Newly qualified therapists are expected to manage CP despite feeling inexperienced and inadequately prepared. Short postgraduate practical training courses could potentially help bridge this readiness gap. However, the value of these short courses in addressing the knowledge and experience gap is unknown. **Objectives:** To establish the value of a short practical training course on the self-perceived readiness of newly qualified South African trained therapists to work with children with CP. **Method:** Secondary analysis of records on therapists' immediate evaluation of a short practical training course on CP management was completed. The analysis included records from 11 courses collected over a 2-years period (2015-2017). Paired t-tests were used to determine the change in knowledge in the quantitative questionnaire. Qualitative data were analysed inductively to determine themes. **Results:** The majority of therapists had their expectations met by the course. Therapists' self-perceived level of knowledge about various aspects of CP after the course changed significantly. Therapists appreciated the adult teaching and learning methods, conducive learning environment, the relevant and organised content and holistic approach of the course. They demonstrated readiness to adopt positive attitudes, perceptions and practice following the course. **Conclusion:** A short practical postgraduate training course in CP is valuable in addressing the self-perceived lack of readiness amongst therapists with little experience in this area. It is capable of improving the knowledge and changing attitudes, perceptions and practice intentions positively, and thereby potentially improving the quality of service offered to children with CP.

PMID: [32391247](#)

17. Anxiety in Children and Adolescents With Cerebral Palsy

Jane McMahon, Adrienne Harvey, Susan M Reid, Tamara May, Giuliana Antolovich

J Paediatr Child Health. 2020 May 15. doi: 10.1111/jpc.14879. Online ahead of print.

Aims: To describe the prevalence of, and factors associated with, anxiety in 6-18-year-old children with cerebral palsy (CP) and determine how often clinicians screen for and manage anxiety in this group. **Methods:** Using a population CP register as the sampling pool, 569 families were approached by email, and 172 (mean age of children 12 years 7 months [SD 3 years 5 months]; 96 males) participated. Parents and, where able, children completed the Screen for Child Anxiety Related Emotional

Disorders (SCARED). Parents also completed the Strengths and Difficulties Questionnaire. Children's medical records were searched for previous anxiety diagnoses and treatments. Results: Clinically significant anxiety was identified in 38% of children on parent reports and 46% on child reports. Girls were twice as likely to have anxiety ($p = 0.02$). Parent- and child-reported scores were strongly correlated ($r = 0.853$). Fewer parents of children with intellectual and communication impairments completed the survey. Based on the SCARED parent reports, anxiety was not identified by a clinician in 16 children (43%) with clinically significant anxiety. Conclusion: Anxiety symptoms are prominent among children with CP, indicating a need for routine screening. Available screening tools are unsuitable for children with more severe limitations in cognition and communication; further research is needed to address this gap.

PMID: [32412671](#)

18. Inter-Day Reliability and Changes of Surface Electromyography on Two Postural Muscles Throughout 12 Weeks of Hippotherapy on Patients With Cerebral Palsy: A Pilot Study

Hélène Viruega, Inès Gaillard, Laura Briatte, Manuel Gaviria

Brain Sci. 2020 May 6;10(5):E281. doi: 10.3390/brainsci10050281.

Cerebral palsy (CP) is an umbrella term covering a group of permanent developmental disorders of movement and posture characterized by highly variable clinical features. The aim of this study was to assess the short-term and mid-term effects of neurorehabilitation via hippotherapy on the contractile properties of two key postural muscles during functional sitting in such patients. Thirty-minute hippotherapy sessions were conducted biweekly for 12 weeks in 18 patients (18.1 ± 5.7 years old). Surface electromyography (EMG) was implemented bilaterally in rectus abdominis and adductor magnus. We quantitatively analyzed the amplitude of EMG signals in the time domain and its spectral characteristics in the frequency domain. EMGs were recorded at the beginning and end of each session on day one and at week six and week twelve. Statistical analysis revealed a substantial inter-day reliability of the EMG signals for both muscles, validating the methodological approach. To a lesser extent, while beyond the scope of the current study, quantitative changes suggested a more selective recruitment/contractile properties' shift of the examined muscles. Exploring postural control during functional activities would contribute to understanding the relationship between structural impairment, activity performance and patient capabilities, allowing the design of neurorehabilitation programs aimed at improving postural and functional skills according to each individual's needs. The present study provides basic quantitative data supporting the body of scientific evidence making hippotherapy an approach of choice for CP neurorehabilitation.

PMID: [32384678](#)

19. Can Hippotherapy Make a Difference in the Quality of Life of Children With Cerebral Palsy? A Pragmatic Study

Debbie J Silkwood-Sherer, Nancy H McGibbon

Physiother Theory Pract. 2020 May 14;1-11. doi: 10.1080/09593985.2020.1759167. Online ahead of print.

Objective: To determine if the addition of 12 weekly therapy sessions, incorporating hippotherapy as the primary intervention to each child's usual therapy program, will improve balance, participation, and quality of life. Methods: Pragmatic, multi-center, randomized, controlled trial of 13 children with cerebral palsy (CP), ages 3 to 6 years. A treatment group received 12 weeks of weekly hippotherapy intervention in addition to their usual therapy. A control group continued with their usual therapy only. Assessments were completed for the treatment group pre-intervention (P0), post intervention (P1), and 12 weeks post no intervention (P2). Control group assessments occurred in the same timeframe: baseline, 12 weeks and 24 weeks. Results: The only significant difference between the groups, post intervention, was on the Pediatric Balance Scale (PBS). Within group analysis showed no significant changes for the control group between any pretest/posttest measures. The treatment group demonstrated significant improvement on the PBS (P0-P1, $p = .02$; P0-P2, $p = .02$) and Activities Scale for Kids (P0-P1, $p = .02$; P0-P2, $p = .02$) with delayed improvement on the 1 Minute Walk Test (P1-P2, $p = .02$) and Pediatric Quality of Life - CP Module (P0-P2, $p = .03$). Conclusions: Improvements in balance in children with CP may promote increased participation and quality of life when hippotherapy is added to their treatment plan.

PMID: [32406798](#)

20. Bone Microarchitecture Assessed by Trabecular Bone Score Is Independent of Mobility Level or Height in Pediatric Patients With Cerebral Palsy

Mirko Rehberg, Manuela Azim, Kyriakos Martakis, Renaud Winzenrieth, Heike Hoyer-Kuhn, Eckhard Schoenau, Oliver Semler, Ibrahim Duran

J Bone Miner Res. 2020 May 12. doi: 10.1002/jbmr.4047. Online ahead of print.

Bone strength and fracture risk do not only depend on bone density, but also on bone structure. The Trabecular Bone Score (TBS) evaluates homogeneity of bone microarchitecture indirectly by measuring gray-level variations of two-dimensional DXA images. Although TBS is well-established for adults, there have been only few publications in pediatrics. In this monocentric retrospective analysis, we investigated TBS in children and adolescents with Cerebral Palsy (CP), a patient group vulnerable to low bone mineral mass due to impaired mobility. The influence of different parameters on TBS and areal BMD (aBMD) were evaluated, as well as the relationship between TBS and aBMD. We compared TBS values of our study population to a reference population. 472 LS-DXA scans of children and adolescents with CP (205 female), aged between 4 and 18 years, were analyzed. The DXA-scans were part of the routine examination. The children had no records of fractures or specific bone diseases. Our study population with CP had similar TBS as the reference population. TBS did not increase with age until an inflection point at 10 (12) years in females (males). Girls had significantly higher TBS than boys ($p=0.049$) and pubertal girls aged 8-13 years had significantly higher TBS than prepubertal girls ($p=0.009$). TBS standard deviation score for age (SDS-TBS) and aBMD Z-scores correlated weakly ($p<0.001$; $R=0.276$ (males), $R=0.284$ (females)). Other than for aBMD Z-scores, SDS-TBS was not influenced by age-adjusted height Z-scores and there was no significant difference in SDS-TBS when grouped by mobility levels, using the Gross Motor Function Classification System. Our results indicate for children with CP to have a similar homogeneous distribution of trabecular microarchitecture as controls. Puberty initiation appears to be essential for increase of TBS with age and for sex differences. TBS seems less influenced by body composition, height and mobility than aBMD. This article is protected by copyright. All rights reserved.

PMID: [32395832](#)

21. PREDICTIVE VALUE OF THE GENERAL MOVEMENTS ASSESSMENT IN PRETERM INFANTS: A META-ANALYSIS [Article in Portuguese, English]

Camila da Silva Pires, Sérgio Tadeu Martins Marba, Jamil Pedro de Siqueira Caldas, Mônica de Carvalho Sanchez Stopiglia

Rev Paul Pediatr. 2020;38:e2018286. doi: 10.1590/1984-0462/2020/38/2018286. Epub 2020 May 8.

Objective: To discuss the predictive value of the General Movements Assessment for the diagnosis of neurodevelopment disorders in preterm newborns. **Data source:** We conducted a systematic literature review using the following databases: Scientific Electronic Library Online (SciELO), National Library of Medicine, National Institutes of Health (PubMed), and Excerpta Medica Database (EMBASE). The articles were filtered by language, year of publication, population of interest, use of Prechtl's Method on the Qualitative Assessment of General Movements, and presence of variables related to the predictive value. The Quality Assessment of Diagnostic Accuracy Studies 2 was used to assess the methodology of the included studies. Sensitivity, specificity, Diagnostic Odds Ratio, positive and negative likelihood ratio, and parameter of accuracy were calculated. **Data synthesis:** Six of 342 articles were included. The evaluation of Writhing Movements is a good indicator for recognizing cerebral palsy, as it has high values for the sensitivity and accuracy parameters. The evaluation of Fidgety Movements has the strongest predictive validity for cerebral palsy, as it has high values in all measures of diagnostic accuracy. The quality assessment shows high risk of bias for patient selection and flow and timing of the evaluation. Therefore, the scale has potential to detect individuals with neurodevelopment disorders. However, the studies presented limitations regarding the selection of subjects and the assessment of neurological outcomes. **Conclusions:** Despite the high predictive values of the tool to identify neurological disorders, research on the subject is required due to the heterogeneity of the current studies.

PMID: [32401947](#)

22. Editorial: Patient Empowerment and Person-Centered Care in Movement Disorders

Adolfo Ramirez-Zamora, Pedro Chana, Mayela Rodríguez-Violante

Editorial Front Neurol. 2020 Apr 28;11:317. doi: 10.3389/fneur.2020.00317. eCollection 2020.

PMID: [32411083](#)

23. Burden of Caregivers of Children With Cerebral Palsy: An Intersectional Analysis of Gender, Poverty, Stigma, and Public Policy

K Vadivelan, P Sekar, S Shri Sruthi, Vijayaprasad Gopichandran

BMC Public Health. 2020 May 8;20(1):645. doi: 10.1186/s12889-020-08808-0.

Background: Caregivers of children with cerebral palsy suffer from a substantial psychosocial burden. However, there is a scarcity of documentation of the various sources of burden in low- and middle-income settings. **Methods:** We conducted qualitative in-depth interviews among mothers of children with cerebral palsy attending a physiotherapy facility. We purposively sampled mothers from rural and peri-urban areas in Tamil Nadu, India, till the point of data saturation. We analysed the transcripts using the socio-ecological model to identify the major dimensions of psychosocial burden among these mothers. **Results:** At the individual level the mothers perceived aches and pains due to the heavy physical activity of caregiving. They also suffered from a feeling of guilt about the child's condition. Due to the difficulty in balancing family and work, they had significant financial burdens. They also perceived a lack of knowledge and awareness about possible options for the treatment of their child. At the interpersonal level, the mothers lacked support from their husband and family in the process of caregiving. They also had to suffer the ill effects of alcoholism and domestic violence from their husbands. They had to compromise on the care they provided to the other family members and their children without cerebral palsy. At the community level, the mothers had no support from the community members and felt isolated from others. The mothers also reported discrimination and lack of participation in social events. Environmental stressors like lack of inclusive public spaces, lack of options for public transport and unfriendly work timings and environment were major sources of burden. The mothers felt that the disability welfare support offered by the government was grossly insufficient and there was no platform for interactions with other peers and mothers suffering from a similar burden. **Conclusion:** Caregivers of children with cerebral palsy have unique burdens in a typical low- and middle-income setting including an intersection of gender norms, poverty, stigmatization and non-inclusive public policy, which need to be addressed to improve the quality of life of caregivers.

PMID: [32384875](https://pubmed.ncbi.nlm.nih.gov/32384875/)

24. Prediction of Childhood Brain Outcomes in Infants Born Preterm Using Neonatal MRI and Concurrent Clinical Biomarkers (PREBO-6): Study Protocol for a Prospective Cohort Study

Joanne M George, Alex M Pagnozzi, Samudragupta Bora, Roslyn N Boyd, Paul B Colditz, Stephen E Rose, Robert S Ware, Kerstin Pannek, Jane E Bursle, Jurgen Fripp, Karen Barlow, Kartik Iyer, Shaneen J Leishman, Rebecca L Jendra

BMJ Open. 2020 May 12;10(5):e036480. doi: 10.1136/bmjopen-2019-036480.

Introduction: Infants born very preterm are at risk of adverse neurodevelopmental outcomes, including cognitive deficits, motor impairments and cerebral palsy. Earlier identification enables targeted early interventions to be implemented with the aim of improving outcomes.

Methods and analysis: Protocol for 6-year follow-up of two cohorts of infants born <31 weeks gestational age (PPREMO: Prediction of Preterm Motor Outcomes; PREBO: Prediction of Preterm Brain Outcomes) and a small term-born reference sample in Brisbane, Australia. Both preterm cohorts underwent very early MRI and concurrent clinical assessment at 32 and 40 weeks postmenstrual age (PMA) and were followed up at 3, 12 and 24 months corrected age (CA). This study will perform MRI and electroencephalography (EEG). Primary outcomes include the Movement Assessment Battery for Children second edition and Full-Scale IQ score from the Wechsler Intelligence Scale for Children fifth edition (WISC-V). Secondary outcomes include the Gross Motor Function Classification System for children with cerebral palsy; executive function (Behavior Rating Inventory of Executive Function second edition, WISC-V Digit Span and Picture Span, Wisconsin Card Sorting Test 64 Card Version); attention (Test of Everyday Attention for Children second edition); language (Clinical Evaluation of Language Fundamentals fifth edition), academic achievement (Woodcock Johnson IV Tests of Achievement); mental health and quality of life (Development and Well-Being Assessment, Autism Spectrum Quotient-10 Items Child version and Child Health Utility-9D). **Aims:** Examine the ability of early neonatal MRI, EEG and concurrent clinical measures at 32 weeks PMA to predict motor, cognitive, language, academic achievement and mental health outcomes at 6 years CA. Determine if early brain abnormalities persist and are evident on brain MRI at 6 years CA and the relationship to EEG and concurrent motor, cognitive, language, academic achievement and mental health outcomes. **Ethics and dissemination:** Ethical approval has been obtained from Human Research Ethics Committees at Children's Health Queensland (HREC/19/QCHQ/49800) and The University of Queensland (2019000426). Study findings will be presented at national and international conferences and published in peer-reviewed journals. Trial registration number: ACTRN12619000155190p. WEB ADDRESS OF TRIAL: <http://>

www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12619000155190p.

PMID: [32404396](#)

25. Congenital Malformations in Children With Cerebral Palsy: Is Prematurity Protective?

Marcel Sévère, Pamela Ng, Carmen Messerlian, John Andersen, David Buckley, Darcy Fehlings, Adam Kirton, Louise Koclas, Nicole Pigeon, Esias Van Rensburg, Ellen Wood, Michael Shevell, Maryam Oskoui

Pediatr Neurol. 2020 Feb 12;S0887-8994(20)30056-4. doi: 10.1016/j.pediatrneurol.2020.02.002. Online ahead of print.

Background: Congenital malformations are more common in children who are born prematurely, and prematurity is the leading risk factor for cerebral palsy. The primary objective of this study was to describe the profile of congenital malformations in a Canadian cohort of children with cerebral palsy. The secondary objectives were to compare the profiles of children with cerebral palsy with and without a congenital malformation and explore the possible role of prematurity. **Methods:** This retrospective cohort study utilized data from the Canadian Cerebral Palsy Registry, a population based registry of children with a confirmed diagnosis of cerebral palsy. Differences between groups were compared using Pearson's chi-square and Student t test as appropriate. Odds ratios and 95% confidence intervals were calculated. **RESULTS:** Congenital malformations were present in 23% participants. In term-born children, brain malformations were the most common, whereas heart and gastrointestinal malformations were more common in children born prematurely. Children with a malformation had higher odds of being born term (odds ratio 1.57, 95% confidence interval 1.20 to 2.04); having hypotonic, ataxic, or dyskinetic cerebral palsy (odds ratio 1.92, 95% confidence interval 1.35 to 2.72); being nonambulatory (odds ratio 1.70, 95% confidence interval 1.29 to 2.25); and having cerebral palsy-associated comorbidities. **Conclusions:** One in four children with cerebral palsy have an associated congenital malformation. Their profile of term birth, higher Apgar scores, and lower frequency of perinatal seizures suggests a distinct causal pathway.

PMID: [32386793](#)

26. Is the Blood Oxygenation Level-Dependent fMRI Response to Motor Tasks Altered in Children After Neonatal Stroke?

Mariam Al Harrach, François Rousseau, Samuel Groeschel, Stéphane Chabrier, Lucie Hertz-Pannier, Julien Lefevre, Mickael Dinomais

Front Hum Neurosci. 2020 Apr 29;14:154. doi: 10.3389/fnhum.2020.00154. eCollection 2020.

Functional MRI is increasingly being used in the assessment of brain activation and connectivity following stroke. Many of these studies rely on the Blood Oxygenation Level Dependent (BOLD) contrast. However, the stability, as well as the accuracy of the BOLD response to motor task in the ipsilesional hemisphere, remains ambiguous. In this work, the BOLD signal acquired from both healthy and affected hemispheres was analyzed in 7-year-old children who sustained a Neonatal Arterial Ischemic Stroke (NAIS). Accordingly, a repetitive motor task of the contralesional and the ipsilesional hands was performed by 33 patients with unilateral lesions. These patients were divided into two groups: those without cerebral palsy (NAIS), and those with cerebral palsy (CP). The BOLD signal time course was obtained from distinctly defined regions of interest (ROIs) extracted from the functional activation maps of 30 healthy controls with similar age and demographic characteristics as the patients. An ROI covering both the primary motor cortex (M1) and the primary somatosensory cortex (S1) was also tested. Compared with controls, NAIS patients without CP had similar BOLD amplitude variation for both the contralesional and the ipsilesional hand movements. However, in the case of NAIS patients with CP, a significant difference in the averaged BOLD amplitude was found between the healthy and affected hemisphere. In both cases, no progressive attenuation of the BOLD signal amplitude was observed throughout the task epochs. Besides, results also showed a correlation between the BOLD signal percentage variation of the lesioned hemisphere and the dexterity level. These findings suggest that for patients who sustained a NAIS with no extensive permanent motor impairment, BOLD signal-based data analysis can be a valuable tool for the evaluation of functional brain networks.

PMID: [32410976](#)

27. Histologic Chorioamnionitis and Risk of Neurodevelopmental Impairment at Age 10 Years Among Extremely Preterm Infants Born Less Than 28 Weeks of Gestation

Kartik K Venkatesh, Alan Leviton, Jonathan L Hecht, Robert M Joseph, Laurie M Douglass, Jean A Frazier, Julie L Daniels, Rebecca C Fry, T Michael O'shea, Karl Ck Kuban

Am J Obstet Gynecol. 2020 May 6;S0002-9378(20)30525-1. doi: 10.1016/j.ajog.2020.05.001. Online ahead of print.

Background: Children born extremely preterm whose placenta had histologic evidence of chorioamnionitis have early brain dysfunction, but little is known about neurological development at 10 years of age. **Objective:** We investigated the association between histologic chorioamnionitis and neurodevelopmental impairment at 10 years among children born <28 weeks gestation (extremely preterm). **Methods:** The multicenter Extremely Low Gestational Age Newborn (ELGAN) Study enrolled extremely preterm newborns from 2002-2004 at 14 U.S. hospitals. Chorioamnionitis was defined by histologic stage (early, moderate, and advanced) and grade (mild/moderate and severe) of chorionic plate and umbilical cord inflammation. The children were evaluated for cerebral palsy at 2 years, and autism spectrum disorder, cognitive impairment (intelligence quotient >2 standard deviations below the mean), and epilepsy at age 10 years by blinded evaluators using validated measures. Multivariable logistic regression with generalized estimating equations was used. **Results:** Among 805 placenta, 43% (347/805) had histologic chorioamnionitis by moderate or advanced maternal stage, 36% (286/805) by severe maternal grade, 18% (132/737) by moderate or advanced fetal stage, and 1% (10/737) by severe fetal grade. The frequencies of impairments were 11% (88/767) for cerebral palsy, 7% (56/773) for autism spectrum disorder, 15% (120/788) for cognitive impairment, and 7% (52/763) for epilepsy. Adjusted for maternal age, body mass index, race, insurance status, maternal education, tobacco use, infant sex, and multiple gestations, the adjusted odds (AOR) for the association between histologic chorioamnionitis and cerebral palsy years was increased with advanced maternal stage (AOR 2.5, 95% CI 1.6 to 3.9), severe maternal grade (AOR 2.0, 95% CI 1.2 to 3.4), moderate fetal stage (AOR 2.20, 95% CI 2.1 to 2.2), and mild or moderate fetal grade (AOR 1.5, 95% CI 1.0 to 2.2). Similarly, the AOR for the association between histologic chorioamnionitis and epilepsy was increased with advanced maternal stage (AOR 1.5, 95% CI 1.3 to 1.6) and severe fetal grade (AOR 5.9, CI 1.9 to 17.8). In addition, the AOR for the association between histologic chorioamnionitis and autism spectrum disorder was increased with mild or moderate fetal grade (AOR 1.7, 95% CI 1.0 to 2.9). Histologic chorioamnionitis was not associated with cognitive impairment. These findings held after adjustment for gestational age at delivery. In contrast to histological chorioamnionitis, a clinical diagnosis of chorioamnionitis was not associated with neurodevelopmental impairment. **Conclusion:** Histologic chorioamnionitis may be associated with some forms of neurodevelopmental impairment at 10 years of life among infants born <28 weeks gestation.

PMID: [32387324](#)

28. MiR-29b Is Associated With Perinatal Inflammation in Extremely Preterm Infants

Lecann R Pavlek, Sundari Vudatala, Christopher W Bartlett, Irina A Buhimschi, Catalin S Buhimschi, Lynette K Rogers

Pediatr Res. 2020 May 9. doi: 10.1038/s41390-020-0943-1. Online ahead of print.

Background: Inflammation is strongly associated with premature birth and neonatal morbidities. Increases in infant haptoglobin, haptoglobin-related protein (Hp&HpRP), and interleukin-6 (IL-6) levels are indicators of intra-amniotic inflammation (IAI) and have been linked to poor neonatal outcomes. Inflammation causes epigenetic changes, specifically suppression of miR-29 expression. The current study sought to determine whether miR-29b levels in cord blood or neonatal venous blood are associated with IAI, identified by elevated IL-6 and Hp, and subsequent clinical morbidities in the infant. **Methods:** We tested 92 cord blood samples from premature newborns and 18 venous blood samples at 36 weeks corrected gestational age. MiR-29b, Hp&HpRP, and IL-6 were measured by polymerase chain reaction and enzyme-linked immunosorbent assay, respectively. **Results:** Decreased levels of miR-29b were observed in infants exposed to IAI with elevated Hp&HpRP and IL-6 levels and in infants delivered by spontaneous preterm birth. Lower miR-29 levels were also observed in women diagnosed with histological chorioamnionitis or funisitis and in infants with cerebral palsy. Higher levels of miR-29 were measured in infants small for gestational age and in venous samples from older infants. **Conclusions:** MiR-29 may be an additional biomarker of IAI and a potential therapeutic target for treating poor newborn outcomes resulting from antenatal exposure to IAI. **Impact:** Decreases in miR-29b are associated with intrauterine inflammation. Hp&HpRP increases are associated with decreased miR-29b. MiR-29b may be an additional biomarker for neonatal outcomes and a potential therapeutic target for intrauterine inflammation.

PMID: [32386397](#)

29. Autologous Transplantation of Umbilical Cord Blood-Derived Cells in Extreme Preterm Infants: Protocol for a Safety and Feasibility Study

Atul Malhotra, Iona Novak, Suzanne Lee Miller, Graham Jenkin

BMJ Open. 2020 May 11;10(5):e036065. doi: 10.1136/bmjopen-2019-036065.

Introduction: Preterm brain injury continues to be an important complication of preterm birth, especially in extremely premature infants. Umbilical cord blood-derived cells (UCBCs) are increasingly being evaluated for their neuroprotective and neuroreparative properties in preclinical and clinical studies. There remains a paucity of information on the feasibility and safety of autologous UCBC transplantation in extremely premature infants. **Methods and analysis:** A single centre safety and feasibility study in preterm babies born before 28 weeks gestation. Cord blood will be collected after birth and if sufficient blood is obtained, UCB mononuclear cells will be harvested from the cord blood, characterised and stored. After excluding infants who have already suffered severe preterm brain injury, based on cranial ultrasounds in first week of life, preterm infants will be infused with autologous UCBCs via the intravenous route at a dose of 25-50 million UCBCs/kg body weight of live cells, with the cell number being the maximum available up to 50 million cells/kg. A minimum of 20 infants will be administered autologous UCBCs. Primary outcomes will include feasibility and safety. Feasibility will be determined by access to sufficient cord blood at collection and UCBCs following processing. Safety will be determined by lack of adverse events directly related to autologous UCBC administration in the first few days after cell administration. Secondary outcomes studied will include neonatal and neurodevelopmental morbidities till 2 years of life. Additional outcomes will include cell characteristics of all collected cord blood, and cytokine responses to cell administration in transplanted infants till 36 weeks' corrected age. **Ethics and dissemination:** Monash Health Human Research Ethics Committee approved this study in December 2019. Recruitment is to commence in July 2020 and is expected to take around 12 months. The findings of this study will be disseminated via peer-reviewed journals and at conferences. Trial registration number: ACTRN12619001637134.

PMID: [32398336](#)

Prevention and Cure

30. A Biomarker for Predicting Responsiveness to Stem Cell Therapy Based on Mechanism-of-Action: Evidence From Cerebral Injury

Richard E Hartman, Neal H Nathan, Nirmalya Ghosh, Cameron D Pernia, Janessa Law, Ruslan Nuryyev, Amy Plaia, Alena Yusof, Beatriz Tone, Melissa Dulcich, Dustin R Wakeman, Nejmi Dilmac, Walter D Niles, Richard L Sidman, Andre Obenaus, Evan Y Snyder, Stephen Ashwal

Cell Rep. 2020 May 12;31(6):107622. doi: 10.1016/j.celrep.2020.107622.

To date, no stem cell therapy has been directed to specific recipients-and, conversely, withheld from others-based on a clinical or molecular profile congruent with that cell's therapeutic mechanism-of-action (MOA) for that condition. We address this challenge preclinically with a prototypical scenario: human neural stem cells (hNSCs) against perinatal/neonatal cerebral hypoxic-ischemic injury (HII). We demonstrate that a clinically translatable magnetic resonance imaging (MRI) algorithm, hierarchical region splitting, provides a rigorous, expeditious, prospective, noninvasive "biomarker" for identifying subjects with lesions bearing a molecular profile indicative of responsiveness to hNSCs' neuroprotective MOA. Implanted hNSCs improve lesional, motor, and/or cognitive outcomes only when there is an MRI-measurable penumbra that can be forestalled from evolving into necrotic core; the core never improves. Unlike the core, a penumbra is characterized by a molecular profile associated with salvageability. Hence, only lesions characterized by penumbral > core volumes should be treated with cells, making such measurements arguably a regenerative medicine selection biomarker.

PMID: [32402283](#)

31. Re: Antenatal Magnesium Sulphate for the Prevention of Cerebral Palsy in Infants Born Preterm: A Double-Blind, Randomised, Placebo-Controlled, Multi-Centre Trial: At Which Gestational Ages Should Magnesium Sulphate Be

Given to Women at Risk of Preterm Birth?

Mads Langager Larsen, Lone Krebs, Gija Rackauskaite, Christina Engel Hoei-Hansen, Gorm Greisen

BJOG. 2020 May 11. doi: 10.1111/1471-0528.16268. Online ahead of print.

PMID: [32394601](https://pubmed.ncbi.nlm.nih.gov/32394601/)