# Cerebral palsy research news

Monday 2 August 2021

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

***Professor Nadia Badawi AM***
CP Alliance Chair of Cerebral Palsy Research

Subscribe to CP Research News

## Interventions and Management

**1. Surgical Results of Selective Dorsal Rhizotomy for the Treatment of Spastic Cerebral Palsy**
Marcelo Volpon Santos, Vinicius M Carneiro, Patricia N B G C Oliveira, Carla A T Caldas, Helio R Machado

J Pediatr Neurosci. Jan-Mar 2021;16(1):24-29. doi: 10.4103/jpn.JPN_26_20. Epub 2021 Jun 25.

Background: Selective dorsal rhizotomy (SDR) is one of the surgical alternatives for treating spasticity, especially in children with spastic diplegia secondary to cerebral palsy (CP). It is becoming increasingly used, and the results of this operation need to be further highlighted. Aim: The main objective of this article was to present the results of such surgical procedure in a cohort of a specialized center, with a particular focus on a quantitative analysis (goniometry). Materials and methods: Retrospective review of the medical records and gait analyses of a cohort of 34 patients diagnosed with CP submitted to elective SDR at our institution, in a period of 6 years, was carried out. All patients underwent a thorough clinical and neurological assessment, gait analysis at a dedicated laboratory, and magnetic resonance imaging of whole neuro-axis. Statistical analysis: For continuous quantitative variables (goniometric angles and muscle tone), a t-student test was used. A scatterplot regression analysis was used for the comparison of modified Ashworth scale (mAS) scores and goniometry measurements. Results and conclusion: In a mean follow-up of 3.2 years, SDR provides a measurable and consistent improvement in the motor function of spastic patients, as per range of motion and tonus scales, with low complication rates. It also allows for patients to reduce their use of muscle relaxants, even though their global mobility does not change significantly. Therefore, it should be considered for CP patients who suffer with the deleterious effects of spasticity.

PMID: 34316304

**2. Outcomes and Complications in Management of Congenital Myopathy Early-Onset Scoliosis**
Lacey Magee, Joshua T Bram, Jason B Anari, Brandon Ramo, Oscar H Mayer, Hiroko Matsumoto, Jaysson T Brooks, Lindsay Andras, Robert Lark, Ryan Fitzgerald, Walter Truong, Ying Li, Lawrence Karlin, Richard Schwend, Stuart Weinstein, David Roye, Brian Snyder, John M Flynn, Matthew Oetgen, John Smith, Patrick J Cahill, PSSG

J Pediatr Orthop. 2021 Jul 29. doi: 10.1097/BPO.0000000000001922. Online ahead of print.

Background: Congenital myopathies (CMs) are complex conditions often associated with early-onset scoliosis (EOS). The purpose of this study was to investigate radiographic outcomes in CM patients undergoing EOS instrumentation as well as complications. Secondarily, we sought to compare these patients to a population with higher prevalence, cerebral palsy (CP) EOS patients. Methods: This is a retrospective study of a prospectively collected multicenter registry. The registry was queried for EOS patients with growth-sparing instrumentation (vertical expandable prosthetic titanium ribs, magnetically controlled growing rods, traditional growing rod, or Shilla) and a CM or CP diagnosis with minimum 2 years follow-up. Outcomes included major curve magnitude, T1-S1 height, kyphosis, and complications. Results: Sixteen patients with CM

were included. Six (37.5%) children with CM experienced 11 complications by 2 years. Mean major curve magnitude for CM patients was improved postoperatively and maintained at 2 years (P<0.01), with no significant increase in T1-S1 height or maximum kyphosis(P>0.05). Ninety-seven patients with CP EOS were included as a comparative cohort. Fewer CP patients required baseline respiratory support compared with CM patients (20.0% vs. 92.9%, P<0.01). Fifty-four (55.7%) CP patients experienced a total of 105 complications at 2 years. There was no evidence that the risk of complication or radiographic outcomes differs between cohorts at 2 years, though CP EOS patients experienced significant improvement in all measurements at 2 years. Conclusions: EOS CM children face a high risk of complication after growing instrumentation, with similar curve correction and risk of complication to CP patients. Level of evidence: Level III.

PMID: 34325442

**3. Health-related quality of life and caregiver burden after hip reconstruction and spinal fusion in children with spastic cerebral palsy**
Rachel L DiFazio, Judith A Vessey, Patricia E Miller, Brian D Snyder, Benjamin J Shore

Dev Med Child Neurol. 2021 Jul 23. doi: 10.1111/dmcn.14994. Online ahead of print.

Aim: To evaluate the effect of hip reconstruction or spinal fusion on health-related quality of life (HRQoL) in non-ambulatory children with spastic cerebral palsy (CP) and caregiver burden. Method: This was a prospective, longitudinal study of changes in HRQoL and caregiver burden over the 5 years after surgical correction of hip instability or scoliosis in children with bilateral spastic CP classified in Gross Motor Function Classification levels IV or V. Serial parent proxy measures of HRQoL and caregiver burden were obtained before and 6 weeks, and 3, 6, 9, 12, 24, and 60 months after surgery using the Caregiver Priorities and Child Health Index of Life with Disabilities and the Assessment of Caregiver Experience with Neuromuscular Disease. Scores 5 years or more after surgery were compared to pre-surgery scores using paired Student's t-tests. Serial outcome trajectories were estimated by linear mixed modelling. Results: Of 69 participants (40 males, 29 females; mean age 11y 6mo, SD 4y 1mo, range 3y 10mo-20y 7mo), 43 had hip reconstruction and 26 had spinal fusion. Clinically significant improvements in HRQoL were detected (average increase 7.6 points) 5 years or more postoperatively, with hip reconstruction providing greater benefit. Domains improved by surgery included positioning, transferring/mobility, comfort/emotions, and health. Caregiver burden did not change as these children remain maximally dependent. Interpretation: Surgical treatment of hip and spine deformity improves HRQoL, especially for painful hip instability, but does not change caregiver burden.

PMID: 34296760

**4. A new technique for proximal femoral resection in non-ambulatory patients with cerebral palsy**
Léonard Duporté, Marion Delpont, Jérôme Cottalorda, Pauline Joly Monrigal, Djamel Louahem M'Sabah, Clément Jeandel

Orthop Traumatol Surg Res. 2021 Jul 21;103019. doi: 10.1016/j.otsr.2021.103019. Online ahead of print.

Proximal femoral resection may be proposed to non-ambulatory patients with cerebral palsy and chronic painful hip dislocation. McCarthy's technique confers good results but does not solve the problems related to femoral reascension (bone migration causing painful osseous or cutaneous conflict). We describe a new technique of resection-interposition of the proximal end of the femur which preserves the greater trochanter by an orthogonal osteotomy below the lesser trochanter while maintaining the gluteal-vastus lateralis strut in continuity. A suture of the remaining joint capsule upon itself and a trans-trochanteric capsulodesis are associated to stabilize the cephalic displacement of the femur.

PMID: 34302999

**5. Contribution of altered corticospinal microstructure to gait impairment in children with cerebral palsy**
Shahla Azizi, Ashkan Irani, Amin Shahrokhi, Elham Rahimian, Mehdi M Mirbagheri

Clin Neurophysiol. 2021 Jul 15;132(9):2211-2221. doi: 10.1016/j.clinph.2021.06.016. Online ahead of print.

Objective: Corticospinal tract (CST) injury may lead to motor disorders in children with Cerebral Palsy (CP). However, the precise underlying mechanisms are still ambiguous. We aimed to characterize the CST structure and function in children with CP and determine their contributions to balance and gait impairments. Method: Twenty-six children with spastic CP participated. Transcranial magnetic stimulation (TMS) and diffusion tensor imaging (DTI) were utilized to characterize CST structure and function. Common clinical measures were used to assess gait speed, endurance and balance, and mobility. Results: CST structure and function were significantly altered in children with CP. Different abnormal patterns of CST structure were identified as either abnormal appearance of brain hemispheres (Group-1) or semi-normal CST appearance (Group-2). We found significant correlations between the DTI parameters of the more affected CST and gait features only in Group-1. Conclusion: CST structure and function are abnormal in children with CP and these abnormalities may contribute to balance and gait impairment in some children with CP. Significance: Our findings may lead to the development of further investigations on the mechanisms underlying gait impairment in children with CP and on decision-making for more effective rehabilitation.

PMID: 34311204

**6. Rectus femoris surgery for the correction of stiff knee gait in cerebral palsy: a systematic review and meta-analysis**
Antoine Josse, Christelle Pons, Camille Printemps, Julie Chan-Waï-Nam, Hassene Affes, Sylvain Brochard, Matthias Thépaut

Review Orthop Traumatol Surg Res. 2021 Jul 24;103022. doi: 10.1016/j.otsr.2021.103022. Online ahead of print.

Introduction: Rectus femoris (RF) transfer was long the gold-standard treatment for stiff knee gait (SKG), but efficacy now seems less than that of distal RF release. The aim of the present study was to compare efficacy between the two. The study hypothesis was that both significantly improve 4 knee kinematic parameters at 1 year. Patients and method: A meta-analysis was performed, using PRISMA criteria, on the Medline, Science Direct, Cochrane Registry, Scopus and Pascal databases. Search was conducted up to March 1, 2020 by two authors (A.J & M.T). Study methodology was assessed on MINORS index. Inclusion criteria comprised patients with SKG, treated by RF transfer or distal release. Endpoints comprised: Peak Knee Flexion in swing phase (PKFSW), Knee Range of Motion (KROM), time to Peak Knee Flexion (t-PKFGC), and Maximum Knee Extension in stance phase (MKEST). Effect size was assessed on Standard Mean Deviation (SMD). Results: 695 studies were identified, 16 of which were included: 14 transfer, 5 release. Data were analyzed for 1,079 limbs in 768 patients. Only transfer improved PKFSW, with small effect size (SMD = 0.29). The other 3 parameters were improved by both techniques, with moderate effect size. Discussion: Results showed improved knee kinematics after RF transfer, but with small or moderate effect size. The effect of distal release on PKF could not be assessed, due to publication bias. The heterogeneity of studies and low levels of evidence call for caution in interpreting the present results. Level of evidence: III.

PMID: 34314902

**7. Evaluation of Complications and Weight Outcomes in Pediatric Cerebral Palsy Patients With Gastrostomy Tubes**
Jihane Jadi, Sudipta Hyder, Nidia P Rodriguez Ormaza, Emma Twer, Michael Phillips, Adesola Akinkuotu, Trista D Reid

Am Surg. 2021 Jul 28;31348211034753. doi: 10.1177/00031348211034753. Online ahead of print.

Background: Feeding difficulties are common in children with cerebral palsy (CP). The goal of this study was to examine pediatric CP patients undergoing gastrostomy tube (G tube) placement and assess the association between patient characteristics and weight after 3 months, 6 months, and 1 year. Methods: This was a retrospective study of all pediatric patients with CP who received a G tube placement between April 2014 and December 2017 at a single institution. Bivariate analysis was used to examine association between patient characteristics and the primary outcome of improvement in weight Z score at 3, 6, and 12 months. Results: Of 63 patients who received a G tube, 81% had an increase in Z score at 3 months, 44% at 6 months, and 64% at 12 months. By 12 months, factors associated with a positive Z score change included moderate and severe malnutrition, lack of prior G tube, and fewer comorbidities. The majority (69.8%) of patients experienced complications. Seven (11%) patients died, with only 1 death related to G tube placement. Discussion: The use of G tubes in CP patients resulted in an increase in an improvement in nutritional status for the majority of patients over the course of a year. Although most complications were minor, patients had a high complication rate and frequently visited the emergency department, highlighting the need for standardized education and follow-up among this patient population.

PMID: 34318698

**8. Recurrent pain in a child with cerebral palsy: Questions**
Andrea Trombetta, Simone Benvenuto, Egidio Barbi

Pediatr Nephrol. 2021 Jul 29. doi: 10.1007/s00467-021-05147-z. Online ahead of print.

PMID: 34324050

**9. Recurrent pain in a child with cerebral palsy: Answers**
Andrea Trombetta, Simone Benvenuto, Egidio Barbi

Pediatr Nephrol. 2021 Jul 29. doi: 10.1007/s00467-021-05156-y. Online ahead of print.

PMID: 34324051

**10. Visual function assessment, ocular examination, and intervention in children with developmental delay: A systematic approach - Part 2**
Deiva Jayaraman, Namita Jacob, Meenakshi Swaminathan

Review Indian J Ophthalmol. 2021 Aug;69(8):2012-2017. doi: 10.4103/ijo.IJO_2396_20.

In India, there is increasing number of children with development delay and vision impairment with or without additional disabilities due to prematurity, brain damage, cerebral palsy, or genetic syndromes. Despite initiatives from Government of India, early intervention for these children remains a challenge across the country due to lack of trained professionals and appropriate resources. This paper describes the developmental screening tools, intervention aspects including Individualized Education Plan, procedures for handling children with cerebral visual impairment, team approach, and guidelines derived from the inputs of experts in vision rehabilitation centers of premier eye institutes in India.

PMID: 34304167

**11. How Did the Lockdown Imposed Due to COVID-19 Affect Patients With Cerebral Palsy?**
Bilinc Dogruoz Karatekin, Afitap İcagasioglu, Seyma Nur Sahin, Gülnihal Kacar, Fethullah Bayram

Pediatr Phys Ther. 2021 Jul 27. doi: 10.1097/PEP.0000000000000818. Online ahead of print.

Background: The novel coronavirus infection (SARS-CoV-2) caused disruption of the treatment and follow-up evaluations of children with cerebral palsy. Aim: The change in mobility, pain, functional status, and spasticity was investigated who were followed in a pediatric rehabilitation unit after the lockdown. Methods: One hundred ten children were evaluated. Pain, severity of spasticity, botulinum toxin administration dates, and continuity of home exercises were recorded. The functional status was evaluated with the Functional Independence Measure for Children (WeeFIM). Results: The WeeFIM self-care and mobility subscale scores and total scores were significantly worse. Only 5 of the participants had pain in the previous evaluations; in the last evaluation, 29 had pain complaints. The pain and spasticity severity of the participants whose botulinum toxin administration was delayed were significantly increased. Conclusions: The children with cerebral palsy should be followed with telemedicine at short intervals, and when necessary, in the hospital.

PMID: 34323865

**12. Diagnostic yield of chromosomal microarray and trio whole exome sequencing in cryptogenic cerebral palsy**
Michal Yechieli, Suleyman Gulsuner, Hilla Ben-Pazi, Aviva Fattal, Adi Aran, Alla Kuzminsky, Liora Sagi, Dafna Guttman, Nira Schneebaum Sender, Varda Gross-Tsur, Tehila Klopstock, Tom Walsh, Paul Renbaum, Sharon Zeligson, Lilach Shemer Meiri, Dorit Lev, Dorit Shmueli, Luba Blumkin, Amnon Lahad, Mary-Claire King, Ephrat Lahad Levy, Reeval Segel

J Med Genet. 2021 Jul 28;jmedgenet-2021-107884. doi: 10.1136/jmedgenet-2021-107884. Online ahead of print.

Objective: To determine the yield of genetic diagnoses using chromosomal microarray (CMA) and trio whole exome sequencing (WES), separately and combined, among patients with cryptogenic cerebral palsy (CP). Methods: Trio WES of patients with prior CMA analysis for cryptogenic CP, defined as disabling, non-progressive motor symptoms beginning before the age of 3 years without known cause. Results: Given both CMA analysis and trio WES, clinically significant genetic findings were identified for 58% of patients (26 of 45). Diagnoses were eight large CNVs detected by CMA and 18 point mutations detected by trio WES. None had more than one severe mutation. Approximately half of events (14 of 26) were de novo. Yield was significantly higher in patients with CP with comorbidities (69%, 22 of 32) than in those with pure motor CP (31%, 4 of 13; p=0.02). Among patients with genetic diagnoses, CNVs were more frequent than point mutations among patients with congenital anomalies (OR 7.8, 95% CI 1.2 to 52.4) or major dysmorphic features (OR 10.5, 95% CI 1.4 to 73.7). Clinically significant mutations were identified in 18 different genes: 14 with known involvement in CP-related disorders and 4 responsible for other neurodevelopmental conditions. Three possible new candidate genes for CP were ARGEF10, RTF1 and TAOK3. Conclusions: Cryptogenic CP is genetically highly heterogeneous. Genomic analysis has a high yield and is warranted in all these patients. Trio WES has higher yield than CMA, except in patients with congenital anomalies or major dysmorphic features, but these methods are complementary. Patients with negative results with one approach should also be tested by the other.

PMID: 34321325

**13. Stretch-induced satellite cell deformation in contractured muscles in children with cerebral palsy**
Peter B Dykstra, Sudarshan Dayanidhi, Henry G Chambers, Richard L Lieber

J Biomech. 2021 Jul 14;126:110635. doi: 10.1016/j.jbiomech.2021.110635. Online ahead of print.

Satellite cells (SCs) are quiescent, adult skeletal muscle stem cells responsible for postnatal muscle growth and repair. Children with cerebral palsy (CP) have muscle contractures with reduced SC abundance, extracellular matrix abnormalities and reduced serial sarcomere number resulting in greatly increased in vivo sarcomere length, perhaps due to impaired sarcomere addition, compared to children with typical development (TD). Stretch is a strong activator of SCs that leads to addition of sarcomeres during bone-muscle growth. Mechanical loading and subsequent deformation of intracellular structures can lead to activation and proliferation, perhaps by cytoskeletal transmissions of extracellular mechanical signals to the nuclei. The primary aim of this study was to determine the effect of ex vivo stretch-induced sarcomere length change on SC deformation in children with CP and TD. Muscle biopsies were obtained from twelve children (7 CP, 5 TD) during surgery. Fiber bundles were labeled with fluorescent antibodies for Pax7 (SC), DRAQ5 (nuclei), and alpha-actinin (sarcomere protein). Fibers were stretched using a custom jig and imaged using confocal microscopy. SC nuclear length, height and aspect ratio underwent increased deformation with increasing sarcomere length ($p < 0.05$) in both groups. Slopes of association for SC nuclear length, aspect ratio and sarcomere lengths were similar between CP and TD. Our results indicate that SC in children with CP undergo similar deformation as TD across sarcomere lengths.

PMID: 34303895

**14. Cardiovascular and Cerebrovascular Implications of Growth Restriction: Mechanisms and Potential Treatments**
Charmaine R Rock, Tegan A White, Beth R Piscopo, Amy E Sutherland, Suzanne L Miller, Emily J Camm, Beth J Allison

Review Int J Mol Sci. 2021 Jul 14;22(14):7555. doi: 10.3390/ijms22147555.

Fetal growth restriction (FGR) is a common complication of pregnancy, resulting in a fetus that fails to reach its genetically determined growth potential. Whilst the fetal cardiovascular response to acute hypoxia is well established, the fetal defence to chronic hypoxia is not well understood due to experiment constraints. Growth restriction results primarily from reduced oxygen

and nutrient supply to the developing fetus, resulting in chronic hypoxia. The fetus adapts to chronic hypoxia by redistributing cardiac output via brain sparing in an attempt to preserve function in the developing brain. This review highlights the impact of brain sparing on the developing fetal cardiovascular and cerebrovascular systems, as well as emerging long-term effects in offspring that were growth restricted at birth. Here, we explore the pathogenesis associated with brain sparing within the cerebrovascular system. An increased understanding of the mechanistic pathways will be critical to preventing neuropathological outcomes, including motor dysfunction such as cerebral palsy, or behaviour dysfunctions including autism and attention-deficit/hyperactivity disorder (ADHD).

PMID: 34299174

**15. Head Circumference within the Normal Range and Neurodevelopmental Outcomes in Preterm Infants**
Elisa T Bushman, Christina Blanchard, Rachael G Sinkey, Stacy Harris, Brian Casey, Alan T Tita, Manimaran Ramani, Lorie M Harper

Am J Perinatol. 2021 Jul 29. doi: 10.1055/s-0041-1732460. Online ahead of print.

Objective: We sought to determine if variation in head circumference (HC) within the range of normal (5th-10th and 90th-95th percentile) is associated with poor neurodevelopmental outcomes (NDO), which defined as mild or moderate delay by Bayley II psychometrics (BSID-II). Study design: This is a secondary analysis of a randomized controlled trial assessing the benefits of magnesium for the prevention of cerebral palsy. Fetuses with a normal HC at birth defined as within 5th to 95th percentile were included. NDO were assessed at age 2 with BSID-II. Moderate delay was defined as a score <70 and mild delay as <85. HC was classified as small normal (5th-10th percentile), normal (10th-90th percentile), and large normal (90th-95th percentile). Logistic regression models adjusted for confounding. Linear regression models estimated the impact for every 1 cm of change in HC. Results: Of 1,236 included infants, 111 (8%) had small normal HC; 1,058 (85%) had normal HC; and 67 (5%) had large normal HC. Baseline characteristics were similar between groups. There was no association with changes in HC within the range of normal and developmental indices. When considered as a continuous variable, every 1 cm increase in HC was also not associated with a significant change in developmental indices. Conclusion: Within the normal range (5th-95th percentile), changes in HC did not correlate with changes in NDO at 2 years as measured by Bayley II scales. Key points: · It is unknown if variations in normal HC are associated with poor neurodevelopmental outcomes. · Alterations in HC within the range of normal (5th-95th percentile) are not associated with adverse NDO. · When considered as a continuous variable, a 1 cm increase in HC is not associated with adverse NDO. · Changes in HC within the range of normal do not appear to be a pathologic change altering NDO.

PMID: 34327687

**16. Necrotizing Enterocolitis in Neonates: Has the Brain Taken a Hit 10 Years Later?**
Ankita Mondal, Devesh Misra, Ahmed Al-Jabir, Dalal Hubail, Thomas Ward, Bijendra Patel

J Pediatr Neurosci. Jan-Mar 2021;16(1):30-34. doi: 10.4103/jpn.JPN_41_20. Epub 2021 Jun 25.

Background: The neonate with necrotizing enterocolitis (NEC) is at risk of developing poor neurodevelopmental outcomes. There is a dearth of long-term follow-up studies in this field, with a majority of studies reporting a follow-up duration of 2 years. The aim of this study was to assess neurodevelopment of babies diagnosed with NEC more than a decade ago. This study was carried out in a tertiary hospital with neonatal surgery and intensive care units. Materials and methods: Retrospective review of notes and telephone interviews with parents of babies diagnosed with NEC between January 2007 and December 2008 was conducted. Evidence of motor, cognitive, and sensory impairment was recorded. Fisher's exact, $\chi 2$, and unpaired t-tests were used. P-values <0.05 were considered significant. Results: Overall mortality in this cohort was 31%. Eighteen patients were followed up to an average age of 11.2 years. Of the 18 patients, 11 (61%) had a neurological impairment. Of the 15 surgically managed patients, 10 (67%) had an impairment and, of the 3 medically managed patients, 1 (33%) had an impairment. Cognitive impairment was the most common (10/18, 56%), followed by motor (6/18, 33%). Ten of 18 (56%) had special education needs, 9 of 18 (50%) had learning difficulties, 6 of 18 (33%) had speaking difficulties, and 4 of 18 (22%) had cerebral palsy. Patients also had behavioral conditions (3/18, 17%), visual impairment (2/18, 11%), and seizures (2/18, 11%). Conclusion: In the field of NEC, there is a hidden neurological burden that neonatal surgeons bequeath to the community. Sixty-one percent of patients are neurologically impaired, affecting the quality of life and function in the long-term. There should be appropriate parent counseling at the point of diagnosis and regular development checks for children with NEC.

PMID: 34316305

**17. Neonatal encephalopathy: Focus on epidemiology and underexplored aspects of etiology**
S McIntyre, K B Nelson, S B Mulkey, M Lechpammer, E Molloy, N Badawi, Newborn Brain Society Guidelines and Publications Committee

Review Semin Fetal Neonatal Med. 2021 Jul 15;101265. doi: 10.1016/j.siny.2021.101265. Online ahead of print.

Neonatal Encephalopathy (NE) is a neurologic syndrome in term and near-term infants who have depressed consciousness, difficulty initiating and maintaining respiration, and often abnormal tone, reflexes and neonatal seizures in varying combinations. Moderate/severe NE affects 0.5-3/1000 live births in high-income countries, more in low- and middle-income countries, and carries high risk of mortality or disability, including cerebral palsy. Reduced blood flow and/or oxygenation around the time of birth, as with ruptured uterus, placental abruption or umbilical cord prolapse can cause NE. This subset of NE, with accompanying low Apgar scores and acidemia, is termed Hypoxic-Ischemic Encephalopathy. Other causes of NE that can present similarly, include infections, inflammation, toxins, metabolic disease, stroke, placental disease, and genetic disorders. Aberrant fetal growth and congenital anomalies are strongly associated with NE, suggesting a major role for maldevelopment. As new tools for differential diagnosis emerge, their application for prevention, individualized treatment and prognostication will require further systematic studies of etiology of NE.

PMID: 34305025

**18. MRI combined with early clinical variables are excellent outcome predictors for newborn infants undergoing therapeutic hypothermia after perinatal asphyxia**
Marianne Thoresen, Sally Jary, Lars Walløe, Mathias Karlsson, Miriam Martinez-Biarge, Ela Chakkarapani, Frances M Cowan

EClinicalMedicine. 2021 May 17;36:100885. doi: 10.1016/j.eclinm.2021.100885. eCollection 2021 Jun.

Background: Binary prediction-models for outcome [death, cognition, presence and severity of cerebral palsy (CP)], using MRI and early clinical data applicable for individual outcome prediction have not been developed. Methods: From Dec 1st 2006 until Dec 31st 2013, we recruited 178 infants into a population-based cohort with moderate or severe hypoxic-ischaemic encephalopathy (HIE) including postnatal collapse (PNC, n = 12) and additional diagnoses (n = 12) using CoolCap/TOBY-trial entry-criteria including depressed amplitude-integrated EEG (aEEG). Early clinical/biochemical variables and MRI scans (median day 8) were obtained in 168 infants. Injury severity was scored for cortex, basal ganglia/thalami (BGT), white matter (WM) and posterior limb of the internal capsule, summating to a total injury score (TIS, range 0-11). Outcome was categorized as adverse or favourable at 18-24 months from Bayley-III domains (cut-off 85) and neurological examination including CP classification. Findings: HIE and entry-aEEG severity were stable throughout the study. Outcome was favourable in 133/178 infants and adverse in 45/178: 17 died, 28 had low Cognition/Language scores, (including 9 with severe CP and 6 mild); seven had mild CP with favourable cognitive outcome. WMxBGT product scores and TIS were strong outcome predictors, and prediction improved when clinical/biochemical variables were added in binary logistic regression. The Positive Predictive Value for adverse outcome was 88%, increasing to 95% after excluding infants with PNC and additional diagnoses. Using WMxBGT in the regression predicted 8 of the 9 children with severe CP. Interpretation: Binary logistic regression with WMxBGT or TIS and clinical variables gave excellent outcome prediction being 12% better than single variable cross-tabulation. Our MRI scoring and regression models are readily accessible and deserve investigation in other cohorts for group and individual prediction. Funding: We thank the National Health Service (NHS) and our Universities and funders in UK and Norway: SPARKS, The Moulton Foundation, The Norwegian Research Council, The Lærdal Foundation for Acute Medicine and charitable donations for their support for cooling therapy.

PMID: 34308304

**19. Medico-legal considerations in the context of neonatal encephalopathy and therapeutic hypothermia**
Jonathan M Fanaroff, Michael G Ross, Steven M Donn, Newborn Brain Society Guidelines and Publications Committee

Review Semin Fetal Neonatal Med. 2021 Jul 8;101266. doi: 10.1016/j.siny.2021.101266. Online ahead of print.

Neonatal encephalopathy (NE) is a significant complication of the peripartum period. It can lead to lifelong neurologic disabilities, including cerebral palsy, cognitive impairments, developmental delays, and epilepsy. Induced hypothermia is the first therapy, which has shown promise in improving the outcomes for neonates with moderate to severe NE following a presumed intrapartum insult. NE is also a frequent source of medical malpractice litigation. In this paper, we will review salient features of the American Tort System as it pertains to medical malpractice. We will discuss the obstetric medico-legal implications of therapeutic hypothermia and suggest a five-step approach to analyzing neonatal cases for causation, etiology, timing of occurrence, responsibility, and liability. We will close with three illustrative clinical cases.

PMID: 34301500

**20. Subcutaneous fat necrosis in an infant with hypoxic ischaemic encephalopathy stage 3: an uncommon association**
Sonalika Mehta, Naveen Parkash Gupta, Anil Batra, Rashmi Sharma

Case Reports BMJ Case Rep. 2021 Jul 28;14(7):e237933. doi: 10.1136/bcr-2020-237933.

Subcutaneous fat necrosis (SCFN) is inflammation and necrosis of adipose tissue associated with hypoxia and hypothermia. It leads to various metabolic abnormalities, of which the most dreaded is hypercalcaemia. We report a case of a 7-week-old boy with history of birth asphyxia (hypoxic ischaemic encephalopathy stage 3) who presented to us with features suggestive of hypercalcaemia with bilateral nephrocalcinosis. On examination, there were multiple subcutaneous nodules on both arms. Evaluation revealed suppressed parathyroid activity along with low levels of 25(OH)vitamin D3 and elevated 1,25-dihydroxyvitamin D3 Skin biopsy confirmed the diagnosis of SCFN. He was managed with intravenous fluids, single dose of intravenous furosemide and oral prednisolone. Hypercalcaemia responded within 14 days of admission, prednisolone was tapered and stopped in a month. SCFN, in our case, can be attributed to the underlying perinatal asphyxia along with use of therapeutic hypothermia. Through this case, we wish to sensitise practicing neonatologists for the need of screening and early identification of these abnormalities, which if missed can be fatal.

PMID: 34321259

**21. Early micro- and macrostructure of sensorimotor tracts and development of cerebral palsy in high risk infants**
Rahul Chandwani, Julia E Kline, Karen Harpster, Jean Tkach, Nehal A Parikh, Cincinnati Infant Neurodevelopment Early Prediction Study (CINEPS) Group

Hum Brain Mapp. 2021 Jul 29. doi: 10.1002/hbm.25579. Online ahead of print.

Infants born very preterm (VPT) are at high risk of motor impairments such as cerebral palsy (CP), and diagnosis can take 2 years. Identifying in vivo determinants of CP could facilitate presymptomatic detection and targeted intervention. Our objectives were to derive micro- and macrostructural measures of sensorimotor white matter tract integrity from diffusion MRI at term-equivalent age, and determine their association with early diagnosis of CP. We enrolled 263 VPT infants (≤32 weeks gestational age) as part of a large prospective cohort study. Diffusion and structural MRI were acquired at term. Following consensus guidelines, we defined early diagnosis of CP based on abnormal structural MRI at term and abnormal neuromotor exam at 3-4 months corrected age. Using Constrained Spherical Deconvolution, we derived a white matter fiber orientation distribution (fOD) for subjects, performed probabilistic whole-brain tractography, and segmented nine sensorimotor tracts of interest. We used the recently developed fixel-based (FB) analysis to compute fiber density (FD), fiber-bundle cross-section (FC), and combined fiber density and cross-section (FDC) for each tract. Of 223 VPT infants with high-quality diffusion MRI data, 14 (6.3%) received an early diagnosis of CP. The cohort's mean (SD) gestational age was 29.4 (2.4) weeks and postmenstrual age at MRI scan was 42.8 (1.3) weeks. FD, FC, and FDC for each sensorimotor tract were significantly associated with early CP diagnosis, with and without adjustment for confounders. Measures of sensorimotor tract integrity enhance our understanding of white matter changes that antecede and potentially contribute to the development of CP in VPT infants.

PMID: 34322949

**22. Measuring the impact of dyskinesia on function in children with dyskinetic cerebral palsy**
Kate Himmelmann

Dev Med Child Neurol. 2021 Jul 23. doi: 10.1111/dmcn.14992. Online ahead of print.

PMID: 34297844

**23. Meridian acupuncture plus massage for children with spastic cerebral palsy**
Kunzhi Chen, Shiju Shu, Mei Yang, Shengbing Zhong, Feng Xu

Am J Transl Res. 2021 Jun 15;13(6):6415-6422. eCollection 2021.

Objective: To evaluate the effect of combination therapy of meridian acupuncture and massage on motor development in children with spastic cerebral palsy (SCP). Methods: A total of 113 children with SCP in our hospital were allocated into research group (63 cases, treated with meridian acupuncture plus massage) and control group (50 cases, treated with routine rehabilitation measures). Clinical efficacy and alterations of inflammatory factors were observed. Peabody Developmental Motor Scale (PDMS) and gross motor function measure (GMFM-88; sitting, standing, walking) were employed for the assessment of motor ability. Changes in muscle tension were monitored with the Ashworth scale (AS), and modified Barthel index (MBI) and Gesell's Developmental Schedule (GDS) were used to evaluate children's daily activities, language, fine motor skills, and adaptability. Finally, the development of children in the two groups was monitored. Results: The research group had higher total effective rate than the control group (P=0.018). After treatment, the levels of interleukin 6 (IL-6) and tumor necrosis factor-α (TNF-α) in the research group were lower than those in the control group (P<0.05); the PDMS and AS scores were reduced in both groups, and the reduction was greater in research group (P<0.05); GFMF-88, Barthel and GDS scores increased in both groups, especially in the research group; children in research group were better developed than those in control group (P<0.05). Conclusion: Meridian acupuncture plus massage contributes to a significant improvement of motor development in children with SCP.

PMID: 34306381

**24. Vitamin D Status in Children on Anticonvulsant Therapy**
Madhava Vijayakumar, Ajitha Bk, Biju George, Vijayalakshmi Bhatia

Indian J Pediatr. 2021 Jul 28. doi: 10.1007/s12098-021-03853-y. Online ahead of print.

Objective: To assess vitamin D status of children on long-term anticonvulsants, including the less studied widely used levetiracetam, and the potential risk factors for deficiency. Method: Children on antiepileptic drugs (cases, n = 269) were compared with controls (n = 295) for serum biochemistry, 25OHD, parathormone (PTH), sun exposure, dietary calcium, and vitamin D intake. Results: Cases had lower serum 25OHD [median (IQR) 18.4 (11.5-24.1) ng/mL] compared to controls [20.8 (15.4-26.2] ng/mL, p < 0.001), as well as more frequent vitamin D deficiency (25OHD < 12 ng/mL, 27.1%) and insufficiency (25OHD < 20 ng/mL, 57.6%) than did controls (11.2% and 46.1%, respectively). Significantly lower median (IQR) serum calcium [8.8 (8.1-9.4) vs. 9.2 (8.5-10.0) mg/dL], phosphorous [3.8 (3.3-4.2) vs. 4.7 (4.0-5.3) mg/dL), and higher PTH [58.4 (42.9-85.8) vs. 38.9 (24.6-55.5) pg/mL, p < 0.001 for all] and proportion of elevated alkaline phosphatase (11.2% vs. 5.1%, p < 0.01) was seen in cases versus controls. Vitamin D deficiency was present in 53.4% of children with cerebral palsy (CP) versus 19.9% in those without CP (p < 0.001). Serum 25OHD did not differ between patients on cytochrome P450 inducers versus noninducers, neither among the 3 major groups, users of carbamazepine, valproate, and levetiracetam. Logistic regression analysis showed serum 25OHD < 12 ng/mL to be independently influenced by case or control status, presence of CP, and season of sampling. Conclusion: Vitamin D deficiency is common with anticonvulsant therapy, especially in those having CP. In Kerala, the hot, dry season from March to May is protective.

PMID: 34318406

**25. Video Visual Scene Displays with Dynamic Text: Effect on Single-Word Reading by an Adolescent with Cerebral Palsy**

Kelsey Mandak, Janice Light, David McNaughton

Perspect ASHA Spec Interest Groups. 2020 Oct;5(5):1272-1281. doi: 10.1044/2020_persp-20-00068.

Purpose: The purpose of this study was to investigate the effect of the Transition to Literacy (T2L) feature within video visual scene displays (VSDs) on the single-word reading of academic vocabulary concepts (i.e., weather concepts) by a pre-literate adolescent with cerebral palsy and minimal speech. Method: A single-subject, multiple probe, across word sets design was used to evaluate the effects of the intervention. The intervention used an AAC app programmed with video VSDs embedded with hotspots with the T2L feature to teach the adolescent 12 academic vocabulary words. Results: The adolescent acquired all target words successfully with only minimal exposure to the written words through the app and was able to generalize her learning to two novel tasks. Using Tau-U to evaluate the size of the observed effects, there were very large effects across all word sets. Conclusion: The findings from this study demonstrate the effectiveness of the T2L feature to improve single-word reading in pre-literate individuals with minimal speech. The use of video VSDs and T2L technology together may offer professionals a unique way to complement current AAC devices and literacy instruction for adolescents with minimal speech who are pre-literate.

PMID: 34307883