Cerebral palsy research news

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Macquarie Group Foundation Chair of Cerebral Palsy

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Interventions and Management

1. Effectiveness of robotic-assisted therapy for upper extremity function in children and adolescents with cerebral palsy: a systematic review protocol
Sasithorn Sung-U, Badur Un Nisa, Kayano Yotsumoto, Rumi Tanemura

BMJ Open. 2021 May 11;11(5):e045051. doi: 10.1136/bmjopen-2020-045051.

Introduction: The application of advanced technologies in paediatric rehabilitation to improve performance and enhance everyday functioning shows considerable promise. The aims of this systematic review are to investigate the effectiveness of robotic-assisted therapy for upper extremity function in children and adolescents with cerebral palsy and to extend the scope of intervention from empirical evidence. Methods and analysis: Multiple databases, including MEDLINE (Ovid), PubMed, CINAHL, Scopus, Web of Science, Cochrane Library and IEEE Xplore, will be comprehensively searched for relevant randomised controlled trials and non-randomised studies. The grey literature will be accessed on the ProQuest Dissertations & Theses Global database, and a hand search from reference lists of previous articles will be performed. The papers written in English language will be considered, with no limitation on publication date. Two independent reviewers will identify eligible studies, evaluate the level of evidence (the Oxford Centre for Evidence-Based Medicine) and appraise methodological quality and risk of bias (the Standard quality assessment criteria for evaluating primary research papers from a variety of fields (QualSyst tool); the Grading of Recommendations Assessment, Development and Evaluation). Data will be appropriately extracted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline. A narrative synthesis will be provided to summarise the results, and a meta-analysis will be conducted if there is sufficient homogeneity across outcomes. Prospero registration number: CRD42020205818. Ethics and dissemination: Ethical approval is not required for this study. The findings will be disseminated via a peer-reviewed journal and international conferences.

PMID: 33980527

2. Relative independence of upper limb position sense and reaching in children with hemiparetic perinatal stroke
Andrea M Kuczynski, Adam Kirton, Jennifer A Semrau, Sean P Dukelow

J Neuroeng Rehabil. 2021 May 12;18(1):80. doi: 10.1186/s12984-021-00869-5.

Background: Studies using clinical measures have suggested that proprioceptive dysfunction is related to motor impairment of the upper extremity following adult stroke. We used robotic technology and clinical measures to assess the relationship between position sense and reaching with the hemiparetic upper limb in children with perinatal stroke. Methods: Prospective term-born children with magnetic resonance imaging-confirmed perinatal ischemic stroke and upper extremity deficits were recruited from a population-based cohort. Neurotypical controls were recruited from the community. Participants completed two tasks in the Kinarm robot: arm position-matching (three parameters: variability [Varxy], contraction/expansion [Areaxy], systematic spatial shift [Shiftxy]) and visually guided reaching (five parameters: posture speed [PS], reaction time [RT], initial

direction error [IDE], speed maxima count [SMC], movement time [MT]). Additional clinical assessments of sensory (thumb localization test) and motor impairment (Assisting Hand Assessment, Chedoke-McMaster Stroke Assessment) were completed and compared to robotic measures. Results: Forty-eight children with stroke (26 arterial, 22 venous, mean age: 12.0 ± 4.0 years) and 145 controls (mean age: 12.8 ± 3.9 years) completed both tasks. Position-matching performance in children with stroke did not correlate with performance on the visually guided reaching task. Robotic sensory and motor measures correlated with only some clinical tests. For example, AHA scores correlated with reaction time ($R = - 0.61$, $p < 0.001$), initial direction error ($R = - 0.64$, $p < 0.001$), and movement time ($R = - 0.62$, $p < 0.001$). Conclusions: Robotic technology can quantify complex, discrete aspects of upper limb sensory and motor function in hemiparetic children. Robot-measured deficits in position sense and reaching with the contralesional limb appear to be relatively independent of each other and correlations for both with clinical measures are modest. Knowledge of the relationship between sensory and motor impairment may inform future rehabilitation strategies and improve outcomes for children with hemiparetic cerebral palsy.

PMID: 33980254

3. Sleep-related breathing disorders associated with intrathecal baclofen therapy to treat patients with cerebral palsy: A cohort study and discussion
Ricky T Mohon, Kim Sawyer, Kaci Pickett, Samantha Bothwell, John T Brinton, Michelle Sorbemonte-King, Lourdes M DelRosso

NeuroRehabilitation. 2021 Apr 30. doi: 10.3233/NRE-210012. Online ahead of print.

Background: Patients with cerebral palsy and other static encephalopathies (CP) are known to be at increased risk of sleep-related breathing disorders (SRBD). Few studies have reviewed whether intrathecal baclofen (ITB) can contribute to SRBD. Objective: To assess the prevalence of SRBD in patients with CP receiving ITB by using nocturnal polysomnography (NPSG). Methods: We performed a retrospective chart review of patients receiving ITB who had NPSG at Children's Hospital Colorado (CHCO) and Seattle Children's Hospital (SCH) from 1995 to 2019. The Gross Motor Function Classification System (GMFCS) measured the severity of motor disability. Screening sleep questionnaires collected subjective data and NPSG provided objective data of SRBD. Results: All patients except one were GMFCS 4 or 5 with median age at ITB pump placement of 9.7 years. The screening questionnaire for SRBD detected one or more nighttime symptoms in > 82%of all patient groups. Pre-ITB criteria for a SRBD was met in 83%of patients at CHCO and 91%at SCH. Post-ITB prevalence remained similarly high. Conclusions: NPSG identified a high prevalence of SRBD in these cohorts from CHCO and SCH. Our study showed neither improvement nor worsening of SRBD in patients receiving ITB.

PMID: 33967066

4. Pediatric Intrathecal Baclofen Pumps: A Descriptive Analysis of Hospital Course and Associated Costs
Jonathan Dallas, Robert P Naftel, Chevis N Shannon

Pediatr Neurosurg. 2021 May 7;1-11. doi: 10.1159/000515988. Online ahead of print.

Introduction: The purpose of this study was to identify predictors of increased cost and postoperative length-of-stay (LOS) following intrathecal baclofen pump (ITBP) placement. Methods: Patients were derived from the 2009/2012 kids' inpatient database. Inclusion criteria were selected for patients with ICD-9 codes 343.X (infantile cerebral palsy), 86.06 (infusion pump insertion), 03.90 (spinal catheter insertion), and elective hospitalizations. Nonparametric univariate analysis and subsequent gamma log-link general linear modeling were used to identify significant predictors of cost/LOS ($p < 0.05$). Results: 529 unweighted patients (787 with survey weights applied) met criteria. Median LOS was 3.00 days, and median cost was USD 23,284. Following multivariate modeling, predictors of increased LOS (in days) included increased hospital ITBP volume ($p = 0.027$), small hospital size (+0.55, $p = 0.004$), device complications (+0.95, $p < 0.001$), procedural complications (+1.40, $p < 0.001$), additional procedures (+0.86, $p < 0.001$), electrolyte abnormalities (+3.74, $p < 0.001$), and neurological comorbidities (+1.60, $p < 0.001$). Factors associated with decreased LOS were paralysis (-0.53, $p < 0.001$), Northeastern hospital region (-0.55, $p = 0.018$), and investor-owned hospital status (-0.75, $p = 0.001$). Similarly, predictors of increased cost included race of Hispanic (+USD 1,156, $p = 0.033$) or "other" (+USD 2,158, $p = 0.001$), Northeast hospital region (+USD 4,120, $p < 0.001$), small (+USD 4,139, $p < 0.001$) or medium (+USD 3,368, $p < 0.001$) hospital sizes, additional procedures (+USD 1,649, $p < 0.001$), neurological comorbidities (+USD 3,222, $p = 0.003$), and increased LOS ($p < 0.001$). Factors associated with decreased cost included Western hospital region (-USD 1,594, $p = 0.001$), government hospitals (-USD 1,391, $p = 0.019$), and investor-owned hospitals (-USD 2,057, $p = 0.021$). Conclusion: This study found multiple variables associated with increased cost/LOS following ITBP placement. Broadly, this analysis demonstrates national trends associated with increased cost following ITBP

placement.

PMID: 33965955

5. Low Rate of Intrathecal Baclofen Pump Catheter-Related Complications: Long-Term Study in Over 100 Adult Patients Associated With Reinforced Catheter
Christina N Feller, Ahmed J Awad, Mary Elizabeth S Nelson, Nicholas Ketchum, Peter A Pahapill

Neuromodulation. 2021 May 11. doi: 10.1111/ner.13412. Online ahead of print.

Objectives: Intrathecal baclofen (ITB) is a cost-effective therapy for patients with severe spasticity. The most common complications are catheter-related complications (CRCs) including kinking/occlusion, blockage, migration, fracture, disconnection, and CSF leak. Our objective was to determine the CRC rate in a large cohort of adults with newly implanted ITB pump systems with polymer reinforced silicone catheters. Materials and methods: This is a retrospective study of a prospectively maintained database consisting of patients who had undergone implantation of ITB pump systems with Ascenda (Medtronic, Minneapolis) catheters from 2013 to 2020. Over this seven-year period, 141 patients underwent ITB pump system implantations; 126 of which had a minimum of one-year follow-up. Results: The 126 patients with a minimum of one year follow-up (average 43 month; range 12-89), had an average age of 51 years (63% male). Severe spasticity was due to spinal cord injury (38%), traumatic brain injury (15%), cerebral palsy (13%), multiple sclerosis (11%), stroke (10%), and other (13%). Nine (7.1%) CRCs occurred in 7 (5.6%) patients (median 6 mo. post-implant): 5 intrathecal catheter occlusions (range 3 -52 months post-implant), two fractures in one patient (6 months), one disconnection at the catheter pump interface (2 months), and one due to kinking at 84 months No migrations occurred. Conclusions: Reported CRCs have been high for ITB pump systems. Ours is the first large cohort, long-term study of CRCs related to reinforced catheters; additionally, our low CRC rate compares favorably to previously published data. Thus, implantation of reinforced catheters may be associated with a low CRC rate.

PMID: 33974333

6. Effects of Physical Therapist Intervention on the Pulmonary Function in Children With Cerebral Palsy: A Systematic Review and Meta-Analysis
Magdalena Rutka, Waclaw M Adamczyk, Paweł Linek

Phys Ther. 2021 May 13;pzab129. doi: 10.1093/ptj/pzab129. Online ahead of print.

Objective: The purpose of this study was to evaluate the effects of physical therapy on pulmonary function and respiratory muscle strength in children with cerebral palsy (CP). Methods: A search of 10 databases was conducted for this systematic review. Initially, there were no language, study design, or time frame restrictions. All studies assessing the effect of physical therapy on the respiratory system in children with CP were included. Two reviewers independently extracted and documented data. The extraction of the data included description of the intervention (duration, therapeutic method) and study results (change of spirometric parameters, respiratory muscle strength). The effects of physical therapist treatment were calculated using software. Results: A total of 269 children aged 5 to 18 years from 10 studies were included. The included studies consisted of 5 different therapeutic methods (inspiratory muscle training [IMT], aerobic training, swimming, respiratory exercise, exercise with elastic bands). Physical therapist intervention led to a significant increase in the maximal expiratory pressure (MEP) (I2 = 0%), peak expiratory flow (I2 = 0%), and maximum oxygen consumption (I2 = 37%). A separate analysis of the most frequently used therapy (IMT) showed a positive effect on MEP (I2 = 0%) and maximal inspiratory pressure (I2 = 35%). Conclusions: Various forms of physical therapy have potential to demonstrate a positive effect on maximal inspiratory pressure, MEP, and peak expiratory flow in children with CP. There is no possibility to recommend the best method and duration of the physical therapy; however, it can be suggested that physical therapy should be applied for at least 4 weeks and include IMT. Impact: CP is one of the most common causes of physical disabilities in children, and pulmonary dysfunction is the leading cause of death in people with CP. Thus, it is warranted to seek different approaches that may improve pulmonary function in people with CP. This review has shown that various forms of physical therapy have potential to improve the pulmonary function of children with CP.

PMID: 33989407

7. The effect of musculoskeletal model scaling methods on ankle joint kinematics and muscle force prediction during gait for children with cerebral palsy and equinus gait
Yunru Ma, Shuyun Jiang, Kumar Mithraratne, Nichola Wilson, Yan Yu, Yanxin Zhang

Comput Biol Med. 2021 May 5;134:104436. doi: 10.1016/j.compbiomed.2021.104436. Online ahead of print.

Clinical gait analysis incorporated with neuromusculoskeletal modelling could provide valuable information about joint movements and muscle functions during ambulation for children with cerebral palsy (CP). This study investigated how imposing pre-calculated joint angles during musculoskeletal model scaling influence the ankle joint angle and muscle force computation. Ten children with CP and equinus gait underwent clinical gait analysis. For each participant, a "default" (scaled without pre-calculated joint angles) and a "PJA" (scaled with pre-calculated ankle joint angles) model were generated to simulate their gait. Ankle joint angles were calculated with an inverse kinematic (IK) and direct kinematic (DK) approach. Triceps surae and tibialis anterior muscle forces were predicted by static optimisation and EMG-assisted modelling. We found that PJA-derived ankle angles showed a better agreement with what derived from the DK approach. The tibialis anterior muscle prediction was more likely to be affected by the scaling methods for the static optimisation approach and the gastrocnemius muscle force prediction was more likely to be influenced for the EMG-assisted modelling. This study recommends using the PJA model since the good consistency between IK and DK-derived joint angles facilitates communication among different research disciplines.

PMID: 33984750

8. Exercise load and physical activity intensity in relation to dystonia and choreoathetosis during powered wheelchair mobility in children and youth with dyskinetic cerebral palsy
Saranda Bekteshi, Ioana Gabriela Nica, Sotirios Gakopoulos, Marco Konings, Rozanne Maes, Benoit Cuyvers, Jean-Marie Aerts, Hans Hallez, Elegast Monbaliu

Disabil Rehabil. 2021 May 10;1-12. doi: 10.1080/09638288.2021.1921064. Online ahead of print.

Purpose: To explore the relation between exercise load, physical activity intensity, and movement disorders during powered wheelchair (PW) mobility in people with severe dyskinetic cerebral palsy (DCP). Methods: Ten participants with DCP, 6-21 years old, users of a head/foot steering system were included. Dystonia and choreoathetosis were assessed using the Dyskinesia Impairment Mobility Scale (DIMS), heart rate (HR) was used to assess the exercise load of the tasks on the participants, and the accelerometry-based activity index (AI) to measure the physical activity intensity and energy expenditure during mobility task performance. Results: Neck- and distal arm dystonia showed significant correlations with HR ($0.64 < rs < 0.77$; $0.009 < p < 0.048$), whereas neck- and proximal arm choreoathetosis with AI ($0.64 < rs < 0.76$, $0.011 < p < 0.044$). Total-body AI was strongly correlated to the AI of the arms ($0.66 < rs < 0.90$, $< 0.001 < p < 0.038$), but not to the AI of the head. Conclusions: During PW mobility tasks, dystonia is associated to exercise load and choreoathetosis to physical activity intensity and energy expenditure. Findings highlight the difficulties in measuring exercise load and activity intensity in PW users with DCP due to the involuntary hypertonic and/or hyperkinetic hallmark of the movement disorders. Nevertheless, a relaxed surrounding with minimal distractions during PW training may increase learning efficiency. Future studies with a bigger sample size are highly recommended to fully establish the relationship between the variables and to allow generalizability of results. Implications for rehabilitation: Dystonia is positively related to heart rate during powered mobility, which may be explained by the hypertonic hallmark of dystonia causing an increase in exercise load. Choreoathetosis is positively related to the physical activity index during powered mobility where the hyperkinetic hallmark of choreoathetosis may lead to an increase in physical activity intensity and energy expenditure. Arm overflow movements are the component which contribute the most to total-body activity index, thus, minimizing these movements may lower the overall energy expenditure during powered mobility. Mobility training in a relaxed surrounding with minimal distractions and minimized arm overflow movements may lead to a less-demanding powered wheelchair mobility experience and increased learning efficiency.

PMID: 33970729

9. The progression of BMI status over time in Irish ambulant children with cerebral palsy
Karen Brady, Damien Kiernan, Andrea Marron

Ir J Med Sci. 2021 May 14. doi: 10.1007/s11845-021-02635-x. Online ahead of print.

Background: An increasing prevalence of overweight and obesity in children has been reported globally. Most studies examining the trajectory of BMI in children over time have tended to focus on children with typical development. Our group previously reported static prevalence rates in children with cerebral palsy. However, concern remains within our multi-disciplinary team that progression into higher BMI categories is apparent as children with cerebral palsy age. Aims: To examine the progression of BMI status as children with cerebral palsy age and determine the severity of obesity. Methods: A retrospective analysis was conducted of the National Movement Laboratory database yielding 574 participants that met inclusion criteria. BMI was calculated retrospectively, and age adjusted BMI centiles were used for analysis. A chi-square test for homogeneity was used to compare differences in proportions. Differences in age, weight and height between assessments were assessed using a Wilcoxon signed rank test. Statistical significance was set at $p < 0.05$. Results: No statistically significant differences were present in proportions for any BMI classifications between first and repeat assessments. Small increases were evident in both the obesity (7.8 to 11.5%) and overweight (10.8 to 12.4%) categories. Eighty percent of children remained in a normal BMI category between assessments while 56% remained either overweight or moved into a category of obesity. Conclusion: The majority of children with cerebral palsy who presented with a normal BMI at first assessment maintained this BMI classification at follow-up. The results of this study highlight the importance of maintaining a healthy BMI status.

PMID: 33988804

10. Watchwords for management of developmental disabilities in developing countries
Ashok N Johari

Editorial Dev Med Child Neurol. 2021 Jun;63(6):629. doi: 10.1111/dmcn.14864.

PMID: 33973239

11. Childhood neurodevelopmental outcomes of survivors of acute bilirubin encephalopathy: A retrospective cohort study
Vinod Kumar, Praveen Kumar, Venkataseshan Sundaram, Sanjay Kumar Munjal, Prahbhjot Malhi, Naresh Kumar Panda

Early Hum Dev. 2021 Apr 29;158:105380. doi: 10.1016/j.earlhumdev.2021.105380. Online ahead of print.

Background: Reports on childhood neurodevelopmental and neurosensory outcomes following acute bilirubin encephalopathy from low- and middle-income countries are scarce. Aim: This study aimed to analyze the neurodevelopmental and neurosensory outcomes of survivors of acute bilirubin encephalopathy. Study design: Retrospective cohort. Subjects: Neonates with admission diagnosis of acute bilirubin encephalopathy were followed up and assessed for neuromotor, neurodevelopmental and neurosensory functions between 18 m and 12.5 years of age. Results: In 67 neonates with acute bilirubin encephalopathy, a composite outcome of cerebral palsy or death was observed in 33 (49%) subjects. Choreo-athetoid cerebral palsy [19 (73%)] was the most common type observed. Sensori-neural hearing loss was observed in 46 (79%) subjects. Subjects with cerebral palsy had significantly low Developmental profile-3 scores in all assessed domains. Neonates with an early-stage acute bilirubin encephalopathy (aOR (95% C.I): 0.12 (0.05-0.71); $p = 0.02$) and those with a normal neurological examination at discharge (aOR (95% C.I): 0.11 (0.06-0.7); $p = 0.049$) had significantly lower odds of the primary outcome. Conclusions: Majority of survivors of acute bilirubin encephalopathy had adverse outcomes during childhood in the form of cerebral palsy and sensory-neural hearing loss. Cognitive functions were better preserved than the language and general development in the affected children.

PMID: 33990043

12. Cognition in cerebral palsy: White matter matters
Christopher M Filley

Editorial Eur J Paediatr Neurol. 2021 May 4;S1090-3798(21)00100-8. doi: 10.1016/j.ejpn.2021.05.005. Online ahead of print.

PMID: 33975788

13. The importance of dystonia in cerebral palsy
Darcy Fehlings

Editorial Eur J Paediatr Neurol. 2021 May 4;S1090-3798(21)00098-2. doi: 10.1016/j.ejpn.2021.05.003. Online ahead of print.

PMID: 33966981

14. Fracture characteristics by age, sex, and ambulatory status among individuals with cerebral palsy: a descriptive study
Sanjana Kannikeswaran, Zachary P French, Kevin Walsh, Jennylee Swallow, Michelle S Caird, Daniel G Whitney

Disabil Rehabil. 2021 May 7;1-7. doi: 10.1080/09638288.2021.1921860. Online ahead of print.

Purpose: To evaluate clinically relevant fracture characteristics by age, sex, and ambulatory status among individuals with cerebral palsy. Methods: Fracture location, energy of fracture, and activities that lead to a fracture were assessed among a clinic -based sample of children (0-17 years; n = 57) and adults (18-70 years; n = 58) with cerebral palsy that sustained a fracture by sex and gross motor function classification system (GMFCS) I-III vs. IV/V. Results: Proportion of fractures that were low-energy was 67-99% for children and 69-84% for adults. ~2/3rds of fractures were at the lower extremities, with the distal femur being the most common site for children (44%) and the foot/ankle for adults (40%); however, there were age, sex, and ambulatory effects, such that 43% of adults GMFCS IV/V and 32% of women had a distal femur fracture. GMFCS I-III were more likely to fracture from functionally complex activities, while GMFCS IV/V were more likely to fracture from wheelchair/ transfers/limb-stuck and incidental findings. Conclusions: The majority of fractures were low-energy and occurred in the lower extremities, with effects by age, sex, and GMFCS. Activities that led to a fracture also differed by age and GMFCS, which can be used to design fracture prevention interventions in addition to bolstering skeletal mass and architecture. Implications for rehabilitation: Skeletal fragility is a major problem for individuals with cerebral palsy (CP) across the lifespan leading to an increased risk of fragility fractures. Rehabilitation is a prime clinical intervention to prevent fractures from occurring and improving post-fracture healing and function; yet, effective rehabilitation interventions require knowledge of fracture characteristics, such as where fractures are occurring and the activities that lead to the fracture event specific to individuals with CP. Using a clinic-based sample of 0-70 year olds with CP, we describe salient fracture characteristics based on age, sex, and ambulatory status to enhance translation into clinical and rehabilitation practice.

PMID: 33962527

15. Preterm and writhing movements: is it possible to predict fidgety movements in preterm infants?
Felipe A Souza, Caroline C L Nogueira, Andrea J Silva, Paula S C Chagas, Jaqueline S Frônio

J Perinatol. 2021 May 13. doi: 10.1038/s41372-021-01064-z. Online ahead of print.

Background: Preterm infants who do not have fidgety movements at 3 months of corrected age have up to ten times greater risk of developing cerebral palsy or other alterations in motor development, compared to infants who exhibit such movements. The General Movements Assessment (GMA) is a validated tool that may predict the fidgety movement period. Objective: This study aimed to describe the trajectory of the General Movements Assessment (GMA) during the preterm and writhing movements periods in preterm infants and determine the best time point to predict the fidgety movements period. Study design: Fifty-two preterm newborns were evaluated by the GMA method. Results: GMA assessment at the age of 5 weeks post term was found the most predictive of neuromotor development disorders in at-risk newborns, with a sensitivity and specificity of 86% and 58%, respectively, and a high negative predictive value (92%) and increased hit ratio (69% accuracy). Conclusion: Preterm infants with ≤34 weeks of gestational age have a high prevalence of poor repertoire classifications on the GMA and one single assessment with GMA near the time of NICU discharge seems to be the best time to determine infants who need to be followed more carefully, but the best time point to predict the fidgety movements period was 5 weeks post term.

PMID: 33986474

16. Postnatal Corticosteroids to Prevent or Treat Bronchopulmonary Dysplasia
Lex W Doyle

Review Neonatology. 2021 May 11;1-8. doi: 10.1159/000515950. Online ahead of print.

Bronchopulmonary dysplasia (BPD) remains a major morbidity for infants born preterm. Postnatal corticosteroids might reduce the risk of developing BPD, or reduce its severity when it occurs, because of their powerful anti-inflammatory effects. However, corticosteroids have adverse effects, including on the developing brain. There have been numerous randomized clinical trials of corticosteroids given via various routes, of varying types, and started at different postnatal ages. There is some evidence that inhaled corticosteroids started earlier in the postnatal period may reduce BPD, but increase mortality. Inhaled corticosteroids started after the first week of age have little effect, but data are sparse. Systemic corticosteroids started in the first week after birth reduce BPD but increase cerebral palsy. Systemic corticosteroids started after the first week of age reduce both BPD and mortality, without evidence of long-term neurological harm. However, no studies have been powered to look for important adverse long-term neurological effects. Of the 2 systemic corticosteroids assessed, most effects relate to dexamethasone and not to hydrocortisone, but hydrocortisone in the first week after birth may reduce mortality, and is worthy of further study. There are limited data directly comparing inhaled versus systemic corticosteroids, with no evidence of superiority of one mode over the other. Corticosteroids instilled into the trachea using surfactant as a vehicle to distribute the drug through the lungs offer promise in preventing BPD. For current clinical practice, systemic corticosteroids should be avoided in the first week of life, and thereafter used only in infants at high risk of BPD.

PMID: 33975319

17. Altered distributions and functions of natural killer T cells and γδ T cells in neonates with neonatal encephalopathy, in school-age children at follow-up, and in children with cerebral palsy
Nawal A B Taher, Lynne A Kelly, Alhanouf I Al-Harbi, Mary I O'Dea, Zunera Zareen, Emer Ryan, Eleanor J Molloy, Derek G Doherty

J Neuroimmunol. 2021 Apr 29;356:577597. doi: 10.1016/j.jneuroim.2021.577597. Online ahead of print.

We enumerated conventional and innate lymphocyte populations in neonates with neonatal encephalopathy (NE), school-age children post-NE, children with cerebral palsy and age-matched controls. Using flow cytometry, we demonstrate alterations in circulating T, B and natural killer cell numbers. Invariant natural killer T cell and Vδ2+ γδ T cell numbers and frequencies were strikingly higher in neonates with NE, children post-NE and children with cerebral palsy compared to age-matched controls, whereas mucosal-associated invariant T cells and Vδ1 T cells were depleted from children with cerebral palsy. Upon stimulation ex vivo, T cells, natural killer cells and Vδ2 T cells from neonates with NE more readily produced inflammatory cytokines than their counterparts from healthy neonates, suggesting that they were previously primed or activated. Thus, innate and conventional lymphocytes are numerically and functionally altered in neonates with NE and these changes may persist into school-age.

PMID: 33964735

18. Transcriptional analysis of muscle tissue and isolated satellite cells in spastic cerebral palsy
Karyn G Robinson, Erin L Crowgey, Stephanie K Lee, Robert E Akins

Dev Med Child Neurol. 2021 May 14. doi: 10.1111/dmcn.14915. Online ahead of print.

Aim: To analyze transcriptomes from muscle tissue and cells to improve our understanding of differences in gene expression and molecular function in cerebral palsy (CP) muscle. Method: In this case-control study, eight participants with CP (five males, three females; mean [SD] age 14y 2mo [1y 8mo]) and 11 comparison individuals (eight males, three females; mean [SD] age 14y 0mo [2y 6mo]) were enrolled after informed consent/assent and skeletal muscle was obtained during surgery.

RNA was extracted from tissue and from primary satellite cells grown to form myotubes in vitro. RNA sequencing data were analyzed using validated informatics pipelines. Results: Analysis identified expression of 6308 genes in the tissue samples and 7459 in the cultured cells. Significant differential expression between CP and control was identified in 87 genes in the tissue and 90 genes in isolated satellite cell-derived myotube cultures. Interpretation: Both tissue and cell analyses identified differential expression of genes associated with muscle development and multiple pathways of interest.

PMID: 33987836

19. Genetic Testing Contributes to Diagnosis in Cerebral Palsy: Aicardi-Goutières Syndrome as an Example
Diane Beysen, Chania De Cordt, Charlotte Dielma, Benson Ogunjimi, Julie Dandelooy, Edwin Reyniers, Katrien Janssens, Marije M E Meuwissen

Front Neurol. 2021 Apr 22;12:617813. doi: 10.3389/fneur.2021.617813. eCollection 2021.

Cerebral palsy (CP) is a non-progressive neurodevelopmental disorder characterized by motor impairments, often accompanied by co-morbidities such as intellectual disability, epilepsy, visual and hearing impairment and speech and language deficits. Despite the established role of hypoxic-ischemic injury in some CP cases, several studies suggest that birth asphyxia is actually an uncommon cause, accounting for <10% of CP cases. For children with CP in the absence of traditional risk factors, a genetic basis to their condition is increasingly suspected. Several recent studies indeed confirm copy number variants and single gene mutations with large genetic heterogeneity as an etiology in children with CP. Here, we report three patients with spastic cerebral palsy and a genetically confirmed diagnosis of Aicardi-Goutières syndrome (AGS), with highly variable phenotypes ranging from clinically suggestive to non-specific symptomatology. Our findings suggest that AGS may be a rather common cause of CP, that frequently remains undiagnosed without additional genetic testing, as in only one case a clinical suspicion of AGS was raised. Our data show that a diagnosis of AGS must be considered in cases with spastic CP, even in the absence of characteristic brain abnormalities. Importantly, a genetic diagnosis of AGS may have significant therapeutic consequences, as targeted therapies are being developed for type 1 interferonopathies, the group of diseases to which AGS belongs. Our findings demonstrate the importance of next generation sequencing in CP patients without an identifiable cause, since targeted diagnostic testing is hampered by the often non-specific presentation.

PMID: 33967934