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Cerebral palsy research news

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Professor Nadia Badawi AM
CP Alliance Chair of Cerebral Palsy Research

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Interventions and Management

1. Upper Limb Onabotulinumtoxin A Injections in Children Under 2 Years with Cerebral Palsy: A Retrospective Chart Review
Danni Centorame, Barry Rawicki, Sabine Hennel, Brian Hoare

J Child Neurol. 2022 Sep 15;8830738221124365. doi: 10.1177/08830738221124365. Online ahead of print.

To report on the safety of using Onabotulinumtoxin A (OnaA) in the upper limb(s) of children <2 years of age with cerebral palsy and to describe a proactive clinical model of care in the management of upper limb impairment in children with cerebral palsy. Methods and procedures: Retrospective chart audit of 65 infants aged 13-23 months (mean 18.69) who received upper limb OnaA injections. Administration procedures, trends in muscle selection, and adverse events were examined. Results: Adverse events were reported in 6 (4%) of the 65 children. Across the study period, muscles that control thumb and forearm movements were most commonly injected. The number of OnaA injections to subscapularis and flexor digitorum profundus increased over this period. Conclusions and implications: OnaA is a safe treatment option for the short-term management of focal upper limb muscle overactivity in children under 2 years of age with cerebral palsy. In line with existing evidence, OnaA should always be considered as an adjunct to evidence-based therapy.

PMID: 36113444

2. Development of a Clinical Framework for the Assessment of Dyskinesia and Function in the Upper Limb in Children with Cerebral Palsy
Edward Ralph, Kate Carroll, Marcella Danks, Adrienne Harvey

Phys Occup Ther Pediatr. 2022 Sep 12;1-13. doi: 10.1080/01942638.2022.2104149. Online ahead of print.

Objective: Dyskinesia in cerebral palsy (CP) is a complex movement disorder that can significantly impact upper limb function. Despite a range of available tools, there is no consensus on best practice assessment of upper limb function in children with CP and dyskinesia. This study aimed to develop a clinical framework for the assessment of the impact of dyskinesia on upper limb function in children with CP. Design: Modified Delphi study using expert consensus. Methods: An expert panel of six highly experienced Australian therapists ranked assessment tools sourced from existing evidence-based literature using a five-point Likert scale. Tools rated as important for use "most" or "all" of the time, by 80% of respondents were accepted into the framework following two survey rounds and a third stage discussion. Results: Of 21 tools, 12 were included in the framework under five categories: (i) screening for dyskinesia; (ii) measuring the severity of dyskinesia; (iii) Classifying upper limb functional ability; (iv) measuring upper limb functional ability; and (v) measuring upper limb movement. Conclusions: The framework for assessing the impact of dyskinesia on upper limb function in CP aims to guide clinicians to improve assessment consistency and facilitate individualized goal-directed management. Further studies with a

larger number of expert clinicians and researchers will further strengthen the utility of the framework.

PMID: 36097697

3. Cerebral Palsy: Hip Surveillance
Angielyn M San Juan, Vineeta T Swaroop

Pediatr Ann. 2022 Sep;51(9):e353-e356. doi: 10.3928/19382359-20220706-06. Epub 2022 Sep 1.

Patients with cerebral palsy are known to be at risk for hip displacement and dislocation. Progressive hip displacement is known to cause a variety of problems including pain, impaired sitting balance, difficulty with perineal care, and decreased quality of life. To avoid these problems, hip reconstruction may be recommended and has been shown to lead to significant improvements in pain and health-related quality of life. To properly identify patients in need of intervention for hip displacement, hip surveillance is an active program consisting of clinical and radiographic monitoring in patients with cerebral palsy that allows for early detection of hip displacement in those at risk. As such, all children with cerebral palsy should be referred for hip surveillance at age 2 years. A growing body of literature has shown that hip surveillance along with appropriate orthopedic management decreases or prevents the incidence of hip dislocations, with direct implications on overall quality of life, in children with cerebral palsy. [Pediatr Ann. 2022;51(9):e353-e356.].

PMID: 36098607

4. Bilateral pericapsular nerves group (PENG) block for analgesia in pediatric hip surgery
J A Anido Guzmán, F J Robles Barragán, I Funcia de la Torre, F Alfonso Sanz, I A Becerra Cayetano, C de la Hoz Serrano

Case Reports Rev Esp Anestesiol Reanim (Engl Ed). 2022 Sep 7;S2341-1929(22)00135-4. doi: 10.1016/j.redare.2021.05.017. Online ahead of print.

Effective management and control of peri- and postoperative pain in hip surgery is essential in order to minimize the use of opioids and their adverse effects. Effective regional analgesia for hip pain is made particularly challenging by the complex innervation of the hip joint. Standard regional techniques can be associated with complications, including incomplete anesthesia, hypotension, or lower limb weakness. We present the case of a 5-year-old girl with a history of infantile cerebral palsy who underwent bilateral varus derotation osteotomy and adductor tenotomy due to paralytic dislocation. She received bilateral PENG block and femoral cutaneous nerve block-a simple technique that covers all the nerves involved in the sensory innervation of the joint capsule without the need for multiple injections.

PMID: 36088271

5. Orthopedic surgical outcomes that matter in children with cerebral palsy
M Wade Shrader

Dev Med Child Neurol. 2022 Sep 9. doi: 10.1111/dmcn.15407. Online ahead of print.

No abstract available

PMID: 36082484

6. Idiopathic Toe Walking: An Update on Natural History, Diagnosis, and Treatment
Jeremy P Bauer, Susan Sienko, Jon R Davids

J Am Acad Orthop Surg. 2022 Sep 7. doi: 10.5435/JAAOS-D-22-00419. Online ahead of print.

Toe walking is a common presenting report to an orthopaedic practice. Evaluation of a child with toe walking includes a thorough history and physical examination to elucidate the diagnosis. When no other diagnosis is suspected, a diagnosis of idiopathic toe walking is often given. Despite the high prevalence of the condition, there is notable controversy of the nomenclature of the disease. Recent research has shed more light on both the natural history and the genetic basis. The use of motion analysis, including EMG and multisegment foot model, may help both differentiate children with mild forms of cerebral palsy and evaluate outcomes after treatment. Early treatment for young children with adequate range of motion (ROM) is generally reassurance because most young children with idiopathic toe walking are expected to resolve spontaneously. When the toe walking persists, treatment options include both surgical and nonsurgical management. Nonsurgical management centers on obtaining ROM through stretching and serial casting, followed by gait retraining and bracing treatment. Surgical lengthening at either the Achilles or gastrocnemius level improves the ROM of the ankle and then similarly requires therapy and bracing treatment to obtain a more normalized gait.

PMID: 36084329

7. Patterns of asymmetry and energy cost generated from predictive simulations of hemiparetic gait
Russell T Johnson, Nicholas A Bianco, James M Finley

PLoS Comput Biol. 2022 Sep 9;18(9):e1010466. doi: 10.1371/journal.pcbi.1010466. Online ahead of print.

Hemiparesis, defined as unilateral muscle weakness, often occurs in people post-stroke or people with cerebral palsy, however it is difficult to understand how this hemiparesis affects movement patterns as it often presents alongside a variety of other neuromuscular impairments. Predictive musculoskeletal modeling presents an opportunity to investigate how impairments affect gait performance assuming a particular cost function. Here, we use predictive simulation to quantify the spatiotemporal asymmetries and changes to metabolic cost that emerge when muscle strength is unilaterally reduced and how reducing spatiotemporal symmetry affects metabolic cost. We modified a 2-D musculoskeletal model by uniformly reducing the peak isometric muscle force unilaterally. We then solved optimal control simulations of walking across a range of speeds by minimizing the sum of the cubed muscle excitations. Lastly, we ran additional optimizations to test if reducing spatiotemporal asymmetry would result in an increase in metabolic cost. Our results showed that the magnitude and direction of effort-optimal spatiotemporal asymmetries depends on both the gait speed and level of weakness. Also, the optimal speed was 1.25 m/s for the symmetrical and 20% weakness models but slower (1.00 m/s) for the 40% and 60% weakness models, suggesting that hemiparesis can account for a portion of the slower gait speed seen in people with hemiparesis. Modifying the cost function to minimize spatiotemporal asymmetry resulted in small increases (~4%) in metabolic cost. Overall, our results indicate that spatiotemporal asymmetry may be optimal for people with hemiparesis. Additionally, the effect of speed and the level of weakness on spatiotemporal asymmetry may help explain the well-known heterogenous distribution of spatiotemporal asymmetries observed in the clinic. Future work could extend our results by testing the effects of other neuromuscular impairments on optimal gait strategies, and therefore build a more comprehensive understanding of the gait patterns observed in clinical populations.

PMID: 36084139

8. Efficacy of conservative treatment for spastic cerebral palsy children with equinus gait: a systematic review and meta -analysis
Krongkaew Klaewkasikum, Tanyaporn Patathong, Patarawan Woratanarat, Thira Woratanarat, Kunlawat Thadanipon, Sasivimol Rattanasiri, Ammarin Thakkinstian

Meta-Analysis J Orthop Surg Res. 2022 Sep 8;17(1):411. doi: 10.1186/s13018-022-03301-3.

Background: Comparisons between various conservative managements of spastic equinus deformity in cerebral palsy demonstrated limited evidences, to evaluate the efficacy of conservative treatment among cerebral palsy children with spastic

equinus foot regarding gait and ankle motion. Methods: Studies were identified from PubMed and Scopus up to February 2022. Inclusion criteria were randomized controlled trial (RCT), conducted in spastic cerebral palsy children with equinus deformity, aged less than 18 years, compared any conservative treatments (Botulinum toxin A; BoNT-A, casting, physical therapy, and orthosis), and evaluated gait improvement (Physician Rating Scale or Video Gait Analysis), Observational Gait Scale, Clinical Gait Assessment Score, ankle dorsiflexion (ankle dorsiflexion at initial contact, and passive ankle dorsiflexion), or Gross Motor Function Measure. Any study with the participants who recently underwent surgery or received BoNT-A or insufficient data was excluded. Two authors were independently selected and extracted data. Risk of bias was assessed using a revised Cochrane risk-of-bias tool for randomized trials. I2 was performed to evaluate heterogeneity. Risk ratio (RR), the unstandardized mean difference (USMD), and the standardized mean difference were used to estimate treatment effects with 95% confidence interval (CI). Results: From 20 included studies (716 children), 15 RCTs were eligible for meta-analysis (35% had low risk of bias). BoNT-A had higher number of gait improvements than placebo (RR 2.64, 95% CI 1.71, 4.07, I2 = 0). Its combination with physical therapy yielded better passive ankle dorsiflexion at knee extension than physical therapy alone (USMD = 4.16 degrees; 95% CI 1.54, 6.78, I2 = 36%). Casting with or without BoNT-A had no different gait improvement and ankle dorsiflexion at knee extension when compared to BoNT-A. Orthosis significantly increased ankle dorsiflexion at initial contact comparing to control (USMD 10.22 degrees, 95 CI% 5.13, 15.31, I2 = 87%). Conclusion: BoNT-A and casting contribute to gait improvement and ankle dorsiflexion at knee extension. BoNT-A specifically provided gait improvement over the placebo and additive effect to physical therapy for passive ankle dorsiflexion. Orthosis would be useful for ankle dorsiflexion at initial contact. Trial registration PROSPERO number CRD42019146373.

PMID: 36076293

9. Neuromuscular electrical stimulation to augment lower limb exercise and mobility in individuals with spastic cerebral palsy: A scoping review
Kelly R Greve, Christopher F Joseph, Blake E Berry, Kornel Schadl, Jessica Rose

Review Front Physiol. 2022 Aug 30;13:951899. doi: 10.3389/fphys.2022.951899. eCollection 2022.

Background: Neuromuscular Electrical Stimulation (NMES) is an emerging assistive technology applied through surface or implanted electrodes to augment skeletal muscle contraction. NMES has the potential to improve function while reducing the neuromuscular impairments of spastic cerebral palsy (CP). This scoping review examines the application of NMES to augment lower extremity exercises for individuals with spastic CP and reports the effects of NMES on neuromuscular impairments and function in spastic CP, to provide a foundation of knowledge to guide research and development of more effective treatment. Methods: A literature review of Scopus, Medline, Embase, and CINAHL databases were searched from 2001 to 2 November 2021 with identified inclusion and exclusion criteria. Results: Out of 168 publications identified, 33 articles were included. Articles on three NMES applications were identified, including NMES-assisted strengthening, NMES-assisted gait, and NMES for spasticity reduction. NMES-assisted strengthening included the use of therapeutic exercises and cycling. NMES-assisted gait included the use of NMES to improve gait patterns. NMES-spasticity reduction included the use of transcutaneous electrical stimulation or NMES to decrease tone. Thirteen studies investigated NMES-assisted strengthening, eleven investigated therapeutic exercise and demonstrated significant improvements in muscle structure, strength, gross motor skills, walking speed, and functional mobility; three studies investigated NMES-assisted cycling and demonstrated improved gross motor skills and walking distance or speed. Eleven studies investigated NMES-assisted gait and demonstrated improved muscle structure, strength, selective motor control, gross motor skills, and gait mechanics. Seven studies investigated NMES for spasticity reduction, and five of the seven studies demonstrated reduced spasticity. Conclusion: A growing body of evidence supports the use of NMES-assisted strengthening, NMES-assisted gait, and NMES for spasticity reduction to improve functional mobility for individuals with spastic CP. Evidence for NMES to augment exercise in individuals with spastic CP remains limited. NMES protocols and parameters require further clarity to translate knowledge to clinicians. Future research should be completed to provide richer evidence to transition to more robust clinical practice.

PMID: 36111153

10. Psychosocial aspects of sports medicine in pediatric athletes: Current concepts in the 21 st century
Donald E Greydanus, Berrin Ergun-Longmire, Maria Demma Cabral, Dilip R Patel, Cheryl A Dickson

Dis Mon. 2022 Sep 10;101482. doi: 10.1016/j.disamonth.2022.101482. Online ahead of print.

Behavioral aspects of organized sports activity for pediatric athletes are considered in a world consumed with winning at all

costs. In the first part of this treatise, we deal with a number of themes faced by our children in their sports play. These concepts include the lure of sports, sports attrition, the mental health of pediatric athletes (i.e., effects of stress, anxiety, depression, suicide in athletes, ADHD and stimulants, coping with injuries, drug use, and eating disorders), violence in sports (i.e., concepts of the abused athlete including sexual abuse), dealing with supervisors (i.e., coaches, parents), peers, the talented athlete, early sports specialization and sports clubs. In the second part of this discussion, we cover ergolytic agents consumed by young athletes in attempts to win at all costs. Sports doping agents covered include anabolic steroids (anabolic-androgenic steroids or AAS), androstenedione, dehydroepiandrostenedione (DHEA), human growth hormone (hGH; also its human recombinant homologue: rhGH), clenbuterol, creatine, gamma hydroxybutyrate (GHB), amphetamines, caffeine and ephedrine. Also considered are blood doping that includes erythropoietin (EPO) and concepts of gene doping. In the last section of this discussion, we look at disabled pediatric athletes that include such concepts as athletes with spinal cord injuries (SCIs), myelomeningocele, cerebral palsy, wheelchair athletes, and amputee athletes; also covered are pediatric athletes with visual impairment, deafness, and those with intellectual disability including Down syndrome. In addition, concepts of autonomic dysreflexia, boosting and atlantoaxial instability are emphasized. We conclude that clinicians and society should protect our precious pediatric athletes who face many challenges in their involvement with organized sports in a world obsessed with winning. There is much we can do to help our young athletes find benefit from sports play while avoiding or blunting negative consequences of organized sport activities.

PMID: 36100481

11. Measuring advanced motor skills in children with cerebral palsy: development of normative data and percentile curves for the Challenge-20 assessment
Darko Milaščević, F Virginia Wright, Milan Milošević, David Neubauer

Int J Rehabil Res. 2022 Sep 12. doi: 10.1097/MRR.0000000000000546. Online ahead of print.

The Challenge-20 is an assessment of advanced motor skills of children with cerebral palsy. The purpose of this study was to develop age-related norms and percentile curves for the Challenge-20 with typically developing children (n = 150, 7 through 11 years), and compare Challenge-20 scores of independently ambulatory children with CP, Gross Motor Function Classification System level I (n = 135) and II (n = 56) to these age norms. Younger TD children (7 years) scored lowest, and older children (11 years) scored highest on the Challenge-20, showing similar developmental trajectories. Challenge-20 scores of 15% of children in GMFCS level I were situated above the lower 2.5th percentile curve of the typically developing children's Challenge-20 growth curve, that is, overlapping into the typically developing child zone. The Challenge-20 is sensitive to the progression of advanced gross motor skills in typically developing children. Children with cerebral palsy, GMFCS I follow similar, albeit lower, Challenge score trajectory to that of typically developing children, and in some cases come close to lower level abilities of typically developing children. The reference values with typically developing children extend the Challenge-20's utility when assessing advanced gross motor skill of independently ambulatory children with cerebral palsy for physiotherapy intervention and physical activity planning and open the door to re-thinking more about advanced gross motor interventions for children with cerebral palsy in GMFCS levels I and II given their potential to progress along the developmental trajectory.

PMID: 36083590

12. Physical activity, quality of life and parenting stress in children with cerebral palsy
Mi-Jeong Yoon, Hyehoon Choi, Joon-Sung Kim, Seong Hoon Lim, Yeun-Jie Yoo, Bo Young Hong

Pediatr Int. 2022 Jan;64(1):e15295. doi: 10.1111/ped.15295.

Background: Children with cerebral palsy (CP) are less physically active than their typically developing peers. The effects of decreased physical activity on children's quality of life (QOL) or caregiver's lives are not well understood. This study aimed to investigate the association between physical activity, QOL, and parenting stress in children with CP. Methods: A prospective cross-sectional study was done in children with CP. Daily physical activity was measured over 7 days using an accelerometer (ActiGraph™). Caregivers completed the Child Health Questionnaire - Parent Form 50 and Parenting Stress Index - Short Form. Multiple regression analysis was used. Results: In total, data from 65 children with Gross Motor Function Classification System (GMFCS) levels I-V, aged 4-13 years, were analyzed. Non-ambulatory (GMFCS IV-V) children had significantly lower activity counts and moderate to vigorous physical activity (MVPA) in comparison with ambulatory (GMFCS I-II) and marginally ambulatory (GMFCS III) children. The ambulatory group had better physical QOL than the non-ambulatory group.

Caregivers of the non-ambulatory or marginally ambulatory children with CP reported higher parenting stress levels than those of the ambulatory group. Time spent in MVPA and activity counts were positively associated with physical QOL in children with CP. Low activity counts and low amounts of MVPA of children with CP were significant predictors of high parenting stress. Conclusions: Physical activity in children with CP is associated with children's QOL and parenting stress. These results suggest that clinicians should conduct physical activity assessment and counseling to promote physical activity.

PMID: 36112040

13. Factors Affecting Mothers' Adherence to Home Exercise Programs Designed for Their Children with Cerebral Palsy
Reem M Alwhaibi, Asma B Omer, Ruqaiyah Khan

Int J Environ Res Public Health. 2022 Aug 30;19(17):10792. doi: 10.3390/ijerph191710792.

Cerebral palsy is a common motor disorder that results in long-term impairment. The purpose of this study was to find out what factors influence Saudi mothers' compliance with their Children with Cerebral Palsy (C-CP) Home Exercise Program (HEP). A self-administered online questionnaire was used to perform this qualitative research study on a group of 113 mothers who had children with CP. The study included mothers with children from birth to 12 years old who had received a HEP prescription from a physiotherapist. The measuring instrument tool was a questionnaire with two sections: demographic characteristics and a questionnaire about the parents' adherence to the HEP. The questionnaire utilized in this study was subjected to a reliability analysis, and the derived Cronbach's alpha was found to be 0.814 for the questionnaire (which had 17 phrases). These results imply that the questionnaire is reliable. A total of 113 responses were received, with 4 incomplete responses being eliminated. The majority of mothers (66.1%) did not follow the HEP, according to the findings of this survey. The demographics of the mothers revealed that 20-25-year-old mothers were more adherent than the other age groups. The findings of this study demonstrated that the physical therapist's treatment of the mother influenced exercise compliance.

PMID: 36078507

14. The Effects of Swallowing Disorders and Oral Malformations on Nutritional Status in Children with Cerebral Palsy
Mustapha Mouilly, Adil El Midaoui, Aboubaker El Hessni

Nutrients. 2022 Sep 4;14(17):3658. doi: 10.3390/nu14173658.

Nutrition plays an important role both from a nutrition and a socio-psychological point of view; this part seems to be even more crucial in cerebral palsy where undernutrition is responsible for an increase in morbidity and mortality. The objective of this study was to evaluate the effects of swallowing disorders and oral malformations on the nutritional status of children with cerebral palsy. We evaluated 65 patients aged 2 to 17 years using a cross-sectional, descriptive and observational approach. All patients had a definite diagnosis of cerebral palsy. The measurement of anthropometric variables (weight, height, Body Mass Index (BMI) and circumferences) was performed according to recognized techniques and measurements. The Z-score was also calculated using the World Health Organization (WHO) references. The 5-level Gross Motor Function Classification System was used, providing a standardized classification of motor disability patterns for children with cerebral palsy. The population had a median age of 9.25 (4.50-16.00) and was about 53% female. Furthermore, 75% of the patients had a height inferior to 158 cm. The results of our study show that 42 (64.6%) had false routes, 17 (26.2%) had oral-facial malformations and 51 (78.5%) did not have lip prehensions during meals. The results also show that growth retardation is closely related to gross motor function with p = 0.01, as well as all nutritional indices (Z-score weight for age, Z-score height for age and Z-score BMI for age) are affected by swallowing disorders and oral malformations, with statistically significant values < 0.05. In conclusion, a preventive and curative management specific to this population of children with cerebral palsy must be implemented with an interdisciplinary concertation.

PMID: 36079915

15. Surgical outcomes and observation in exotropia cerebral palsy children with cortical visual impairment
Haiyun Ye, Qingyu Liu, Qijia Zhan, Yidan Zhang, Xiaodong Du, Xiaoxiao Zhang, Yue Di, Tong Qiao

BMC Ophthalmol. 2022 Sep 8;22(1):364. doi: 10.1186/s12886-022-02581-x.

Purpose: Cortical visual impairment (CVI) is the common cause of pediatric visual impairment in cerebral palsy (CP) while exotropia is the most common strabismus associated with CP. We aim to observe the strabismic surgery outcomes in pediatric patients with CP and CVI. Method: Our medical records were collected from pediatric patients treated in our hospital from May 1, 2017 to Jan 1, 2022. With normal intelligence assessment and diagnosis of exotropia in children with CP and CVI, microsurgeries were performed under intravenous combined inhalation anesthesia. The strabismus was examined by the prism test under best vision correction and the contrast sensitivity testing (CST) was measured at five levels of spatial frequencies. Result: A total of 38 exotropia patients with CP and CVI were identified and included for analysis during the study period with age ranged from 5 to 12 years (mean 8.45 years) and mean follow up duration was 8.7 months (6-42 months). After bilateral lateral rectus recession (with/without medial rectus resection or inferior oblique transposition), the exotropia amount of participants were obviously revealed from - 30 ~ - 140 (median, IQR: - 50, 40) prism diopters (PD) preoperatively to 0 ~ - 15 (0, 5) PD postoperatively. Statistically significantly improvements were observed at all levels of spatial frequency on CST postoperatively, especially at high spatial frequency areas ($p < 0.05$). Conclusion: Our results demonstrated that the effect of strabismus surgery on exotropia in children with CP and CVI were stable and monocular contrast sensitivity post- operation increased significantly at all spatial frequencies levels.

PMID: 36076198

16. Health-related quality of life from 20 to 32 years of age in very low birth weight individuals: a longitudinal study
Elias Kjølseth Berdal, Arnt Erik Karlsen Wollum, Ingrid Marie Husby Hollund, Johanne Marie Iversen, Eero Kajantie, Kari Anne I Evensen

Health Qual Life Outcomes. 2022 Sep 14;20(1):136. doi: 10.1186/s12955-022-02044-3.

Background: Preterm birth with very low birth weight (VLBW, birth weight < 1500 g) is associated with health problems later in life. How VLBW individuals perceive their physical and mental health-related quality of life (HRQoL) is important to understand their putative burden of disease. Previous studies have shown mixed results, and longitudinal studies into adulthood have been requested. This study aimed to investigate differences in HRQoL between preterm VLBW and term born individuals at 32 years of age, and to study changes in HRQoL from 20 to 32 years. Methods: In a geographically based longitudinal study, 45 VLBW and 68 term born control participants completed the Short Form 36 Health Survey (SF-36) at 32 years of age. Data from three previous timepoints was also available (20, 23 and 28 years of age). The SF-36 yields eight domain scores as well as a physical and a mental component summary. Between-group differences in these variables were investigated. We also performed subgroup analyses excluding individuals with disabilities, i.e., cerebral palsy and/or low estimated intelligence quotient. Results: At 32 years of age, the physical component summary was 5.1 points lower (95% confidence interval (CI): 8.6 to 1.6), and the mental component summary 4.1 points lower (95% CI: 8.4 to - 0.3) in the VLBW group compared with the control group. For both physical and mental component summaries there was an overall decline in HRQoL from 20 to 32 years of age in the VLBW group. When we excluded individuals with disabilities (n = 10), group differences in domain scores at 32 years were reduced, but physical functioning, bodily pain, general health, and role-emotional scores remained lower in the VLBW subgroup without disabilities compared with the control group. Conclusion: We found that VLBW individuals reported lower HRQoL than term born controls at 32 years of age, and that HRQoL declined in the VLBW group from 20 to 32 years of age. This was in part, but not exclusively explained by VLBW individuals with disabilities.

PMID: 36104723

17. Pain coping tools for children and young adults with a neurodevelopmental disability: A systematic review of measurement properties
Nadine L Smith, Meredith G Smith, Noula Gibson, Christine Imms, Ashleigh L Thornton, Adrienne R Harvey

Review Dev Med Child Neurol. 2022 Sep 16. doi: 10.1111/dmcn.15410. Online ahead of print.

Aim: To systematically identify and evaluate the measurement properties of patient-reported outcome measures (PROMs) and observer-reported outcome measures (parent proxy report) of pain coping tools that have been used with children and young adults (aged 0-24 years) with a neurodevelopmental disability. Method: A two-stage search using MEDLINE, Embase, CINAHL, Web of Science, and PsycInfo was conducted. Search 1 in August 2021 identified pain coping tools used in neurodevelopmental disability and search 2 in September 2021 located additional studies evaluating the measurement properties of these tools. Methodological quality was assessed using the COnsensus-based Standards for the Selection of Health Measurement INstruments (COSMIN) guidelines (PROSPERO protocol registration no. CRD42021273031). Results: Sixteen studies identified seven pain coping tools, all PROMs and observer-reported outcome measures (parent proxy report) versions. The measurement properties of the seven tools were appraised in 44 studies. No tool had high-quality evidence for any measurement property or evidence for all nine measurement properties as outlined by COSMIN. Only one tool had content validity for individuals with neurodevelopmental disability: the Cerebral Palsy Quality of Life tool. Interpretation: Pain coping assessment tools with self-report and parent proxy versions are available; however, measurement invariance has not been tested in young adults with a neurodevelopmental disability. This is an area for future research.

PMID: 36111806

18. Harnessing cognitive strategy use for functional problems and proposed underlying mechanisms in childhood-onset dystonia
Kailee Butchereit, Michael Manzini, Helene J Polatajko, Jean-Pierre Lin, Verity M McClelland, Hortensia Gimeno

Eur J Paediatr Neurol. 2022 Sep 8;41:1-7. doi: 10.1016/j.ejpn.2022.08.007. Online ahead of print.

Background: There is a significant gap in knowledge about rehabilitation techniques and strategies that can help children and young people with hyperkinetic movement disorders (HMD) including dystonia to successfully perform daily activities and improve overall participation. A promising approach to support skill acquisition is the Cognitive Orientation to daily Occupational Performance (CO-OP) intervention. CO-OP uses cognitive strategies to help patients generate their own solutions to overcome self-identified problems encountered in everyday living. Purpose: 1. To identify and categorize strategies used by children with HMD to support skill acquisition during CO-OP; 2. To review the possible underlying mechanisms that might contribute to the cognitive strategies, in order to facilitate further studies for developing focused rehabilitation approaches. Methods: A secondary analysis was performed on video-recorded data from a previous study exploring the efficacy of CO-OP for childhood onset HMD, in which CO-OP therapy sessions were delivered by a single occupational therapist. For the purpose of this study, we reviewed a total of 40 randomly selected hours of video footage of CO-OP sessions delivered to six participants (age 6-19 years) over ten intervention sessions. An observational recording sheet was applied to identify systematically the participants' or therapist's verbalizations of cognitive strategies during the therapy. The strategies were classified into six categories in line with published literature. Results: Strategies used by HMD participants included distraction, externally focussed attention, internally focussed attention, emotion self-regulation, motor imagery and mental self-guidance. We postulate different underlying working mechanisms for these strategies, which have implications for the therapeutic management of children and young people with HMD including dystonia. Conclusions: Cognitive strategy training can fundamentally change and improve motor performance. On-going work will address both the underlying neural mechanisms of therapeutic change and the mediators and moderators that influence how change unfolds.

PMID: 36108454

19. Iterative Development of a Software to Facilitate Independent Home Use of BCI Technologies for Children with Quadriplegic Cerebral Palsy
Erica D Floreani, Dion Kelly, Danette Rowley, Brian Irvine, Eli Kinney-Lang, Adam Kirton

Annu Int Conf IEEE Eng Med Biol Soc. 2022 Jul;2022:3361-3364. doi: 10.1109/EMBC48229.2022.9871105.

Brain-computer interfaces (BCIs) are emerging as a new solution for children with severe disabilities to interact with the world. However, BCI technologies have yet to reach end-users in their daily lives due to significant translational gaps. To address these gaps, we applied user-centered design principles to establish a home BCI program for children with quadriplegic cerebral palsy. This work describes the technical development of the software we designed to facilitate BCI use at home. Children and their families were involved at each design stage to evaluate and provide feedback. Since deployment, seven families have successfully used the system independently at home and continue to use BCI at home to further enable participation and independence for their children. Clinical relevance- The design and successful implementation of user-centered software for

home use will both inform on the feasibility of BCI as a long-term access solution for children with neurological disabilities as well as decrease barriers of accessibility and availability of BCI technologies for end-users.

PMID: 36086125

20. Individuals with moderate to severe hand impairments may struggle to use EMG control for assistive devices
Tess B Meier, Alison R Brecheisen, Katie Y Gandomi, Paulo A Carvalho, Gretchen R Meier, Edward A Clancy, Gregory S Fischer, Christopher J Nycz

Annu Int Conf IEEE Eng Med Biol Soc. 2022 Jul;2022:2864-2869. doi: 10.1109/EMBC48229.2022.9871351.

Neurological trauma, such as stroke, traumatic brain injury (TBI), spinal cord injury, and cerebral palsy can cause mild to severe upper limb impairments. Hand impairment makes it difficult for individuals to complete activities of daily living, especially bimanual tasks. A robotic hand orthosis or hand exoskeleton can be used to restore partial function of an intact but impaired hand. It is common for upper extremity prostheses and orthoses to use electromyography (EMG) sensing as a method for the user to control their device. However some individuals with an intact but impaired hand may struggle to use a myoelectrically controlled device due to potentially confounding muscle activity. This study was conducted to evaluate the application of conventional EMG control techniques as a robotic orthosis/exoskeleton user input method for individuals with mild to severe hand impairments. Nine impaired subjects and ten healthy subjects were asked to perform repeated contractions of muscles in their forearm and then onset analysis and feature classification were used to determine the accuracy of the employed EMG techniques. The average accuracy for contraction identification across employed EMG techniques was 95.4% ± 4.9 for the healthy subjects and 73.9% ± 13.1 for the impaired subjects with a range of 47.0% ± 19.1 - 91.6% ± 8.5. These preliminary results suggest that the conventional EMG control technologies employed in this paper may be difficult for some impaired individuals to use due to their unreliable muscle control.

PMID: 36085874

21. Design of a multifunctional specialized wheelchair mechanism for cerebral palsy in children
Alyssa N Maguina, Leslie M Urdiales-Bonelli, Piero G Latorre-Quevedo, Lizardo K Torres-Ayala, Dante A Elias

Annu Int Conf IEEE Eng Med Biol Soc. 2022 Jul;2022:2527-2530. doi: 10.1109/EMBC48229.2022.9871696.

This paper describes and evaluates an approximation of the proposed position-changing mechanism of a cerebral palsy wheelchair for children using only one actuator. Only details the functional requirements that allow the change of position: wheelchair mode, standing frame mode, and stretcher mode. To evaluate the mechanism, a video was recorded and evaluated in Kinovea, and MATLAB software to obtain the functional angular range of the backrest reclination and the seat elevation. The scaled prototype has a mean error of 2.58% in comparison with the original design. The results indicate that this mechanism effectively provided compliance with the proposed angles and comfort for the patient.

PMID: 36086058

22. AEPUS: a tool for the Automated Extraction of Pennation angles in Ultrasound images with low Signal-to-noise ratio for plane-wave imaging
S Vostrikov, A Cossettini, C Leitner, C Baumgartner, L Benini

Annu Int Conf IEEE Eng Med Biol Soc. 2022 Jul;2022:1520-1526. doi: 10.1109/EMBC48229.2022.9871297.

The penetrating ability of ultrasound (US) com-bined with its real-time operation make it the perfect tool for investigating muscle contraction mechanics during complex functional tasks, e.g., locomotion. Changes in fascicle lengths and pennation angles of muscle fascicles strongly correlate with the capacity of skeletal muscles to produce forces, thereby represent fundamental parameters to be tracked. While the gold standard for extracting these features from US images is still based on manual annotation, the availability of recording devices capable of generating big data of muscle dynamics makes such manual

approach unfeasible, setting the need for automated muscle images annotation tools. Existing approaches, however, are seriously limited, also in view of the continuous developments and technology ad-vancements for ultrafast US and plane-wave imaging. In fact, they rely on conventional (slow) B-mode imaging, make use of point tracking approaches (which often fail due to out-of-plane motion), or can only operate on very high quality images. To overcome all these limitations, we present AEPUS, an automated image labeling tool capable of extracting pennation angles from low quality images using a very small number of plane waves, therefore making it capable of exploiting all the benefits of ultrafast US. Clinical Relevance - Ultrasound is a standard research tool to investigate alterations of spastic muscles in children with Cerebral Palsy. We propose a reliable and time-efficient method to track muscle features in ultrasound images and support clinical biomechanists in their analyses.

PMID: 36086389

23. Epidemiology of fractures in children with cerebral palsy: a Swedish population-based registry study
Gustaf Linton, Gunnar Hägglund, Tomasz Czuba, Ann I Alriksson-Schmidt

BMC Musculoskelet Disord. 2022 Sep 15;23(1):862. doi: 10.1186/s12891-022-05813-9.

Background: Children with cerebral palsy (CP) form a heterogeneous group and may have risk or protective factors for fractures compared with typically developing children. The fracture sites may also differ from those of children who do not have CP. We analyzed the fracture epidemiology in a total population of children with CP. Methods: This was a retrospective registry study based on data from the Swedish Cerebral Palsy Follow-Up Program (CPUP) and the Swedish National Patient Register. All children in the CPUP born in 2000-2015 were included. The Gross Motor Function Classification System (GMFCS) level, reported fractures, fracture site, and epilepsy diagnosis were recorded up to 2018. Hazards and hazard ratios were calculated for first-time fractures. Results: Of the 3,902 participants, 368 (9.4%) had at least one reported fracture. The cumulative risk of sustaining a fracture before age 16 years was 38.3% (95% confidence interval 33.9-42.4). The hazard for fracture was 7 times higher in children with epilepsy. The overall fracture incidence was not statistically significantly related to sex or GMFCS level. Fractures in the upper extremities were most prevalent in children with a lower GMFCS level, and femoral fractures were most prevalent in children at GMFCS level V. Most fractures occurred in early childhood and after 8 years of age. Conclusions: Children with CP were at similar risk of sustaining fractures as typically developing children, but the risk was higher in children with comorbid epilepsy. Fractures occurred in children at GMFCS levels I-III at sites similar to those for typically developing children; fractures in the upper extremities were the most frequent. Children at GMFCS levels IV or V and those with epilepsy were more likely to have a fracture in the lower extremities, and the femur was the most frequent site.

PMID: 36104768

24. Epidemiology of cerebral palsy among children in the remote Gorkha district of Nepal: findings from the Nepal cerebral palsy register
Israt Jahan, Mahmudul Hassan Al Imam, Mohammad Muhit, Amir Banjara Chhetri, Nadia Badawi, Gulam Khandaker

Disabil Rehabil. 2022 Sep 14;1-10. doi: 10.1080/09638288.2022.2118871. Online ahead of print.

Purpose: To describe the epidemiology of cerebral palsy (CP) among children in Gorkha, Nepal. Methods: We established the first population-based register of children with CP aged <18 y in Gorkha, Nepal (i.e., Nepal CP Register). Children with suspected CP underwent detailed neurodevelopmental assessment by a multidisciplinary assessment team. Socio-demographic, etiology, motor severity, rehabilitation, and educational status were documented. Results: Between January and October 2018, 182 children with confirmed CP were registered (mean (standard deviation (SD)) age: 10 years 1 months (4 years 10 months), 37.4% females). The majority (88.3%) had CP acquired pre- or perinatally. Mean (SD) age of CP diagnosis was four years five months. Mothers who did not receive any formal schooling had 4.5, 3.1, and 6.3 times higher odds of having inadequate antenatal care, homebirth, and unskilled birth attendants, respectively, when adjusted for other factors. Most children had spastic CP (77.5%) and Gross Motor Function Classification System level III-V (54.9%). Overall, 45.8% had never received rehabilitation services, 58.0% of school-aged children were not attending schools. The median age of receiving rehabilitation services was three years zero months. Conclusions: The delayed diagnosis and clinical severity indicate the overall poor health status of children with CP in Nepal which could be improved by ensuring early diagnosis and intervention. Implications for rehabilitationThe first population-based cerebral palsy register in Nepal suggests diagnosis of CP is considerably delayed among children.The high burden of severe motor impairment and poor communication skill with limited access to timely

rehabilitation among children with CP in Nepal is concerning. Capacity development of community-based health workers and mothers of children with CP could help implementing community-based programs for prevention and early diagnosis of CP, and to promote early intervention for children with CP in remote Gorkha, Nepal.

PMID: 36102553

25. Cerebral palsy and developmental intellectual disability in children younger than 5 years: Findings from the GBD-WHO Rehabilitation Database 2019

Bolajoko O Olusanya, Melissa Gladstone, Scott M Wright, Mijna Hadders-Algra, Nem-Yun Boo, M K C Nair, Nihad Almasri, Vijaya Kancherla, Maureen E Samms-Vaughan, Angelina Kakooza-Mwesige, Tracey Smythe, Christie Del Castillo-Hegyi, Ricardo Halpern, Olaf K de Camargo, Jalal Arabloo, Aziz Eftekhari, Amira Shaheen, Sheffali Gulati, Andrew N Williams, Jacob O Olusanya, Donald Wertlieb, Charles R J Newton, Adrian C Davis

Front Public Health. 2022 Aug 25;10:894546. doi: 10.3389/fpubh.2022.894546. eCollection 2022.

Objective: Children with developmental disabilities are associated with a high risk of poor school enrollment and educational attainment without timely and appropriate support. Epidemiological data on cerebral palsy and associated comorbidities required for policy intervention in global health are lacking. This paper set out to report the best available evidence on the global and regional prevalence of cerebral palsy (CP) and developmental intellectual disability and the associated "years lived with disability" (YLDs) among children under 5 years of age in 2019. Methods: We analyzed the collaborative 2019 Rehabilitation Database of the Global Burden of Disease (GBD) Study and World Health Organization for neurological and mental disorders available for 204 countries and territories. Point prevalence and YLDs with 95% uncertainty intervals (UI) are presented. Results: Globally, 8.1 million (7.1-9.2) or 1.2% of children under 5 years are estimated to have CP with 16.1 million (11.5-21.0) or 2.4% having intellectual disability. Over 98% resided in low-income and middle-income countries (LMICs). CP and intellectual disability accounted for 6.5% and 4.5% of the aggregate YLDs from all causes of adverse health outcomes respectively. African Region recorded the highest prevalence of CP (1.6%) while South-East Asia Region had the highest prevalence of intellectual disability. The top 10 countries accounted for 57.2% of the global prevalence of CP and 62.0% of the global prevalence of intellectual disability. Conclusion: Based on this Database, CP and intellectual disability are highly prevalent and associated with substantial YLDs among children under 5 years worldwide. Universal early detection and support services are warranted, particularly in LMICs to optimize school readiness for these children toward inclusive education as envisioned by the United Nations' Sustainable Development Goals.

PMID: 36091559

26. The Global Pregnancy Collaboration (CoLab) symposium on short- and long-term outcomes in offspring whose mothers had preeclampsia: A scoping review of clinical evidence

Steven J Korzeniewski, Elizabeth Sutton, Carlos Escudero, James M Roberts

Review Front Med (Lausanne). 2022 Aug 30;9:984291. doi: 10.3389/fmed.2022.984291. eCollection 2022.

Preeclampsia is a maternal syndrome characterized by the new onset of hypertension after 20 weeks of gestation associated with multisystemic complications leading to high maternal and fetal/neonatal morbidity and mortality. However, sequelae of preeclampsia may extend years after pregnancy in both mothers and their children. In addition to the long-term adverse cardiovascular effects of preeclampsia in the mother, observational studies have reported elevated risk of cardiovascular, metabolic, cerebral and cognitive complications in children born from women with preeclampsia. Less clear is whether the association between maternal preeclampsia and offspring sequelae are causal, or to what degree the associations might be driven by fetal factors including impaired growth and the health of its placenta. Our discussion of these complexities in the 2018 Global Pregnancy Collaboration annual meeting prompted us to write this review. We aimed to summarize the evidence of an association between maternal preeclampsia and neurobehavioral developmental disorders in offspring in hopes of generating greater research interest in this important topic.

PMID: 36111112

27. Genomic and phenotypic characterization of 404 individuals with neurodevelopmental disorders caused by CTNNB1 variants
Sayaka Kayumi, Luis A Pérez-Jurado, María Palomares, Sneha Rangu, Sarah E Sheppard, Wendy K Chung, Michael C Kruer, Mira Kharbanda, David J Amor, George McGillivray, Julie S Cohen, Sixto García-Miñaúr, Clare L van Eyk, Kelly Harper, Lachlan A Jolly, Dani L Webber, Christopher P Barnett, Fernando Santos-Simarro, Marta Pacio-Míguez, Angela Del Pozo, Somayeh Bakhtiari, Matthew Deardorff, Holly A Dubbs, Kosuke Izumi, Katheryn Grand, Christopher Gray, Paul R Mark, Elizabeth J Bhoj, Dong Li, Xilma R Ortiz-Gonzalez, Beth Keena, Elaine H Zackai, Ethan M Goldberg, Guiomar Perez de Nanclares, Arrate Pereda, Isabel Llano-Rivas, Ignacio Arroyo, María Ángeles Fernández-Cuesta, Christel Thauvin-Robinet, Laurence Faivre, Aurore Garde, Benoit Mazel, Ange-Line Bruel, Michael L Tress, Eva Brilstra, Amena Smith Fine, Kylie E Crompton, Alexander P A Stegmann, Margje Sinnema, Servi C J Stevens, Joost Nicolai, Gaetan Lesca, Laurence Lion-François, Damien Haye, Nicolas Chatron, Amelie Piton, Mathilde Nizon, Benjamin Cogne, Siddharth Srivastava, Jennifer Bassetti, Candace Muss, Karen W Gripp, Rebecca A Procopio, Francisca Millan, Michelle M Morrow, Melissa Assaf, Andres Moreno-De-Luca, Shelagh Joss, Mark J Hamilton, Marta Bertoli, Nicola Foulds, Shane McKee, Alastair H MacLennan, Jozef Gecz, Mark A Corbett

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Purpose: Germline loss-of-function variants in CTNNB1 cause neurodevelopmental disorder with spastic diplegia and visual defects (NEDSDV; OMIM 615075) and are the most frequent, recurrent monogenic cause of cerebral palsy (CP). We investigated the range of clinical phenotypes owing to disruptions of CTNNB1 to determine the association between NEDSDV and CP. Methods: Genetic information from 404 individuals with collectively 392 pathogenic CTNNB1 variants were ascertained for the study. From these, detailed phenotypes for 52 previously unpublished individuals were collected and combined with 68 previously published individuals with comparable clinical information. The functional effects of selected CTNNB1 missense variants were assessed using TOPFlash assay. Results: The phenotypes associated with pathogenic CTNNB1 variants were similar. A diagnosis of CP was not significantly associated with any set of traits that defined a specific phenotypic subgroup, indicating that CP is not additional to NEDSDV. Two CTNNB1 missense variants were dominant negative regulators of WNT signaling, highlighting the utility of the TOPFlash assay to functionally assess variants. Conclusion: NEDSDV is a clinically homogeneous disorder irrespective of initial clinical diagnoses, including CP, or entry points for genetic testing.

PMID: 36083290

28. Cerebral Palsy Prediction with Frequency Attention Informed Graph Convolutional Networks
Haozheng Zhang, Hubert P H Shum, Edmond S L Ho

Annu Int Conf IEEE Eng Med Biol Soc. 2022 Jul;2022:1619-1625. doi: 10.1109/EMBC48229.2022.9871230.

Early diagnosis and intervention are clinically con-sidered the paramount part of treating cerebral palsy (CP), so it is essential to design an efficient and interpretable automatic prediction system for CP. We highlight a significant difference between CP infants' frequency of human movement and that of the healthy group, which improves prediction performance. However, the existing deep learning-based methods did not use the frequency information of infants' movement for CP prediction. This paper proposes a frequency attention informed graph convolutional network and validates it on two consumer-grade RGB video datasets, namely MINI-RGBD and RVI-38 datasets. Our proposed frequency attention module aids in improving both classification performance and system interpretability. In addition, we design a frequency-binning method that retains the critical frequency of the human joint position data while filtering the noise. Our prediction performance achieves state-of-the-art research on both datasets. Our work demonstrates the effectiveness of frequency information in supporting the prediction of CP non-intrusively and provides a way for supporting the early diagnosis of CP in the resource-limited regions where the clinical resources are not abundant.

PMID: 36086367

29. Identification to Intervention: A Perspective From Parents of Children with Cerebral Palsy
Nancy J Wise, Patricia A Gellasch

Nurs Res. 2022 Sep 12. doi: 10.1097/NNR.0000000000000619. Online ahead of print.

Background: Early diagnosis of cerebral palsy (CP) promotes early intervention, symptom management, and support for parents. There is little evidence showing whether parents actually receive these benefits. Objectives: The objectives of this study were to explore and describe the experiences of parents of children with CP, including their journey to diagnosis, access to services and resources, and what they would want other parents or health care providers to know and understand about their experiences. Methods: Using a qualitative descriptive design, semistructured interviews were conducted from January 2021 to April 2021. A purposive sampling method with a snowball effect was used to recruit parents through therapists, a children's hospital, a pediatric rehabilitation center, and social media CP support groups. An inductive approach to content analysis was used to categorize the data. ATLAS.ti® was employed to arrange and code data. Results: Three themes emerged: (a) Something Was Off: I Simply Didn't Know; (b) Coping With the Unknown: Uncharted Territory; and (c) What We Needed Then and Now: Advocacy, Education, and Research. Discussion: Parents emphasized a lack of knowledge of developmental milestones and their inability to recognize delays in their children. Health care providers dismissed persistent unexplained symptoms and developmental delays; parents were expected to 'watch and wait' for their child to catch up. The CP diagnosis, although delayed, validated their concerns and gut intuitions about their child's symptoms and connected them to early intervention services and specialty care. Therapists became a lifeline for parents, providing education, answering questions, obtaining adaptive equipment, and offering care management strategies. Parent support groups provided emotional support, lessened parent isolation, and offered realistic hope. Parents reported a need for an earlier diagnosis and earlier access to services, direct and open communication about CP diagnosis, and follow-up phone calls after the diagnosis. They also asked for a tip sheet to guide them after the diagnosis.

PMID: 36096981

30. Impact of Cerebellar Injury on Neurodevelopmental Outcomes in Preterm Infants with Cerebral Palsy

Yoo Jinie Kim, Ee-Kyung Kim, Jung-Eun Cheon, Huijin Song, Moon Suk Bang, Hyung-Ik Shin, Seung Han Shin, Han-Suk Kim

Am J Phys Med Rehabil. 2022 Aug 29. doi: 10.1097/PHM.0000000000002099. Online ahead of print.

Objective: We aimed to analyze brain imaging findings and neurodevelopmental outcomes of preterm infants diagnosed with cerebral palsy (CP). Design: Brain magnetic resonance imaging (MRI) of preterm infants born between 23 and 32 weeks' gestation and diagnosed with CP at two years corrected age (CA) were evaluated. Brain lesions were categorized as periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and cerebellar hemorrhage (CBH) and graded by the severity. Neurodevelopmental outcomes were assessed using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) at 18-24 months CA, and the Korean Ages and Stages Questionnaire (K-ASQ) at 18 and 24 months CA. Results: CP was found in 38 (6.1%) children among 618 survivors. Cerebellar injury (CI) of high-grade CBH and/or atrophy accounted for 25%. Among patients with supratentorial lesions, those having CI showed significantly lower scores on each K-ASQ domain except gross motor than patients without CI. They also revealed a high proportion of patients below the cut-off value of K-ASQ in language, fine motor, and problem-solving domains ($P < 0.05$), and lower Bayley-III language composite scores ($P = 0.038$). Conclusions: Poor neurodevelopmental outcomes other than motor function were associated with CI. Evaluation of the cerebellum may help predict functional outcomes of patients with CP.

PMID: 36075880

31. Cerebellar Cortex Stimulation for Acquired Dystonia: A Case Report and Review of Its Role in Modern Surgical Practice

Anna Stroud, Stephen Tisch, Benjamin P Jonker

Review Stereotact Funct Neurosurg. 2022 Sep 12;1-10. doi: 10.1159/000526072. Online ahead of print.

Background: Cerebral palsy (CP) is a common cause of acquired dystonia, which can lead to significant interference with quality of life and societal participation. In the last two decades, the surgical treatment of dystonia has primarily focused on deep brain stimulation targeting the basal ganglia and thalamic circuits. However, stimulation of the basal ganglia has generally been less effective in acquired combined forms of dystonia, including dystonic CP. These limitations, along with growing evidence for the role of the cerebellum in the pathophysiology of dystonia, have led to renewed interest in the cerebellum as a target for therapeutic stimulation in dystonia. Nevertheless, there are very few contemporary studies demonstrating its use. We

present the case of a patient with generalized dystonia due to dyskinetic CP who was successfully treated with stimulation of the cerebellar cortex in the modern era. We also review the evidence underpinning targeting of the cerebellum in surgical therapy for dystonia and examine the latest reports of this approach in the surgical literature. Summary: The patient derived significant improvement in the control of her dystonic symptoms, with a reduction in her BFMDRS score from 83 to 25. No complications were observed during more than 3 years of postoperative follow-up. Since the turn of the 21st century, there have been only 7 reports of cerebellar stimulation for dystonia, recruiting a total of 18 patients. These studies have exclusively targeted deep brain structures, making the present report of cortical cerebellar stimulation particularly unique. Key messages: In the 21st century, cerebellar stimulation has predominantly been a second-line treatment for dystonia, after the failure of DBS targeting more mainstream loci within the thalamus and globus pallidus. However, there is increasing recognition of the role of the cerebellum in movement disorders, with multiple convergent lines of evidence supporting its involvement in dystonia pathophysiology. The cerebellum is worthy of greater consideration as a target for neurostimulation in dystonia, particularly in cases of acquired etiology.

PMID: 36096124

Prevention and Cure

32. Editorial: Preterm brain injury: Understanding injurious processes and new strategies for promoting neuroprotection and neuro-repair
Megan Finch-Edmondson, Rod W Hunt, Jens Bo Nielsen, Madison C B Paton

Editorial Front Physiol. 2022 Aug 29;13:994521. doi: 10.3389/fphys.2022.994521. eCollection 2022.

No abstract available

PMID: 36105287

33. Tumour necrosis factor blockade after asphyxia in foetal sheep ameliorates cystic white matter injury
Christopher A Lear, Benjamin A Lear, Joanne O Davidson, Jialin Sae-Jiw, Johanna M Lloyd, Simerdeep K Dhillon, Alistair J Gunn, Laura Bennet

Brain. 2022 Sep 10;awac331. doi: 10.1093/brain/awac331. Online ahead of print.

Cystic white matter injury (WMI) is highly associated with severe neurodevelopmental disability and cerebral palsy in preterm infants, yet its pathogenesis remains poorly understood and there is no established treatment. In the present study we tested the hypothesis that slowly evolving cystic WMI after hypoxia-ischaemia is mediated by programmed necrosis initiated by tumour necrosis factor (TNF). TNF blockade was begun 3 days after hypoxia-ischaemia in order to target the tertiary phase of injury, when the majority of secondary cell death is thought to be complete. Chronically instrumented preterm fetal sheep (0.7 gestation) received 25 minutes of hypoxia-ischaemia induced by complete umbilical cord occlusion (UCO) or sham-UCO (controls, n = 10), followed by intracerebroventricular infusion of the soluble TNF inhibitor, Etanercept, at 3, 8 and 13 days after UCO (UCO-Etanercept, n = 9) or vehicle (UCO-vehicle, n = 9). Fetal brains were processed for histology at 21 days after UCO. UCO-vehicle was associated with a spectrum of macroscopic white matter degeneration, including white matter atrophy, ventriculomegaly and overt temporal lobe cystic WMI. Oligodendrocyte maturational arrest and impaired labelling of myelin proteins, characteristic of diffuse WMI, was observed in the parietal lobe and surrounding the cystic lesions in the temporal lobe. Etanercept markedly attenuated cystic WMI on the side of the intracerebroventricular infusion, with partial contralateral protection. Further, Etanercept improved oligodendrocyte maturation and labelling of myelin proteins in the temporal and parietal lobes. The present study shows that cystic WMI reflects late-onset tertiary cell death mediated by delayed neuroinflammation through the TNF pathway. Delayed TNF blockade markedly attenuated cystic WMI and restored oligodendrocyte maturation and deficits in myelin protein expression. These data suggest that delayed TNF blockade may represent a viable therapeutic strategy to reduce the risk of cystic and diffuse WMI and potentially cerebral palsy after preterm birth, with a surprisingly wide therapeutic window.

PMID: 36087304