Cerebral palsy research news

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Interventions and Management

1. Hip reconstruction in closed triradiate cartilage: long-term outcomes in patients with cerebral palsy
Thomas Schlemmer, Reinald Brunner, Bernhard Speth, Carlo Camathias, Johannes Mayr, Erich Rutz

Arch Orthop Trauma Surg. 2021 May 28. doi: 10.1007/s00402-021-03970-5. Online ahead of print.

Introduction: Hip reconstruction is an established procedure in pediatric patients with neurogenic hip dislocation. An open triradiate cartilage provides the advantage of a high plasticity of the bone which prevents an intraarticular fracture and postoperative adaptation of shape. Some patients with dislocated hips, however, arrive late. A hip reconstruction is still feasible as shown earlier but the long-term risk for osteoarthritis, and recurrence of dislocation, and functional outcome is unknown. It is the aim of our investigation to evaluate long-term clinical and radiological outcomes of hip reconstruction by Dega type pelvic osteotomy performed after fusion of the triradiate epiphyseal cartilage in patients suffering from cerebral palsy. Material and methods: We retrospectively analyzed 43 hips in 37 patients with a hip reconstruction for correction of hip dislocation or subluxation. In all patients, the triradiate cartilage was fused before surgery. Age at surgery was 15 years and 2 months on average and follow-up time was mean 13 years 5 months. Results: Mean Kellgren Lawrence score at final follow-up was significantly higher than at preoperative investigation ($P < 0.00001$). At long-term follow-up 3 of 43 hips had developed pain, and 1 of them required arthroplasty. Reimers´ migration index was stable over the years and was not higher at last follow-up compared to the index observed shortly after surgery ($P = 0.857$), so was the Sharp angle ($P = 0.962$). We found no significant reduction in the range of motion of the hip in the sagittal plane. Conclusion: We noted mild radiological signs of osteoarthritis which possibly occur due to an intraarticular acetabulum fracture during bending down the acetabulum. Nevertheless, hip reconstruction in patients with cerebral palsy and closed triradiate cartilage remains a valuable option as it results in a stable, painless hip for more than a decade.

PMID: 34050376

2. Intraoperative neuromonitoring during distal femoral extension osteotomy in children with cerebral palsy
Ozan A Erdal, Baris Gorgun, Ilker A Sarikaya, Muharrem Inan

J Pediatr Orthop B. 2021 May 28. doi: 10.1097/BPB.0000000000000882. Online ahead of print.

Objectives: The most common treatment method for a fixed knee flexion contracture more than 10 degrees in cerebral palsy (CP) is distal femoral extension osteotomy (DFEO). However, a serious complication after a DFEO is neurological impairment. Its rates were reported as 5- 40%. Intraoperative neuromonitoring (IONM), widely used in spinal surgery and in other fields, is a valuable tool to define any neurological injury during operation. The aim of our study was to determine surgical steps with risk of neurological injury and to report if precautions would be effective in recovering signal loss. Methods: We performed IONM during DFEO of 23 knees of 12 children with CP. IONM was performed by recording somatosensory evoked potentials, transcranial motor evoked potentials and free-run electromyography during defined steps

throughout the surgery. Preoperative and postoperative popliteal angles, flexion contractures and physeal posterior distal femoral angles were evaluated. Results: We detected alert signals at osteotomy or manipulation steps of surgeries of all patients. We observed persistent alert signals in two cases (2 out of 23 knees; Group 2). In this group, the action potentials recovered only after 5 and 10 degrees of undercorrection at the osteotomy sites. Alert signals disappeared after a brief period of waiting in other cases. Throughout mean 37 months of follow-up, none of our patients experienced any neurological complication. Conclusions: The study concludes that the surgical steps in DFEO with a higher risk for a neurological complication were the osteotomy and manipulation steps. Alert signals were detected with the help of IONM, and preventive measures were effective in recovering neuromonitoring recordings.

PMID: 34074918

3. Neurophysiological Assessments of Brain and Spinal Cord Associated with Lower Limb Functions in Children with Cerebral Palsy: A Protocol for Systematic Review and Meta-Analysis
Leonard Ubalde, Jing-Nong Liang

Brain Sci. 2021 May 13;11(5):628. doi: 10.3390/brainsci11050628.

Background: Task-dependent neurophysiological adaptations in people with cerebral palsy have been examined using various techniques such as functional magnetic resonance imaging, peripheral nerve stimulation in order to assess H-reflexes, and transcranial magnetic stimulation. This activity-dependent plasticity is hypothesized to improve specific gross motor function in individuals with cerebral palsy. Although these adaptations have been examined extensively, most studies examined tasks utilizing the upper limbs. The aim of this review is to assess the neurophysiological adaptations of the central nervous system in individuals with cerebral palsy during lower limb functional tasks. Methods: A systematic review and meta-analysis will be conducted to evaluate the neurophysiological changes in the brain and spinal cord associated with lower extremity tasks in individuals with cerebral palsy. We will search within PubMed, MEDLINE, Embase, PsychINFO, and CINAHL using a predetermined search string to identify and evaluate relevant studies. Two independent reviewers will screen these studies against our inclusion criteria and risks of bias, and will extract the data from each study. A third reviewer will be used to resolve any disagreement regarding the inclusion of a study between reviewers. Randomized controlled trials as well as cross-sectional studies published in English 10 years before May 2021 that investigate the neurophysiological adaptations in the brain and spinal cord in people with cerebral palsy will be included if they meet the eligibility criteria. Primary outcomes will include scalar values of fractional anisotropy (FA), H-reflex gains or measures of amplitude, as well as motor cortex (M1) cortical excitability as measured by transcranial magnetic stimulation. Discussion: Since no identifiable data will be involved in this study, no ethical approval is required. Our results will provide insight into the neurophysiological adaptations in children with cerebral palsy, which will be useful in guiding directions for clinical decision making and future development of targeted interventions in pediatrics rehabilitation for children with cerebral palsy. Systematic review registration: The protocol for this systematic review is registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42020215902).

PMID: 34068265

4. Review on the monograph "Improving quality of life for individuals with cerebral palsy through treatment of gait impairment"
Wendy Pierce

Review J Pediatr Rehabil Med. 2021 May 21. doi: 10.3233/PRM-210029. Online ahead of print.

PMID: 34057106

5. Analgesic Effect of Botulinum Toxin in Children with Cerebral Palsy: A Systematic Review
Stramkauskaite Almina, Ylaite Karile, Prasauskiene Audrone, Bakaniene Indre

Review Toxicon. 2021 May 31;S0041-0101(21)00159-8. doi: 10.1016/j.toxicon.2021.05.012. Online ahead of print.

This review aims to determine the analgesic efficacy of botulinum toxin (BTX) for the management of pain in children with cerebral palsy (CP). During July and August 2020, a systematic literature search was performed using a mixture of subject

headings and free text. The eligibility criteria for inclusion in the review were: (1) interventional studies, (2) participants: children aged 0-18 with CP, (3) participants were treated with BTX, (4) an outcome measure of pain or satisfaction with pain management, and (5) published in an English-language peer-reviewed journal. Eleven studies met the eligibility criteria; nine studies explored analgesic effects of BTX for hypertonia related pain and two for postoperative pain. The studies were of level II to level IV evidence. We identified one high-quality study, which provides level II evidence, and two observational studies that supported BTX therapy for muscle hypertonia related pain in non-ambulant children with CP (GMFCS levels IV and V). For children in GMFCS levels I to III, the evidence for the analgesic effects of BTX was contradictory possibly due to the heterogeneity of the studies and/or weak study design. Mixed evidence for the use of BTX to reduce pain after hip surgery was found likely due to differences in the surgical method, injection protocols, and outcome measures.

PMID: 34081932

6. Dietary approaches for atherosclerotic cardiovascular disease prevention in cerebral palsy
Jessica R Iyer, Alexander C Razavi

Dev Med Child Neurol. 2021 Jun 2. doi: 10.1111/dmcn.14945. Online ahead of print.

PMID: 34080182

7. Nutritional Disorders in a Group of Children and Adolescents with Syndromes or Diseases Involving Neurodysfunction
Justyna Podgórska-Bednarz, Lidia Perenc, Mariusz Drużbicki, Agnieszka Guzik

Nutrients. 2021 May 24;13(6):1786. doi: 10.3390/nu13061786.

A study of the literature shows the lack of data on a comprehensive analysis of eating disorders in children with neurodysfunction, which constitute a clinical subgroup with an increased risk of abnormalities in this area. Therefore, the aim of this study was to determine the relationship between the coexistence of nutritional disorders and diseases or syndromes associated with neurodysfunction based on data collected during hospitalization at a rehabilitation center for children and adolescents. A retrospective analysis was carried out in a group of 327 children and adolescents aged 4-18 years. The study group covered various types of diseases or syndromes involving damage to the central nervous system. A retrospective analysis of baseline data (age, sex, main and additional diagnosis and Body Mass Index-BMI) was performed. Two assessment criteria of nutritional status were taken into account (z-score BMI and other previously published normative values). In the study group, malnutrition was found more frequently (18.0% of the respondents) than obesity (11.3% of the subjects). Hypothyroidism coexisting with malnutrition was identified in the study group (N% = 43.8%, p = 0.011) and malnutrition with tetraplegia in the subgroup of spastic cerebral palsy (N% = 34.2 %, p = 0.029).

PMID: 34073813

8. Sleep Disordered Breathing in Adults with Cerebral Palsy: What Do We Know So Far?
Hannah Hayward, Mariam Louis, Linda Edwards, Rafik Jacob

South Med J. 2021 Jun;114(6):339-342. doi: 10.14423/SMJ.0000000000001264.

As advances in medicine continue to extend the lifespan of patients with cerebral palsy (CP), emphasis must be placed on evaluating patients for chronic health issues common in the general adult population. Sleep-disordered breathing (SDB) affects a large number of otherwise healthy adults and is even more common in individuals with disability. SDB includes the following subtypes: obstructive sleep apnea, central sleep apnea, and sleep-related hypoventilation/hypoxemia. SDB consequences include poor daytime functioning from sleepiness and an increased risk of cardiovascular morbidity and mortality. There is a paucity of data available in the literature about the association between SDB and CP in the adult population. More research is needed to understand the true prevalence and management strategies of SDB in patients with CP. This review focuses on three major subtypes of SDB: obstructive sleep apnea, central sleep apnea, and sleep-related hypoventilation/hypoxemia.

PMID: 34075423

9. Usability and inter-rater reliability of the NeuroMotion app: A tool in General Movements Assessments
Katarina A Svensson, Maria Örtqvist, Arend F Bos, Ann-Christin Eliasson, Heléne Ek Sundelin

Eur J Paediatr Neurol. 2021 May 18;33:29-35. doi: 10.1016/j.ejpn.2021.05.006. Online ahead of print.

Background: Early intervention after perinatal brain insults requires early detection of infants with cerebral palsy (CP). General Movements Assessments (GMA) in the fidgety movement period has a high predictive value for CP. Aim: To investigate the NeuroMotion™ app's usability regarding film quality and user experience and to assess the inter-rater reliability of GMA in a neonatal risk group. Methods: GMA, inter-rater reliability and film quality was assessed in a cohort consisting of 37 infants enrolled in a multicentre study of GMA as part of the Swedish neonatal follow-up program for high-risk infants. Some of these infants were filmed twice. For evaluation of user experience 95 parents of 52 infants were addressed with a web-based questionnaire. A GMA expert assessed film quality and performed GMA and three on-site assessors, individually performed GMA. Inter-rater reliability was computed using Krippendorff's alpha (k-alpha). Results: In all, 45 films showed good or excellent quality. The response rate of the questionnaire survey was 40% and revealed predominantly positive perceptions of the NeuroMotion™ app. GMA in 36 infants resulted in substantial agreement (k-alpha = 0.72, 95%CI = 0.3-1.0) between the three on-site assessors' consensus and the GMA expert. Inter-rater reliability for GMA between the on-site assessors was moderate (k-alpha = 0.48, 0.18-0.74). Conclusion: The NeuroMotion™ app produces good technical quality films and the app user experience was overall positive. High agreement was observed between the on-site assessors and the GMA expert. The study design is feasible for more extensive GMA studies in cohorts of infants at risk of CP.

PMID: 34052727

10. Parents' Perspectives on a Computer Game-Assisted Rehabilitation Program for Manual Dexterity in Children With Cerebral Palsy: Qualitative Analysis of Expectations, Child Engagement, and Benefits
Anuprita Kanitkar, Sanjay Tejraj Parmar, Tony J Szturm, Gayle Restall, Gina Rempel, Nariman Sepehri

JMIR Rehabil Assist Technol. 2021 May 31;8(2):e24337. doi: 10.2196/24337.

Background: Children with motor impairments affecting the upper extremity benefit from task-specific therapy, such as constraint-induced movement therapy. However, there is a need to improve engagement and compliance with task-specific exercise programs that target manual dexterity for children with cerebral palsy (CP). A computer game-based rehabilitation (GRP) platform was developed that combines fine manipulation and gross movement exercises with engaging game activities appropriate for young children with CP. Objective: The objectives of this qualitative analysis were to compare parents' perspectives and opinions about expectations, challenges, and benefits between 2 interventions. Methods: A mixed methods, randomized controlled trial (RCT) was conducted to examine the feasibility and estimate the effect size of 2 exercise programs for rehabilitation of manual dexterity of children with CP using either GRP or conventional therapy. Parents of 26 of the children who completed the GRP program (n=33) and parents of 15 of the children who completed the conventional therapy program (n=27) participated in the interviews. A general conductive approach was used to analyze the data recorded during the parents' interviews. Results: Five themes captured the range of the parent's experiences, viewpoints, and ideas: (1) parents' expectations, (2) child's engagement with therapy, (3) positive effects of the interventions, (4) challenges, and (5) improving the protocol. Conclusions: Parents from both groups recognized that their expectations related to improving children's object handling and manipulation skills including participation in activities of daily life were addressed during the 16-week therapy program. Parents perceived a change in the children's level of independence in their daily tasks at home, school, and leisure activities. Trial registration: ClinicalTrials.gov NCT02728375; https://clinicaltrials.gov/ct2/show/NCT02728375.

PMID: 34057424

11. Risk Factors for Cerebral Palsy in Moldova
Ecaterina Bufteac Gincota, Reidun Jahnsen, Larisa Spinei, Guro L Andersen

Medicina (Kaunas). 2021 May 28;57(6):540. doi: 10.3390/medicina57060540.

Background and Objectives: This is the first study assessing risk factors for cerebral palsy (CP) among children born in Moldova. The aim of this study was to identify and describe risk factors for cerebral palsy (CP) among children born in Moldova, which is one of the low-middle income countries in Europe. Materials and Methods: We identified 351 children with CP born during 2009 and 2010 in Moldova. Detailed information on 417 children without CP served as a reference group. Logistic regression analyses were applied to the calculate crude and adjusted odds ratios (OR) for CP with 95% confidence intervals (CI) in addition to attributable fraction (AF). Results: Among children with CP (40.5% girls), 26% had spastic unilateral, 54% bilateral, 13% dyskinetic, 5% ataxic and 2% unclassified CP. Significant risk factors for CP included maternal alcohol consumption during pregnancy (OR 1.7, $p = 0.002$), maternal hypertension (OR 2.0, $p < 0.001$), children born to mothers from the rural areas (OR 1.6, $p < 0.001$), maternal age ≥35 years (OR 0.6, $p = 0.018$), maternal epilepsy (OR 4.3, $p < 0.001$), breech delivery (OR 3.1, $p = 0.001$), home births (OR 6.3, $p = 0.001$), umbilical cord around neck (OR 2.2, $p < 0.001$), AVD (OR 3.1, $p < 0.001$), male gender (OR 1.3, $p < 0.001$), SGA (OR 1.3, $p = 0.027$), multiple gestations (OR 1.7, $p < 0.001$) and hyperbilirubinemia (OR 4.5, $p < 0.001$). Multivariable analyses showed that the AF of CP was 64% for rural residence (OR 2.8, $p = 0.002$), 87% for home birth (7.6, $p = 0.005$), 79% for pre-labor rupture of membrane (OR 4.9, $p = 0.001$), 66% for breech delivery (OR 2.9, $p = 0.002$) and 81% for hyperbilirubinemia (OR 5.4, $p < 0.001$). Conclusions: A combination of factors related to the mother, the delivery and the child were risk factors for CP in Moldova, many of them possibly avoidable. Improved pregnancy and maternity care would potentially reduce the risk of CP. A national CP registry in Moldova is suggested as an opportunity to follow up on these findings.

PMID: 34071238

12. Patterns of Health Service Use Among Young People With Cerebral Palsy in England
Jennifer M Ryan, Grace Lavelle, Nicola Theis, Cherry Kilbride, Marika Noorkoiv

Front Neurol. 2021 May 12;12:659031. doi: 10.3389/fneur.2021.659031. eCollection 2021.

Background: Although the provision of healthcare for people with cerebral palsy (CP) is typically focussed on childhood, many people with CP require access to services periodically throughout their life. Few studies have examined patterns of health service use among young people with CP in England. Understanding patterns of use may inform future service development. Objective: To describe patterns of visits to rehabilitation and medical professionals among ambulatory young people with CP living in England, and identify factors associated with service use. Methods: Sixty-two young people with CP aged 10-19 years [mean (SD) age 13.7 (2.5) years] in Gross Motor Function Classification System (GMFCS) levels I-III reported visits to a range of health professionals, hospital admissions and visits to the emergency department over a median duration of 34 weeks (min-max: 12-34 weeks). Negative binomial models were used to examine factors associated with number of visits. Results: Physiotherapists were the most commonly used professional, with 67.7% of participants visiting a physiotherapist at least once, followed by dentists (66.1%), general practitioners (48.4%), occupational therapists (40.3%) and orthopaedic surgeons (40.3%). Physiotherapists were also the most frequently visited professional with a total of 473 visits (13.3 visits per person-year). Speech and language therapists (5.0 visits per person-year), occupational therapists (4.5 visits per person-year) and nurses (4.3 per person-year) were the next most frequently visited professionals. Age, GMFCS level, and speech impairment were associated with rate of visits to a physiotherapist. Conclusions: The proportion of young people who visited medical and rehabilitation professionals during the study period varied considerably depending on the profession. Generally, the proportion of young people using services was low. In the context of limited resources, data on service use in combination with data on unmet need, may support the reorganisation of services to maximise benefits to young people with CP.

PMID: 34054701

13. Cerebral palsy in ART children has declined substantially over time: a Nordic study from the CoNARTaS group
Anne Lærke Spangmose, Lene Hee Christensen, Anna-Karina Aaris Henningsen, Julie Forman, Signe Opdahl, Liv Bente Romundstad, Kate Himmelmann, Christina Bergh, Ulla-Britt Wennerholm, Aila Tiitinen, Mika Gissler, Anja Pinborg

Hum Reprod. 2021 May 29;deab122. doi: 10.1093/humrep/deab122. Online ahead of print.

Study question: Are the decreasing multiple birth rates after ART associated with a simultaneous drop in the incidence of cerebral palsy (CP) in ART children over time? Summary answer: The relative odds of CP in ART children have declined in the Nordic countries over the past two decades concurrently with declining multiple birth rates. What is known already: In the Nordic countries, the rate of twin pregnancies after ART has decreased from 30% in the early 1990s to 4-13% in 2014, following the implementation of elective single embryo transfer (SET). Consequently, preterm birth rates have declined substantially in ART pregnancies. However, whether the risk of CP, a known consequence of preterm birth, has decreased correspondingly is still unknown. Study design, size, duration: Retrospective register-based cohort study based on data on all

singletons, twins, and higher-order multiples born in Denmark (birth year 1994-2010), Finland (1990-2010), and Sweden (1990 -2014), corresponding to 111 844 ART children and 4 679 351 spontaneously conceived children. Participants/material, setting, methods: Data were obtained from a large Nordic cohort of children born after ART and spontaneous conception initiated by the Committee of Nordic ART and Safety-CoNARTaS. The CoNARTaS cohort was established by cross-linking national register data using the unique personal identification number, allocated to every citizen in the Nordic countries. Data from the National Medical Birth Registers, where information on maternal, obstetric, and perinatal outcomes is recorded, were cross-linked to data from the National ART- and Patients Registers to obtain information on fertility treatments and CP diagnoses. Relative risks of CP for ART compared to spontaneous conception were estimated as odds ratios from multivariate logistic regression analyses across all birth years, as well as for the following birth year categories: 1990-1993, 1994-1998, 1999-2002, 2003-2006, 2007-2010, and 2011-2014. Analyses were made for all children and for singletons and twins, separately. Main results and the role of chance: The main outcome measure was the relative odds of CP in different time periods for ART versus spontaneously conceived children. CP was diagnosed in 661 ART children and 16 478 spontaneously conceived children born between 1990 and 2014. In 1990-1993, the relative odds of CP were substantially higher in all ART children (adjusted odds ratio (aOR) 2.76 (95% CI 2.03-3.67)) compared with all spontaneously conceived children, while in 2011-2014, it was only moderately higher (aOR 1.39 (95% CI 1.01-1.87)). In singletons, the higher relative odds of CP in ART children diminished over time from 1990 to 1993 (aOR 2.02 (95% CI 1.22-3.14)) to 2003-2006 (aOR 1.18 (95% CI 0.91-1. 49)) and was not significantly increased for birth cohorts 2007-2010 and 2011-2014. For ART twins versus spontaneously conceived twins, the relative odds of CP was not statistically significantly increased throughout the study period. Limitations, reasons for caution: The main limitation of the study was a shorter follow-up time and younger age at first CP diagnosis for ART children compared with spontaneously conceived children. However, analyses ensuring a minimum of bias from differences in age at CP diagnosis and follow-up time confirmed the results, hence, we do not consider this to cause substantial bias. Wider implications of the findings: A SET policy in ART treatments has the potential to reduce the increased risk of cerebral palsy in the ART population due to lower rates of multiple deliveries. At a time with high survival rates of frozen/thawed embryos, this study provides a strong argument against the continued use of multiple embryo transfer in most ART settings. Larger cohort studies including also the number of gestational sacs in early pregnancy will be preferable to show an effect of vanishing twins on the risk of CP in the ART population. Study funding/competing interest(s): The study was financed by grants from NordForsk (grant number 71450), Elsass Foundation (19-3-0444), the ALF-agreement (ALFGBG 70940), and The Research Fund of Rigshospitalet, Copenhagen University Hospital. There are no conflicts of interest to declare. Trial registration number: ISRCTN11780826.

PMID: 34051081

14. Effect of position on gross motor function and spasticity in spastic cerebral palsy children
Wardah Rauf, Samia Sarmad, Iqra Khan, Muhammad Jawad

J Pak Med Assoc. 2021 Mar;71(3):801-805. doi: 10.47391/JPMA.1213.

Objectives: To evaluate the effect of positioning on gross motor function and spasticity in spastic quadriplegic cerebral palsy children with Gross Motor Function Classification System level IV and V. Methods: A quasi-experimental study was conducted at two Paediatric Physical Therapy Centres from November 2018 to July 2019. The study comprised of seventy four children with quadriplegic cerebral palsy aged between 3 to 8 years. Data was obtained and gross motor functional abilities and spasticity were assessed by GMFM-88 and Modified Ashworth Scale, respectively. Twenty four-hour positioning in specific seats, night positioning and standing frames for six months. The child was being positioned 24 hours according to his challenges for the period of six months. Semi reclined positioning was performed to manage aspiration, oral leak and to develop retention. Prone positioning was done to develop righting reactions, functional sitting position was used in the treatment regime to attain better upright position and neutral pelvic standing using standing frames. SPSS 24 was used to analyse the data. Results: Paired t-test reported significant improvement in the test scores in lying position, rolling, sitting position, crawling, kneeling, standing, walking or running. Fifty-nine subjects exhibited improvement in spasticity before and after interventional procedures, while 15 showed no improvement ($p<0.05$). Conclusions: Twenty-Four-hour proper body positioning and postural techniques improved gross motor functioning in all five dimensions of functioning. The overall spasticity in quadriplegic cerebral palsy children was also reduced due to appropriate positioning techniques.

PMID: 34057924

15. Botulinum Toxin Type A injections for pediatric spasticity: Keeping our patients informed and practices safe
Edward Wright, Lauren Fetsko

Review J Pediatr Rehabil Med. 2021 May 13. doi: 10.3233/PRM-210031. Online ahead of print.

Serious adverse events (serious AEs) following the therapeutic use of Botulinum Toxin Type A (BoNT-A) are infrequent. Children with pediatric spasticity often have comorbidities that can cloud causation around an adverse event (AE). If a serious AE occurs, clear documentation of information sharing and informed consent as well as the provider-patient relationship are critical to minimizing litigation risks. Reviewing the litigation that has occurred following BoNT-A for pediatric spasticity can offer insight into how providers' perspectives regarding this intervention may differ from those of the public who might serve as jurists. This article offers suggestions for content sharing during the consent process to optimize patient understanding about potential adverse events.

PMID: 34057107

16. Rehabilitation in childhood-onset hyperkinetic movement disorders including dystonia: Treatment change in outcomes across the ICF and feasibility of outcomes for full trial evaluation
Hortensia Gimeno, Helene J Polatajko, Victoria Cornelius, Jean-Pierre Lin, Richard G Brown

Eur J Paediatr Neurol. 2021 May 6;S1090-3798(21)00095-7. doi: 10.1016/j.ejpn.2021.04.009. Online ahead of print.

Background: Childhood-onset hyperkinetic movement disorders (HMD), including dystonia are notoriously difficult to treat and there are limited studies showing successful medical, surgical or non-pharmacological interventions. Methods: This prospective study used grouped data (n = 22) from two studies of the Cognitive Orientation to daily Occupational Performance (CO-OP) Approach for patient-selected goals. Eligibility included aged 6-21 years, deep brain stimulation in place, with manual ability classification system level I-IV. Outcome was assessed on a range of patient-reported and clinician-rated measures across the International Classification of Function at end-treatment (10 weekly sessions) (series 1 and 2) and 3-month follow-up (series 1). Feasibility of outcomes to be used in a full trial were explored. Findings: Nineteen participants completed the intervention and were included in the analysis. Of the primary outcome measures, the self-reported Canadian Occupational Performance Measure showed improvement in goal performance (mean change 4.08, 95% CI [3.37,4.79] post-; 4.18 [5.10,5.26] follow-up), and satisfaction (4.03 [3.04,5.03) post-; 4.44 [3.07,5.82] follow-up]. The Assessment of Motor and Process Skills showed improved motor score (0.52 [0.01,1.03] at follow-up only, while the process score did not change. Objective blind-rated pooled data using the Performance Quality Rating Scale-individualized indicated significant change for trained goals (3.79 [3.37,4.21] post-; (4.01,5.10) follow-up] and untrained goals (1.90 [1.24,2.55] post 1.91 [0.23,3.60] follow-up]. Motor impairment assessed by the Burke-Fahn Motor Disability Rating Scale was unchanged (-3.26 [-6.62,0.09] post-; -1.11 [-8.05,5.82] follow-up). Improvement was also observed in self-efficacy (0.97 [0.47,1.47] post-; 1.37 [1.91-0.83] follow-up) and Quality of Life (0.12 [0.03-0.22] follow-up). Goal improvement; self-efficacy and quality of life captured significant change post-intervention. This improvement was shown despite no change on impairment-related measures and were shown to be feasible measures to use in a larger study of CO-OP for this population.

PMID: 34052114

17. Environmental factors associated with participation and its related concepts among children and youth with cerebral palsy: a rapid review
Jet van der Kemp, Marjolijn Ketelaar, Jan Willem Gorter

Disabil Rehabil. 2021 May 30;1-12. doi: 10.1080/09638288.2021.1923839. Online ahead of print.

Purpose: To provide an overview of environmental factors associated with participation and participation-related constructs in children and youth with cerebral palsy (CP). Methods: A rapid review following the principles from scoping methodology was performed with a literature search in September 2019. The CINAHL, Embase, Ovid MEDLINE and PsychINFO databases were searched to identify original articles which addressed participation in children and youth (aged 0-18) with CP. Results: In total, 9511 unique articles were identified, of which 34 met all inclusion criteria. Many different measures for environmental factors were used. Most common environmental factors associated with participation (i.e., attendance and involvement) were family ecology, type of school, and parental stress. Regarding participation-related constructs (activity competence, sense of self and preferences), most common factors were parental stress and the physical environment. Conclusions: While environmental factors are found to be associated with participation attendance and activity competence in children with CP, there is a lack of research of environmental factors in relation to both participation involvement and other participation-related constructs. To increase impact in clinical practice, future research should involve structured assessments of the environment and focus more on modifiable factors, to help service providers develop treatment paradigms needed for meaningful participation outcomes. IMPLICATIONS FOR REHABILITATION: Family ecology, type of school, and parental stress were the most common factors associated with participation. Future research should focus on modifiable factors associated with participation outcomes. Modifiable environmental factors associated with participation included parental stress, family activity

and type of school. In clinical practice, environmental factors are to be assessed in a more systematic way in relation to current or future participation restrictions.

PMID: 34057002

18. Association of Severe Retinopathy of Prematurity and Bronchopulmonary Dysplasia with Adverse Neurodevelopmental Outcomes in Preterm Infants without Severe Brain Injury
Seong Phil Bae, Seung Han Shin, Young Mi Yoon, Ee-Kyung Kim, Han-Suk Kim

Brain Sci. 2021 May 26;11(6):699. doi: 10.3390/brainsci11060699.

Although impaired neurodevelopment is strongly associated with severe brain injury, most preterm infants survive without severe brain injury. In this study, the association of impaired neurodevelopment and neonatal morbidities of preterm infants was assessed after excluding those with severe brain injury. This was a retrospective study of very low birthweight infants in a single tertiary center. After excluding infants with severe brain injury, the study population was categorized as infants without intraventricular hemorrhage (IVH) and with low-grade IVH. Neurodevelopmental outcomes at a corrected age (CA) of 18-24 months were evaluated using the Bayley Scales of Infant and Toddler Development 3rd Edition (Bayley-III). Cerebral palsy (CP), hearing impairment and blindness were also assessed and compared. Of 240 infants, 25 (11.6%) infants had combined neurodevelopmental impairment (NDI). In the multivariate analysis for combined NDI, small for gestational age (SGA) (adjusted OR 6.820, 95% confidence intervals (CI) 1.770-26.307), moderate to severe bronchopulmonary dysplasia (BPD) (aOR 3.21, 95% CI 1.032-9.999) and severe retinopathy of prematurity (ROP) (aOR 5.669, 95% CI 1.132-28.396) were associated with combined NDI. Among neonatal morbidities, moderate to severe BPD and severe ROP were associated with adverse neurodevelopmental outcomes in preterm infants without severe brain injury.

PMID: 34073292

19. Sibling umbilical cord blood infusion is safe in young children with cerebral palsy
Jessica M Sun, Laura E Case, Mohamad A Mikati, Joan M Jasien, Colleen McLaughlin, Barbara Waters-Pick, Gordon Worley, Jesse Troy, Joanne Kurtzberg

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Preclinical and early phase clinical studies suggest that an appropriately dosed umbilical cord blood (CB) infusion has the potential to help improve motor function in young children with cerebral palsy (CP). As many children with CP do not have their own CB available, use of allogeneic cells would extend access to this potentially beneficial therapy to more children. In this phase I, open-label study, 15 children, aged 1 to 6 years, with moderate to severe spastic CP were treated with a single intravenous infusion of allogeneic human leukocyte antigen (HLA) matched or partially matched sibling CB with a cell dose of ≥2.5 × 107 cells/kg based on the pre-cryopreservation count (median infused cell dose, 3.3 × 107 ; range, 1.8-5.2 × 107). There were a total of 49 adverse events (AEs) over a 2-year time period, but there were no AEs related to the CB infusions. Specifically, there were no acute infusion reactions and no antibody formation against platelets, red blood cells, or donor-specific HLA antigens. Donor cells were not detected in peripheral blood 6 months later. Six months after infusion, participants were assessed for response and experienced a mean ± SD increase of 4.7 ± 2.5 points on the Gross Motor Function Measure-66 and 1 ± 2.9 points on the Peabody Gross Motor Quotient. Appropriately dosed, allogeneic partially or fully HLA-matched sibling CB infusion is well tolerated and potentially beneficial in young children with CP.

PMID: 34085782

20. Deep Brain Stimulation and Hypoxemic Perinatal Encephalopathy: State of Art and Perspectives
Gaëtan Poulen, Emilie Chan-Seng, Emily Sanrey, Philippe Coubes

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Cerebral palsy (CP) is a heterogeneous group of non-progressive syndromes with lots of clinical variations due to the extent of brain damages and etiologies. CP is majorly defined by dystonia and spasticity. The treatment of acquired dystonia in CP is

very difficult. Many pharmacological treatments have been tried and surgical treatment consists of deep brain stimulation (continuous electrical neuromodulation) of internal globus pallidus (GPi). A peculiar cause of CP is neonatal encephalopathy due to an anoxic event in the perinatal period. Many studies showed an improvement of dystonia in CP patients with bilateral GPi DBS. However, it remains a variability in the range of 1% to 50%. Published case-series concerned mainly small population with a majority of adult patients. Selection of patients according to the clinical pattern, to the brain lesions observed on classical imaging and to DTI is the key of a high success rate of DBS in children with perinatal hypoxemic encephalopathy. Only a large retrospective study with a high number of patients in a homogeneous pediatric population with a long-term follow -up or a prospective multicenter trial investigation could answer with a high degree of certitude of the real interest of this therapeutic in children with hypoxemic perinatal encephalopathy.

PMID: 34070634

21. Cell-based treatment for perinatal hypoxic-ischemic encephalopathy
You Jeong Park, Cesario V Borlongan, Mari Dezawa

Review Brain Circ. 2021 Mar 30;7(1):13-17. doi: 10.4103/bc.bc_7_21. eCollection Jan-Mar 2021.

Hypoxic-ischemic encephalopathy (HIE) is a major cause of acute neonatal brain injury and can lead to disabling long-term neurological complications. Treatment for HIE is limited to supportive care and hypothermia within 6 h injury which is reserved for full-term infants. Preclinical studies suggest the potential for cell-based therapies as effective treatments for HIE. Some clinical trials using umbilical cord blood cells, placenta-derived stem cells, mesenchymal stem cells (MSCs), and others have yielded promising results though more studies are needed to optimize protocols and multi-center trials are needed to prove safety and efficacy. To date, the therapeutic effects of most cell-based therapies are hypothesized to stem from the bystander effect of donor cells. Transplantation of stem cells attenuate the aberrant inflammation cascade following HIE and provide a more ideal environment for endogenous neurogenesis and repair. Recently, a subset of MSCs, the multilineage-differentiating stress-enduring (Muse) cells have shown to treat HIE and other models of neurologic diseases by replacing dead or ischemic cells and have reached clinical trials. In this review, we examine the different cell sources used in clinical trials and evaluate the underlying mechanism behind their therapeutic effects. Three databases-PubMed, Web of Science, and ClinicalTrials.gov-were used to review preclinical and clinical experimental treatments for HIE.

PMID: 34084971

22. In-depth analysis reveals complex molecular aetiology in a cohort of idiopathic cerebral palsy
Na Li, Pei Zhou, Hongmei Tang, Lu He, Xiang Fang, Jinxiang Zhao, Xin Wang, Yifei Qi, Chuanbo Sun, Yunting Lin, Fengying Qin, Miaomiao Yang, Zhan Zhang, Caihua Liao, Shuxin Zheng, Xiaofang Peng, Ting Xue, Qianying Zhu, Hong Li, Yan Li, Liru Liu, Jingyu Huang, Li Liu, Changgeng Peng, Angela M Kaindl, Jozef Gecz, Dingding Han, Dong Liu, Kaishou Xu, Hao Hu

Brain. 2021 Jun 2;awab209. doi: 10.1093/brain/awab209. Online ahead of print.

Cerebral palsy is the most prevalent physical disability in children; however, its inherent molecular mechanisms remain unclear. In the present study, we performed in-depth clinical and molecular analysis on 120 idiopathic cerebral palsy families, and identified underlying detrimental genetic variants in 45% of these patients. In addition to germline variants, we found disease-related postzygotic mutations in approximately 6.7% of cerebral palsy patients. We found that patients with more severe motor impairments or a comorbidity of intellectual disability had a significantly higher chance of harboring disease-related variants. By a compilation of 114 known cerebral-palsy-related genes, we identified characteristic features in terms of inheritance and function, from which we proposed a dichotomous classification system according to the expression patterns of these genes and associated cognitive impairments. In two patients with both cerebral palsy and intellectual disability, we revealed that the defective TYW1, a tRNA hypermodification enzyme, caused primary microcephaly and problems in motion and cognition by hindering neuronal proliferation and migration. Furthermore, we developed an algorithm and demonstrated in mouse brains that this malfunctioning hypermodification specifically perturbed the translation of a subset of proteins involved in cell cycling. This finding provided a novel and interesting mechanism for congenital microcephaly. In another cerebral palsy patient with normal intelligence, we identified a mitochondrial enzyme GPAM, the hypomorphic form of which led to hypomyelination of the corticospinal tract in both human and mouse models. In addition, we confirmed that the aberrant Gpam in mice perturbed the lipid metabolism in astrocytes, resulting in suppressed astrocytic proliferation and a shortage of lipid contents supplied for oligodendrocytic myelination. Taken together, our findings elucidate novel aspects of the etiology of cerebral palsy and provide insights for future therapeutic strategies.

PMID: 34077496

23. Parent-Reported PEDI-CAT Mobility and Gross Motor Function in Infants with Cerebral Palsy
Kimberley Scott, Jessica Lewis, Xueliang Pan, Jill Heathcock

Pediatr Phys Ther. 2021 Jun 3. doi: 10.1097/PEP.0000000000000801. Online ahead of print.

Purpose: The purpose of this study is to determine the relationship between the Pediatric Evaluation of Disability Index-Computer Adapted Test (PEDI-CAT), a parent-reported outcome measure, and therapist-administered measures of motor function for infants with cerebral palsy (CP) with moderate to severe motor impairments. Methods: A prospective, cohort study included 54 infants, ages 6 to 24 months, with CP or high risk of CP, Gross Motor Function Classification System (GMFCS) levels III to V. Measures included the Gross Motor Function Measure (GMFM) and the mobility domain of the PEDI-CAT (PEDI-mob). Results: A significant correlation was found between PEDI-mob and GMFM scores. Significant differences were found in PEDI-mob scores as a function of GMFCS level. Conclusions: The PEDI-mob adds value to motor evaluations of infants with CP. Parents can accurately contribute information about daily motor performance for goal setting and treatment planning. The PEDI-mob offers a practical solution when longer assessments cannot be completed.

PMID: 34086623

24. Classification of functional abilities of children and adolescents with cerebral palsy
Robert J Palisano

Child Neurol. 2021 Jun 2. doi: 10.1111/dmcn.14928. Online ahead of print.

PMID: 34080179

25. Validity and Reliability of the Caregiving Difficulty Scale in Mothers of Children with Cerebral Palsy
Eun-Young Park

Int J Environ Res Public Health. 2021 May 26;18(11):5689. doi: 10.3390/ijerph18115689.

This study was conducted to determine the construct validity and reliability of the Caregiving Difficulty Scale, a tool developed to measure difficulties experienced by parents of children with cerebral palsy. To this end, a survey was conducted with 215 mothers of children with cerebral palsy, and the resultant data were analyzed. A confirmatory factor analysis was performed to verify the construct validity of this scale, and the intra-item fit value was calculated for reliability analysis. Validity analysis confirmed that a bi-factor model comprising four sub-factors, Concern for the Child, Impact on Self, Support for Caregiving, and Social and Economic Strain, was suitable for the Caregiving Difficulty Scale. In addition, the reliability analysis results showed that the reliability coefficients of three of these areas, excluding Social and Economic Strain, and the reliability of the entire scale were acceptable. Therefore, the Caregiving Difficulty Scale is an appropriate tool to measure the burden of caregiving for children with cerebral palsy, and the findings emphasize the need to improve its reliability by comparing sub-factors' reliability.

PMID: 34073272

26. Evidence-Based Recommendations for an Optimal Prenatal Supplement for Women in the U.S., Part Two: Minerals
James B B Adams, Jacob C C Sorenson, Elena L L Pollard, Jasmine K K Kirby, Tapan Audhya

Review Nutrients. 2021 May 28;13(6):1849. doi: 10.3390/nu13061849.

The levels of many essential minerals decrease during pregnancy if un-supplemented, including calcium, iron, magnesium, selenium, zinc, and possibly chromium and iodine. Sub-optimal intake of minerals from preconception through pregnancy increases the risk of many pregnancy complications and infant health problems. In the U.S., dietary intake of minerals is often

below the Recommended Dietary Allowance (RDA), especially for iodine and magnesium, and 28% of women develop iron deficiency anemia during their third trimester. The goal of this paper is to propose evidence-based recommendations for the optimal level of prenatal supplementation for each mineral for most women in the United States. Overall, the evidence suggests that optimal mineral supplementation can significantly reduce a wide range of pregnancy complications (including anemia, gestational hypertension, gestational diabetes, hyperthyroidism, miscarriage, and pre-eclampsia) and infant health problems (including anemia, asthma/wheeze, autism, cerebral palsy, hypothyroidism, intellectual disability, low birth weight, neural tube defects, preterm birth, rickets, and wheeze). An evaluation of 180 commercial prenatal supplements found that they varied widely in mineral content, often contained only a subset of essential minerals, and the levels were often below our recommendations. Therefore, there is a need to establish recommendations on the optimal level of mineral supplementation during pregnancy.

PMID: 34071548

27. Making cerebral palsy visible across the globe
Nigel Paneth

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PMID: 34060078