Cerebral Palsy Alliance

NEWS
Cerebral Palsy Research

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Interventions and Management

1. Effects of Suit-Orthosis on Postural Adjustments During Seated Reaching Task in Children With Cerebral Palsy.

Pavão SL, Visicato LP, da Costa CSN, de Campos AC, Rocha NACF.

Pediatr Phys Ther. 2018 Jul;30(3):231-237. doi: 10.1097/PEP.0000000000000519.

To investigate suit-orthosis effects on postural sway during anticipatory and compensatory postural adjustments (APA and CPA, respectively) in a seated reaching task performed by children with cerebral palsy (CP). Twenty-nine children were divided according to Manual Ability Classification System (MACS) I and II-III. Participants were instructed to reach forward toward an object both in a no-suit condition and in a suit-orthosis condition. Using the suit-orthosis, children at MACS II-III decreased velocity of center-of-pressure (CoP) sway during APA, whereas children at MACS I increased the anterior-posterior CoP displacement during CPA. Suit-orthosis improved postural stability in children at MACS II-III during APA. The suit may assist with arm function control during postural sway when preparing to reach for objects. Suit-orthoses in therapy should be individually prescribed considering the intended activity and person's motor impairment.

PMID: 29924076

2. Commentary on "Effects of Suit-Orthosis on Postural Adjustments During Seated Reaching Task in Children With Cerebral Palsy".

Bailes AF, Dorich J.

Pediatr Phys Ther. 2018 Jul;30(3):237. doi: 10.1097/PEP.0000000000000526.

PMID: 29924077

3. Gait Analysis Parameters and Walking Activity Pre- and Postoperatively in Children With Cerebral Palsy.

Nicholson K, Lennon N, Church C, Miller F.

Pediatr Phys Ther. 2018 Jul;30(3):203-207. doi: 10.1097/PEP.0000000000000512.

This study examined the relationship between the Gait Deviation Index (GDI) and walking activity preoperatively and postoperatively. The GDI and walking activity from 74 youth with cerebral palsy (CP) were included in the analysis. The preoperative GDI was calculated using gait parameters collected during a clinical gait analysis 1 to 16 months prior to surgery. The postoperative GDI was calculated using gait parameters collected during a clinical gait analysis 10 to 26 months following surgery. A weak correlation was present between the change in the average GDI and the change in strides. A moderate correlation was found between the change in the Surgery GDI and the change in strides. Single-event multilevel surgery improves gait deviations in children with CP.

However, the improvement in gait pattern has limited correlation with postoperative change in walking activity. Our results demonstrate a need to pair surgical with additional intervention to affect long-term improvements in walking activity.

PMID: 29924068

4. Commentary on "Gait Analysis Parameters and Walking Activity Pre- and Postoperatively in Children With Cerebral Palsy".

Andrews M, Bjornson K.

Pediatr Phys Ther. 2018 Jul;30(3):208. doi: 10.1097/PEP.0000000000000522.

PMID: 29924069

5. Outcome of Single Event Multilevel Soft Tissue Release for Spastic Diplegic Cerebral Palsy.

Gajaseni P, Cheewakongkiat P, Surijamorn P, Srisaarn T.

J Med Assoc Thai. 2017 Mar;100(3):301-5.

We evaluated the results of single event multilevel surgery for treatment of contractures of lower extremities in spastic diplegic cerebral palsy patients in Phramongkutklao Hospital. The present study included 40 patients (23 boys, 17 girls, mean age 8.9 years) with spastic diplegic cerebral palsy, who underwent single event multilevel surgery for the treatment of soft tissue contractures in lower extremities secondary to spasticity between 2006 and 2009. Evaluations were based on pre- and post-operative (follow-up for three years), physical examination, and video observational gait pattern on the Gross Motor Function Classification System (GMFCS) scores and Functional Mobility scales (FMS). Range of motion of all operated joints were increased post-operatively, resulting in significant improvement in posture, gait, and balance of patients. The mean GMFCS scores were 4.2 pre-operatively, 4.1 at post-operatively 1-year, 3.8 at post-operative 2-year, and 3.0 at post-operative 3-year, which were significantly improved two and three years post-operative period ($p<0.05$). The mean FMS scores were improved at 5 meters post-operative at 1-, 2-, and 3-year ($p<0.05$). The mean FMS scores at 50 meters were improved at 3-year post-operative period. Single event multilevel surgery can help spastic diplegic cerebral palsy patients improve range of motions, gait patterns, and mobility functions.

PMID: 29911788

6. A novel surgical correction and innovative splint for swan neck deformity in hypermobility syndrome.

Vishwanathan K, Ganjiwale D.

J Family Med Prim Care. 2018 Jan-Feb;7(1):242-245. doi: 10.4103/jfmpc.jfmpc_14_17.

Splinting is a great domain of occupational therapy profession. Making a splint for the patient would depend on the need or requirement of the problems and deformities. Swan neck deformity is an uncommon condition, and it can be seen in rheumatoid arthritis, cerebral palsy, and after trauma. Conservative treatment of the swan neck deformity is available by different static splints only. There are very few reports of surgical correction of swan-neck deformity in benign hypermobility syndrome. This case report describes the result of novel surgical intervention and an innovative hand splint in a 20-year-old female with a history of cardiovascular stroke with no residual neurological deficit. She presented with correctable swan neck deformity and failed to improve with static ring splints to correct the deformity. She underwent volar plate plication of the proximal interphalangeal joint of the left ring finger along with hemitenodesis of ulnar slip of flexor digitorum superficialis (FDS) tendon whereby, the ulnar slip of FDS was passed through a small surgically created rent in A2 pulley and sutured back to itself. Postoperatively, the patient was referred to occupational therapy for splinting with the instruction that the splint would work sometimes for as static and some time as dynamic for positional and correction of the finger. After occupational therapy intervention and splinting, the patient had a full correction of the swan-neck deformity with near full flexion of the operated finger and can work independently.

PMID: 29915767

7. Influence of Rehabilitation Medicine Residency Training in Performing Chemodenervation in Children with Cerebral Palsy in Thailand.

Buntragulpoontawee M, O'Brien TE, Kovindha A.

J Med Assoc Thai. 2017 Mar;100(3):347-52.

Chemodenervation (CD) involves injecting drugs such as phenol, botulinum toxin, or alcohol to reduce muscle spasticity. However, they interfere with daily activities of children with cerebral palsy (CP). Rehabilitation residency training in Thailand currently requires performing a minimum of five CD procedures. However, the effect of this policy on post-training practice is unknown. To explore the influence of CD training during residency on post-training clinical practice and their current use of it in treating CP patients. The questionnaires were sent to 431 Thai physiatrists nationwide by both electronic and postal mails. The responses were collected within a three-month period. Of 116 (27%) respondents with usable questionnaires, 85 (73%) were trained during their residency to perform CD and 46 (40%) performed it in their practice. Those trained to perform CD were more likely in their subsequent practice to do so ($p = 0.0140$), and younger age was associated with performing it ($p = 0.0055$). The number of CD procedures performed during residency correlated directly with reported confidence in performing the procedure in later practice ($p<0.0001$). The most common reasons for not performing CD were few CP cases in their care, and unavailable equipment or injection agent. Although only a cross-sectional study, the findings suggest that increasing the number of CD procedures required in rehabilitation residency may increase the use of CD to benefit CP patients in future clinical practice.

PMID: 29911799

8. Long-term results of multilevel surgery in adults with cerebral palsy.

Putz C, Blessing AK, Erhard S, Fiethen K, Geisbüsch A, Niklasch M, Döderlein L, Wolf SI, Dreher T.

Int Orthop. 2018 Jun 20. doi: 10.1007/s00264-018-4023-7. [Epub ahead of print]

Deterioration of gait in adolescent and adult patients with cerebral palsy can be associated with multiple factors. Multilevel surgery (MLS) is one option in adults with cerebral palsy to improve gait function with encouraging short-term results. It is a question whether these improvements are maintained over time. In a retrospective consecutive cohort study, adults with bilateral spastic cerebral palsy (BSCP) treated with MLS between 1995 and 2011 were scanned for potential inclusion. Patients needed to fulfill the following inclusion criteria: age at MLS > 17, standardized three-dimensional gait analysis (3D-GA) including clinical examination at pre-operative (E0), a short-term follow-up (E1) and at least seven years (E2) after the index MLS. Twenty adults (10 women, 10 men) with a Gross Motor Function Classification Level (GMFCS) I-III and a mean age at MLS of 24.8 years were included in this study. The average long-term follow-up was 10.9 years. The Gait Profile Score (GPS) was used as primary outcome measure. The GPS improved significantly from 13.8° before surgery to 11.2° at short-term ($p = 0.007$) and to 11.3° at long-term follow-up ($p = 0.002$). Mean GPS showed a slight deterioration between E1 and E2 due to a minority of six patients (30%) who showed a significant loss of correction. Surgical treatment in adults with BSCP was feasible and effective in the long-term. Significant improvement of gait and function was maintained in the majority of patients, while some patients were prone to develop crouch gait, hip flexion contractures, or pain.

PMID: 29922840

9. The Musculoskeletal Aspects of Obesity in Neuromuscular Conditions.

Conklin MJ, Pearson JM.

Orthop Clin North Am. 2018 Jul;49(3):325-333. doi: 10.1016/j.ocl.2018.02.006. Epub 2018 Apr 16.

Obesity is a common problem in children and adolescents with neuromuscular disease. The available literature on obesity in cerebral palsy, spina bifida, and Duchenne muscular dystrophy as it relates to orthopedic treatment is reviewed, including the demographics and measurement of obesity as well as the mechanisms of obesity in these individuals. In addition, the effect of obesity on function, patient evaluation, and orthopedic treatment are reviewed.

PMID: 29929714

10. Assessment of pain in children with cerebral palsy focused on translation and clinical feasibility of the revised FLACC score.

Pedersen LK, Rahbek O, Nikolajsen L, Møller-Madsen B.

Scand J Pain. 2017 Dec 29;9(1):49-54. doi: 10.1016/j.sjpain.2015.06.005.

PMID: 29911641

11. The revised FLACC score: Reliability and validation for pain assessment in children with cerebral palsy.

Pedersen LK, Rahbek O, Nikolajsen L, Møller-Madsen B.

Scand J Pain. 2017 Dec 29;9(1):57-61. doi: 10.1016/j.sjpain.2015.06.007.

PMID: 29911640

12. Preliminary Efficacy of a Friendly Constraint-Induced Therapy (Friendly-CIT) Program on Motor and Psychosocial Outcomes in Children with Cerebral Palsy.

Chen YL, Chen HL, Shieh JY, Wang TN.

Phys Occup Ther Pediatr. 2018 Jun 18:1-12. doi: 10.1080/01942638.2018.1484407. [Epub ahead of print]

Constraint-induced therapy (CIT) is effective, but concerns have been repeatedly raised regarding the generalizability, feasibility, and potentially intrusive nature of restraining a child's unimpaired upper limb. We examined the feasibility and efficacy of friendly-CIT, which uses home-based model, a caregiver-determined schedule, and gentle restraint, in children with cerebral palsy. In a one-group pre-post intervention trial, 15 children (median of age = 8 years, 4 months) participated in 8 weeks of friendly-CIT (36 hours). Motor and psychosocial outcomes were investigated. Participants showed significant improvement on the manual dexterity subtest of the Bruininks-Oseretsky Test of Motor Proficiency ($p = 0.004$); the how often ($p = 0.01$) and how well ($p = 0.02$) scales of the Revised Pediatric Motor Activity Log; and the functional skills score on the Chinese version of the Pediatric Evaluation of Disability Inventory ($p = 0.002$). For psychosocial outcomes, children with CP consistently demonstrated high engagement and increased playfulness ($p < 0.0001$) during the 8-week intervention. Parents showed no change in stress status and high satisfaction with friendly-CIT. Friendly-CIT is feasible and promising for improving a child's motor and psychosocial outcomes without increasing parental stress.

PMID: 29912601

13. Acupuncture for cerebral palsy: A meta-analysis of randomized controlled trials.

Li LX, Zhang MM, Zhang Y, He J.

Neural Regen Res. 2018 Jun;13(6):1107-1117. doi: 10.4103/1673-5374.233455.

To evaluate the efficacy and safety of acupuncture therapy for children with cerebral palsy. We conducted electronic searches of PUBMED (1950/2017), EMBASE (1974/2017), ScienceDirect (1986/2017), Academic Source Premier (1887/2017), the Cochrane Library (Issue 4, April 2017), Science Citation Index Expanded (1900/2017), China National Knowledge Infrastructure (1915/2017), China Biological Medicine (1990/2017-04), WanFang (1980/2017), VIP (1989/2017), and Chinese Science Citation Database (1989/2017). We included randomized controlled trials that aimed to compare the effect of acupuncture plus rehabilitation training versus rehabilitation training alone. Data about functional motor abilities, daily activity/social participation, effective rate, intellectual development, and adverse effects were included. We used Revman 5.2 software for statistical analysis. The primary outcomes included functional motor abilities, daily activity, and effective rate. The secondary outcomes included intellectual development and adverse effects. Twenty-one studies with a total of 1718 participants met the inclusion criteria. The effect size of gross motor function (SMD = 0.64, 95% CI: 0.52 to 0.76, $P < 0.00001$; $I2 = 0\%$, $P = 0.69$; in 13 studies with 1144 patients) and the total effective rate (RR = 1.28, 95% CI: 1.20 to 1.37, $P < 0.00001$; $I2 = 18\%$, $P = 0.27$; in 12 studies with 1106 patients) suggested that acupuncture plus rehabilitation produced a significant improvement in gross motor function and a high total effective rate. The pooled fine motor function (SMD = 3.48, 95% CI: 2.62 to 4.34, $P < 0.00001$; $I2 = 64\%$, $P = 0.10$; in 2 studies with 193 patients), modified Ashworth scale scores (SMD = -0.31, 95% CI: -0.52 to -0.11, $P = 0.003$; $I2 = 74\%$, $P = 0.004$; in 5 studies with 363 patients) and activities of daily living (SMD = 1.45, 95% CI: 1.20 to 1.71, $P < 0.00001$; $I2 = 78\%$, $P = 0.004$; in 4 studies with 313 patients) also indicated improvements in children with cerebral palsy. Publication bias was not observed.

Only mild adverse events related to acupuncture were reported. Acupuncture plus rehabilitation training improved gross motor function, reduced muscle spasms, and enhanced daily life activities in children with cerebral palsy. However, this conclusion should be interpreted with caution due to the small number of randomized controlled trials available and the small sample sizes. More high-quality and large-scale studies are needed.

PMID: 29926839

14. A multicentre cross-sectional study to evaluate the clinical characteristics and nutritional status of children with cerebral palsy.

Aydin K; Turkish Cerebral Palsy Study Group.

Clin Nutr ESPEN. 2018 Aug;26:27-34. doi: 10.1016/j.clnesp.2018.05.002. Epub 2018 May 31.

This study was designed to assess clinical characteristics and nutritional status of pediatric outpatients with cerebral palsy (CP) and to determine prevalence of malnutrition based on physicians' clinical judgment and on anthropometric data in relation to percentile reference values. A total of 1108 pediatric neurology outpatients (mean ± SEM age: 7.2 ± 0.1 years, 59.3% were males) diagnosed with CP were included in this cross-sectional, non-interventional multicenter single-visit study conducted between October 2015 and July 2016 at 20 centers across Turkey. Data on patient and CP characteristics, concomitant nonneuromotor impairments and gastrointestinal disorders as well as anthropometrics, outcome of nutritional status assessment (via physicians' clinical judgment and Gomez classification and Waterlow classification of anthropometric data) and physician's view on nutritional care in CP patients were collected at a single visit. The most common CP etiology was asphyxia (62.5%). The most common clinical category was spastic CP (87.5%) with quadriplegic (54.0%) topography and level V gross motor dysfunction (45.4%) in most of patients. The prevalence of malnutrition was considered to be 57.2% based on physicians' clinical judgment, while shown to be 94.3% (3rd degree in 86.7%) according to Gomez classification of Neyzi weight for age (WFA) percentiles and to be 91.3% (severe in 88.3%) according to Waterlow classification of Neyzi height for age (HFA) percentiles. In conclusion, our findings revealed high prevalence of malnutrition, while also emphasize the likelihood of overestimation of malnutrition in children with CP when anthropometric assessment was based on use of growth charts for general pediatric population. This large-scale survey provided valuable data regarding nutritional assessment practice and malnutrition prevalence among children with CP in Turkey, which may be utilized for future proactive strategies in the prevention and treatment of malnutrition in this population.

PMID: 29908679

15. Tuina for children with cerebral palsy: A protocol for a systematic review: Erratum.

Medicine (Baltimore). 2018 Jun;97(25):e11267. doi: 10.1097/MD.0000000000011267.

PMID: 29924057

16. Is hiragana decoding impaired in children with periventricular leukomalacia?

Kurahashi N, Futamura Y, Nonobe N, Ogaya S, Maki Y, Yoshimura I, Suzuki T, Hosokawa Y, Yamada K, Aso K, Maruyama K, Nakamura M.

Brain Dev. 2018 Jun 13. pii: S0387-7604(18)30242-0. doi: 10.1016/j.braindev.2018.05.018. [Epub ahead of print]

There are few studies on hiragana reading skill and phonological awareness in Japanese schoolchildren with periventricular leukomalacia (PVL). Three seven-year-old children with PVL who had no intellectual disabilities or dysarthria were recruited. Their perinatal information, brain magnetic resonance image (MRI) at term equivalent age, accompanying neurodevelopmental disorders, ophthalmologic features, Kaufman Assessment Battery for Children (K-ABC), a hiragana reading test (four tasks), and a phonological awareness task (mora reversal tasks) were analyzed. Patient (Pt) 1 and pt2 were male. Pt2 and pt3 were siblings of triplets. Their gestational age was 28 or 32 weeks, and their birth weights were 1196, 1554, and 1848 g, respectively. Their brain MRI revealed cystic or non-cystic periventricular white matter injury involving the deep white matter at the trigone of both lateral ventricles. Pt1 had attention-deficit/hyperactivity disorder and pt3 had pervasive developmental disorder not otherwise specified. All patients had strabismus with spared best-corrected visual acuity. Scores of Reading/Decoding in K-ABC ranged from 89 to 99. As for the single mora reading task or the non-word reading task in the kana reading test, Z scores of their reading time ranged from 2.3 to 5.9 compared to control children. Pt1 and pt3 made significant errors in the mora reversal task of three-mora words, whereas all patients could answer all words correctly in the mora reversal task of two-mora words. All children showed significantly prolonged reading time despite their adequate letter recognition.

Two patients showed delayed phonological awareness. It was suggested that hiragana decoding impairment due to subcortical and/or cortical injury related to PVL affected their reading ability.

PMID: 29908673

17. Fifteen-minute consultation: Modern-day art and science of managing cerebral palsy.

Cadwgan J, Goodwin J, Fairhurst C.

Arch Dis Child Educ Pract Ed. 2018 Jun 15. pii: edpract-2017-313793. doi: 10.1136/archdischild-2017-313793. [Epub ahead of print]

While there remains limited intervention to address the damage to the developing brain, current multidisciplinary management of cerebral palsy (CP) needs to minimise the impact of secondary musculoskeletal complications. A focus on comorbidities to maximise function for activity and participation by supporting the child and family in their environment is required. Comprehensive clinical guidance was published by National Institute for Health and Care Excellence (NICE) earlier this year. This article aims to provide a practical clinical approach to the child and family based on:(1) art: empathy, listening and weighing up the clinical picture of the child and family in context; diagnosis, the need for support and space; and care coordination at the right time; and (2) science: the current science in CP care is rapidly expanding in terms of plasticity, pathophysiology, functional assessments and treatments.

PMID: 29907583

Prevention and Cure

18. Association Between rs3833912/rs16944 SNPs and Risk for Cerebral Palsy in Mexican Children.

Torres-Merino S, Moreno-Sandoval HN, Thompson-Bonilla MDR, Leon JAO, Gomez-Conde E, Leon-Chavez BA, Martinez-Fong D, Gonzalez-Barrios JA.

Mol Neurobiol. 2018 Jun 21. doi: 10.1007/s12035-018-1178-6. [Epub ahead of print]

Perinatal asphyxia in the neonatal brain triggers a robust inflammatory response in which nitric oxide (NO) generation plays a hazardous role. Increased levels of NO can be maintained by the activity of inducible NO synthase (NOS2A) on its own or activated by IL-1beta (IL-1β) gene transcription and positive back stimulation of the NOS2 (CCTTT)n microsatellite by IL-1β, thus potentiating brain injury after ischemic perinatal asphyxia. We investigated whether the risk for cerebral palsy (CP) increases when an expansion of the - 2.5 kb (CCTTT)n microsatellite in the NOS2A gene and a single nucleotide polymorphism (SNP) in -C511T of the IL- IL-1β gene promoter occur in patients after perinatal hypoxic-ischemic encephalopathy. Genomic DNA was purified from peripheral leukocytes of 48 patients with CP and of 57 healthy control children. IL-1β SNP genotypes were established using a real-time PCR technique and fluorogenic probes and were validated by restriction fragment length polymorphism (RFLP) analysis using the AvaI restriction enzyme. The length of the CCTTTn microsatellite in the NOS2 gene promoter was determined by automated sequencing. The 14 repeat-long allele of the CCTTTn NOS2A microsatellite was present in 27% of CP patients vs 12.3% of controls, showing an odds ratio (OR) = 2.6531 and 95% confidence interval (CI) = 0.9612-7.3232 (P < 0.0469). The -511 TT genotype frequency showed an OR = 2.6325 (95% CI = 1.1348-6.1066, P = 0.0189). Interestingly, the haplotype CCTTT14/TT showed an OR = 9.561 (95%, CI = 1.1321-80.753; P = 0.0164). The haplotype (CCTTT)14/TT, formed by the expansion of the - 2.5 kb (CCTTT)n microsatellite in the NOS2A gene promoter and the -511 C→ T SNP of the IL-1β gene promoter, might be a useful marker to identify patients who are at high risk for developing CP after hypoxic-ischemic encephalopathy.

PMID: 29931509

19. Antenatal Prevention of Cerebral Palsy and Childhood Disability - Is the Impossible Possible?

Ellery SJ, Kelleher M, Grigsby P, Burd I, Derks JB, Hirst J, Miller SL, Sherman LS, Tolcos M, Walker D.

J Physiol. 2018 Jun 21. doi: 10.1113/JP275595. [Epub ahead of print]

PMID: 29928763

20. Neonatal interventions for preventing cerebral palsy: an overview of Cochrane Systematic Reviews.

Shepherd E, Salam RA, Middleton P, Han S, Makrides M, McIntyre S, Badawi N, Crowther CA.

Cochrane Database Syst Rev. 2018 Jun 20;6:CD012409. doi: 10.1002/14651858.CD012409.pub2. [Epub ahead of print]

Cerebral palsy is an umbrella term that encompasses disorders of movement and posture attributed to non-progressive disturbances occurring in the developing foetal or infant brain. As there are diverse risk factors and aetiologies, no one strategy will prevent cerebral palsy. Therefore, there is a need to systematically consider all potentially relevant interventions for prevention. Primary To summarise the evidence from Cochrane Systematic Reviews regarding effects of neonatal interventions for preventing cerebral palsy (reducing cerebral palsy risk).Secondary To summarise the evidence from Cochrane Systematic Reviews regarding effects of neonatal interventions that may increase cerebral palsy risk. We searched the Cochrane Database of Systematic Reviews (27 November 2016) for reviews of neonatal interventions reporting on cerebral palsy. Two review authors assessed reviews for inclusion, extracted data, and assessed review quality (using AMSTAR and ROBIS) and quality of the evidence (using the GRADE approach). Reviews were organised by topic; findings were summarised in text and were tabulated. Interventions were categorised as effective (high-quality evidence of effectiveness); possibly effective (moderate-quality evidence of effectiveness); ineffective (high-quality evidence of harm); probably ineffective (moderate-quality evidence of harm or lack of effectiveness); and no conclusions possible (low- to very low-quality evidence). Forty-three Cochrane Reviews were included. A further 102 reviews pre-specified the outcome cerebral palsy, but none of the included randomised controlled trials (RCTs) reported this outcome. Included reviews were generally of high quality and had low risk of bias, as determined by AMSTAR and ROBIS. These reviews involved 454 RCTs; data for cerebral palsy were available from 96 (21%) RCTs involving 15,885 children. Review authors considered interventions for neonates with perinatal asphyxia or with evidence of neonatal encephalopathy (3); interventions for neonates born preterm and/or at low or very low birthweight (33); and interventions for other specific groups of 'at risk' neonates (7). Quality of evidence (GRADE) ranged from very low to high. Interventions for neonates with perinatal asphyxia or with evidence of neonatal encephalopathy. Effective interventions: high-quality evidence of effectiveness. Researchers found a reduction in cerebral palsy following therapeutic hypothermia versus standard care for newborns with hypoxic ischaemic encephalopathy (risk ratio (RR) 0.66, 95% confidence interval (CI) 0.54 to 0.82; seven trials; 881 children).No conclusions possible: very low-quality evidence. One review observed no clear differences in cerebral palsy following therapeutic hypothermia versus standard care. Interventions for neonates born preterm and/or at low or very low birthweight. Possibly effective interventions: moderate-quality evidence of effectiveness. Researchers found a reduction in cerebral palsy with prophylactic methylxanthines (caffeine) versus placebo for endotracheal extubation in preterm infants (RR 0.54, 95% CI 0.32 to 0.92; one trial; 644 children).Probably ineffective interventions: moderate-quality evidence of harm. Researchers reported an increase in cerebral palsy (RR 1.45, 95% CI 1.06 to 1.98; 12 trials; 1452 children) and cerebral palsy in assessed survivors (RR 1.50, 95% CI 1.13 to 2.00; 12 trials; 959 children) following early (at less than eight days of age) postnatal corticosteroids versus placebo or no treatment for preventing chronic lung disease in preterm infants. Probably ineffective interventions: moderate-quality evidence of lack of effectiveness. Trial results showed no clear differences in cerebral palsy following ethamsylate versus placebo for prevention of morbidity and mortality in preterm or very low birthweight infants (RR 1.13, 95% CI 0.64 to 2.00; three trials, 532 children); volume expansion versus no treatment (RR 0.76, 95% CI 0.48 to 1.20; one trial; 604 children); gelatin versus fresh frozen plasma (RR 0.94, 95% CI 0.52 to 1.69; one trial, 399 children) for prevention of morbidity and mortality in very preterm infants; prophylactic indomethacin versus placebo for preventing mortality and morbidity in preterm infants (RR 1.04, 95% CI 0.77 to 1.40; four trials; 1372 children); synthetic surfactant versus placebo for respiratory distress syndrome in preterm infants (RR 0.76, 95% CI 0.55 to 1.05; five trials; 1557 children); or prophylactic phototherapy versus standard care (starting phototherapy when serum bilirubin reached a pre-specified level) for preventing jaundice in preterm or low birthweight infants (RR 0.96, 95% CI 0.50 to 1.85; two trials; 756 children).No conclusions possible: low- to very low-quality evidence. No clear differences in cerebral palsy were observed with interventions assessed in 21 reviews. Interventions for other specific groups of 'at risk' neonates. No conclusions possible: low- to very low-quality evidence. Review authors observed no clear differences in cerebral palsy with interventions assessed in five reviews. This overview summarises evidence from Cochrane Systematic Reviews regarding effects of neonatal interventions on cerebral palsy, and can be used by researchers, funding bodies, policy makers, clinicians, and consumers to aid decision-making and evidence translation. To formally assess other benefits and/or harms of included interventions, including impact on risk factors for cerebral palsy, review of the included Reviews is recommended. Therapeutic hypothermia versus standard care for newborns with hypoxic ischaemic encephalopathy can prevent cerebral palsy, and prophylactic methylxanthines (caffeine) versus placebo for endotracheal extubation in preterm infants may reduce cerebral palsy risk. Early (at less than eight days of age) postnatal corticosteroids versus placebo or no treatment for preventing chronic lung disease in preterm infants may increase cerebral palsy risk. Cerebral palsy is rarely identified at birth, has diverse risk factors and aetiologies, and is diagnosed in approximately one in 500 children. To date, only a small proportion of Cochrane Systematic Reviews assessing neonatal interventions have been able to report on this outcome. There is an urgent need for long-term follow-up of RCTs of such interventions addressing risk factors for cerebral palsy (through strategies such as data linkage with registries) and for consideration of the use of relatively new interim assessments (including the General Movements Assessment). Such RCTs must be rigorous in their design and must aim for consistency in cerebral palsy outcome measurement and reporting to facilitate pooling of data and thus to maximise research efforts focused on prevention.

PMID: 29926474

21. Epigenetic machine learning: utilizing DNA methylation patterns to predict spastic cerebral palsy.

Crowgey EL, Marsh AG, Robinson KG, Yeager SK, Akins RE.

BMC Bioinformatics. 2018 Jun 21;19(1):225. doi: 10.1186/s12859-018-2224-0.

Spastic cerebral palsy (CP) is a leading cause of physical disability. Most people with spastic CP are born with it, but early diagnosis is challenging, and no current biomarker platform readily identifies affected individuals. The aim of this study was to evaluate epigenetic profiles as biomarkers for spastic CP. A novel analysis pipeline was employed to assess DNA methylation patterns between peripheral blood cells of adolescent subjects (14.9 ± 0.3 years old) with spastic CP and controls at single CpG site resolution. Significantly hypo- and hyper-methylated CpG sites associated with spastic CP were identified. Nonmetric multidimensional scaling fully discriminated the CP group from the controls. Machine learning based classification modeling indicated a high potential for a diagnostic model, and 252 sets of 40 or fewer CpG sites achieved near-perfect accuracy within our adolescent cohorts. A pilot test on significantly younger subjects (4.0 ± 1.5 years old) identified subjects with 73% accuracy. Adolescent patients with spastic CP can be distinguished from a non-CP cohort based on DNA methylation patterns in peripheral blood cells. A clinical diagnostic test utilizing a panel of CpG sites may be possible using a simulated classification model. A pilot validation test on patients that were more than 10 years younger than the main adolescent cohorts indicated that distinguishing methylation patterns are present earlier in life. This study is the first to report an epigenetic assay capable of distinguishing a CP cohort.

PMID: 29925314

22. Bone Morphogenetic Protein (BMP)-3b Gene Depletion Causes High Mortality in a Mouse Model of Neonatal Hypoxic-Ischemic Encephalopathy.

Ogawa Y, Tsuji M, Tanaka E, Miyazato M, Hino J.

Front Neurol. 2018 Jun 5;9:397. doi: 10.3389/fneur.2018.00397. eCollection 2018.

Bone morphogenetic proteins (BMPs) are a group of proteins that induce the formation of bone and the development of the nervous system. BMP-3b, also known as growth and differentiation factor 10, is a member of the BMPs that is highly expressed in the developing and adult brain. BMP-3b is therefore thought to play an important role in the brain even after physiological neurogenesis has completed. BMP-3b is induced in peri-infarct neurons in aged brains and is one of the most highly upregulated genes during the initiation of axonal sprouting. However, little is known about the role of BMP-3b in neonatal brain injury. In the present study, we aimed to describe the effects of BMP-3b gene depletion on neonatal hypoxic-ischemic encephalopathy, which frequently results in death or lifelong neurological disabilities, such as cerebral palsy and mental retardation. BMP-3b knockout and wild type mice were prepared at postnatal day 12. Mice of each genotype were divided into sham-surgery, mild hypoxia-ischemia (HI), and severe HI groups (n = 12-45). Mice in the HI groups were subjected to left common carotid artery ligation followed by 30 min (mild HI) or 50 min (severe HI) of systemic hypoxic insult. A battery of tests, including behavioral tests, was performed, and the brain was then removed and evaluated at 14 days after insult. Compared with wild type pups, BMP-3b knockout pups demonstrated the following characteristics. (1) The males exposed to severe HI had a strikingly higher mortality rate, and as many as 70% of the knockout pups but none of the wild type pups died; (2) significantly more hyperactive locomotion was observed in males exposed to severe HI; and (3) significantly more hyperactive rearing was observed in both males and females exposed to mild HI. However, BMP-3b gene depletion did not affect other parameters, such as cerebral blood flow, cylinder test and rotarod test performance, body weight gain, brain weight, spleen weight, and neuroanatomical injury. The results of this study suggest that BMP-3b may play a crucial role to survive in severe neonatal hypoxic-ischemic insult.

PMID: 29922215

23. Antenatal magnesium sulfate treatment for women at risk of preterm birth is safe and might decrease the risk of cerebral palsy.

Huusom LD.

BMJ Evid Based Med. 2018 Jun 19. pii: bmjebm-2018-110897. doi: 10.1136/bmjebm-2018-110897. [Epub ahead of print]

PMID: 29921710

24. Corpus callosum and cerebellar vermis size in very preterm infants: Relationship to long-term neurodevelopmental outcome.

Wu PM, Shih HI, Yu WH, Chen LW, Wang LC, Huang CC, Tu YF.

Pediatr Neonatol. 2018 Jun 1. pii: S1875-9572(17)30546-6. doi: 10.1016/j.pedneo.2018.05.012. [Epub ahead of print]

The neonatal changes of corpus callosum or cerebellar volume in preterm infants have been shown to link with abnormal mentality and motor disability in early childhood. This study aims to predict the long-term neurological outcomes by measuring these changes on neonatal brain ultrasound in preterm infants. Our cohort consisted of infants aged below 32 weeks' gestation with very low birth body weights who completed neuro-assessments at 5 years of age. Corpus callosum or cerebellar vermis were measured at 28-30 weeks and at 37-40 weeks gestational age in premature infants with cerebral palsy (CP), mental retardation (MR) and normal control premature infants. There are 12 patients in MR group, 12 in CP group and 27 patients as controls for final analysis. There was no significant difference in other factors between study groups except lower gestational age (P = 0.043) in CP group. Respiratory distress syndrome was more common in MR group (P = 0.037) and cystic periventricular leukomalacia was more common in CP group (P < 0.001) than controls. After adjusting for sex and birth body weight, the MR group had smaller cerebellar vermis area at 37-40 gestational weeks (P = 0.002) than controls. They also reduced the growth of corpus callosum area (difference = -0.12 ± 0.16, P = 0.029) and cerebellar vermis area (difference = 1.10 ± 0.44, P = 0.020) from 28 to 30 gestational weeks to 37-40 gestational weeks compared with controls (difference = 0.03 ± 0.15, 1.92 ± 0.70, respectively). In contrast, the CP group had reduced the growth of corpus callosum body (difference = -0.02 ± 0.18, P = 0.034) compared with controls (difference = 0.03 ± 0.04). They subsequently had smaller body thickness of corpus callosum (0.10 ± 0.02, P = 0.015) at 37-40 gestational weeks than controls (0.14 ± 0.04). Serial monitoring corpus callosum and cerebellar vermis size in early life of very preterm babies may predict the motor or mentality neurological outcome at 5 years of age.

PMID: 29910162

25. Genetic burden and associations with adverse neurodevelopment in neonates with congenital heart disease.

Blue GM, Ip E, Walker K, Kirk EP, Loughran-Fowlds A, Sholler GF, Dunwoodie SL, Harvey RP, Giannoulatou E, Badawi N, Winlaw DS.

Am Heart J. 2018 Jul;201:33-39. doi: 10.1016/j.ahj.2018.03.021. Epub 2018 Apr 5.

Up to 20% of children with congenital heart disease (CHD) undergoing cardiac surgery develop neurodevelopmental disabilities (NDD), with some studies reporting persistent impairment. Recent large-scale studies have demonstrated shared genetic mechanisms contributing to CHD and NDD. In this study, a targeted approach was applied to assess direct clinical applicability of this information. A gene panel comprising 148 known CHD and/or NDD genes was used to sequence 15 patients with CHD + NDD, 15 patients with CHD, and 15 healthy controls. The number and types of variants between the 3 groups were compared using Poisson log-linear regression, and the SNP-set (Sequence) Kernel Association Test-Optimized was used to conduct single-gene and gene-pathway burden analyses. A significant increase in rare (minor allele frequency < 0.01) and novel variants was identified between the CHD + NDD cohort and controls, P < .001 and P = .001, respectively. There was also a significant increase in rare variants in the CHD cohort compared with controls (P = .04). Rare variant burden analyses implicated pathways associated with "neurotransmitters," "axon guidance," and those incorporating "RASopathy" genes in the development of NDD in CHD patients. These findings suggest that an increase in novel and rare variants in known CHD and/or NDD genes is associated with the development of NDD in patients with CHD. Furthermore, burden analyses point toward rare variant burden specifically in pathways related to brain development and function as contributors to NDD. Although promising variants and pathways were identified, further research, utilizing whole-genome approaches, is required prior to demonstrating clinical utility in this patient group.

PMID: 29910053

26. Neurologic Consequences of Preterm Birth.

Ream MA, Lehwald L.

Curr Neurol Neurosci Rep. 2018 Jun 16;18(8):48. doi: 10.1007/s11910-018-0862-2.

Preterm birth is the leading cause of death worldwide in children < 5 years of age; however, technology and advances in medical knowledge are increasing the survival of children born even at the fringes of viability. With increased survival comes increased risk of long-term neurologic impairments. This paper aims to review recent findings related to changes in brain development associated with prematurity and its impact on neurodevelopmental disabilities. Advanced imaging techniques, longitudinal follow-up of individuals born extremely preterm into adulthood and improved understanding of risk factors associated with neurologic impairment contribute to recent discoveries. Sensory impairments are often associated with later cognitive and social impairments and therefore represent targets for therapy. All aspects of neurologic development can be affected by preterm delivery. Future research is needed to further elucidate targets for prenatal and postnatal interventions for neuroprotection and to improve outcomes of prematurity.

PMID: 29907917

27. Early developmental brain injury/interference: moving on from cerebral palsy.

Fahey M.

Dev Med Child Neurol. 2015 Jul;57(7):681. doi: 10.1111/dmcn.12776.

PMID: 29927489

28. For and against the term cerebral palsy.

Baxter P.

Dev Med Child Neurol. 2015 Jul;57(7):592. doi: 10.1111/dmcn.12802.

PMID: 29927488

29. Epidemiological and clinical profile of cerebral palsy at the Bobo-dioulasso university hospital (Burkina Faso).
[Article in French; Abstract available in French from the publisher]

Gandema S, Sanouo, Ouedraogo AS, Nacro B.

Mali Med. 2015;30(3):50-54.

Cerebral palsy is the leading cause of motor disability in children. To describe the epidemiological and clinical profiles of cerebral palsy in children seen at the of Bobo-Dioulasso University Hospital. This is a descriptive cross-sectional study prospectively conducted at the Department of Physical Medicine at the University Hospital of Bobo-Dioulasso over a period of one year from 1 July 2012 to 30 June 2013. Our study population consisted of all children aged between 0 and 15 years received during the study period displaying cerebral palsy symptoms. We studied 174 patients including 106 boys and 68 girls. The average age was 32.79 months. Etiological factors were dominated by prematurity (34.5%) and cerebral anoxia (25.86%). The main clinical presentations were diplegia (50%), quadriplegia (19.54%), hemiplegia (14.37%), monoplegia (10.34%) and triplegia (5.75%). The most common associated symptoms were epilepsy (15%), eye disorders (12.6%), and hearing problems (10%). Due to its frequency and disabling potential, cerebral palsy is a major public health problem in Burkina Faso. Its support in the African environment is heavily complicated by self-medication and traditional therapy.

PMID: 29927169