NEWS
Cerebral Palsy Research

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## Interventions and Management

**1. Infant hand development in unilateral cerebral palsy: filling the knowledge gap.**
Holmefur M.

Dev Med Child Neurol. 2019 Jan 15. doi: 10.1111/dmcn.14164. [Epub ahead of print]

PMID: 30644546

**2. Upper Limb Function of Children with Unilateral Cerebral Palsy After a Magic-Themed HABIT: A Pre-Post-Study with 3- and 6-Month Follow-Up.**
Hines A, Bundy AC, Black D, Haertsch M, Wallen M.

Phys Occup Ther Pediatr. 2019 Jan 16:1-16. doi: 10.1080/01942638.2018.1505802. [Epub ahead of print]

AIMS: To examine changes in upper limb function, and performance in everyday tasks, for children with unilateral cerebral palsy who participated in a magic-themed hand-arm bimanual intensive therapy (HABIT). METHODS: Twenty-eight children participated; mean age 10 y 6 mo (SD 2 y 2 mo), n = 15 male and n = 13 female. Using a single group, pre-and post-test design, the magic-themed HABIT was delivered for 60 hours over 10 days. Bimanual and unimanual hand function were measured using the Assisting Hand Assessment (AHA) and Box and Blocks Test (BBT). Occupational performance was rated using the Canadian Occupational Performance Measure (COPM). Two parent questionnaires explored change in bimanual hand use in everyday activities; ABILHAND-Kids and Children's Hand-use Experience Questionnaire (CHEQ). Assessments were completed pre-, immediately post, 3 months and 6 months after the intervention. RESULTS: Friedman's ANOVA revealed a significant improvement for COPM and CHEQ grasp subscale. Repeated measures ANOVA revealed a significant improvement in BBT, and ABILHAND-Kids, and no significant change for AHA. CONCLUSIONS: Children who participated in the magic-themed HABIT experienced improved occupational performance, unimanual skills, and parent ratings of performance in challenging everyday tasks.

PMID: 30648457

**3. Reproducibility of the Kids Balance Evaluation Systems Test (Kids-BESTest) and the Kids-Mini-BESTest for children with cerebral palsy.**
Dewar R, Claus AP, Tucker K, Ware RS, Johnston LM.

Arch Phys Med Rehabil. 2019 Jan 9. pii: S0003-9993(19)30002-4. doi: 10.1016/j.apmr.2018.12.021. [Epub ahead of print]

OBJECTIVE: To evaluate the reproducibility, including reliability and agreement, of the Kids Balance Evaluation Systems Test (Kids-BESTest) and short-form Kids-Mini-BESTest for measuring postural control in school-aged children with cerebral palsy. DESIGN: Psychometric study of intra-rater, inter-rater and test-retest reliability and agreement; SETTING: Clinical laboratory and home. PARTICIPANTS: Convenience sample of 18 children aged 8 to 17 years with ambulant cerebral palsy (Gross Motor Function Classification System I-II) with spastic or ataxic motor type. INTERVENTION: Not applicable. MAIN OUTCOME MEASURES: Postural control was assessed using the Kids-BESTest and the short-form Kids-Mini-BESTest. An experienced physiotherapist assessed all children in real-time and the testing session was videoed. The same physiotherapist viewed and scored the video twice, at least two weeks apart, to assess intra-rater reproducibility. Another experienced physiotherapist scored the same video to determine inter-rater reproducibility. Thirteen children returned for a repeat assessment with the first physiotherapist within 6 weeks and their test-retest performance was rated in real time and with video. RESULTS: Excellent reliability was observed for both the Kids-BESTest (ICC 0.96 to 0.99) and Kids-Mini-BESTest (ICC 0.79 to 0.98). The Smallest Detectable Change was good to excellent for all Kids-BESTest agreement analyses (5% to 9%), but poor to good for Kids-Mini-BESTest analyses (9% to 16%). CONCLUSION: The Kids-BESTest shows an excellent ability to discriminate postural control abilities of school-aged children with cerebral palsy and it has a low Smallest Detectable Change, suitable for use as a pre-post intervention outcome measure. Although the Kids-Mini-BESTest is 5-10 min shorter to administer, it has poorer reproducibility and focuses only on falls-related balance, which excludes two domains of postural control.

PMID: 30639271

**4. Postoperative epidural analgesia versus systemic analgesia for thoraco-lumbar spine surgery in children.**
Guay J, Suresh S, Kopp S, Johnson RL.

Cochrane Database Syst Rev. 2019 Jan 16;1:CD012819. doi: 10.1002/14651858.CD012819.pub2. [Epub ahead of print]

BACKGROUND: Spine surgery may be associated with severe acute postoperative pain. Compared with systemic analgesia alone, epidural analgesia may offer better pain control. However, epidural analgesia has sometimes been associated with rare but serious complications. Therefore, it is critical to quantify the real benefits of epidural analgesia over other modes of pain treatment. OBJECTIVES: To assess the effectiveness and safety of epidural analgesia compared with systemic analgesia for acute postoperative pain control after thoraco-lumbar spine surgery in children. SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and Cumulative Index to Nursing and Allied Health Literature on 14 November 2018, together with the references lists of related reviews and retained trials, and two trials registers. SELECTION CRITERIA: We included all randomized controlled trials performed in children undergoing any type of thoraco-lumbar spine surgery comparing epidural analgesia with systemic analgesia for postoperative pain. We applied no language or publication status restriction. DATA COLLECTION AND ANALYSIS: We assessed risk of bias of included trials using the Cochrane tool. We analysed data using random-effects models. We rated the quality of the evidence according to the GRADE scale. MAIN RESULTS: We included 11 trials (559 participants) in the review, and seven trials (249 participants) in the analysis: 140 participants received epidural analgesia and 109 received systemic analgesia. Most studies included adolescents. Three trials included in the analysis contained some participants older than 18 years. The types of surgery were posterior spinal fusion for idiopathic scoliosis (nine trials), anterior correction for idiopathic scoliosis (one trial), or selective dorsal rhizotomy in children with cerebral palsy (one trial). The mean numbers of vertebrae operated on were between nine and 14.5 and the mean numbers of spinal levels were between three and four and a half. The length of surgery varied between three and six and a half hours. Compared with systemic analgesia, epidural analgesia reduced pain at rest at all time points. At six to eight hours, the mean pain score on a 0 to 10 scale with systemic analgesia was 3.1 (standard deviation 0.7) and with epidural analgesia was -1.32 points (95% confidence interval (CI) -1.83 to -0.82; 4 studies, 116 participants; moderate-quality evidence). At 72 hours, the mean pain score with epidural analgesia was equivalent to a -0.8 point reduction on a 0 to 10 scale (standardized mean difference (SMD) -0.65, 95% CI -1.19 to -0.10; 5 studies, 157 participants; moderate-quality evidence). Return of gastrointestinal function There was no difference for nausea and vomiting between groups (risk ratio (RR) 0.87, 95% CI 0.58 to 1.30; 6 studies, 215 participants; low-quality evidence). One study found epidural analgesia with local anaesthetics may have increased the number of participants who had their first flatus within 48 hours (RR 1.63, 95% CI 1.08 to 2.47; 30 participants; very low-quality evidence). Two studies found epidural analgesia with local anaesthetics may have increased the number of participants in whom first bowel movement occurred within 48 hours (RR 11.52, 95% CI 2.36 to 56.26; 60 participants; low-quality evidence). It was uncertain whether epidural analgesia reduced the time to first bowel movement (MD 0.09 days, 95% CI -0.32 to 0.50; 1 study, 60 participants; very low-quality evidence) and time to first liquid ingestion following epidural infusion of an opioid alone or a local anaesthetic plus an opioid (mean difference (MD) -5.02 hours, 95% CI -13.15 to 3.10; 2 studies, 56 participants; very low-quality evidence). Epidural analgesia with local anaesthetics may have increased the risk of having first solid food ingestion within 48 hours (RR 7.00, 95% CI 1.91 to 25.62; 1 study, 30 participants; very low-quality evidence). Secondary outcomes It was uncertain whether there was a difference in time to ambulate (MD 0.08 days, 95% CI -0.24 to 0.39; 1 study, 60 participants; very low-quality evidence) and hospital length of stay (MD -0.29 days, 95% CI -0.69 to 0.10; 2 studies, 89 participants; very low-quality evidence). Two studies found participants were more satisfied when treated with epidural analgesia (MD 1.62 on a scale from 0 to 10, 95% CI 1.26 to 1.97; 60 participants; very low-quality evidence). It was unclear whether there was a difference in parent satisfaction for epidural analgesia with an opioid alone (MD

0.60, 95% CI -0.81 to 2.01; 1 trial, 27 participants; very low-quality evidence). Complications It was uncertain whether there was a difference in the risk of complications such as: respiratory depression (risk difference (RD) -0.05, 95% CI -0.16 to 0.05; 4 studies, 126 participants; very low-quality evidence); wound infection (RD 0.01, 95% CI -0.05 to 0.08; 2 trials, 93 participants; very low-quality evidence); epidural abscess (RD 0, 95% CI -0.05 to 0.05; 3 trials, 120 participants; very low-quality evidence); and neurological complications (RD 0.01, 95% CI -0.04 to 0.06; 4 studies, 151 participants; very low-quality evidence). AUTHORS' CONCLUSIONS: There is moderate- and low-quality evidence that there may be a small additional reduction in pain up to 72 hours after surgery with epidural analgesia compared with systemic analgesia. Two very small studies showed epidural analgesia with local anaesthetic alone may accelerate the return of gastrointestinal function. The safety of this technique in children undergoing thoraco-lumbar surgery is uncertain due to the very low-quality of the evidence. The study in 'Studies awaiting classification' may alter the conclusions of the review once assessed.

PMID: 30650189

**5. Preoperative botulinum neurotoxin A for children with bilateral cerebral palsy undergoing major hip surgery: a randomized double-blind placebo-controlled trial.**
Will E, Magill N, Arnold R, Davies M, Doherty G, Fairhurst C, Roposch A, Lundy C, Norman-Taylor F.

Dev Med Child Neurol. 2019 Jan 15. doi: 10.1111/dmcn.14145. [Epub ahead of print]

AIM: To assess whether preoperative botulinum neurotoxin A (BoNT-A) affects pain after major hip surgery for children with bilateral cerebral palsy (CP). METHOD: This was a randomized, parallel arms, placebo-contolled trial. Children with hypertonic CP aged 2 to 15 years awaiting bony hip surgery at a tertiary hospital were randomized to receive either BoNT-A or placebo injections into the muscles of the hip on a single occasion immediately before surgery. The primary outcome was the paediatric pain profile (PPP), which was assessed at baseline and weekly for 6 weeks. Treatment allocation was by minimization. Participants, clinicians, and outcome assessors were masked to group assignment. RESULTS: Twenty-seven participants (17 males, 10 females; mean 8y 8mo [SD 3y 9mo], range 3y 4mo-15y 10mo) were allocated to BoNT-A and 27 participants (14 males, 13 females; mean 8y 11mo [SD 3y 5mo], range 4y 1mo-15y 2mo) to placebo. Mean (SD) PPP at 6 weeks for the BoNT-A group (n=24 followed up) was 10.96 (7.22) and for the placebo group (n=26) was 10.04 (8.54) (p=0.69; 95% confidence interval [CI] -4.82, 3.18). There were 16 serious adverse events in total during 6 months of follow-up (n=6 in BoNT-A group). INTERPRETATION: Use of BoNT-A immediately before bony hip surgery for reducing postoperative pain for children with CP was not supported. WHAT THIS PAPER ADDS: Botulinum neurotoxin A (BoNT-A) does not reduce postoperative pain following bony hip surgery. BoNT-A also does not affect postoperative quality of life.

PMID: 30644541

**6. Pelvic Tilt Changes After Hamstring Lengthening in Children With Cerebral Palsy.**
Wijesekera MPC, C Wilson N, Trinca D, Holmes G, Bass A, Wright DM, Walton R.

J Pediatr Orthop. 2019 Jan 14. doi: 10.1097/BPO.0000000000001326. [Epub ahead of print]

BACKGROUND: Flexion deformity of the knee is a common presentation in children with cerebral palsy with hamstring surgery as an option for addressing this. However, concerns with regard to increased pelvic tilt have been raised. The purpose of this study was to compare preoperative and postoperative pelvic tilt after isolated hamstring lengthening versus combined hamstring lengthening and the influence of Gross Motor Function Classification System (GMFCS) levels on pelvic tilt. METHODS: This retrospective study included 46 ambulatory children with cerebral palsy who had had open medial hamstring lengthening (mean age at surgery, 11 y 11 mo; SD, 2 y 11 mo; GMFCS I, 16; GMFCS II 20; GMFCS III 10). Twelve children underwent isolated surgery and 34 children underwent combined surgery. The isolated hamstring procedures could be combined with foot and/or ankle-level surgery, as only the hamstring procedure would affect the pelvic tilt. Combined surgery was defined as hamstring lengthening with other procedures performed at the knee or more proximally. The preoperative and postoperative 3-dimensional gait analysis data were evaluated in this study. RESULTS: Both the isolated and combined hamstring lengthening groups showed no significant change in pelvic tilt ([INCREMENT]1.28, P=0.203; [INCREMENT]1.47, P=0.113, respectively). A significant change in pelvic tilt was seen in children functioning at GMFCS III ([INCREMENT]4.66, P=0.009) but not GMFCS I and II ([INCREMENT]0.37, P=0.718; [INCREMENT]0.48, P=0.697). Significant postoperative decreases in the knee flexion angle at initial contact were seen for both isolated ([INCREMENT]5.72, P=0.010) and combined hamstring lengthening ([INCREMENT]10.95, P<0.001). CONCLUSIONS: Hamstring lengthening, for the majority of patients, did not lead to a clinically significant change in mean pelvic tilt and improved knee flexion angle at initial contact. Children who functioned at GMFCS level III had an increase in anterior pelvic tilt and caution should be exercised in this group. STUDY DESIGN: Level IV evidence-case series.

PMID: 30649081

**7. Long-term outcome of knee hyperextension in children with cerebral palsy.**
Abousamra O, Connor J, Church C, Taylor D, Lennon N, Del Pilar Duque Orozco M, Henley J, Sees J, Miller F.

J Pediatr Orthop B. 2019 Jan 14. doi: 10.1097/BPB.0000000000000564. [Epub ahead of print]

This study evaluated knee hyperextension course in children with cerebral palsy over a 5-year follow-up. Knee hyperextension was identified in 308 knees, of which 97 had follow-up greater than 5 years. Between the tests, 40% of limbs had plantar flexor lengthening (PFL). Overall, knee flexion and ankle dorsiflexion in stance increased (P<0.0001). Similar changes were noted between limbs that had PFL and those that did not. PFL is indicated in cases associated with equinus. However, the role of multilevel surgery in the treatment of knee hyperextension needs to be further determined.

PMID: 30649088

**8. Effects of Vojta approach on diaphragm movement in children with spastic cerebral palsy.**
Ha SY, Sung YH.

J Exerc Rehabil. 2018 Dec 27;14(6):1005-1009. doi: 10.12965/jer.1836498.249. eCollection 2018 Dec.

The purpose of this study was to examine the effects of Vojta approach on the gross motor function and diaphragm movement in children with spastic cerebral palsy (CP). Ten children with spastic CP were randomly assigned to a general physiotherapy group (trunk strengthening exercise and gait training) (n=5) and a Vojta approach group (n=5). Interventions were implemented for 30 min per time, 3 times a week for a total of 6 weeks. Ultrasonography was used to measure the areas of the diaphragm (during inspiration, expiration) before and after the interventions, the gross motor function measure (GMFM)-88 was used for evaluation of the gross motor function. In the results of this study, there was a significant difference between before and after GMFM-sitting in the experimental group (P<0.05), a significant difference in changes of inspiration between the two groups (P<0.05). Given these results, Vojta approach may be presented as an effective treatment method for improving sitting position and diaphragm movement during inspiration in children with spastic CP.

PMID: 30656162

**9. Correlation between the dimensions of diaphragm movement, respiratory functions and pressures in accordance with the gross motor function classification system levels in children with cerebral palsy.**
Kwon HY, Kim BJ.

J Exerc Rehabil. 2018 Dec 27;14(6):998-1004. doi: 10.12965/jer.1836422.211. eCollection 2018 Dec.

This study was executed as correlation study to investigate the correlation between the dimensions of diaphragm movement, and respiratory functions and pressures in accordance with the Gross Motor Function Classification System (GMFCS) levels on children with cerebral palsy as the participants. Forty-three children in the age range of 5-13 years diagnosed with cerebral palsy as the research participants were divided into three groups (levels I, II, and III) through systematic stratified random sampling in accordance with their GMFCS levels. Pearson correlation analysis was executed to examine the correlation between dimensions of diaphragm movement, and respiratory functions and pressures in accordance with the GMFCS levels of the participants. There was no significant correlation between the dimensions of diaphragm movement, and respiratory functions and pressures in all of the three groups in accordance with the GMFCS levels of the participants. Therefore, it is deemed that although measurement of the dimensions of diaphragm movement of children with cerebral palsy by using diagnostic ultrasonic M-mode imaging device can be considered as auxiliary tool in predicting the breathing capabilities, it cannot be used as independent measurement equipment.

PMID: 30656161

**10. Impairments of Visuospatial Attention in Children with Unilateral Spastic Cerebral Palsy.**
Ickx G, Hatem SM, Riquelme I, Friel KM, Henne C, Araneda R, Gordon AM, Bleyenheuft Y.

Neural Plast. 2018 Dec 17;2018:1435808. doi: 10.1155/2018/1435808. eCollection 2018.

AIM: This observational study aimed at assessing the prevalence of visuospatial attention deficits in children with unilateral spastic cerebral palsy (USCP), taking into consideration the affected hemibody and the localization of the brain lesion. METHOD: Seventy-five children with USCP were assessed with four visuospatial attention tests: star cancellation, Ogden figure copy, line bisection, and proprioceptive pointing. RESULTS: A majority (64%) of children with USCP presented a deficit in at least one test compared to the reference values. The alterations observed in children with left or right USCP were related to egocentric or allocentric neglect, respectively. Children with cortico/subcortical lesion presented more often visuospatial attention deficits than children with periventricular lesion. Visuospatial attention deficits were not associated with brain lesion locations. INTERPRETATION: Visuospatial attention deficits are prevalent in children with USCP and should be taken into account during their rehabilitation process. The present results shed new light on the interpretation of motor impairments in children with USCP as they may be influenced by the frequent presence of visuospatial deficits.

PMID: 30647728

**11. Caries experience and oral health-related quality of life (OHRQoL) of children and adolescents with cerebral palsy in a low-resource setting.**
Akhter R, Hassan NMM, Martin EF, Muhit M, Smithers-Sheedy H, Badawi N, Khandaker G.

BMC Oral Health. 2019 Jan 15;19(1):15. doi: 10.1186/s12903-018-0704-2.

BACKGROUND: Children with complex neurodevelopmental disabilities such as cerebral palsy (CP), have a higher risk of dental disease related at least in part to greater difficulties in performing and maintaining effective oral hygiene and oral care practices. However, to date, there are very few studies that have considered the impact of dental disease on the Oral Health-Related Quality of Life (OHRQoL) of children and adolescents with cerebral palsy. This study aimed to investigate the association between dental caries experience and oral health related quality of life (OHRQoL) among children and adolescents with cerebral palsy in a low-resource setting (Bangladesh). METHODS: A total of 90 children and adolescents with CP, 2-17 years old (median age 10 years; 37.8% female and 62.2% male) were randomly selected from the Bangladesh Cerebral Palsy Register (BCPR) The decayed, missing and filled teeth (dmft/DMFT) index was used to measure caries experience. Child Perceptions Questionnaire (CPQ) and Family Impact Scale (FIS) were used to assess oral health-related quality of life (OHRQoL). Binary logistic regression was used to investigate factors that may contribute to dental caries experience. RESULTS: Dental caries were observed among 55.6% of the participants. After adjusting for age and gender, binary logistic regression analysis showed that dental caries experience was significantly associated with those who had teeth/mouth pain (rate ratio 7.3; P = 0.02), food caught between teeth (rate ratio: 6.4; P = 0.02), difficulty in eating and drinking (rate ratio 5.9; p = 0.02) and those who felt frequently upset (rate ratio: 54.7; P = 0.02). CONCLUSION: In this study, we found that children and adolescents with CP in a low-resource setting had high dental caries experience and that dental caries had a negative impact on OHRQoL amongst these participants and their parents/caregivers. Health care professionals should be aware of the importance of dental health and oral hygiene in this population. These findings highlight the need for oral health promotion programs for children and adolescents with CP in these settings to reduce pain and to improve quality of life.

PMID: 30646890

**12. Cross-cultural validation of the Bengali version KIDSCREEN-27 quality of life questionnaire.**
Power R, Akhter R, Muhit M, Wadud S, Heanoy E, Karim T, Badawi N, Khandaker G.

BMC Pediatr. 2019 Jan 15;19(1):19. doi: 10.1186/s12887-018-1373-7.

BACKGROUND: Measuring the health-related quality of life (HRQoL) of adolescents, including those with cerebral palsy (CP) (the major cause of childhood physical disability worldwide) in Bangladesh is pertinent although there is a dearth of validated instruments for assessing this concept. For application in a case-control study comparing HRQoL between adolescents with CP and peers without disability in Bangladesh (a typical low- and middle-income country) we cross-culturally translated and psychometrically tested KIDSCREEN-27. METHODS: KIDSCREEN-27 was translated to Bengali using forward and backwards translation protocol and interviewer administered to adolescents with CP and their age and sex matched peers without disability. Primary caregivers were included for proxy-report. Sociodemographic characteristics and clinical information were extracted from the Bangladesh Cerebral Palsy Register (BCPR) and adolescent mental health was assessed using the Bengali version Strengths and Difficulties Questionnaire (SDQ). Feasibility, floor and ceiling effect, internal consistency, content and construct validity of KIDSCREEN-27 were tested. RESULTS: Feasibility, floor and ceiling effect and internal consistency of KIDSCREEN-27 was good for both self- and proxy-report questionnaires; nil missing scores except 'school environment' (11.0% to 74.7%) which correlated to rates of non-school attendance; floor and ceiling effect ≤10.4% except 'peers and social support' 23.4%; Cronbach's alpha 0.67 to 0.91. Instrument validity was strong; factor analysis reflected original instrument dimensions within one to three factors and difference in known groups was observed by CP and adolescent

mental health ($p < 0.05$). CONCLUSION: KIDSCREEN-27 successfully translated to Bengali and both the self and proxy-report questionnaires showed good psychometric properties indicating suitability for case-control assessment of HRQoL between adolescents with CP and peers without disability in Bangladesh.

PMID: 30646887

**13. Sensory-motor network functional connectivity in children with unilateral cerebral palsy secondary to perinatal stroke.**
Woodward KE, Carlson HL, Kuczynski A, Saunders J, Hodge J, Kirton A.

Neuroimage Clin. 2019 Jan 9:101670. doi: 10.1016/j.nicl.2019.101670. [Epub ahead of print]

BACKGROUND: Perinatal stroke is the most common cause of unilateral cerebral palsy. Mechanisms of post-stroke developmental plasticity in children are poorly understood. To better understand the relationship between functional connectivity and disability, we used resting-state fMRI to compare sensorimotor connectivity with clinical dysfunction. METHODS: School-aged children with periventricular venous infarction (PVI) and unilateral cerebral palsy were compared to controls. Resting-state BOLD signal was acquired on 3 T MRI and analyzed using CONN in SPM12. Functional connectivity was computed between S1, M1, supplementary motor area (SMA), and thalamus of the left/non-lesioned and right/lesioned hemisphere. Primary outcome was connectivity expressed as a Fisher-transformed correlation coefficient. Motor function was measured using the Assisting Hand Assessment (AHA), and Melbourne Assessment (MA). Proprioceptive function was measured using a robotic position matching task (VarXY). RESULTS: Participants included 15 PVI and 21 controls. AHA and MA in stroke patients were negatively correlated with connectivity (increased connectivity = poorer performance). Position sense was inversely correlated with connectivity (increased connectivity = improved performance) between the non-lesioned S1 and thalamus/SMA. In controls, VarXY was positively correlated with connectivity between the thalamus and bilateral sensorimotor regions. CONCLUSIONS: Resting state fMRI measures of sensorimotor connectivity are associated with clinical sensorimotor function in children with unilateral cerebral palsy secondary to PVI. Greater insight into understanding reorganization of brain networks following perinatal stroke may facilitate personalized rehabilitation.

PMID: 30642756

**14. Thalamic diaschisis following perinatal stroke is associated with clinical disability.**
Craig BT, Carlson HL, Kirton A.

Neuroimage Clin. 2019 Jan 4:101660. doi: 10.1016/j.nicl.2019.101660. [Epub ahead of print]

BACKGROUND: Perinatal stroke causes most hemiparetic cerebral palsy and leads to lifelong disability. Understanding developmental neuroplasticity following early stroke is increasingly translated into novel therapies. Diaschisis refers to alterations brain structures remote from, but connected to, stroke lesions. Ipsilesional thalamic diaschisis has been described following adult stroke but has not been investigated in perinatal stroke. We hypothesized that thalamic diaschisis occurs in perinatal stroke and its degree would be inversely correlated with clinical motor function. METHODS: Population-based, controlled cohort study. Participants were children (<19 years) with unilateral perinatal stroke (arterial ischemic stroke [AIS] or periventricular venous infarction [PVI]), anatomical magnetic resonance imaging (MRI) >6 months of age, symptomatic hemiparetic cerebral palsy, and no additional neurologic disorders. Typically developing controls had comparable age and gender proportions. T1-weighted anatomical scans were parcellated into 99 regions of interest followed by generation of regional volumes. The primary outcome was thalamic volume expressed as ipsilesional (ILTV), contralesional (CLTV) and thalamic ratio (CLTV/ILTV). Standardized clinical motor assessments were correlated with thalamic volume metrics. RESULTS: Fifty-nine participants (12.9 years old ±4.0 years, 46% female) included 20 AIS, 11 PVI, and 28 controls. ILTV was reduced in both AIS and PVI compared to controls ($p < .001$, $p = .029$, respectively). Ipsilesional thalamic diaschisis was not associated with clinical motor function. However, CLTV was significantly larger in AIS compared to both controls and PVI ($p = .005$, $p < .001$, respectively). CLTV was inversely correlated with all four clinical motor assessments (all $p < .003$). CONCLUSION: Bilateral thalamic volume changes occur after perinatal stroke. Ipsilesional volume loss is not associated with clinical motor function. Contralesional volume is inversely correlated with clinical motor function, suggesting the thalamus is involved in the known developmental plasticity that occurs in the contralesional hemisphere after early unilateral injury.

PMID: 30639178

**15. Exosomes populate the cerebrospinal fluid of preterm infants with post-haemorrhagic hydrocephalus.**
Spaull R, McPherson B, Gialeli A, Clayton A, Uney J, Heep A, Cordero-Llana Ó.

Int J Dev Neurosci. 2019 Jan 9;73:59-65. doi: 10.1016/j.ijdevneu.2019.01.004. [Epub ahead of print]

BACKGROUND: Preterm infants are at risk of germinal matrix haemorrhage-intraventricular haemorrhage (GMH-IVH) which leads to post-haemorrhagic hydrocephalus (PHH) in 30% of infants; this is associated with moderate-severe neurodevelopmental impairment and confers significant risk of cerebral palsy. There are however no predictive indicators of the severity or long-term outcome after GMH-IVH. In recent years, endosome-derived extracellular vesicles (EVs) or exosomes have been isolated from biofluids and shown to mediate intercellular communication via selective enrichment in proteins and micro-RNAs. METHODS: This study aimed to isolate and characterise EVs from the cerebrospinal fluid (CSF) of 3 preterm infants with PHH using nanoparticle tracking analysis (NTA), transmission electron microscopy (TEM) with immunogold protein labelling, and micro-RNA analysis. RESULTS: NTA of unaltered CSF revealed a heterogeneous and dynamic population of EVs. Exosomal-sized EVs were isolated by differential ultracentrifugation and TEM confirmed the presence of CD63+ and CD81+ exosomes. The micro-RNAs miR-9, miR-17, miR-26a, miR-124 and miR-1911 were detected within the exosome-enriched fraction and profiled over time. CONCLUSION: This is the first reported characterisation of exosomes from the CSF of preterm infants with post-haemorrhagic hydrocephalus.

PMID: 30639393

**16. Association of Infants Exposed to Prenatal Zika Virus Infection With Their Clinical, Neurologic, and Developmental Status Evaluated via the General Movement Assessment Tool.**
Einspieler C, Utsch F, Brasil P, Panvequio Aizawa CY, Peyton C, Hydee Hasue R, Françoso Genovesi F, Damasceno L, Moreira ME, Adachi K, Marschik PB, Nielsen-Saines K; GM Zika Working Group.

JAMA Netw Open. 2019 Jan 4;2(1):e187235. doi: 10.1001/jamanetworkopen.2018.7235.

IMPORTANCE: There is an urgent need to assess neurodevelopment in Zika virus (ZIKV)-exposed infants. OBJECTIVES: To perform general movement assessment (GMA) at 9 to 20 weeks' postterm age and to evaluate whether the findings are associated with neurodevelopmental outcomes at age 12 months in infants prenatally exposed to acute maternal illness with rash in Brazil during the ZIKV outbreak and in age-matched controls. DESIGN, SETTING, AND PARTICIPANTS: In this cohort study, infants prenatally exposed to acute maternal illness with rash were recruited at medical institutions in Rio de Janeiro and Belo Horizonte, Brazil, from February 1, 2016, to April 30, 2017, while infants without any exposure to maternal illness originated from the Graz University Audiovisual Research Database for the Interdisciplinary Analysis of Neurodevelopment. Participants were 444 infants, including 76 infants without congenital microcephaly, 35 infants with microcephaly, and 333 neurotypical children matched for sex, gestational age at birth, and age at GMA. MAIN OUTCOMES AND MEASURES: General movement assessment performed at 9 to 20 weeks' postterm age, with negative predictive value, positive predictive value, sensitivity, and specificity generated, as well as clinical, neurologic, and developmental status (Bayley Scales of Infant and Toddler Development, Third Edition [Bayley-III] scores) at age 12 months. Motor Optimality Scores were generated based on the overall quality of the motor repertoire. Adverse outcomes were defined as a Bayley-III score less than 2 SD in at least 1 domain, a score less than 1 SD in at least 2 domains, and/or atypical neurologic findings. RESULTS: A total of 444 infants were enrolled, including 111 children prenatally exposed to a maternal illness with rash and 333 children without any prenatal exposure to maternal illness (57.7% male and mean [SD] age, 14 [2] weeks for both groups); 82.1% (46 of 56) of ZIKV-exposed infants without congenital microcephaly were healthy at age 12 months. Forty-four of 46 infants were correctly identified by GMA at 3 months, with a negative predictive value of 94% (95% CI, 85%-97%). Seven of 10 ZIKV-exposed children without microcephaly with adverse neurodevelopmental outcomes were identified by GMA. The GMA positive predictive value was 78% (95% CI, 46%-94%), sensitivity was 70% (95% CI, 35%-93%), specificity was 96% (95% CI, 85%-99%), and accuracy was 91% (95% CI, 80%-97%). Children with microcephaly had bilateral spastic cerebral palsy; none had normal movements. The Motor Optimality Score differentiated outcomes: the median Motor Optimality Score was 23 (interquartile range [IQR], 21-26) in children with normal development, 12 (IQR, 8-19) in children with adverse outcomes, and 5 (IQR, 5-6) in children with microcephaly, a significant difference (P = .001). CONCLUSIONS AND RELEVANCE: This study suggests that although a large proportion of ZIKV-exposed infants without microcephaly develop normally, many do not. The GMA should be incorporated into routine infant assessments to enable early entry into targeted treatment programs.

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**17. Live birth after perimortem cesarean delivery in a 36-year-old out-of-hospital cardiac arrest nulliparous woman.**
Wu SH, Li RS, Hwu YM.

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OBJECTIVE: The aim of this study is to share a valuable experience of perimortem Cesarean delivery (PMCD) when no signs of spontaneous circulation were detected after 4 min of resuscitation. The time interval between maternal cardiac arrest and neonatal delivery was evaluated and reviewed. CASE REPORT: We present the case of an out-of-hospital cardiac arrest (OHCA) in a nulliparous woman who survived a car accident with only seatbelt injuries. The term infant was delivered by PMCD at our emergency department at least 43 min after maternal cardiac arrest. The mother only had concussion and was healthy at the time of discharge. The infant survived but had moderate neurological growth impairment (cerebral palsy) at the age of 7 months. CONCLUSION: Contrary to previous studies and case reports, maternal and neonatal outcomes seem to be better when performing PMCD within 10 min. Multidisciplinary teamwork is the key for optimal outcomes in such situations.

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