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Interventions and Management

1. Ipsilesional volume loss of basal ganglia and thalamus is associated with poor hand function after ischemic perinatal stroke
Nigul Ilves, Silva Lõo, Norman Ilves, Rael Laugesaar, Dagmar Loorits, Pille Kool, Tiina Talvik, Pilvi Ilves

BMC Neurol. 2022 Jan 12;22(1):23. doi: 10.1186/s12883-022-02550-3.

Background: Perinatal stroke (PS) is the leading cause of hemiparetic cerebral palsy (CP). Involvement of the corticospinal tract on neonatal magnetic resonance imaging (MRI) is predictive of motor outcome in patients with hemiparetic CP. However, early MRI is not available in patients with delayed presentation of PS and prediction of hemiparesis severity remains a challenge. Aims: To evaluate the volumes of the basal ganglia, amygdala, thalamus, and hippocampus following perinatal ischemic stroke in relation to hand motor function in children with a history of PS and to compare the volumes of subcortical structures in children with PS and in healthy controls. Methods: Term born PS children with arterial ischemic stroke (AIS) (n = 16) and with periventricular venous infarction (PVI) (n = 18) were recruited from the Estonian Pediatric Stroke Database. MRI was accuired during childhood (4-18 years) and the volumes of the basal ganglia, thalamus, amygdala and hippocampus were calculated. The results of stroke patients were compared to the results of 42 age- and sex-matched healthy controls. Affected hand function was evaluated by Assisting Hand Assessment (AHA) and classified by the Manual Ability Classification System (MACS). Results: Compared to the control group, children with AIS had smaller volumes of the ipsi- and contralesional thalami, ipsilesional globus pallidus, nucleus accumbens and hippocampus ($p < 0.005$). Affected hand function in children with AIS was correlated with smaller ipsilesional thalamus, putamen, globus pallidus, hippocampus, amygdala and contralesional amygdala ($r > 0.5$; $p < 0.05$) and larger volume of the contralesional putamen and hippocampus ($r < - 0.5$; $p < 0.05$). In children with PVI, size of the ipsilesional caudate nucleus, globus pallidus, thalamus ($p \leq 0.001$) and hippocampus ($p < 0.03$) was smaller compared to controls. Smaller volume of the ipsi- and contralesional thalami and ipsilesional caudate nucleus was correlated with affected hand function ($r > 0.55$; $p < 0.05$) in children with PVI. Conclusions: Smaller volume of ipsilesional thalamus was associated with poor affected hand function regardless of the perinatal stroke subtype. The pattern of correlation between hand function and volume differences in the other subcortical structures varied between children with PVI and AIS. Evaluation of subcortical structures is important in predicting motor outcome following perinatal stroke.

PMID: 35022000

2. Reconstruction of paralyzed arm function in patients with hemiplegia through contralateral seventh cervical nerve cross transfer: a multicenter study and real-world practice guidance
Juntao Feng, Tie Li, Minzhi Lv, Sangsoo Kim, Joon-Ho Shin, Naiqing Zhao, Qingzhong Chen, Yanpei Gong, Yucheng Sun, Zaixing Zhao, Ning Zhu, Jihua Cao, Wen Fang, Bin Chen, Song Zheng, Zhu Xu, Xin Jin, Yundong Shen, Yanqun Qiu, Huawei Yin, Su Jiang, Jie Li, Ying Ying, Liwen Chen, Ying Liu, Jie Jia, Chuntao Zuo, Jianguang Xu, Yudong Gu, Wendong Xu

EClinicalMedicine. 2022 Jan 4;43:101258. doi: 10.1016/j.eclinm.2021.101258. eCollection 2022 Jan.

Background: A previous randomized controlled trial showed contralateral seventh cervical nerve (CC7) cross transfer to be safe and effective in restoring the arm function of spastic arm paralysis patients in a specified population. Guidance on indications, safety and expected long-term improvements of the surgery are needed for clinical practice. Methods: This is a retrospective, multicenter, propensity score-matched cohort study. All patients registered between 2013 and 2019 with unilateral spastic arm paralysis over 1 year who were registered at one of five centers in China and South Korea were included. Patients received CC7 cross transfer or rehabilitation treatment in each center. Primary outcome was the change in the upper-extremity Fugl-Meyer (UEFM) score from baseline to 2-year follow-up; larger increase indicated better functional improvements. Findings: The analysis included 425 eligible patients. After propensity score matching, 336 patients who were 1:1 matched into surgery and rehabilitation groups. Compared to previous trial, patient population was expanded on age (< 12 and > 45 years old), duration of disease (< 5 years) and severity of paralysis (severe disabled patients with UEFM < 20 points). In matched patients, the overall increases of UEFM score from preoperative evaluation to 2-year follow-up were 15.14 in the surgery group and 2.35 in the rehabilitation group (difference, 12.79; 95% CI: 12.02-13.56, $p < 0.001$). This increase was 16.58 at 3-year and 18.42 at 5-year follow-up compared with the surgery group baseline. Subgroup analysis revealed substantial increase on UEFM score in each subgroup of age, duration of disease, severity of paralysis and cause of injury. No severe complication or disabling sequela were reported in the surgery group. Interpretation: This study showed that CC7 cross transfer can provide effective, safe and stable functional improvements in long-term follow-up, and provided evidences for expanding the indications of the surgery to a wider population of patients with hemiplegia.

PMID: 35028546

3. Assessing spino-cortical proprioceptive processing in childhood unilateral cerebral palsy with corticokinematic coherence

Josselin Démas, Mathieu Bourguignon, Xavier De Tiège, Vincent Wens, Nicolas Coquelet, Antonin Rovai, Sandra Bouvier, Rodolphe Bailly, Sylvain Brochard, Mickael Dinomais, Patrick Van Bogaert

Neurophysiol Clin. 2022 Jan 4;S0987-7053(21)00129-5. doi: 10.1016/j.neucli.2021.12.003. Online ahead of print.

Objective: To develop an electrophysiological marker of proprioceptive spino-cortical tracts integrity based on corticokinematic coherence (CKC) in young children with unilateral cerebral palsy (UCP), in whom behavioral measures are not applicable. Methods: Electroencephalography (EEG) signals from 12 children with UCP aged 19 to 57 months were recorded using 128-channel EEG caps while their fingers were moved at 2 Hz by an experimenter, in separate sessions for the affected and non-affected hands. The coherence between movement kinematics and EEG signals (i.e., CKC) was computed at the sensor and source (using a realistic head model) levels. Peaks of CKC obtained for the affected and non-affected hands were compared for location and strength. The relation between CKC strength on the lesion-side, the lesion-type (cortico-subcortical vs. subcortical) and the level of manual ability were studied with 2-way repeated-measures ANOVA. Results: At the individual level, a significant CKC peak at the central area contralateral to the moved hand was found in all young children with their non-affected hand and in 8 out of 12 children with their affected hand. At the group level, CKC to the affected hand movements was weaker than CKC to the non-affected hand movements. This difference was influenced by the type of lesion, the effect being predominant in the subgroup ($n = 5$) with cortico-subcortical lesions. Conclusion: CKC is measurable with EEG in young children with UCP and provides electrophysiological evidence for altered proprioceptive spino-cortical tracts on the lesioned brain hemisphere, particularly in children with cortico-subcortical lesions.

PMID: 34996694

4. Tranexamic acid use decreases transfusion rate in children with cerebral palsy undergoing proximal femoral varus derotational osteotomy

Edward Compton, Rachel Y Goldstein, Alexander Nazareth, Stephen J Shymon, Lydia Andras, Robert M Kay

Medicine (Baltimore). 2022 Jan 14;101(2):e28506. doi: 10.1097/MD.0000000000028506.

Previous studies demonstrated the safety of tranexamic acid (TXA) use in cerebral palsy (CP) patients undergoing proximal femoral varus derotational osteotomy (VDRO), but were underpowered to determine if TXA alters transfusion rates or estimated blood loss (EBL). The purpose of this study was to investigate if intraoperative TXA administration alters transfusion rates or EBL in patients with CP undergoing VDRO surgery. We conducted a retrospective review of 390 patients with CP who

underwent VDRO surgery between January 2004 and August 2019 at a single institution. Patients without sufficient clinical data and patients with preexisting bleeding or coagulation disorders were excluded. Patients were divided into 2 groups: those who received intraoperative TXA and those who did not. Out of 390 patients (mean age 9.4 ± 3.8 years), 80 received intravenous TXA (TXA group) and 310 did not (No-TXA group). There was no difference in mean weight at surgery (P = .25), Gross Motor Function Classification System level (P = .99), American Society of Anesthesiologist classification (P = .50), preoperative feeding status (P = .16), operative time (P = .91), or number of procedures performed (P = .12) between the groups. The overall transfusion rate was lower in the TXA group (13.8%; 11/80) than the No-TXA group (25.2%; 78/310) (P = .04), as was the postoperative transfusion rate (7.5%; 6/80 in the TXA group vs 18.4%; 57/310 in the No-TXA group) (P = .02). The intraoperative transfusion rate was similar for the 2 groups (TXA: 7.5%; 6/80 vs No-TXA: 10.3%; 32/310; P = .53). The EBL was slightly lower in the TXA group, although this was not significant (TXA: 142.9 ± 113.1 mL vs No-TXA: 177.4 ± 169.1 mL; P = .09). The standard deviation for EBL was greater in the No-TXA group due to more high EBL outliers. The percentage of blood loss based on weight was similar between the groups (TXA: 9.2% vs No-TXA: 10.1%; P = .40). The number needed to treat (NNT) with TXA to avoid one peri-operative blood transfusion in this series was 9.The use of intraoperative TXA in patients with CP undergoing VDRO surgery lowers overall and postoperative transfusion rates. Level of evidence: III, Retrospective Comparative Study.

PMID: 35029205

5. Hallux valgus surgery in children with cerebral palsy: A systematic review
T L Lewis, K Patel, K L Shepherd, P MacInnes, R Ray, M Kokkinakis

Foot Ankle Surg. 2021 Dec 24;S1268-7731(21)00262-9. doi: 10.1016/j.fas.2021.12.009. Online ahead of print.

Background: Children with cerebral palsy are highly likely to develop foot deformities, some of which may require surgical intervention. Hallux valgus is a common forefoot deformity which can cause issues with pain, footwear, orthotic splints and soft tissues. It remains unclear what the optimal surgical treatment is for children with cerebral palsy and hallux valgus deformity. Objective: To systematically review studies reporting the clinical and radiological outcomes of surgical correction of hallux valgus deformity in children with cerebral palsy. Methods: A systematic review of studies published in electronic databases (Medline, Embase, Pubmed and Cochrane library) from inception until January 2021. Keywords related to hallux valgus and cerebral palsy were included. Results: 58 studies were identified of which 7 met the criteria for inclusion. 200 feet in 134 patients with a mean age of 13.5 years were included, with a mean follow up period of 43 months. A range of clinical and radiographic outcomes were assessed. A treatment framework for the assessment and management of hallux valgus in children with cerebral palsy based on the published evidence is presented. Conclusion: Non-ambulant children with cerebral palsy with symptomatic hallux valgus should primarily undergo first MTPJ arthrodesis whilst those who are ambulant should undergo first metatarsal osteotomy± soft tissue correction.

PMID: 35012870

6. Exploring the factors that influence stakeholders' expectations and subsequent perception of lower limb orthopaedic surgical outcomes for ambulant children with cerebral palsy - a qualitative study
Hajar Almoajil, Tim Theologis, Helen Dawes, Jo Pierce, Andrew Meaney, Aziz Baklouti, Lara Poverini, Sally Hopewell, Francine Toye

Disabil Rehabil. 2022 Jan 12;1-8. doi: 10.1080/09638288.2021.2025272. Online ahead of print.

Purpose: To explore the perspectives of children with CP, their parents or carers, and health professionals on factors affecting expectations and perceptions of surgical outcomes for lower limb orthopaedic surgery. Materials and methods: Semi-structured interviews were conducted with 10 healthcare professionals, 10 children and young people with CP, and 8 parents. Interview data were analysed by content analysis supported by the Framework Approach using the International Classification of Functioning, Disability, and Health (ICF-CY). Results: A comprehensive list of 10 factors including facilitators, barriers, motivational and demotivational factors were identified and categorized into two overreaching themes (Environmental and Personal factors): interdisciplinary collaboration, communication and information resources, holistic care, and shared goal setting are reported as environment facilitators of outcomes expectations. In contrast, reported barriers include lack of time and resources and divergent expectations. Personal motivators include family encouragement, patient's self-determination, and previous experiences, whereas personal demotivators include fear of a new environment. Conclusion: The recognition of potential factors influencing expectations and perceptions of surgical outcomes could assist clinical reasoning when planning

surgical interventions for ambulant children with CP. If these factors are integrated into the healthcare practice, it will most likely enhance the positive stakeholders' experiences postoperatively. IMPLICATION FOR REHABILITATION: Understanding relevant stakeholders' experiences offer a positive contribution to holistic and person-centred approaches in healthcare. People with cerebral palsy and their caregivers require adequate information on surgery and post-surgical rehabilitation regime in order to reach informed decisions. Previous experiences can influence surgical expectations and subsequent perceptions of the outcome.

PMID: 35019783

7. Acute Response to One Bout of Dynamic Standing Exercise on Blood Glucose and Blood Lactate Among Children and Adolescents With Cerebral Palsy Who are Nonambulant
Petra Lundström, Katarina Lauruschkus, Åsa Andersson, Åsa B Tornberg

Pediatr Exerc Sci. 2022 Jan 10;1-6. doi: 10.1123/pes.2021-0098. Online ahead of print.

Purpose: To investigate the acute exercise effects of dynamic standing exercise on blood glucose and blood lactate among children and adolescents with cerebral palsy who are nonambulant. Methods: Twenty-four participants with cerebral palsy who are nonambulant performed 30 minutes of dynamic standing exercise using a motorized device enabling assisted passive movements in an upright weight-bearing position. Capillary blood samples were taken from the fingertip for measurement of blood glucose and blood lactate at rest and at the end of exercise. Results: At rest, the participants had hyperlactatemia that was unaffected after exercise, presented as median and interquartile range at rest 1.8 (1.3:2.7) mmol/L, and after exercise 2.0 (1.1:2.5) mmol/L. Children and adolescents with Gross Motor Function Classification System, level V, had higher lactate levels at rest (2.5 [1.8:2.9] vs 1.4 [1.0:2.0]; P = .030) and after exercise (2.3 [2.0:2.6] vs 1.2 [0.9:2.2]; P = .032) compared with children and adolescents with Gross Motor Function Classification System, level IV, respectively. A statistically significant larger decrease in blood lactate levels after exercise was observed in children and adolescents with higher resting blood lactate levels (ρ = .56; P = .004). There were no statistically significant changes in blood glucose. Conclusions: Forty percentage of the participants had mild hyperlactatemia at rest and participants with the highest blood lactate levels at rest had the greatest decrease in blood lactate levels after one bout of exercise. Children and adolescents who were classified with the highest level of the Gross Motor Function Classification Scale had higher blood lactate levels. More studies are needed on how to prevent chronically high resting levels of lactate with exercise in children with cerebral palsy who are nonambulant.

PMID: 35016158

8. Glycopyrrolate for drooling in children with medical complexity under three years of age
Eleonora Lovardi, Maria Antonietta De Ioris, Donatella Lettori, Caterina Geremia, Susanna Staccioli, Gessica Della Bella, Raffaella Scrocca, Alessia Scarselli, Marcella Aversa, Francesco De Peppo, Andrea Campana, Enrico Castelli

Ital J Pediatr. 2022 Jan 8;48(1):2. doi: 10.1186/s13052-021-01195-1.

Background: The aim of the study is to determine that Glycopirrolate is safe and effective in decreasing drooling in children with medical complexity under 3 years of age. Medical treatment is based on anticholinergic drugs as transdermal scopolamine, benzotropine and GLY. GLY (Glycopyrronium bromide) is a synthetic quaternary ammonium anticholinergic agent with poor blood-brain barrier penetration and consequently has limited central effects. Actually, the oral GLY formulation was approved by the United States Food and Drug Administration (FDA) to treat drooling in children aged 3-16 years. Five studies reported on GLY use for the treatment of drooling in children with cerebral palsy and other conditions with neurological impairment; four are prospective studies while one a retrospective review. Methods: this is a case report of eighteen children (sex ratio 11/8, median age 17 months, range 2-36 months) under three years of age, followed by a multidisciplinary team at the Bambino Gesù Children Hospital. The median follow-up was of 31.5 months (range 1-69 months). Response to treatment was assessed according to the Drooling Impact Scale administered at time 0 and after 1 month. All patients have an important neurological impairment: nine patients have a cerebral palsy (Gross Motor Function Classification System class V) and nine a genetic/ malformative syndrome. Twelve patients have a tracheostomy and two need mechanical ventilation. Gastrostomy is present in 16 out of 18 patients. All patients received Glycopirrolate. The median starting daily dose was 0.065 mg/kg/die (range 0.02-0.21 mg/kg/die) three times a day. The drooling impact scale was administered at time O and after 1 month. Results: Four out 18 patients stopped treatment for adverse event, lack of efficacy or parental decision. The mean Drooling Impact Scale at time 0 was 89 (range 81-100) and after 1 month 61(range 43-78); the difference was statistically significant (P < 0.001). The overall response to treatment was 94%. Conclusions: This is the first study to determine the safety and effectiveness of Glycopyrrolate

in decreasing drooling in a specific subset of patients. No major side effects were observed. Further comparative studies are needed to confirm our results.

PMID: 34998418

9. Use of Vitamin D Bolus in Fortified Juice for Improving Vitamin D Status in Children with Cerebral Palsy
Antonia Karagiannis, Julia Nisiotou, Anna Challa, Anargyros N Moulas

Adv Exp Med Biol. 2021;1339:257-264. doi: 10.1007/978-3-030-78787-5_31.

Children with cerebral palsy (CP) are at risk of poor nutrition due to a number of factors. Feeding, eating, drinking, and swallowing (FEDS) problems are common in these children and may result in protein-calorie malnutrition usually accompanied by micronutrient deficiencies. Vitamin D is among the elements whose uptake is obstructed. Insufficient exposure to solar radiation in children and adolescents with CP adds to further decreasing serum vitamin D levels thus potentially affecting growth, bone density, and muscle function. Since maintaining long-term adherence to daily oral administration of vitamin D in this population is often difficult, bolus therapy by using vitamin D-fortified products could be an alternative way of effective and safe vitamin D intake. Purpose: Assessing the efficacy of administration of bolus vitamin D in fortified juice for increasing 25(OH)D levels in a group of 15 children with CP. Results: The juice was well tolerated, and a significant increase in 25(OH)D levels was observed from 54.1 to 110.3 nmol/L ($p < 0.0001$) 4 weeks after the administration without any case of hypercalcemia. Conclusion: Bolus therapy with vitamin D3-fortified juice is well tolerated and effectively increases 25(OH)D levels in children with CP.

PMID: 35023113

10. Scurvy Masquerading as Septic Arthritis in a Case of Cerebral Palsy
Deepak S Jain, Tushar Agrawal, Parimal K Malviya

Case Reports J Orthop Case Rep. 2021 Aug;11(8):107-110. doi: 10.13107/jocr.2021.v11.i08.2388.

Introduction: Scurvy is a rarely seen in pediatric patients nowadays, seen more in those with developmental delay, autism or those who are severely malnourished. Epiphyseal separations are known to occur in scurvy, but only a few such cases have been reported in children with cerebral palsy. The diagnosis is often misleading since other morbidities as trauma, malignancies, coagulopathies, septic arthritis, osteomyelitis, or rheumatologic disorders are often considered at first. We report the case of 4-year-old female child with cerebral palsy in whom the initial concern was septic arthritis/osteomyelitis based upon clinical presentation, ultrasonic and magnetic resonance imaging, led to a surgery revealing subperiosteal hematomas. Case report: A 4-year-old girl was admitted in the pediatrics department for fever and bilateral knee joint pain for 3 days. She was a diagnosed case of with cerebral palsy, psyco-developmental delay, and epileptogenic disorder put under valproic acid. She was toxic and febrile. Within 4 h after admission, both knees developed tense shiny intense swelling associated with pain, redness, and local rise of temperature with limited active range of motion. Near-complete passive range of motion was noted. There were no abnormal findings on the rest of the musculoskeletal examination. Aspiration of the knee revealed subperiosteal hematoma diagnostic of scurvy. Conclusion: Scurvy is exceedingly rare in children nowadays; however, its presentation among risky populations should not be forgotten. Musculoskeletal revelations, mostly subperiosteal hematoma, are the main manifestation of scurvy in the pediatric population. Scurvy as a differential diagnosis for trauma, osteomyelitis, septic arthritis will always be a bane for orthopedic surgeons. A heightened awareness is needed to avoid unnecessary surgery, unnecessary tests, and procedures and to be able to start treatment for a potentially fatal but easily curable disease.

PMID: 35004388

11. Acceptability and feasibility of a vestibular nerve stimulation headset protocol in children with cerebral palsy
Karen McConnell, Daniel Topley, Jason McKeown, Claire Kerr

BMC Pediatr. 2022 Jan 11;22(1):34. doi: 10.1186/s12887-021-03093-1.

Background: Research suggests electrical Vestibular Nerve Stimulation (VeNS) may improve balance for people with neurological impairments. This study aimed to assess the feasibility and acceptability of a VeNS headset protocol in children with cerebral palsy (CP). Methods: Children aged 5-18 years with ambulant CP, their parents, and healthcare professionals were recruited via social media. Children completed a battery of balance tests and wore a sham VeNS headset one hour per day for four weeks. Perspectives on the balance tests and headset were ascertained from children, parents and healthcare professionals using semi-structured interviews. Interview data were analysed thematically. Results: Two families and four healthcare professionals participated. Balance outcome measures were fully completed and deemed acceptable. Adherence with wearing the headset was 89-100% but discomfort with self-adhesive electrodes was reported. Four themes emerged from interview data: headset issues, perceptions about VeNS, the importance of balance, and modifications for future study. Conclusions: Although the VeNS headset had high acceptability, the volunteer sample was small, potentially suggesting limited interest in VeNS as a treatment for children with CP, or reluctance to trial a 'non-active' headset. Recruitment via clinicians known to the family and use of an 'active' headset may increase participation in future research.

PMID: 35016677

12. Effects of Hinged versus Floor-Reaction Ankle-Foot Orthoses on Standing Stability and Sit-to-Stand Performance in Children with Spastic Diplegic Cerebral Palsy
Yu-Lin Wang, Wen-Chou Chi, Chiung-Ling Chen, Cheng-Hsieh Yang, Ya-Ling Teng, Kwok-Tak Yeung

Int J Environ Res Public Health. 2022 Jan 4;19(1):542. doi: 10.3390/ijerph19010542.

Hinged ankle-foot orthoses (HAFOs) and floor reaction ankle-foot orthoses (FRAFOs) are frequently prescribed to improve gait performance in children with spastic diplegic cerebral palsy (CP). No study has investigated the effects of FRAFO on sit-to-stand (STS) performance nor scrutinized differences between the application of HAFOs and FRAFOs on postural control. This study compared the effects of HAFOs and FRAFOs on standing stability and STS performance in children with spastic diplegic CP. Nine children with spastic diplegic CP participated in this crossover repeated-measures design research. Kinematic and kinetic data were collected during static standing and STS performance using 3-D motion analysis and force plates. Wilcoxon signed ranks test was used to compare the differences in standing stability and STS performance between wearing HAFOs and FRAFOs. The results showed that during static standing, all center of pressure (COP) parameters (maximal anteroposterior/mediolateral displacement, maximal velocity, and sway area) were not significantly different between FRAFOs and HAFOs. During STS, the floor reaction force in the vertical direction was significantly higher with FRAFOs than with HAFOs ($p = 0.018$). There were no significant differences in the range of motion in the trunk, knee, and ankle, the maximal velocity of COP forward displacement, completion time, and the force of hip, knee, and ankle joints between the two orthoses. The results suggest both FRAFOs and HAFOs have a similar effect on standing stability, while FRAFOs may benefit STS performance more compared to HAFOs.

PMID: 35010802

13. A randomized crossover study of functional electrical stimulation during walking in spastic cerebral palsy: the FES on participation (FESPa) trial
Irene Moll, Rik G J Marcellis, Marcel L P Coenen, Sabine M Fleuren, Paul J B Willems, Lucianne A W M Speth, M Adhiambo Witlox, Kenneth Meijer, R Jeroen Vermeulen

BMC Pediatr. 2022 Jan 13;22(1):37. doi: 10.1186/s12887-021-03037-9.

Background: Spastic cerebral palsy is the most common cause of motor disability in children. It often leads to foot drop or equinus, interfering with walking. Ankle-foot orthoses (AFOs) are commonly used in these cases. However, AFOs can be too restrictive for mildly impaired patients. Functional electrical stimulation (FES) of the ankle-dorsiflexors is an alternative treatment as it could function as a dynamic functional orthosis. Despite previous research, high level evidence on the effects of FES on activities and participation in daily life is missing. The primary aim of this study is to evaluate whether FES improves the activity and participation level in daily life according to patients, and the secondary aim is to provide evidence of the effect of FES at the level of body functions and activities. Furthermore, we aim to collect relevant information for decisions on its clinical implementation. Methods: A randomized crossover trial will be performed on 25 children with unilateral spastic cerebral palsy. Patients aged between 4 and 18 years, with Gross Motor Functioning Classification System level I or II and

unilateral foot drop of central origin, currently treated with AFO or adapted shoes, will be included. All participants will undergo twelve weeks of conventional treatment (AFO/adapted shoes) and 12 weeks of FES treatment, separated by a six-week washout-phase. FES treatment consists of wearing the WalkAide® device, with surface electrodes stimulating the peroneal nerve during swing phase of gait. For the primary objective, the Goal Attainment Scale is used to test whether FES improves activities and participation in daily life. The secondary objective is to prove whether FES is effective at the level of body functions and structures, and activities, including ankle kinematics and kinetics measured during 3D-gait analysis and questionnaire-based frequency of falling. The tertiary objective is to collect relevant information for clinical implementation, including acceptability using the device log file and side effect registration, cost-effectiveness based on quality adjusted life years (QALYs) and clinical characteristics for patient selection. Discussion: We anticipate that the results of this study will allow evidence-based use of FES during walking in children with unilateral spastic cerebral palsy. Trial registration: ClinicalTrials.gov: NCT03440632.

PMID: 35027013

14. Effects of Robot-Assisted Therapy on Gait Parameters in Pediatric Patients With Spastic Cerebral Palsy
Faustyna Manikowska, Sabina Brazevic, Anna Krzyżańska, Marek Jóźwiak

Front Neurol. 2021 Dec 23;12:724009. doi: 10.3389/fneur.2021.724009. eCollection 2021.

Background: Gait dysfunction is a crucial factor that restricts independence and quality of life in children with cerebral palsy (CP). Gait training based on robotic-assisted therapy (RAT) is widely used, but information about effectiveness and ideal patient profile is not sufficient. Aim of this study was to assess the effect of RAT on gait parameters in spastic children with CP, and to determine whether changes in gait parameters are different among patients on different ambulatory levels. Method: A total of 26 children with bilateral spastic CP were divided into two groups based on their functional ability: non-assisted ambulator (NAS) or assisted ambulator (AS); and underwent a RAT program (30 training sessions of RAT during 10 weeks). Gait analysis was performed: before the therapy (t1), right after (t2), and 6 weeks later (t3). Results: No significant changes in spatiotemporal parameters or gait deviation index at t2 or t3. Double support symmetry significantly improved (t1 vs. t3, $p = 0.03$) for the whole group (NAS + AS). Walking speed symmetry significantly improved (t2 vs. t3, $p = 0.02$) for group AS. Conclusion: RAT based on our protocol did not change spatiotemporal parameters and kinematics of walking except limited improvement in some aspects of gait symmetry. We did not find differences in changes in selected objective gait parameters among children with CP in different ambulatory levels.

PMID: 35002911

15. Surface Modifications of an Organic Polymer-Based Microwire Platform for Sustained Release of an Anti-Inflammatory Drug
Chuan Liu, Michelle A Nguyen, Anabel Alvarez-Ciara, Melissa Franklin, Cassie Bennett, Justin B Domena, Noah C Kleinhenz, Gabriel A Blanco Colmenares, Sebastian Duque, Aisha F Chebbi, Brianna Bernard, Jean-Hubert Olivier, Abhishek Prasad

ACS Appl Bio Mater. 2020 Jul 20;3(7):4613-4625. doi: 10.1021/acsabm.0c00506. Epub 2020 Jul 8.

Brain machine interfaces (BMIs), introduced into the daily lives of individuals with injuries or disorders of the nervous system such as spinal cord injury, stroke, or amyotrophic lateral sclerosis, can improve the quality of life. BMIs rely on the capability of microelectrode arrays to monitor the activity of large populations of neurons. However, maintaining a stable, chronic electrode-tissue interface that can record neuronal activity with a high signal-to-noise ratio is a key challenge that has limited the translation of such technologies. An electrode implant injury leads to a chronic foreign body response that is well-characterized and shown to affect the electrode-tissue interface stability. Several strategies have been applied to modulate the immune response, including the application of immunomodulatory drugs applied both systemically and locally. While the use of passive drug release at the site of injury has been exploited to minimize neuroinflammation, this strategy has all but failed as a bolus of anti-inflammatory drugs is released at predetermined times that are often inconsistent with the ongoing innate inflammatory process. Common strategies do not focus on the proper anchorage of soft hydrogel scaffolds on electrode surfaces, which often results in delamination of the porous network from electrodes. In this study, we developed a microwire platform that features a robust yet soft biocompatible hydrogel coating, enabling long-lasting drug release via formation of drug aggregates and dismantlement of hydrophilic biodegradable three-dimensional polymer networks. Facile surface chemistry is developed to functionalize polyimide-coated electrodes with the covalently anchored porous hydrogel network bearing large numbers of highly biodegradable ester groups. Exponential long-lasting drug release is achieved using such hydrogels. We

show that the initial state of dexamethasone (Dex) used to formulate the hydrogel precursor solution plays a cardinal role in engineering hydrophilic networks that enable a sustained and long-lasting release of the anti-inflammatory agent. Furthermore, utilization of a high loading ratio that exceeds the solubility of Dex leads to the encapsulation of Dex aggregates that regulate the release of this anti-inflammatory agent. To validate the anti-inflammatory effect of the hydrogel-functionalized Dex-loaded microwires, an in vivo preliminary study was performed in adult male rats (n = 10) for the acute time points of 48 h and 7 days post implant. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to assess the mRNA expression of certain inflammatory-related genes. In general, a decrease in fold-change expression was observed for all genes tested for Dex-loaded wires compared with controls (functionalized but no drug). The engineering of hybrid microwires enables a sustained release of the anti-inflammatory agent over extended periods of time, thus paving the way to fabricate neuroprosthetic devices capable of attenuating the foreign body response.

PMID: 35025460

16. Early detection of Australian Aboriginal and Torres Strait Islander infants at high risk of adverse neurodevelopmental outcomes at 12 months corrected age: LEAP-CP prospective cohort study protocol
Carly R Luke, Katherine Benfer, Leeann Mick-Ramsamy, Robert S Ware, Natasha Reid, Arend F Bos, Margot Bosanquet, Roslyn N Boyd

BMJ Open. 2022 Jan 7;12(1):e053646. doi: 10.1136/bmjopen-2021-053646.

Introduction: Neurodevelopmental disorders (NDD), including cerebral palsy (CP), autism spectrum disorder (ASD) and foetal alcohol spectrum disorder (FASD), are characterised by impaired development of the early central nervous system, impacting cognitive and/or physical function. Early detection of NDD enables infants to be fast-tracked to early intervention services, optimising outcomes. Aboriginal and Torres Strait Islander infants may experience early life factors increasing their risk of neurodevelopmental vulnerability, which persist into later childhood, further compounding the health inequities experienced by First Nations peoples in Australia. The LEAP-CP prospective cohort study will investigate the efficacy of early screening programmes, implemented in Queensland, Australia to earlier identify Aboriginal and Torres Strait Islander infants who are 'at risk' of adverse neurodevelopmental outcomes (NDO) or NDD. Diagnostic accuracy and feasibility of early detection tools for identifying infants 'at risk' of a later diagnosis of adverse NDO or NDD will be determined. Methods and analysis: Aboriginal and/or Torres Strait Islander infants born in Queensland, Australia (birth years 2020-2022) will be invited to participate. Infants aged <9 months corrected age (CA) will undergo screening using the (1) General Movements Assessment (GMA); (2) Hammersmith Infant Neurological Examination (HINE); (3) Rapid Neurodevelopmental Assessment (RNDA) and (4) Ages and Stages Questionnaire-Aboriginal adaptation (ASQ-TRAK). Developmental outcomes at 12 months CA will be determined for: (1) neurological (HINE); (2) motor (Peabody Developmental Motor Scales 2); (3) cognitive and communication (Bayley Scales of Infant Development III); (4) functional capabilities (Paediatric Evaluation of Disability Inventory-Computer Adaptive Test) and (5) behaviour (Infant Toddler Social and Emotional Assessment). Infants will be classified as typically developing or 'at risk' of an adverse NDO and/or specific NDD based on symptomology using developmental and diagnostic outcomes for (1) CP (2) ASD and (3) FASD. The effects of perinatal, social and environmental factors, caregiver mental health and clinical neuroimaging on NDOs will be investigated. Ethics and dissemination: Ethics approval has been granted by appropriate Queensland ethics committees; Far North Queensland Health Research Ethics Committee (HREC/2019/QCH/50533 (Sep ver 2)-1370), the Townsville HHS Human Research Ethics Committee (HREC/QTHS/56008), the University of Queensland Medical Research Ethics Committee (2020000185/HREC/2019/QCH/50533) and the Children's Health Queensland HHS Human Research Ethics Committee (HREC/20/QCHQ/63906) with governance and support from local First Nations communities. Findings from this study will be disseminated via peer-reviewed publications and conference presentations. Trial registration number: ACTRN12619000969167.

PMID: 34996793

17. Impact of gestational age on risk of cerebral palsy: unravelling the role of neonatal morbidity
Ruoqing Chen, Arvid Sjölander, Stefan Johansson, Donghao Lu, Neda Razaz, Kristina Tedroff, Eduardo Villamor, Sven Cnattingius

Int J Epidemiol. 2022 Jan 6;50(6):1852-1863. doi: 10.1093/ije/dyab131.

Background: The contribution of adverse consequences of preterm birth to gestational-age-related risk of cerebral palsy (CP) has rarely been studied. We aimed to assess the potential mediating roles of neonatal morbidity on the association between

gestational age and risk of CP. Methods: In this Swedish population-based study, 1 402 240 singletons born at 22-40 gestational weeks during 1998-2016 were followed from day 28 after birth for a CP diagnosis until 2017. Potential mediators included asphyxia, respiratory-related, infection-/inflammatory-related and neurological-related diseases within 0-27 days of life. Cox regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Causal mediation analysis was performed to estimate the proportion of the association mediated through pathways involving the four sequential mediators. Results: We found an inverse dose-response relationship between gestational age and risk of CP, where the strongest association was observed for 22-24 weeks (HR 47.26, 95% CI 34.09-65.53) vs 39-40 weeks. Compared with non-diseased peers, children with neonatal morbidity, particularly those with neurological-related diseases (HR 31.34, 95% CI 26.39-37.21), had a higher risk of CP. The increased risk of CP was, at 24 weeks, almost entirely explained by neonatal morbidity (91.7%); this proportion decreased to 46.1% and 16.4% at 32 and 36 weeks, respectively. Asphyxia was the main mediating pathway from 22 to 34 weeks, and neurological-related neonatal diseases led the mediating pathways from 34 weeks onwards. Conclusion: Neonatal morbidity mediates a large proportion of the effect of preterm birth on CP, but the magnitude declines as gestational age increases.

PMID: 34999876

18. Correlation between fetal heart rate evolution patterns and magnetic resonance imaging findings in severe cerebral palsy: a longitudinal study
Masahiro Nakao, Yukiko Nanba, Asumi Okumura, Junichi Hasegawa, Satoshi Toyokawa, Kiyotake Ichizuka, Naohiro Kanayama, Shoji Satoh, Nanako Tamiya, Akihito Nakai, Keiya Fujimori, Tsugio Maeda, Hideaki Suzuki, Mitsutoshi Iwashita, Akira Oka, Tomoaki Ikeda

BJOG. 2022 Jan 10. doi: 10.1111/1471-0528.17089. Online ahead of print.

Objective: To investigate the relationship between hypoxic-ischaemic insult timing and brain injury type in infants with severe cerebral palsy (CP). Design: Longitudinal study SETTING: Database of the Recurrence Prevention Committee, Japan Obstetric Compensation System for Cerebral Palsy. Sample: Infants with severe CP born at ≥34 weeks of gestation. Methods: The intrapartum fetal heart rate (FHR) strips were categorised as continuous bradycardia; persistently non-reassuring (NR-NR); reassuring-prolonged deceleration (R-PD); Hon's pattern (R-Hon); persistently reassuring (R-R); and unclassified. The brain magnetic resonance imaging (MRI) scans were categorised based on the predominant site involved: basal ganglia-thalamus (BGT); white matter (WM); watershed (WS); stroke; normal; and unclassified. Main outcome measures: Manifestations of the brain MRI types and the relationship between FHR evolution pattern and MRI type were analysed. Results: Among 672 eligible infants, 76% had BGT-dominant injury, 5.4% WM, 1.2% WS, 1.6% stroke, 1.9% normal, and 14% unclassified. Placental abruption and fetal growth restriction were associated with an increased (adjusted odds ratio [aOR], 8.02) and decreased (aOR, 0.38) risk of BGT injury, respectively. The majority of infants had BGT injury in most FHR groups (bradycardia, 97%; NR-NR, 75%; R-PD, 90%; R-Hon, 76%; and R-R, 45%). The risk profiles in case of BGT in the NR-NR group were similar to those in the R-PD and R-Hon groups. Conclusion: BGT-dominant brain damage accounted for 3/4 of the cases of CP in term or near-term infants, even in prenatal onset cases. Hypoxic-ischaemic insult has a major impact on CP development during the antenatal period.

PMID: 35007405

19. Parenting experiences among fathers of prematurely-born children with cerebral palsy in South Korea
Jisun Park, Kyung-Sook Bang

Child Health Nurs Res. 2021 Jan;27(1):75-85. doi: 10.4094/chnr.2021.27.1.75. Epub 2021 Jan 31.

Purpose: The symptoms and impairments caused by cerebral palsy usually require long-term treatment, resulting in a substantial burden on the family of affected children. This study explored the experiences of fathers with prematurely-born children with cerebral palsy, with a focus on how such experiences influenced their families. Methods: A qualitative case study method was used. Nine subjects were recruited from April 2018 to June 2019 at one hospital, and each was interviewed three times by a neonatal nurse. Results: Five core experiences of fathers were identified: regret for an insufficient initial response, confronting my child born as a premature baby, the position of being a dad who can't do anything, the process of treatment like a tunnel with no exit, and a father's getting meaning in life through children. These stories covered an individual's timeline and family interactions. Conclusion: Our findings suggest that fathers of prematurely-born children tend to suppress their emotions; therefore, a novel intervention program to encourage fathers' emotional expression and to support healthier interactions with

their families is needed. Moreover, our findings could contribute basic information for the construction of a community-based support system to aid families, including prematurely-born children and other persons with impairments.

PMID: 35004499

20. Bobath in Brazil: what is the best study design for intervention for children with cerebral palsy?
Cláudia R M Alcântara de Torre

Dev Med Child Neurol. 2022 Jan 14. doi: 10.1111/dmcn.15147. Online ahead of print.

PMID: 35030264

21. Investigation on Quality of Life and Economic Burden of Children with Cerebral Palsy in Changzhou
Chaorong Bian, Feng Peng, Haibin Guo, Kejin Chen

J Healthc Eng. 2022 Jan 4;2022:1519689. doi: 10.1155/2022/1519689. eCollection 2022.

Based on the data of children with cerebral palsy (CP) in Changzhou obtained by the Disabled Persons' Federation, this study sampled some children with CP and investigated their survival status, treatment cost, and family burden so as to provide scientific decision-making basis and policy suggestions for coping with disease hazards and improving children's quality of life. In this study, a simple random sampling method was used to conduct household surveys of the selected children with CP. The economic burden of CP is measured by direct and indirect methods, and the quality of life of patients of children with CP and their families is analyzed qualitatively and quantitatively by the EuroQol Five Dimensions (EQ-5D) Questionnaire. The average family economic burden of each case of CP in Changzhou was about 4,188,500 yuan, of which the direct medical burden was 205,800 yuan and the indirect economic burden was 3,982,700 yuan. The socioeconomic burden of CP in Changzhou is as high as about 2.244 billion yuan. From the EQ-5D measurement results of 55 children with CP, the average index score was 0.423, which was lower than the national general population level. The proportions of patients with CP who have problems in the five aspects of action, self-care, daily activities, pain/discomfort, and anxiety/depression are 72.73%, 81.82%, 81.82%, 83.64%, and 92.73%, respectively, which are significantly higher than those of the national general population. The average score of the Visual Analogue Scale (VAS) is 58.09, which is significantly lower than the national general population level. The only major factor affecting the quality of life of patients with CP and their families is the health status represented by the EQ-5D score. To liberate and develop the labor ability of patients and their direct caregivers through clinical treatment, rehabilitation, and special education is the most effective way to reduce the socioeconomic burden of CP. Relevant government departments should perform their duties, integrate social assistance resources, implement early intervention, and launch targeted support and assistance policy.

PMID: 35028115

22. The Economic Burden and Determinant Factors of Parents/Caregivers of Children with Cerebral Palsy in Malaysia: A Mixed Methods Study
Aniza Ismail, Ruhana Sk Abd Razak, Leny Suzana Suddin, Aidalina Mahmud, Sazlina Kamaralzaman, Ghazali Yusri

Int J Environ Res Public Health. 2022 Jan 1;19(1):475. doi: 10.3390/ijerph19010475.

The economic burden is a major concern for parents/caregivers of children with cerebral palsy (CP). This study used the sequential explanatory mixed-method approach to explore the economic burden on parents/caregivers with a CP child in Malaysia and the factors associated with the economic burden. The study period spanned April 2020 and December 2020. A total of 106 questionnaire respondents were selected for the quantitative part, and 15 were interviewed to obtain qualitative input. A retrospective costing analysis was conducted based on the cost data obtained from the questionnaire. The majority of the children were Gross Motor Function Classification System (GMFCS) Level 5 (71%), quadriplegic (63%), and aged >4 years (90%). The estimated annual median total economic burden on the parents/caregivers per child in 2020 was RM52,540.00 (~USD12,515.03), with indirect cost being the greatest cost (RM28,800.00, ~USD6860.16), followed by

developmental cost (RM16,200.00, ~USD3858.84), direct healthcare cost (RM4540.00, ~USD1081.43) and direct non-healthcare cost (RM3000.00, ~USD714.60). The annual household income was identified as a significant determinant factor (p=0.019, 95% CI: 0.04, 0.40) of the economic burden. The participants' responses during the in-depth interview in the qualitative part of the study supported the premise that socioeconomic factors play a substantial role in determining the total economic burden. Our findings may aid local policymakers when planning the greater provision of support to the affected families in the future, especially for the parents/caregivers of children with CP, who are facing socioeconomic challenges.

PMID: 35010732

23. The impact of COVID-19 on the lifestyles of adolescents with cerebral palsy in the Southeast United States
Byron Lai, Huacong Wen, Tanvee Sinha, Drew Davis, Erin Swanson-Kimani, Cynthia Wozow, Raven Young, Danielle Powell, James H Rimmer

Disabil Health J. 2021 Dec 17;101263. doi: 10.1016/j.dhjo.2021.101263. Online ahead of print.

Background: The impact of COVID-19 on adolescents with cerebral palsy (CP) and their families is underinvestigated, particularly in the Southeastern United States. Objective/hypothesis: The objective of this study was to examine the impact of COVID-19 on lifestyle activities, general and mental health, and basic needs among a cohort of adolescents with CP in the Southeast U.S. The second purpose was to identify key factors that impacted their lifestyles. Methods: This was a cross-sectional survey of adolescents with CP (aged 10-19 years) who completed a child-modified version of the Coronavirus Disability Survey. Health and behavior items were associated with the perceived lifestyle impact of COVID-19. Results: A total of 101 respondents completed the survey (mean age: 14 ± 2 years). Respondents reported minimal to no change in general health since the COVID-19 outbreak. Basic needs were met for most families. Nearly all participants (94.1%) reported a mental health concern that resulted from COVID-19: 32.7% felt down or depressed; 47.5% felt little pleasure in doing things; and 64.4% felt isolated. Moreover, 74.3% reported decreased socialization, 51.5% reported reduced exercise participation, and 43.6% reported difficulties in obtaining medical care. Most participants (90.1%) were negatively affected by COVID-19, and key associated factors were reduced interactions with friends and family ($p = 0.001$), exercise participation ($p = 0.016$), interest in doing things ($p = 0.005$), worsened depression ($p = 0.015$), increased isolation from others ($p = 0.02$) and at home ($p = 0.006$), technological communication ($p = 0.00$), and virus exposure ($p = 0.008$). Conclusions: Study findings highlight problem areas that warrant urgent intervention among adolescents with CP located within the Southeast U.S.

PMID: 35000878

24. Prelabor rupture of membranes at term: A possible hematological triage in addition to vagino-rectal beta-hemolytic streptococcus screening for early labor induction
Francesco D'Ambrosi, Nicola Cesano, Enrico Iurlaro, Alice Ronchi, Ilaria Giuditta Ramezzana, Matteo Di Maso, Carlo Pietrasanta, Andrea Ronchi, Lorenza Pugni, Enrico Ferrazzi

PLoS One. 2022 Jan 13;17(1):e0261906. doi: 10.1371/journal.pone.0261906. eCollection 2022.

Introduction: A potential complication of term prelabor rupture of membranes (term PROM) is chorioamnionitis with an increased burden on neonatal outcomes of chronic lung disease and cerebral palsy. The purpose of the study was to analyze the efficacy of a standing clinical protocol designed to identify women with term PROM at low risk for chorioamnionitis, who may benefit from expectant management, and those at a higher risk for chorioamnionitis, who may benefit from early induction. Material and methods: This retrospective study enrolled all consecutive singleton pregnant women with term PROM. Subjects included women with at least one of the following factors: white blood cell count ≥ 15×100/μL, C-reactive protein ≥ 1.5 mg/dL, or positive vaginal swab for beta-hemolytic streptococcus. These women comprised the high risk (HR) group and underwent immediate induction of labor by the administration of intravaginal dinoprostone. Women with none of the above factors and those with a low risk for chorioamnionitis waited for up to 24 hours for spontaneous onset of labor and comprised the low-risk (LR) group. Results: Of the 884 consecutive patients recruited, 65 fulfilled the criteria for HR chorioamnionitis and underwent immediate induction, while 819 were admitted for expectant management. Chorioamnionitis and Cesarean section rates were not significantly different between the HR and LR groups. However, the prevalence of maternal fever (7.7% vs. 2.9%; $p = 0.04$) and meconium-stained amniotic fluid was significantly higher in the HR group than in LR group (6.1% vs. 2.2%; $p = 0.04$). This study found an overall incidence of 4.2% for chorioamnionitis, 10.9% for Cesarean section, 0.5% for umbilical artery blood pH < 7.10, and 1.9% for admission to the neonatal intensive care unit. Furthermore, no confirmed cases of neonatal sepsis were encountered. Conclusions: A clinical protocol designed to manage, by immediate induction, only those

women with term PROM who presented with High Risk factors for infection/inflammation achieved similar maternal and perinatal outcomes between such women and women without any risks who received expectant management. This reduced the need for universal induction of term PROM patients, thereby reducing the incidence of maternal and fetal complications without increasing the rate of Cesarean sections.

PMID: 35025890

25. Wavelength and pulse energy optimization for detecting hypoxia in photoacoustic imaging of the neonatal brain: a simulation study
Sadreddin Mahmoodkalayeh, Karl Kratkiewicz, Rayyan Manwar, Meysam Shahbazi, Mohammad Ali Ansari, Girija Natarajan, Eishi Asano, Kamran Avanaki

Biomed Opt Express. 2021 Nov 10;12(12):7458-7477. doi: 10.1364/BOE.439147. eCollection 2021 Dec 1.

Cerebral hypoxia is a severe injury caused by oxygen deprivation to the brain. Hypoxia in the neonatal period increases the risk for the development of neurological disorders, including hypoxic-ischemic encephalopathy, cerebral palsy, periventricular leukomalacia, and hydrocephalus. It is crucial to recognize hypoxia as soon as possible because early intervention improves outcomes. Photoacoustic imaging, using at least two wavelengths, through a spectroscopic analysis, can measure brain oxygen saturation. Due to the spectral coloring effect arising from the dependency of optical properties of biological tissues to the wavelength of light, choosing the right wavelength-pair for efficient and most accurate oxygen saturation measurement and consequently quantifying hypoxia at a specific depth is critical. Using a realistic neonate head model and Monte Carlo simulations, we found practical wavelength-pairs that quantified regions with hypoxia most accurately at different depths down to 22 mm into the cortex neighboring the lateral ventricle. We also demonstrated, for the first time, that the accuracy of the sO2 measurement can be increased by adjusting the level of light energy for each wavelength-pair. Considering the growing interest in photoacoustic imaging of the brain, this work will assist in a more accurate use of photoacoustic spectroscopy and help in the clinical translation of this promising imaging modality. Please note that explaining the effect of acoustic aberration of the skull is not in the scope of this study.

PMID: 35003846

26. Development of muscle tone impairments in high-risk infants: Associations with cerebral palsy and cystic periventricular leukomalacia
Elisabeth J M Straathof, Elisa G Hamer, Kilian J Hensens, Sacha La Bastide-van Gemert, Kirsten R Heineman, Mijna Hadders-Algra

Eur J Paediatr Neurol. 2022 Jan 1;37:12-18. doi: 10.1016/j.ejpn.2021.12.015. Online ahead of print.

Aim: To assess the prevalence and development of muscle tone impairments in infants at high risk of developmental disorders, and their associations with cerebral palsy (CP) and cystic periventricular leukomalacia (cPVL). Method: Longitudinal exploration of muscle tone in 39 infants at high risk of CP (LEARN2MOVE 0-2 project) mostly due to an early lesion of the brain. Muscle tone was assessed ≥4 times between 0 and 21 months corrected age (CA) with the Touwen Infant Neurological Examination. Diagnosis of CP was determined at 21 months CA. Neonatal neuro-imaging was available. Developmental trajectories were calculated using generalized linear mixed effect models. Results: Infants showed atypical muscle tone in three or four body parts in 93% (172/185) of the assessments. The most prevalent muscle tone pattern was hypotonia of neck and trunk with hypertonia of the limbs (28%). From 7 months CA onwards hypertonia of the arms was associated with CP. Asymmetric arm tone during infancy was associated with unilateral CP. At 18-21 months CA ankle hypertonia was associated with CP at 21 months; leg hypertonia in infancy was not associated with CP. Leg hypertonia was associated with cPVL, regardless of age. Interpretation: High-risk infants due to an early lesion of the brain often present with muscle tone impairment. In these infants, hypertonia and asymmetric muscle tone of the arms were from 7 months onwards associated with the diagnosis of CP at 21 months; hypertonia of the legs was not.

PMID: 35007848

27. Long-term efficacy and safety of repeated botulinum toxin a applications based on function and anesthesia type in children with cerebral palsy
Murat Celal Sozbilen, Kubra Evren Sahin

J Orthop. 2021 Dec 30;29:22-27. doi: 10.1016/j.jor.2021.12.005. eCollection Jan-Feb 2022.

Purpose: This study evaluates the motor development of patients undergoing three or more repeated Botulinum toxin A (BoNT -A) applications in a tertiary pediatric hospital as well as the safety of three different types of anesthesia. Methods: Seventy-five children who underwent BoNT-A applications at least three consecutive times at six-month intervals and a total of 320 procedures were examined. Gross Motor Function Classification System (GMFCS) was employed in motor development evaluation. The three anesthesia methods (sedation analgesia, anesthesia with larengeal mask [LMA] and inhalation mask) were compared in terms of sedation, procedure, recovery, and total operation room time. Results: Following the procedures, significant motor development was observed in 60 (80%) patients. In sedation analgesia group during the first three procedures, the recovery time was seen to be significantly shorter, while there was no difference between the anesthesia methods of any procedures following the fourth. Regardless of the type of anesthesia, the recovery times of those having undergone six or more procedures were longer than those with less than six procedures. Conclusions: As repeated BoNT-A application provides motor step progress, it can be applied safely and effectively under anesthesia. Sedation analgesia provides an easier recovery compared to LMA and mask only within the first three applications. However, recovery time increases with four or more repeated applications, specifically increasing as the number of applications increases. Level of evidence: III.

PMID: 35027815

28. Plasma Metabolomic Changes in Children with Cerebral Palsy Exposed to Botulinum Neurotoxin
Hongmei Tang, Tingting Peng, Xubo Yang, Liru Liu, Yunxian Xu, Yiting Zhao, Shiya Huang, Chaoqiong Fu, Yuan Huang, Hongyu Zhou, Jinling Li, Lu He, Wenda Wang, Huiran Niu, Kaishou Xu

J Proteome Res. 2022 Jan 12. doi: 10.1021/acs.jproteome.1c00711. Online ahead of print.

The long-term effect of botulinum neurotoxin A (BoNT-A) on children with cerebral palsy (CP) is unclear, and how the dynamic changes of metabolites impact the duration of effect remains unknown. To tackle this, we collected 120 plasma samples from 91 children with spastic CP for analysis, with 30 samples in each time point: prior to injection and 1, 3, and 6 months after injection. A total of 354 metabolites were identified across all the time points, 39 of which exhibited significant changes (with tentative IDs) (p values <0.05, VIP > 1). Principal component analysis and partial least-squares discriminant analysis disclosed a clear separation between different groups (p values <0.05). Network analysis revealed the coordinated changes of functional metabolites. Pathway analysis highlighted the metabolic pathways associated with energy consumption and glycine, serine, and threonine metabolism and cysteine and methionine metabolism. Collectively, our results identified the significant dynamic changes of plasma metabolite after BoNT-A injections on children with CP. Metabolic pathways associated with energy expenditure might provide a new perspective for the effect of BoNT-A in children with CP. Glycine, serine, and threonine metabolism and cysteine and methionine metabolism might be related to the duration of effect of BoNT-A.

PMID: 35018779

29. Play-based groups for children with cerebral palsy and their parents: a qualitative interview study about the impact on mothers' wellbeing
Kirsten R Prest, Aleksandra J Borek, Anne-Marie R Boylan

Child Care Health Dev. 2022 Jan 12. doi: 10.1111/cch.12962. Online ahead of print.

Background: Cerebral Palsy (CP) is the most common childhood physical disability in developed countries. Parents of children with CP experience difficulties which can result in reduced wellbeing. Health professionals supporting children with CP have been encouraged to focus on parental wellbeing as this forms part of the child's essential environment. There is a lack of evidence about interventions which holistically support the whole family by providing therapeutic input for the child and support for parents. This study aimed to explore parents' experiences of play-based groups for children with CP and their

parents, with a focus on the groups' impact on parents' wellbeing. Methods: Parents of children with CP who had attended play-based groups in the year prior were recruited for this qualitative study. Semi-structured interviews were conducted, audio-recorded and transcribed verbatim. Participants' demographic characteristics were collected as contextual information. Data was analysed using an inductive thematic approach. Results: Ten mothers were interviewed. Overall, mothers had positive experiences of the groups and perceived them as an important influence on their wellbeing. Four themes described mothers' experiences of the groups and the subsequent impact on their wellbeing: (1) Practical Support, (2) Connecting with Others, (3) Transitioning Journeys, and (4) Different Motivators, Different Experiences. Numerous factors influenced mothers' experiences of attending the groups and the subsequent impact on their wellbeing. This included mothers' individual experiences of having a child with CP. Conclusions: Interventions combining practical and social support for the whole family can have a positive impact on the wellbeing of mothers of children with CP. Care should be taken to provide individualised support for each family. There is no 'one size fits all' approach and a package of care can provide multiple services which meet the varying needs of mothers and their children with CP.

PMID: 35023213

30. Guideline to improve physical function in cerebral palsy: too big to succeed
Lynne Romeiser Logan, Kat Kolaski

Dev Med Child Neurol. 2022 Jan 14. doi: 10.1111/dmcn.15134. Online ahead of print.

PMID: 35030263