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## Interventions and Management

### 1. Pain, disability, and quality of life in participants after concurrent onabotulinumtoxinA treatment of upper and lower limb spasticity: Observational results from the ASPIRE study

Ganesh Bavikatte, Gerard E Francisco, Wolfgang H Jost, Alessio Baricich, Esther Duarte, Simon F T Tang, Marc Schwartz, Mariana Nelson, Tiziana Musacchio, Alberto Esquenazi

PM R. 2024 May 30. doi: 10.1002/pmrj.13195. Online ahead of print.

**Introduction:** Upper and lower limb spasticity is commonly associated with central nervous system disorders including stroke, traumatic brain injury, multiple sclerosis, cerebral palsy, and spinal cord injury, but little is known about the concurrent treatment of upper and lower limb spasticity with botulinum toxins. **Objective:** To evaluate onabotulinumtoxinA (onabotA) utilization and to determine if concurrent onabotA treatment of the upper and lower limbs has supported improvements in participants with spasticity. **Design:** Sub-analysis of a 2-year, international, prospective, observational registry (ASPIRE, NCT01930786). **Setting:** International clinic sites (54). **Participants:** Adult spasticity participants across etiologies, who received  $\geq 1$  concurrent onabotA treatment of the upper and lower limbs during the study. **Intervention:** Participants were treated with onabotA at the clinician's discretion. **Outcomes:** Baseline characteristics and outcomes of disability (Disability Assessment Scale [DAS]), pain (Numeric Pain Rating Scale [NPRS]), participant satisfaction, physician satisfaction, and quality of life (QoL; Spasticity Impact Assessment [SIA]) were evaluated. Adverse events were monitored throughout the study. **Results:** Of 744 participants enrolled, 730 received  $\geq 1$  dose of onabotA; 275 participants received treatment with onabotA in both upper and lower limbs during  $\geq 1$  session; 39.3% of participants were naïve to onabotA for spasticity. The mean (SD) total dose per treatment session ranged from 421.2 (195.3) to 499.6 (188.6) U. The most common baseline upper limb presentation was clenched fist ( $n = 194$ , 70.5%); lower limb was equinovarus foot ( $n = 219$ , 66.9%). High physician and participant satisfaction and improvements in pain, disability and QoL were reported after most treatments. Nine participants (3.3%) reported nine treatment-related adverse events; two participants (0.7%) reported three serious treatment-related severe adverse events. No new safety signals were identified. **Conclusion:** More than a third of enrolled participants received at least one concurrent onabotA treatment of the upper and lower limbs, with reduced pain, disability, and improved QoL after treatment, consistent with the established safety profile of onabotA for the treatment of spasticity.

PMID: [38813838](#)

### 2. Efficacy of neuromuscular electrical stimulation and interrupted serial casting in children with spastic diplegia [Abstract in English, Arabic]

Yasser M Abd Elmonem, Elham E Salem, Mohamed A Elshafey, Amr H Mostafa

J Taibah Univ Med Sci. 2024 May 16;19(3):628-636. doi: 10.1016/j.jtumed.2024.05.006. eCollection 2024 Jun.

**Objectives:** This research was aimed at comparing the effects of neuromuscular electrical stimulation (NMES) combined with interrupted serial casting (SC) versus SC alone on various aspects of lower limb function in children with diplegic cerebral palsy. SC is a clinical technique used to increase passive range of motion (ROM), decrease hypertonicity, and improve walking in children with cerebral palsy (CP). **Methods:** This randomized comparative trial involved 33 children with diplegic

CP, who were randomly assigned to group A or group B at recruitment. Group A received SC along with a customized physical therapy program, whereas group B received the same interventions as group A along with NMES applied through cast windows during casting. Evaluations were based on ROM, the Modified Tardieu Scale, handheld dynamometer measurements, and the Observational Gait Scale. Assessments were conducted before and after 8 weeks of intervention. Results: Both groups exhibited significant improvements in dorsiflexion ROM, popliteal angle, gastrocnemius dynamic spasticity, and hamstring dynamic spasticity after the intervention ( $P = 0.0001$  for all). However, significant differences ( $P < 0.05$ ) in dorsiflexor strength, knee extensor strength, and observational gait scale score were observed between groups after the intervention, favoring group B. Conclusions: The use of NMES during SC may help overcome the substantial decrease in strength resulting from casting, thus achieving less reduction of tone, improving ROM without significantly decreasing strength, and attaining greater improvements in gait function.

PMID: [38812723](#)

### 3. Hip displacement in children with post-neonatal cerebral palsy and acquired brain injury: a systematic review

Errolyn Boettcher-Hunt, Roslyn N Boyd, Noula Gibson

Review Brain Inj. 2024 May 26;1-13. doi: 10.1080/02699052.2024.2350049. Online ahead of print.

Aim: To systematically review the prevalence, risk factors and timing of onset of hip displacement in children with a post-neonatal (PNN) brain injury with regards to hip surveillance recommendations. Method: A search of PubMed, MEDLINE, Embase, CINAHL and Web of Science was conducted on 22nd February 2022. Studies were included if they reported presence of, and risk factors for, hip displacement in children with PNN brain injury. Data was extracted on patient characteristics, and analyzed in terms of risk factors of interest and timing of development of hip displacement. Results: Six studies met the inclusion criteria ( $n = 408$  participants). All were cohort studies: five retrospective and one prospective. Rates of hip displacement ranged from 1% to 100%, and were higher in children with diffuse brain injury at an early age, who were non-ambulant and had spastic quadriplegia. Hip displacement and hip dislocation were first identified at one and three months respectively following PNN brain injury. Interpretation: Evidence on hip displacement in children with PNN brain injury is sparse and low quality. Children who remain non-ambulant after diffuse PNN brain injury before five years of age appear most at risk of developing progressive hip displacement and earlier hip surveillance is recommended.

PMID: [38796860](#)

### 4. Lower Extremity Muscle Tendon Interaction Around Knee During Gait Among Adolescent Children with Cerebral Palsy with Varying Crouch Angle

Triveni Shetty, Rajani Mullerpatan, Sailakshmi Ganesan, Ashok N Johari

Indian J Orthop. 2024 May 4;58(6):680-686. doi: 10.1007/s43465-024-01165-9. eCollection 2024 Jun.

Background: Optimal management and surgical planning of severe bony deformities and muscle tendon unit contractures demands comprehensive evaluation of all structures including the dynamic muscle tendon length of all muscles around the joint during gait. Objectives: Present study aimed to explore dynamic muscle-tendon length for all muscles around the knee joint along with pelvis, hip, and ankle joint kinematics among adolescent children with varying crouch angle. Methods: Muscle-tendon length of 29 adolescent children with cerebral palsy with varying crouch angles was computed using a full-body musculo-skeletal model and expressed as a percentage of muscle-tendon length during walking compared to resting condition. Results: Children with knee flexion angle greater than  $25^\circ$  demonstrated lower anterior pelvic tilt and 11% greater muscle-tendon length of semimembranosus and biceps femoris during stance phase of gait compared to children with knee flexion angle less than  $25^\circ$  and typically developing children ( $p < 0.01$ ). Conclusions: The findings of present study reported that routine bedside clinical evaluation in adolescent children with knee flexion angle greater than  $25^\circ$  revealed moderate shortening of hamstring muscle in supine position. Whereas instrumented objective evaluation of gait demonstrated lengthened hamstring muscle and reduced hip extension and relatively lower anterior pelvic tilt. Therefore, it may be valuable to add objective assessment of dynamic muscle-tendon length to kinematics of all lower-extremity joint motion during gait, in order to understand the muscle-joint interactions; particularly in children with severe crouch and plan specific, tailor-made surgical and non-surgical interventions.

PMID: [38812859](#)

### 5. Prevalence and Treatment of Surgical Complications Following Proximal Femoral Osteotomies in Children with Cerebral Palsy: An Analysis of 1085 Hips

Ahmet Imerci, Freeman Miller, Jason J Howard, M Wade Shrader

Indian J Orthop. 2024 Apr 25;58(6):669-679. doi: 10.1007/s43465-024-01144-0. eCollection 2024 Jun.

**Purpose:** Proximal femoral osteotomy (PFO) is a reconstructive surgical option used to improve hip containment or correct internal hip rotation gait in children with cerebral palsy (CP). A few reports describe the risk of surgical complications after PFO. The purpose of this study was to determine the risk factors associated with adverse postoperative surgical outcomes in pediatric patients with CP following PFO and to report the treatment of complications. **Methods:** Following institutional review board approval, 1085 (1003 primary and 82 secondary) PFO procedures were retrospectively reviewed in 563 children with CP with at least 1 year of follow-up after final surgery over an 18-year follow-up period. Demographic characteristics, motor type, gross motor function classification system (GMFCS) level, medical comorbidities, feeding tube status, seizure history, intervention type, and prevalence of PFO-related surgical complications and associated treatments were evaluated. Multivariate regression analysis was performed to determine risk factors for all surgical complications. **Results:** During a 5.8-year ( $\pm$  3.8 years) follow-up, at least 1 surgical complication was identified in 143 (13.1%) hips in 121 (21.5%) patients after PFO in children with CP. Of these complications, the most common was heterotopic ossification (65 [6%] of hips); most of which were asymptomatic and required no treatment. Other complications included 25 (2%) nonunions, 21 (2%) deep or superficial infections, 13 (1%) delayed unions, 12 (1%) peri-implant fractures, and 7 early implant failures (0.64). The rate of revision surgery due to these complications was 13.1% (6.8% of hips), of which 41% (30 revision surgeries) were for the treatment of nonunion. Regarding the development of delayed union or nonunion, dystonia, GMFCS level IV/V, and seizure history were identified as risk factors by multivariate analysis. **Conclusions:** The prevalence of surgical complications after PFO was 13.1% with 6.8% of hips requiring revision surgery. Dystonia, seizure history, and nonambulatory status were the strongest predictors for the need for revision surgery after PFO. These data can be used to help counsel patients and families regarding the risks associated with PFO for children with CP. **Level of proof:** IV; retrospective study.

PMID: [38812872](#)

## **6. Effects of progressive functional ankle exercises in spastic cerebral palsy, plantarflexors versus dorsiflexors: a randomized trial**

Melek Volkan Yazici, Gamze Çobanoğlu, Gökhan Yazici, Bülent Elbasan

Randomized Controlled Trial Turk J Med Sci. 2023 May 31;53(5):1166-1177. doi: 10.55730/1300-0144.5682. eCollection 2023.

**Background/aim:** Children with cerebral palsy (CP), even those who have very mild impairment, have lower muscle strength than their typically developing peers. The ankle dorsiflexors (DFs) and plantarflexors (PFs) of children with CP are especially weak. Weakness in the ankle muscles causes problems in functional skills, mobility, and balance in spastic CP (SCP). The aim of this study was to investigate the effects of progressive functional exercises (PFEs) on the DF, PF, or dorsi-plantar flexor (DPF) muscles in children with SCP, specifically, the functional mobility, balance, and maximum voluntary contraction (MVC), and compare the effects of strengthening these muscles individually or combined. **Materials and methods:** This randomized trial was conducted between December 1st, 2018, and May 15th, 2019, at Gazi University, Department of Physiotherapy and Rehabilitation. Randomly assigned into groups were 27 independently ambulant patients with unilateral/bilateral SCP, where PFEs were applied to the DF, PF, or DPF muscles. Muscle tone, balance, and functional mobility were assessed. The MVC was evaluated by surface electromyography. PFEs were performed 4 times a week, for 6 weeks. **Results:** The spasticity of the PF muscles decreased in all of the groups. PFE of the DF muscles led to an increase in ankle joint range of motion (ROM) and improved functional mobility ( $p < 0.05$ ). PFE of the PF muscles resulted in improvements in balance and functional mobility ( $p < 0.05$ ). PFE of the DPF muscles brought about improvements in balance but not in functional mobility ( $p < 0.05$ ). No significant difference in the MVC was observed in any of the groups ( $p > 0.05$ ). **Conclusion:** Gains are obtained according to the function of a muscle group. By training the DF muscles, it is possible to improve function and ROM. Furthermore, training the PF muscles led to improvements in balance and functional mobility, indicating that it is possible to bring about positive changes in spastic muscles. This study showed that muscle groups must be exercised according to the intended goal.

PMID: [38812998](#)

## **7. Proximal Femur Guided Growth: A Systematic Review**

Joshua C Tadlock, Michael D Eckhoff, Hunter R Graver, Tyler H Doty, Tyler C Nicholson, EStephan J Garcia

J Surg Orthop Adv. 2024 Spring;33(1):49-52.

Children with cerebral palsy (CP) and those with avascular necrosis (AVN) after treatment of developmental hip dysplasia (DDH) are at risk of developing coxa valga. Proximal femur guided growth is a minimally invasive option to correct this deformity. A systematic review of articles that described treatment of coxa valga with proximal femur guided growth (PFGG) and reporting on primary radiographic outcomes, demographic variables, surgical variables and complications. One hundred and seventy-nine hips underwent PFGG (117 with CP and 62 with lateral overgrowth). Average age at surgery was 8.1 years; average follow-up was 52.5 months. Migration percentage improved from 11.2% ( $p < 0.0001$ ). Neck-shaft angle improved by 11.9° ( $p < 0.0001$ ). The most common complication was screw growth out of the physis (30% of cases). PFGG can correct coxa valga, improve radiographic parameters, and in children with CP prevent further subluxation. This technique modulates

proximal femur growth, induces changes to the acetabulum and can correct valgus deformity. Evidence Level III. (Journal of Surgical Orthopaedic Advances 32(4):049-052, 2024).

PMID: [38815079](#)

### **8. Identifying the top 10 priorities of adolescents with a physical disability regarding participation in physical activity: A Delphi study**

Karen Brady, Ronan Cleary, Eva O'Gorman, Suzanne McDonough, Claire Kerr, Damien Kiernan, Elaine McConkey, Jennifer Ryan, Ailish Malone

Dev Med Child Neurol. 2024 May 30. doi: 10.1111/dmcn.15986. Online ahead of print.

**Aim:** To establish consensus among adolescents with a physical disability regarding their priorities for enhancing participation in physical activity and help inform the design of future interventions for participation in physical activity. **Method:** We conducted a national multi-round Delphi study involving adolescents with a physical disability aged 13 to 17 years. Round 1 of the initial survey consisted of open-ended questions. Free-text responses were then analysed thematically, creating items categorized according to the family of participation-related constructs (fPRC). In round 2, participants rated the perceived importance of these items using a 5-point Likert scale. The top 10 priorities were constructed from the highest-ranked items. **Results:** One hundred and sixteen participants (mean age = 14 years 7 months, range = 13-17 years; 66 males; 58 with cerebral palsy; 43 wheelchair users) completed round 1; 108 items were included in round 2. Fifty-eight items were rated as either 'important' or 'really important' by 70% of participants. The top 10 priorities were rated as important or really important by 82% to 94% of participants with a mean Likert score of 4.40 (range = 4.25-4.63). Seven of the top 10 priorities were related to the environmental context of the fPRC. The other three were related to involvement and the related concept of preference. **Interpretation:** The priorities identified will help inform future physical activity interventions for adolescents with a physical disability.

PMID: [38815177](#)

### **9. Effectiveness of action observation treatment based on pathological model in hemiplegic children: a randomized-controlled trial**

Antonino Errante, Laura Beccani, Jessica Verzelloni, Irene Maggi, Mariacristina Filippi, Barbara Bressi, Settimio Ziccarelli, Francesca Bozzetti, Stefania Costi, Adriano Ferrari, Leonardo Fogassi

Eur J Phys Rehabil Med. 2024 May 30. doi: 10.23736/S1973-9087.24.08413-2. Online ahead of print.

**Background:** Action observation treatment (AOT) is an innovative therapeutic approach consisting in the observation of actions followed by their subsequent repetition. The standard version of AOT consists in the observation/imitation of a typically developed individual, which is proposed as model (TDM-AOT). **Aim:** This study aims to compare the effectiveness of AOT based on a pathological ameliorative model (PAM-AOT) versus TDM-AOT in improving upper limb ability in children with unilateral cerebral palsy (UCP). **Design:** The study consists in a prospective randomized controlled, evaluator-blinded trial (RCT), with two active arms, designed to evaluate the effectiveness of AOT based on pathological model (PAM-AOT) as compared to a standard AOT based on TDM (TDM-AOT). **Setting:** The 3-week AOT program was administered in a clinical setting. For some patients, the treatment was delivered at participant's home with the remote support of the physiotherapist (tele-rehabilitation). **Population:** Twenty-six children with UCP (mean age 10.5±3.09 years; 14 females) participated in the study, with the experimental group observing a pathological model and the control group observing a typically developed model. **Methods:** Motor assessments included unimanual and bimanual ability measures conducted at T0 (baseline, before the treatment), T1 (3 weeks after T0), T2 (8-12 weeks after treatment) and T3 (24-28 weeks after treatment); a subset of 16 patients also underwent fMRI motor assessment. Generalized Estimating Equations models were used for statistical analysis. **Results:** Both groups showed significant improvement in bimanual function (GEE, Wald 106.16; P<0.001) at T1 (P<0.001), T2 (P<0.001), and T3 (P<0.001). Noteworthy, the experimental group showed greater improvement than the control group immediately after treatment (P<0.013). Both groups exhibited similar improvement in unimanual ability (GEE, Wald 25.49; P<0.001). The fMRI assessments revealed increased activation of ventral premotor cortex after treatment in the experimental compared with control group (GEE, Wald 6.26; P<0.012). **Conclusions:** Overall, this study highlights the effectiveness of PAM-AOT in achieving short-term improvement of upper limb ability in children with UCP. **Clinical rehabilitation impact:** These findings have significant implications for rehabilitative interventions based on AOT in hemiplegic children, by proposing a non-traditional approach focused on the most functional improvement achievable by imitating a pathological model.

PMID: [38814197](#)

### 10. Effect of botulinum toxin type a combined with physical therapy on functional capacity in children with spastic cerebral palsy: a randomized controlled clinical trial

Maria Eliege de Souza, Caroline Razera Ferreira, Claudia Santos Oliveira, Maria Fernanda Molledo Secco, Paulo Fonseca Junior, Paulo Roberto Garcia Lucareli, Daniela Aparecida Biasotto-Gonzalez, Fabiano Politti

Neurol Res. 2024 May 26:1-7. doi: 10.1080/01616412.2024.2359260. Online ahead of print.

**Objective:** Investigate the effects of botulinum toxin type A (BoNT-A) combined with physical therapy on functional capacity in children with spastic cerebral palsy (CP). **Methods:** Twenty-four children with spastic CP were treated with either BoNT-A and physical therapy or physical therapy alone. **Results:** Significant differences ( $p < 0.05$ ) were found after 30 days of treatment for the Berg Scale, Timed Up and Go (TUG) test, Ashworth Scale and Pediatric Evaluation of Disability Inventory (PEDI) and after three months for the Berg Scale, TUG test and PEDI. No significant differences ( $p > 0.05$ ) were found in the control group. **Discussion:** BoNT-A combined with physical therapy leads to significant improvements in spasticity and functionality in children with CP within a period of three months from the onset of treatment.

PMID: [38797512](#)

### 11. Enhanced EEG power density during painful stretching in individuals with cerebral palsy

Álvaro Sabater-Gárriz, Pedro Montoya, Inmaculada Riquelme

Res Dev Disabil. 2024 May 24:150:104760. doi: 10.1016/j.ridd.2024.104760. Online ahead of print.

**Background:** Pain perception mechanisms in cerebral palsy remain largely unclear. **Aims:** This study investigates brain activity in adults with cerebral palsy during painful and non-painful stretching to elucidate their pain processing characteristics. **Methods and procedures:** Twenty adults with cerebral palsy and 20 controls underwent EEG in three conditions: rest, non-painful stretching, and painful stretching. Time-frequency power density of theta, alpha, and beta waves in somatosensory and frontal cortices was analyzed, alongside baseline pressure pain thresholds. **Outcomes and results:** Cerebral palsy individuals exhibited higher theta, alpha, and beta power density in both cortices during painful stretching compared to rest, and lower during non-painful stretching. Controls showed higher power density during non-painful stretching but lower during painful stretching. Cerebral palsy individuals had higher pain sensitivity, with those more sensitive experiencing greater alpha power density. **Conclusions and implications:** These findings confirm alterations in the cerebral processing of pain in individuals with cerebral palsy. This knowledge could enhance future approaches to the diagnosis and treatment of pain in this vulnerable population.

PMID: [38795555](#)

### 12. Assessment of somatosensory profiles by quantitative sensory testing in children and adolescents with and without cerebral palsy and chronic pain

Johanne Villars Jørgensen, Mads Utke Werner, Josephine Sandahl Michelsen, Christian Nai En Tierp-Wong

Eur J Paediatr Neurol. 2024 May 18:51:32-40. doi: 10.1016/j.ejpn.2024.05.007. Online ahead of print.

**Objective:** We investigated differences in somatosensory profiles (SSPs) assessed by quantitative sensory testing in children and adolescents with cerebral palsy (CCP) with and without chronic pain and compared these differences to those in a group of typically developed children and adolescents (TDC) with and without chronic pain. **Method:** All included subjects were consecutively recruited from and tested at the same outpatient orthopedic clinic by the same investigator. The subjects had their reaction times tested. The SSP consisted of the following tests: warmth (WDT), cool (CDT), mechanical (MDT), and vibration (VDT) detection thresholds; heat (HPT), pressure (PPT), and mechanical (MPT) pain thresholds; wind-up ratio (WUR); dynamic mechanical allodynia (DMA) and cold pressor test (CPT) using a conditioned pain modulation (CPM) paradigm. **Results:** We included 25 CCP and 26 TDC. TDC without chronic pain served as controls. In TDC with chronic pain, WDT, HPT, HPT intensity, and PPT were higher than in controls. No differences in SSPs between CCP with and without chronic pain were observed. In CCP, the MDT, WDT, CDT, and HPT intensity were higher than in controls. CCP had longer reaction times than TDC. There were no differences regarding the remaining variables. **Discussion:** In CCP, the SSPs were independent of pain status and findings on MR images. In all CCP the SSPs resembled TDC with chronic pain, compared to TDC without chronic pain. This suggests that CCP do not have the normal neuroplastic adaptive processes that activate and elicit functional changes in the central and peripheral nervous systems.

PMID: [38795436](#)



### 13. Examining tools for assessing the impact of chronic pain on emotional functioning in children and young people with cerebral palsy: stakeholder preference and recommendations for modification

Meredith Grace Smith, Rachel J Gibson, Remo N Russo, Sophie Karanicolas, Adrienne R Harvey

Qual Life Res. 2024 May 25. doi: 10.1007/s11136-024-03693-1. Online ahead of print.

**Purpose:** To firstly identify tools for assessing the impact of chronic pain on emotional functioning in children and young people with cerebral palsy (CP), and secondly identify suggestions to improve their relevance, comprehensiveness, comprehensibility and feasibility for the CP population. Improving assessment of the impact of pain on emotional functioning can enhance quality of life by improving access to interventions for pain-related physical disability, anxiety and depression. **Methods:** Ethics approval was granted through the Women's and Children's Health Network Human Research Ethics Committee (2022/HRE00154). A mixed methods study with people with lived experience and clinicians, and guided by the Consensus-based Standards for Measurement Instruments (COSMIN), was undertaken. An online survey identified the highest rated tools for validation and/or modification for young people with CP and chronic pain. Focus groups and interviews investigated content validity and feasibility of the tools identified as highest rated. **Results:** The Fear of Pain Questionnaire for Children-SF (FOPQ-C-SF) and Modified Brief Pain Inventory (mBPI) were the highest rated for pain coping and multidimensional assessment (respectively) from the online survey (n = 61) of eight tools presented. Focus group and interview data (n = 30), including 58 unique modification suggestions, were coded to six categories: accessibility, comprehensibility, feasibility, relevance, presentation and comprehensiveness. **Conclusion:** Potential modifications have been identified to improve the appropriateness and feasibility of the FOPQ-C-SF and mBPI for children and young people with CP. Future research should implement and test these modifications, prioritising the involvement of people with lived experience to ensure their needs are met alongside clinicians.

PMID: [38795198](#)

### 14. Comparing the Effects of Virtual Reality Breathing Exercise and Incentive Spirometry Exercise on Improving Pulmonary Function in Children with Spastic Diplegic Cerebral Palsy

Rajesh S, Vadivelan Kanniappan, B S Santhosh Kanna, Veeragoudhaman T S

Cureus. 2024 Apr 27;16(4):e59149. doi: 10.7759/cureus.59149. eCollection 2024 Apr.

**Introduction:** Children with cerebral palsy (CP) have a higher incidence of respiratory dysfunction than healthy children. Virtual reality breathing therapy is an assistive technology that is becoming popular in the rehabilitation of children with CP. **Methods:** This experimental study included a total of 32 children with spastic diplegic CP who were divided into two groups: the virtual reality breathing training (VRBT) group and the incentive spirometry (IST) group. Individuals classified as levels I to III on the gross motor function classification system (GMFCS) were recruited using the simple random sampling method. **Result:** The results of comparing the values of forced vital capacity (FVC), forced expiratory volume at one second (FEV1), and the ratio of FVC/FEV1 showed a significant difference between groups. A significant difference was found in the VRBT group compared to the IST group, except for the peak expiratory flow (PEF) values, which showed a nonsignificant difference between the groups. **Conclusion:** There were significant differences in FVC and FEV1 between the VRBT and IST groups. It has been concluded that VRBT has additional benefits in improving pulmonary functions.

PMID: [38803793](#)

### 15. Long-Term Pulmonary and Neurodevelopmental Outcomes of Meconium Aspiration Syndrome Affected Infants: A Retrospective National Population-Based Study in Taiwan

Shang-Po Shen, Yin-Ting Chen, Hsiao-Yu Chiu, Ming-Luen Tsai, Hao-Wen Cheng, Kuang-Hua Huang, Yu-Chia Chang, Hung-Chih Lin

Neonatology. 2024 May 24;1-10. doi: 10.1159/000538925. Online ahead of print.

**Introduction:** Meconium aspiration syndrome (MAS) may cause severe pulmonary and neurologic injuries in affected infants after birth, leading to long-term adverse pulmonary or neurodevelopmental outcomes. **Methods:** This retrospective population-based cohort study enrolled 1,554,069 mother-child pairs between 2004 and 2014. A total of 8,049 infants were in the MAS-affected group, whereas 1,546,020 were in the healthy control group. Children were followed up for at least 3 years. According to respiratory support, MAS was classified as mild, moderate, and severe. With the healthy control group as the reference, the associations between MAS severity and adverse pulmonary outcomes (hospital admission, intensive care unit (ICU) admission, length of hospital stay, or invasive ventilator support during admission related to pulmonary problem) or adverse neurodevelopmental outcomes (cerebral palsy, needs for rehabilitation, visual impairment, or hearing impairment) were accessed. **Results:** MAS-affected infants had a higher risk of hospital and ICU admission and longer length of hospital stay, regardless of severity. Infants with severe MAS had a higher risk of invasive ventilator support during re-admission (odds ratio: 17.50, 95% confidence interval [CI]: 7.70-39.75, p < 0.001). Moderate (hazard ratio [HR]: 1.66, 95% CI: 1.30-2.13, p <

0.001) and severe (HR: 4.94, 95% CI: 4.94-7.11,  $p < 0.001$ ) MAS groups had a higher risk of adverse neurodevelopmental outcome, and the statistical significance remained remarkable in severe MAS group after adjusting for covariates (adjusted HR: 2.28, 95% CI: 1.54-3.38,  $p < 0.001$ ) Conclusions: Adverse pulmonary or neurodevelopmental outcomes could occur in MAS-affected infants at birth. Close monitoring and follow-up of MAS-affected infants are warranted.

PMID: [38797163](#)

## **16. Prevalence of Sensory Processing Deficits in Children with Spastic Cerebral Palsy - An Indian Caregiver's Perspective: Correspondence**

Josef Finsterer, Walter Strobl

Indian J Pediatr. 2024 May 29. doi: 10.1007/s12098-024-05175-1. Online ahead of print.

No abstract available

PMID: [38806968](#)

## **17. "Congenital cytomegalovirus in Sub-Saharan Africa-a narrative review with practice recommendations"**

Helen Payne, Shaun Barnabas

Review Front Public Health. 2024 May 15;12:1359663. doi: 10.3389/fpubh.2024.1359663. eCollection 2024.

Cytomegalovirus (CMV) is the most common cause of congenital infection internationally, occurring in 0.67% of births, and increasingly recognised as a major public health burden due to the potential for long-term neurodevelopmental and hearing impairment. This burden includes estimates of 10% of childhood cerebral palsy and up to 25% of childhood deafness. In Sub-Saharan Africa, where CMV-seroprevalence is almost ubiquitous, prevalence of congenital CMV (cCMV) is higher than the global average, and yet there is a dearth of research and initiatives to improve recognition, diagnosis and treatment. This narrative review outlines the epidemiology and clinical presentation of cCMV, discusses issues of case identification and treatment in Sub-Saharan Africa, and recommends a framework of strategies to address these challenges. Considering the significant burden of cCMV disease in this setting, it is undoubtedly time we embark upon improving diagnosis and care for these infants.

PMID: [38813410](#)

## **18. Cerebral Palsy: A Current Perspective**

Sanjeet Panda, Ajay Singh, Hugo Kato, Artemiy Kokhanov

Review Neoreviews. 2024 Jun 1;25(6):e350-e360. doi: 10.1542/neo.25-6-e350.

Cerebral palsy (CP) is the most common cause of motor disability in children. Insults to the brain at different times lead to diverse injuries. As a result, CP is an extremely heterogeneous clinical diagnosis, presenting differently in each individual and at various ages. With improving survival rates of preterm newborns, increasing active resuscitation of extremely preterm newborns, and widespread availability of extensive genetic testing soon after birth, it is imperative to focus on earlier diagnosis and long-term outcomes of CP. CP is primarily classified into 4 categories based on type of motor impairment, functional ability, distribution, and etiology. As the understanding of CP has evolved significantly in the last 2 decades, the methods of early detection of CP have consequently advanced. Appropriate diagnosis is essential for proper education and counseling of affected families, and introduction of therapeutic interventions as early as possible. In this review, we focus on early brain development and provide an overview of the etiology, classification, diagnosis, early therapeutic options, and prognosis of CP.

PMID: [38821909](#)

## **19. The Hammersmith Infant Neurological Exam Scoring Aid supports early detection for infants with high probability of cerebral palsy**

Darcy Fehlings, Amber Makino, Paige Church, Rudaina Banihani, Karen Thomas, Maureen Luther, Sophie Lam-Damji, Brigitte Vollmer, Leena Haataja, Frances Cowan, Dominico Romeo, Joanne George, Swetlana Kumar

Dev Med Child Neurol. 2024 May 31. doi: 10.1111/dmcn.15977. Online ahead of print.

No abstract available

PMID: [38818710](#)

## 20. Prevalence of Sensory Processing Deficits in Children with Spastic Cerebral Palsy - An Indian Caregiver's Perspective: Authors' Reply

Sapna Dhiman, Ramesh K Goyal, Aakash Mahesan, Puneeta Ajmera, G Shankar Ganesh, Sheffali Gulati

Indian J Pediatr. 2024 May 30. doi: 10.1007/s12098-024-05176-0. Online ahead of print.

No abstract available

PMID: [38814511](#)

## 21. Neonatal Hypoglycemia

Kiley Edmundson, Amy J Jnah

Review Neonatal Netw. 2024 May 1;43(3):156-164. doi: 10.1891/NN-2023-0068.

Neonatal hypoglycemia (NH) is broadly defined as a low plasma glucose concentration that elicits hypoglycemia-induced impaired brain function. To date, no universally accepted threshold (reference range) for plasma glucose levels in newborns has been published, as data consistently indicate that neurologic responses to hypoglycemia differ at various plasma glucose concentrations. Infants at risk for NH include infants of diabetic mothers, small or large for gestational age, and premature infants. Common manifestations include jitteriness, poor feeding, irritability, and encephalopathy. Neurodevelopmental morbidities associated with NH include cognitive and motor delays, cerebral palsy, vision and hearing impairment, and poor school performance. This article offers a timely discussion of the state of the science of NH and recommendations for neonatal providers focused on early identification and disease prevention.

PMID: [38816219](#)

## 22. The Burden of Stroke in Neonates Undergoing Congenital Heart Surgery: A Large Multicenter Analysis

Muhammad Faateh, Kevin Kulshrestha, Hosam F Ahmed, David Lehenbauer, Michael A Carlisle, Michael Gaies, David L S Morales, Awais Ashfaq

Ann Thorac Surg. 2024 May 28:S0003-4975(24)00388-6. doi: 10.1016/j.athoracsur.2024.05.011. Online ahead of print.

Background: Stroke affects surgical decision making and outcomes of neonatal cardiac surgery(CHS). We sought to assess the burden of stroke in this population from a large multi-center database. Methods: We analyzed neonates undergoing CHS with cardiopulmonary bypass from the Pediatric Health Information System database(2004-2022). The cohort was divided into stroke-group which included pre/post-op ischemic, hemorrhagic-subtypes and grade III-IV intraventricular hemorrhages and compared in-hospital and follow-up outcomes to non-stroke group. Results: Of 14,228 neonates, 800(5.6%) had a peri-operative stroke. Stroke-group was more likely to have hypoplastic left-heart syndrome (HLHS)(30.5% vs 20.7%), born pre-term(19.4% vs 11.7%), low-birthweight(17.8% vs 11.9%) and require ECMO(48.8% vs 13.8%)(all,  $p<0.001$ ). Outcomes comparing stroke vs no-stroke were, mortality:33.1% vs 8.9%, non-home discharge:12.5% vs 6.9%, length of stay:41 vs 24 days, hospitalization-costs:\$354,521 vs \$180,489(all,  $p<0.05$ ). Stroke increased odds of mortality by two-fold[OR 2.20(1.75-2.77),  $p<0.001$ ] after adjusting for ECMO, prematurity among other significant factors. On follow-up, stroke-group had higher incidence of hydrocephalus(9.5% vs 1.3%), cerebral palsy (6.2% vs 1.3%), autism spectrum disorder(7.1% vs 3.5%) and had higher one- and five- year mortality among survivors of index admission(5.3% and 11.3% vs 3.3% and 5.9%, respectively) (all  $p<0.05$ ). Conclusions: Neonatal CHS patients born prematurely, diagnosed with HLHS or those requiring ECMO are disproportionately affected by stroke. The occurrence of stroke is marked by significantly higher mortality. Future research should seek to identify factors leading to stroke, in order to increase rescue after stroke and for improvement of long-term outcomes.

PMID: [38815846](#)

## 23. Intraventricular haemorrhage in premature infants: the role of immature neuronal salt and water transport

Fatemeh Bahari, Volodymyr Dzhala, Trevor Balena, Kyle P Lillis, Kevin J Staley

Brain. 2024 May 30:awae161. doi: 10.1093/brain/awae161. Online ahead of print.

Intraventricular hemorrhage (IVH) is a common complication of premature birth. Survivors are often left with cerebral palsy, intellectual disability, and/or hydrocephalus. Animal models suggest that brain tissue shrinkage with subsequent vascular



stretch and tear is an important step in the pathophysiology, but the cause of this shrinkage is unknown. Clinical risk factors for IVH are biomarkers of hypoxic-ischemic stress, which causes mature neurons to swell. However, immature neuronal volume might shift in the opposite direction under these conditions. This is because immature neurons express the chloride salt and water transporter NKCC1, which subserves regulatory volume increases in nonneural cells, whereas mature neurons express KCC2, which subserves regulatory volume decreases. When hypoxic ischemic conditions reduce active ion transport and increase the cytoplasmic membrane permeability, the effects of these transporters will be diminished. As a consequence, while mature neurons swell (cytotoxic edema) immature neurons might shrink. After hypoxic-ischemic stress, *in vivo* and *in vitro* multi-photon imaging of perinatal transgenic mice demonstrated shrinkage of viable immature neurons, bulk tissue shrinkage, and blood vessel displacement. Neuronal shrinkage was correlated with age-dependent membrane salt and water transporter expression using immunohistochemistry. Shrinkage of immature neurons was prevented by prior genetic or pharmacological inhibition of NKCC1 transport. These findings open new avenues of investigation for the detection of acute brain injury by neuroimaging, as well as prevention of neuronal shrinkage and the ensuing IVH, in premature infants.

PMID: [38815055](#)

#### 24. Noise or sound management in the neonatal intensive care unit for preterm or very low birth weight infants

Greta Sibrecht, Katarzyna Wróblewska-Seniuk, Matteo Bruschetti

Review Cochrane Database Syst Rev. 2024 May 30;5(5):CD010333. doi: 10.1002/14651858.CD010333.pub4.

**Background:** Infants in the neonatal intensive care unit (NICU) are subjected to different types of stress, including sounds of high intensity. The sound levels in NICUs often exceed the maximum acceptable level recommended by the American Academy of Pediatrics, which is 45 decibels (dB). Hearing impairment is diagnosed in 2% to 10% of preterm infants compared to only 0.1% of the general paediatric population. Bringing sound levels under 45 dB can be achieved by lowering the sound levels in an entire unit; by treating the infant in a section of a NICU, in a 'private' room, or in incubators in which the sound levels are controlled; or by reducing sound levels at the individual level using earmuffs or earplugs. By lowering sound levels, the resulting stress can be diminished, thereby promoting growth and reducing adverse neonatal outcomes. This review is an update of one originally published in 2015 and first updated in 2020. **Objectives:** To determine the benefits and harms of sound reduction on the growth and long-term neurodevelopmental outcomes of neonates. **Search methods:** We used standard, extensive Cochrane search methods. On 21 and 22 August 2023, a Cochrane Information Specialist searched CENTRAL, PubMed, Embase, two other databases, two trials registers, and grey literature via Google Scholar and conference abstracts from Pediatric Academic Societies. **Selection criteria:** We included randomised controlled trials (RCTs) or quasi-RCTs in preterm infants (less than 32 weeks' postmenstrual age (PMA) or less than 1500 g birth weight) cared for in the resuscitation area, during transport, or once admitted to a NICU or stepdown unit. We specified three types of intervention: 1) intervention at the unit level (i.e. the entire neonatal department), 2) at the section or room level, or 3) at the individual level (e.g. hearing protection). **Data collection and analysis:** We used the standardised review methods of Cochrane Neonatal to assess the risk of bias in the studies. We used the risk ratio (RR) and risk difference (RD), with their 95% confidence intervals (CIs), for dichotomous data. We used the mean difference (MD) for continuous data. Our primary outcome was major neurodevelopmental disability. We used GRADE to assess the certainty of the evidence. **Main results:** We included one RCT, which enrolled 34 newborn infants randomised to the use of silicone earplugs versus no earplugs for hearing protection. It was a single-centre study conducted at the University of Texas Medical School in Houston, Texas, USA. Earplugs were positioned at the time of randomisation and worn continuously until the infants were 35 weeks' postmenstrual age (PMA) or discharged (whichever came first). Newborns in the control group received standard care. The evidence is very uncertain about the effects of silicone earplugs on the following outcomes. • Cerebral palsy (RR 3.00, 95% CI 0.15 to 61.74) and Mental Developmental Index (MDI) (Bayley II) at 18 to 22 months' corrected age (MD 14.00, 95% CI 3.13 to 24.87); no other indicators of major neurodevelopmental disability were reported. • Normal auditory functioning at discharge (RR 1.65, 95% CI 0.93 to 2.94) • All-cause mortality during hospital stay (RR 2.07, 95% CI 0.64 to 6.70; RD 0.20, 95% CI -0.09 to 0.50) • Weight (kg) at 18 to 22 months' corrected age (MD 0.31, 95% CI -1.53 to 2.16) • Height (cm) at 18 to 22 months' corrected age (MD 2.70, 95% CI -3.13 to 8.53) • Days of assisted ventilation (MD -1.44, 95% CI -23.29 to 20.41) • Days of initial hospitalisation (MD 1.36, 95% CI -31.03 to 33.75) For all outcomes, we judged the certainty of evidence as very low. We identified one ongoing RCT that will compare the effects of reduced noise levels and cycled light on visual and neural development in preterm infants. **Authors' conclusions:** No studies evaluated interventions to reduce sound levels below 45 dB across the whole neonatal unit or in a room within it. We found only one study that evaluated the benefits of sound reduction in the neonatal intensive care unit for hearing protection in preterm infants. The study compared the use of silicone earplugs versus no earplugs in newborns of very low birth weight (less than 1500 g). Considering the very small sample size, imprecise results, and high risk of attrition bias, the evidence based on this research is very uncertain and no conclusions can be drawn. As there is a lack of evidence to inform healthcare or policy decisions, large, well designed, well conducted, and fully reported RCTs that analyse different aspects of noise reduction in NICUs are needed. They should report both short- and long-term outcomes.

PMID: [38813836](#)

## 25. Randomised controlled trial of an online cognitive training program in school-aged children with cerebral palsy

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Res Dev Disabil. 2024 May 25;150:104752. doi: 10.1016/j.ridd.2024.104752. Online ahead of print.

**Background:** Children with cerebral palsy (CP) experience deficits in nonverbal reasoning. The SMART online cognitive intervention has been associated with gains in IQ and nonverbal IQ in previous studies in typically developing school-aged children and children experiencing learning difficulties. **Aim:** To assess the efficacy of an online cognitive intervention in school-aged children with CP. **Methods and procedures:** 21 children with CP (male  $n = 17$ ; 76.2%), mean age 9 y 8 m, SD 1 y 1 month (range 8 y 3 m to 12 y 6 m) were randomised into the intervention group ( $n = 9$ ) or a waitlist control group. A mixed-methods approach with an explanatory sequential design was used, with a randomised controlled trial followed by qualitative interviews. Participants were assessed on measures of intelligence, academic ability, attention and executive functioning, and social-emotional functioning at baseline, then after completing the training, or the waitlist period. Analyses included ANCOVAs and paired samples  $t$  tests. Semi-structured interviews explored participants' experiences with the training. **Results and outcomes:** Training completion was low with a mean of 16.9 modules completed out of 55 available. No significant effect of training was found for the primary outcome of intelligence, or for any secondary outcomes. Participants reported barriers and facilitators for accessing the program. **Implications:** Cognitive training programs addressing relational framing ability may require significant modifications before they can be effectively tested with children with CP.

PMID: [38797157](#)

## Prevention and Cure

### 26. Prenatal Magnesium Sulfate and Functional Connectivity in Offspring at Term-Equivalent Age

Steven Ufkes, Eleanor Kennedy, Tanya Poppe, Steven P Miller, Benjamin Thompson, Jessie Guo, Jane E Harding, Caroline A Crowther

Randomized Controlled Trial JAMA Netw Open. 2024 May 1;7(5):e2413508. doi: 10.1001/jamanetworkopen.2024.13508.

**Importance:** Understanding the effect of antenatal magnesium sulfate (MgSO<sub>4</sub>) treatment on functional connectivity will help elucidate the mechanism by which it reduces the risk of cerebral palsy and death. **Objective:** To determine whether MgSO<sub>4</sub> administered to women at risk of imminent preterm birth at a gestational age between 30 and 34 weeks is associated with increased functional connectivity and measures of functional segregation and integration in infants at term-equivalent age, possibly reflecting a protective mechanism of MgSO<sub>4</sub>. **Design, setting, and participants:** This cohort study was nested within a randomized placebo-controlled trial performed across 24 tertiary maternity hospitals. Participants included infants born to women at risk of imminent preterm birth at a gestational age between 30 and 34 weeks who participated in the MAGENTA (Magnesium Sulphate at 30 to 34 Weeks' Gestational Age) trial and underwent magnetic resonance imaging (MRI) at term-equivalent age. Ineligibility criteria included illness precluding MRI, congenital or genetic disorders likely to affect brain structure, and living more than 1 hour from the MRI center. One hundred and fourteen of 159 eligible infants were excluded due to incomplete or motion-corrupted MRI. Recruitment occurred between October 22, 2014, and October 25, 2017. Participants were followed up to 2 years of age. Analysis was performed from February 1, 2021, to February 27, 2024. Observers were blind to patient groupings during data collection and processing. **Exposures:** Women received 4 g of MgSO<sub>4</sub> or isotonic sodium chloride solution given intravenously over 30 minutes. **Main outcomes and measures:** Prior to data collection, it was hypothesized that infants who were exposed to MgSO<sub>4</sub> would show enhanced functional connectivity compared with infants who were not exposed. **Results:** A total of 45 infants were included in the analysis: 24 receiving MgSO<sub>4</sub> treatment and 21 receiving placebo; 23 (51.1%) were female and 22 (48.9%) were male; and the median gestational age at scan was 40.0 (IQR, 39.1-41.1) weeks. Treatment with MgSO<sub>4</sub> was associated with greater voxelwise functional connectivity in the temporal and occipital lobes and deep gray matter structures and with significantly greater clustering coefficients (Hedge  $g$ , 0.47 [95% CI, -0.13 to 1.07]), transitivity (Hedge  $g$ , 0.51 [95% CI, -0.10 to 1.11]), local efficiency (Hedge  $g$ , 0.40 [95% CI, -0.20 to 0.99]), and global efficiency (Hedge  $g$ , 0.31 [95% CI, -0.29 to 0.90]), representing enhanced functional segregation and integration. **Conclusions and relevance:** In this cohort study, infants exposed to MgSO<sub>4</sub> had greater voxelwise functional connectivity and functional segregation, consistent with increased brain maturation. Enhanced functional connectivity is a possible mechanism by which MgSO<sub>4</sub> protects against cerebral palsy and death.

PMID: [38805222](#)