

# Cerebral palsy research news

Monday 27 February 2023

**Cerebral Palsy Alliance** is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at <u>cerebralpalsy.org.au/our-research</u>

**Professor Nadia Badawi AM**CP Alliance Chair of Cerebral Palsy Research

Subscribe to CP Research News

#### **Interventions and Management**

1. The effect of a thumb web spacer splint on hand function in children with hemiplegic cerebral palsy Islam B Ali, Fathy A Elshazly, Mostafa S Ali

J Taibah Univ Med Sci. 2022 Nov 15;18(3):429-435. doi: 10.1016/j.jtumed.2022.10.008. eCollection 2023 Jun.

Objective: Many children with hemiplegic cerebral palsy (HCP) cannot maintain thumb abduction and experience obstruction caused by the thumb remaining in the palm. A web spacer splint maintains the thumb web space and opposition of the thumb for a more functional position. The aim of this study was to analyze the impact of a thumb web spacer as a functional splint on hand function in children with hemiplegic cerebral palsy. Methods: Thirty children with hemiplegic cerebral palsy (ages 4-7 years) were randomly divided into two groups (a control group and a study group). The treatment program for the control group was administered for 45 min three times/week for 8 successive weeks and the study group underwent the identical treatment regimen as the control group, as well as wearing a web spacer splint during the treatment program. Thereafter, the Peabody Developmental Motor Scale (PDMS-2) was used to assess hand function. Results: Post-treatment values in the study group demonstrated a substantial improvement in grasping and visual motor integration in the PDMS-2 when compared to the control group. Therefore, there was a significant improvement in total fine motor quotient when compared post-treatment ( $86.93 \pm 8.94$ ,  $145.73 \pm 15.04$ ) in the control and study groups, respectively (p > 0.05). Conclusion: A web spacer splint can be a viable tool for improving hand function in children with HCP.

PMID: 36818181

2. Efficacy of intrathecal morphine administration in pediatric patients undergoing selective dorsal rhizotomy Jared Pennington, Shawnelle Contini, Miraides Brown, Nupur Goel, Tsulee Chen

J Pediatr Rehabil Med. 2023 Feb 16. doi: 10.3233/PRM-220048. Online ahead of print.

Purpose: The purpose of this study was to evaluate the effectiveness of intrathecal morphine following selective dorsal rhizotomy in pediatric patients previously diagnosed with cerebral palsy. Methods: This was a retrospective, cohort analysis over the course of four years. The analysis consisted of a treatment group which received intrathecal morphine (5 mcg/kg) injection and a control group that did not receive the injection prior to dural closure. All patients underwent multilevel laminectomies for selective dorsal rhizotomy at Akron Children's Hospital. The effectiveness of the treatment was measured by total dose of hydromorphone administered on patient-controlled analgesia (PCA), number of days on oral narcotics, and cumulative dose of oral narcotic. Results: Of the analyzed 15 pediatric patients, seven patients received intrathecal morphine injection while the other eight did not receive the treatment prior to dural closure. There was a difference of 1135 mcg in total PCA dose between the study group (3243 mcg) and the control group (4378 mcg). The total PCA dose based on weight was lower in the study group (163 mcg/kg) than in the control group (171 mcg/kg). Conclusion: Based on these findings, the

administration of intrathecal morphine clinically reduces the opiate need in the first 96 hours post-operatively.

PMID: 36806525

## **3.** A systematic review of complications following selective dorsal rhizotomy in cerebral palsy Dipun Mishra, Sitanshu Barik, Vikash Raj, Pankaj Kandwal

Review Neurochirurgie. 2023 Feb 22;101425. doi: 10.1016/j.neuchi.2023.101425. Online ahead of print.

Purpose: The literature lacks a concise overview of complications secondary to selective dorsal rhizotomy (SDR). The aim of this study was to systematically review the literature regarding post-SDR complications, and to present them concisely. Methods: The protocol of the review was registered on Open Science Framework. Studies on SDR in cerebral palsy were included. The studies to be included used SDR for management of spasticity in patients with cerebral palsy. The long-term complications of SDR mentioned in the articles were inventoried. Results: 30 studies were included for qualitative review. Twenty-one types of complication were identified. Structural complications were the commonest: scoliosis (214/1,043, 20.5%), hyperlordosis (101/552, 18.2%), spondylolysis (55/574, 9.5%) and kyphosis (67/797, 8.4%). Neurological complications comprised constipation (70/485, 14.4%), hip subluxation (3/29, 10.3%), spastic syndrome (4/47, 8.5%), sensory changes (106/1290, 8.2%) and urinary incontinence (61/1013, 6%). Conclusion: This review should help surgeons and parents alike to know about the potential complications of SDR. Complications may affect quality of life and should be weighed. Although the majority of these complications were managed conservatively, there would still be a physical, psychological and financial burden which should be taken into account. Screening should be continued vigorously throughout skeletal growth and at reduced frequency thereafter, for timely intervention in case of structural complications.

PMID: 36828056

**4.** Is Minimally Invasive Bipolar Technique a Better Alternative to Long Fusion for Adult Neuromuscular Scoliosis? Stéphane Wolff, Pierre-Emmanuel Moreau, Lotfi Miladi, Guillaume Riouallon

Global Spine J. 2023 Feb 21;21925682231159347. doi: 10.1177/21925682231159347. Online ahead of print.

Study design: Prospective cohort study. Objectives: To report the results for an alternative technique based on minimally invasive fusion-less surgery. This approach is original in that it corrects deformities by proximal and distal fixation, with reliable pelvic fixation through the use of iliosacral screws on osteoporotic bones. Methods: Adult cerebral palsy patients requiring spinal correction surgery were included prospectively between 2015 and 2019. The technique involved the use of a double-rod construct anchored proximally by four clawed hooks and distally by iliosacral screws, in a minimally invasive approach. Cobb angle and pelvic obliquity were measured before and after initial surgery and at final follow-up. Complications and functional results were reviewed. This group (P) was compared with a second group (R) of patients who underwent surgery between 2005 and 2015, for whom data were collected retrospectively. Results: Thirty-one patients were included in group P, and 15 in group R. The two groups were comparable for demographic data and deformity. At most recent follow-up (3 years for group P [2-6] and 5 years for group R [2-16]), neither correction nor surgical complications differed between the two groups. However, group P had 50% less blood loss and a lower medical complication rate than group R. Conclusions: Our results confirm the effectiveness of this minimally invasive technique for neuromuscular scoliosis in adults. The results were similar to those obtained with the usual techniques, but with fewer medical complications. Confirmation of these results is now required for a longer follow-up period.

PMID: 36809191

5. Association of muscles length and strength with balance and functional status among children with diplegic spastic cerebral palsy

Zavata Afnan, Arshad Nawaz Malik, Saira Jahan, Arshad Ali

J Pak Med Assoc. 2023 Feb;73(2):253-257. doi: 10.47391/JPMA.5174.

Objective: To determine the correlation of muscle length and muscle strength with balance and functional status among children with diplegic spastic cerebral palsy. Methods: The cross-sectional study was conducted from February to July 2021 at the Physical Therapy Department of Chal Foundation and Fatima Physiotherapy Centre, Swabi, Pakistan, and comprised children aged 4-12 years with diplegic spastic cerebral palsy. The strength of back and lower limb muscles was assessed through manual muscles testing. Lower limb muscle's length, indicating tightness, was assessed using goniometer. Paediatric balance scale and gross motor function measure scale-88 were used to assess balance and gross motor function. Data was analysed using SPSS 23. Results: Of the 83 subjects, 47(56.6%) were boys and 36(43.4%) were girls. The overall mean age was 7.31±2.02 years, mean weight was 19.71±5.45kg, mean height was 105.5±14cm and mean body mass index was 17.32±1.64 kg/m2. There was a positive and significant correlation of all the lower limb muscles' strength with balance (p<0.01) and functional status (p<0.01). The correlation between the tightness of muscles and balance was significant and negative for all lower limb muscles (p<0.005). The correlation between the muscles' tightness and functional status was negative and significant for all lower limb muscles (p<0.005). Conclusions: Good muscle strength and appropriate flexibility of lower limb muscles enhanced functional status and good balance in children with diplegic spastic cerebral palsy.

PMID: 36800705

#### 6. A core outcome set for lower limb orthopaedic surgery for children with cerebral palsy: An international multistakeholder consensus study

No authors listed

Dev Med Child Neurol. 2023 Feb 19. doi: 10.1111/dmcn.15557. Online ahead of print.

No abstract available

PMID: 36807905

#### 7. Reliability of 3D freehand ultrasound to assess lower limb muscles in children with spastic cerebral palsy and typical development

Britta Ĥanssen, Nicky Peeters, Tijl Dewit, Ester Huyghe, Bernard Dan, Guy Molenaers, Anja Van Campenhout, Lynn Bar-On, Christine Van den Broeck, Patrick Calders, Kaat Desloovere

J Anat. 2023 Feb 20. doi: 10.1111/joa.13839. Online ahead of print.

This study investigated the reliability of 3-dimensional freehand ultrasound (3DfUS) to quantify the size (muscle volume [MV] and anatomical cross-sectional area [aCSA]), length (muscle length [ML], tendon length [TL], and muscle tendon unit length [MTUL]), and echo-intensity (EI, whole muscle and 50% aCSA), of lower limb muscles in children with spastic cerebral palsy (SCP) and typical development (TD). In total, 13 children with SCP (median age 14.3 (7.3) years) and 13 TD children (median age 11.1 (1.7) years) participated. 3DfUS scans of rectus femoris, semitendinosus, medial gastrocnemius, and tibialis anterior were performed by two raters in two sessions. The intra- and inter-rater and intra- and inter-session reliability were defined with relative and absolute reliability measures, that is, intra-class correlation coefficients (ICCs) and absolute and relative standard error of measurement (SEM and SEM%), respectively. Over all conditions, ICCs for muscle size measures ranged from 0.818 to 0.999 with SEM%s of 12.6%-1.6%. For EI measures, ICCs varied from 0.233 to 0.967 with SEM%s of 15.6%-1.7%. Length measure ICCs ranged from 0.642 to 0.999 with SEM%s of 16.0%-0.5%. In general, reliability did not differ between the TD and SCP cohort but the influence of different muscles, raters, and sessions was not constant for all 3DfUS parameters. Muscle length and muscle tendon unit length were the most reliable length parameters in all conditions. MV and aCSA showed comparable SEM%s over all muscles, where tibialis anterior MV was most reliable. EI had low-relative reliability, but absolute reliability was better, with better reliability for the distal muscles in comparison to the proximal muscles. Combining these results with earlier studies describing muscle morphology assessed in children with SCP, 3DfUS seems sufficiently reliable to determine differences between cohorts and functional levels. The applicability on an individual level, for longitudinal follow-up and after interventions is dependent on the investigated muscle and parameter. Moreover, the semitendinosus, the acquisition, and processing of multiple sweeps, and the definition of EI and TL require further investigation. In general, it is recommended, especially for longitudinal follow-up studies, to keep the rater the same, while standardizing acquisition settings and positioning of the subject.

#### 8. A Modified Sliding-Lengthening Approach to Tendon Lengthening with a Locking Mechanism Suture: A Technical Note

Dai Iwase, Yukie Metoki, Jun Aikawa, Kentaro Uchida, Kensuke Fukushima, Takashi Matsuo, Atsushi Matsuo, Gen Inoue, Masashi Takaso

Indian J Orthop. 2023 Jan 30;57(3):505-509. doi: 10.1007/s43465-023-00829-2. eCollection 2023 Mar.

There are various techniques used for tendon lengthening, of which Z-lengthening and sliding-lengthening are the most frequently performed. In patients with cerebral palsy, tendon lengthening may often be necessary at multiple sites. However, they can cause various complications, such as inaccurate extension, overextension, and a lack of tendon continuity. We modified the sliding-lengthening technique with a locking mechanism to address these issues. This technical note aims to describe the surgical technique and pitfalls associated with the modified sliding-lengthening approach and suture locking mechanism. The tendon was exposed and stabilized using sterilized spitz tubes and was then threaded so that each loop length was equivalent to the amount of tendon extension. Symmetrical hemisection of both ends of the tendon was performed, and the tendon was carefully extended to create a tense loop. The modified sliding-lengthening technique with the locking suture mechanism may be an advantageous method that accurately addresses extension volume, prevents hyperextension, and maintains tendon continuity, even when smaller incisions are used.

PMID: 36825275

#### 9. Management Of Spastic Equinovarus Foot in Children with Cerebral Palsy: An Evaluation of Anatomical Landmarks for Selective Nerve Blocks of the Tibial Nerve Motor Branches

Alessandro Picelli, Rita Di Censo, Alessandro Zadra, Silvia Faccioli, Nicola Smania, Mirko Filippetti

Observational Study J Rehabil Med. 2023 Feb 20;55:jrm00370. doi: 10.2340/jrm.v55.4538.

Objective: To define the anatomical landmarks of tibial motor nerve branches for selective motor nerve blocks of the gastrocnemii, soleus and tibialis posterior muscles in the management of spastic equinovarus foot. Design: Observational study. Patients: Twenty-four children with cerebral palsy with spastic equinovarus foot. Methods: Considering the affected leg length, motor nerve branches to the gastrocnemii, soleus and tibialis posterior muscles were tracked using ultrasonography, and located in the space (vertical, horizontal, deep) according to the position of fibular head (proximal/distal) and a virtual line from the middle of popliteal fossa to the Achilles tendon insertion (medial/lateral). Results: Location of motor branches was defined as percentage of the affected leg length. Mean coordinates were: for the gastrocnemius medialis  $2.5 \pm 1.2\%$  vertical (proximal),  $1.0 \pm 0.7\%$  horizontal (medial),  $1.5 \pm 0.4\%$  deep; for the gastrocnemius lateralis  $2.3 \pm 1.4\%$  vertical (proximal),  $1.1 \pm 0.9\%$  horizontal (lateral),  $1.6 \pm 0.4\%$  deep; for the soleus  $2.1 \pm 0.9\%$  vertical (distal),  $0.9 \pm 0.7\%$  horizontal (lateral),  $2.2 \pm 0.6\%$  deep; for the tibialis posterior  $2.6 \pm 1.2\%$  vertical (distal),  $1.3 \pm 1.1\%$  horizontal (lateral),  $3.0 \pm 0.7\%$  deep. Conclusion: These findings may help the identification of tibial motor nerve branches to perform selective nerve blocks in patients with cerebral palsy with spastic equinovarus foot.

PMID: 36807992

# 10. Biomechanical Implications of Congenital Conditions of the Foot/Ankle Karen M Kruger, Peter A Smith, Joseph J Krzak

Review Foot Ankle Clin. 2023 Mar;28(1):27-43. doi: 10.1016/j.fcl.2022.10.003. Epub 2023 Jan 2.

Segmental foot and ankle models are often used as part of instrumented gait analysis when planning interventions for complex congenital foot conditions. More than 40 models have been used for clinical analysis, and it is important to understand the technical differences among models. These models have been used to improve clinical planning of pediatric foot conditions including clubfoot, planovalgus, and equinovarus. They have also been used to identify clinically relevant subgroups among pediatric populations, quantify postoperative outcomes, and explain variability in healthy populations.

PMID: 36822687

4

11. How did youth with cerebral palsy perceive participation in everyday life after participating in a periodical intensive rehabilitation program based on adapted physical activity in groups? A qualitative interview study Anna Ullenhag, Reidun Jahnsen, Nina Klove, Solveig Smedvig, Anita Hoberg

Disabil Rehabil. 2023 Feb 21;1-9. doi: 10.1080/09638288.2023.2180096. Online ahead of print.

Purpose: Explore how youths with CP experience participation in everyday life, their experience of having participated in a periodical intensive rehabilitation programme and their expectations for the future. Materials & methods: A qualitative design that included semi-structured interviews with 14 youths with CP (mean age 17 years). Results: The qualitative content analysis exposed six themes, (1) Everyday life - to get the pieces of your life to fit together, (2) Participation means inclusion and belonging - the meaning of life, (3) Individual and environmental factors influencing participation, (4) Experience of physical and social activities away from home together with like-minded people, (5) To be continued locally, and (6) You do not know the future, anything can happen - visions for the future. Conclusions: Participation in everyday life increases the meaning of life but takes energy. Periodical intensive rehabilitation programme enabled youths to try new activities, make friends and increase self-insight in their own strengths and limitations. IMPLICATIONS FOR REHABILITATION: Young people with cerebral palsy (CP) describe participation as the meaning of life and state that it is essential for inclusion and being able to contribute to society. Adaptation of environmental factors including collaboration across service sectors and capacity building in young people within their preferred life situations appear to be essential. A periodical intensive rehabilitation, including adapted physical activities in groups, is recommended to provide peer learning and mastery experiences in young people with CP. Young people with CP seem to have the same hopes for the future as their typically developing peers.

PMID: 36803505

#### 12. The Relationship between Pain and Spasticity and Tell-Tale Signs of Pain in Children with Cerebral Palsy Christian Wong

Toxins (Basel). 2023 Feb 13;15(2):152. doi: 10.3390/toxins15020152.

Pain and quality of life are closely interrelated in children with cerebral palsy (CCP). Even though 67% of CCP experience pain, it is overlooked and untreated. In this study, our purpose was two-fold: first, to examine the relationship between pain and spasticity by evaluating the effects of AbobotulinumtoxinA/Dysport (BoNT), and second, to describe the symptoms and location of pain in CCP. The subjects were 22 CCP in at least moderate pain. They were evaluated for spasticity by the modified Ashworth and Tardieu scale and for pain by the r-FLACC and the pediatric pain profile. After one injection of BoNT, the subjects were re-evaluated. We found a significant reduction in pain, but no significant relationship between the reduction of pain and spasticity. We found no association between the dose of BoNT and pain or spasticity. Pain in the lower extremity was located primarily in the hip region. The effect of ultrasound-guided intermuscular injections of BoNT suggests that pain in CCP has an extra-articular component. We found that pain in CCP manifests as specific tell-tale signs and problems in daily living. In conclusion, we found no relationship between pain and spasticity. Signs and manifestations of pain are described in detail. Lower extremity (hip) pain seems to have a soft tissue/extra-articular component.

PMID: 36828465

#### 13. Factors Related to Quality of Life in Children With Cerebral Palsy

Montse Blasco, María García-Galant, Olga Laporta-Hoyos, Júlia Ballester-Plané, Anna Jorba-Bertran, Xavier Caldú, Júlia Miralbell, Xènia Alonso, Mar Meléndez-Plumed, Esther Toro-Tamargo, Francisca Gimeno, Roser Pueyo

Pediatr Neurol. 2023 Jan 18;141:101-108. doi: 10.1016/j.pediatrneurol.2023.01.006. Online ahead of print.

Background: We investigated the influence of relevant demographic, clinical, neuropsychological, and psychosocial variables on the proxy-reported quality of life (QOL) of children with cerebral palsy (CP). Methods: The proxy-reported Cerebral Palsy Quality of Life-Child questionnaire (CP QOL-Child) was completed by 58 children with CP (mean age 10.22 years, SD 1.67). Relationships between QOL scores and demographic, clinical, neuropsychological, and psychosocial variables were assessed. CP QOL scores and other variables that correlated significantly were introduced into a multiple linear regression model. Results: Executive functioning and motor functional status were explanatory variables for the CP QOL total score. Executive

functions explained three specific QOL domains: Social Wellbeing and Acceptance, Feelings about Functioning, and Emotional Wellbeing and Self-esteem. Parental stress also explained Social Wellbeing and Acceptance. Motor functional status and visual perception were explanatory variables for the Access to Services domain. Finally, autism spectrum disorder (ASD) traits were an explanatory variable for the Participation and Physical Health domain. Conclusion: Executive functioning and motor functional status importantly influence QOL of children with CP. Visual perception, ASD symptoms, and parental stress variables are related with specific QOL domains. These findings demonstrate that interventions targeting cognitive functions in children with CP may positively influence QOL.

PMID: 36805966

#### 14. Electric field simulations of transcranial direct current stimulation in children with perinatal stroke Helen L Carlson, Adrianna Giuffre, Patrick Ciechanski, Adam Kirton

Front Hum Neurosci. 2023 Feb 2;17:1075741. doi: 10.3389/fnhum.2023.1075741. eCollection 2023.

Introduction: Perinatal stroke (PS) is a focal vascular brain injury and the leading cause of hemiparetic cerebral palsy. Motor impairments last a lifetime but treatments are limited. Transcranial direct-current stimulation (tDCS) may enhance motor learning in adults but tDCS effects on motor learning are less studied in children. Imaging-based simulations of tDCS-induced electric fields (EF) suggest differences in the developing brain compared to adults but have not been applied to common pediatric disease states. We created estimates of tDCS-induced EF strength using five tDCS montages targeting the motor system in children with PS [arterial ischemic stroke (AIS) or periventricular infarction (PVI)] and typically developing controls (TDC) aged 6-19 years to explore associates between simulation values and underlying anatomy. Methods: Simulations were performed using SimNIBS https://simnibs.github.io/simnibs/build/html/index.html using T1, T2, and diffusion-weighted images. After tissue segmentation and tetrahedral mesh generation, tDCS-induced EF was estimated based on the finite element model (FEM). Five 1mA tDCS montages targeting motor function in the paretic (non-dominant) hand were simulated. Estimates of peak EF strength, EF angle, field focality, and mean EF in motor cortex (M1) were extracted for each montage and compared between groups. Results: Simulations for eighty-three children were successfully completed (21 AIS, 30 PVI, 32 TDC). Conventional tDCS montages utilizing anodes over lesioned cortex had higher peak EF strength values for the AIS group compared to TDC. These montages showed lower mean EF strength within target M1 regions suggesting that peaks were not necessarily localized to motor network-related targets. EF angle was lower for TDC compared to PS groups for a subset of montages. Montages using anodes over lesioned cortex were more sensitive to variations in underlying anatomy (lesion and tissue volumes) than those using cathodes over non-lesioned cortex. Discussion: Individualized patient-centered tDCS EF simulations are prudent for clinical trial planning and may provide insight into the efficacy of tDCS interventions in children with PS.

PMID: 36816507

## 15. Safety and Feasibility of Robot-assisted Gait Training in Adults with Cerebral Palsy in an Inpatient Setting - an Observational Study

Fabian Moll, Axel Kessel, Anna Bonetto, Johanna Stresow, Monika Herten, Marcel Dudda, Jens Adermann

J Dev Phys Disabil. 2023 Feb 11;1-16. doi: 10.1007/s10882-023-09895-8. Online ahead of print.

Background: To investigate the safety and feasibility of six sessions of Hybrid Assistive Limb (HAL) robot-assisted gait training (RAGT) integrated into an inpatient therapy concept and their influence on walking speed and gait parameters in adult CP patients. Methods: Eleven subjects (male = 8, female = 3, mean age: 23 years and 2 months,  $\pm$  4.5 years) with spastic CP underwent six 20-minute RAGT sessions with the HAL during an 11-day hospital stay. Additionally, physiotherapy, physician-performed manual medicine, massage and exercise therapy were provided. Pre- (T1) and post- (T2) intervention assessments were: 10-metre walking test (10MWT), 6-minute walking test (6MWT), Gross Motor Function Measure (GMFM-88) and lower extremities passive range of motion (pROM). Results: All subjects completed the study. No adverse events were noted. Walking speed in the 10MWT test increased from 32.5 s ( $\pm$  24.5 s) at T1 to 27.5 s ( $\pm$  21.4 s) at T2, without significance. Slight, but non-significant improvements were detected in the 6MWT, GMFM and pROM. Confounding factors did not significantly affect the results. Conclusion: Intensive therapy including HAL training leads to non-significant improvements. Further studies with more patients and longer intervention time could provide further insights into the RAGT therapy of adult patients with CP. Registration DRKS-ID: DRKS00020275.

## 16. Control strategies used in lower limb exoskeletons for gait rehabilitation after brain injury: a systematic review and analysis of clinical effectiveness

Jesús de Miguel-Fernández, Joan Lobo-Prat, Erik Prinsen, Josep M Font-Llagunes, Laura Marchal-Crespo

Review J Neuroeng Rehabil. 2023 Feb 19;20(1):23. doi: 10.1186/s12984-023-01144-5.

Background: In the past decade, there has been substantial progress in the development of robotic controllers that specify how lower-limb exoskeletons should interact with brain-injured patients. However, it is still an open question which exoskeleton control strategies can more effectively stimulate motor function recovery. In this review, we aim to complement previous literature surveys on the topic of exoskeleton control for gait rehabilitation by: (1) providing an updated structured framework of current control strategies, (2) analyzing the methodology of clinical validations used in the robotic interventions, and (3) reporting the potential relation between control strategies and clinical outcomes. Methods: Four databases were searched using database-specific search terms from January 2000 to September 2020. We identified 1648 articles, of which 159 were included and evaluated in full-text. We included studies that clinically evaluated the effectiveness of the exoskeleton on impaired participants, and which clearly explained or referenced the implemented control strategy. Results: (1) We found that assistive control (100% of exoskeletons) that followed rule-based algorithms (72%) based on ground reaction force thresholds (63%) in conjunction with trajectory-tracking control (97%) were the most implemented control strategies. Only 14% of the exoskeletons implemented adaptive control strategies. (2) Regarding the clinical validations used in the robotic interventions, we found high variability on the experimental protocols and outcome metrics selected. (3) With high grade of evidence and a moderate number of participants (N = 19), assistive control strategies that implemented a combination of trajectory-tracking and compliant control showed the highest clinical effectiveness for acute stroke. However, they also required the longest training time. With high grade of evidence and low number of participants (N = 8), assistive control strategies that followed a threshold-based algorithm with EMG as gait detection metric and control signal provided the highest improvements with the lowest training intensities for subacute stroke. Finally, with high grade of evidence and a moderate number of participants (N = 19), assistive control strategies that implemented adaptive oscillator algorithms together with trajectory-tracking control resulted in the highest improvements with reduced training intensities for individuals with chronic stroke. Conclusions: Despite the efforts to develop novel and more effective controllers for exoskeleton-based gait neurorehabilitation, the current level of evidence on the effectiveness of the different control strategies on clinical outcomes is still low. There is a clear lack of standardization in the experimental protocols leading to high levels of heterogeneity. Standardized comparisons among control strategies analyzing the relation between control parameters and biomechanical metrics will fill this gap to better guide future technical developments. It is still an open question whether controllers that provide an on-line adaptation of the control parameters based on key biomechanical descriptors associated to the patients' specific pathology outperform current control strategies.

PMID: 36805777

## 17. Impact of maternal late hospital arrival on adverse outcome of offspring affected by placental abruption: A regional multicenter nested case-control study in Japan

Hiroshi Kawamura, Nozomu Takahashi, Yumiko Miyazaki, Hideaki Tsuyoshi, Makoto Orisaka, Yoshio Yoshida

J Obstet Gynaecol Res. 2023 Feb 18. doi: 10.1111/jog.15579. Online ahead of print.

Aims: To elucidate the influence of the time-intervals between the onset and arrival (TIME 1), onset and delivery (TIME 2), and the decision to deliver and delivery (TIME 3) on severe adverse outcomes of offspring born to mothers complicated by placental abruption outside the hospital. Methods: This is a multicenter nested case-control study about placental abruption at Fukui Prefecture, a regional area in Japan, through 2013 to 2017. Multiple pregnancy, fetal or neonatal congenital abnormality, and unknown detailed information at onset of placental abruption were excluded. A composite of perinatal death and cerebral palsy or death at 18-36 months of corrected age was defined as the adverse outcome. The relationship between time-intervals and the adverse outcome was analyzed. Results: The 45 subjects for analysis were divided into two groups, including a group with and without adverse outcome (poor, n = 8; and good, n = 37). TIME 1 was longer in the poor group (150 vs. 45 min, p < 0.001). A subgroup analysis targeted to 29 cases with preterm birth at the third trimester indicates that TIME 1 and TIME 2 were longer in the poor group (185 vs. 55 min, p = 0.02; and 211 vs. 125 min, p = 0.03), while TIME 3 was shorter in the poor group (21 vs. 53 min, p = 0.01). Conclusions: Long time-intervals between onset and arrival or onset and delivery may be correlated with perinatal death or cerebral palsy in surviving infants affected by placental abruption.

#### 18. Causes of death in children with congenital Zika syndrome in Brazil, 2015 to 2018: A nationwide record linkage study

Maria da Conceição N Costa, Luciana Lobato Cardim, Cynthia A Moore, Eliene Dos Santos de Jesus, Rita Carvalho-Sauer, Mauricio L Barreto, Laura C Rodrigues, Liam Smeeth, Lavínia Schuler-Faccini, Elizabeth B Brickley, Wanderson K Oliveira, Eduardo Hage Carmo, Julia Moreira Pescarini, Roberto F S Andrade, Moreno M S Rodrigues, Rafael V Veiga, Larissa C Costa, Giovanny V A França, Maria Gloria Teixeira, Enny S Paixão

PLoS Med. 2023 Feb 24;20(2):e1004181. doi: 10.1371/journal.pmed.1004181. eCollection 2023 Feb.

Background: Children with congenital Zika syndrome (CZS) have severe damage to the peripheral and central nervous system (CNS), greatly increasing the risk of death. However, there is no information on the sequence of the underlying, intermediate, immediate, and contributing causes of deaths among these children. The aims of this study are describe the sequence of events leading to death of children with CZS up to 36 months of age and their probability of dying from a given cause, 2015 to 2018. Methods and findings: In a population-based study, we linked administrative data on live births, deaths, and cases of children with CZS from the SINASC (Live Birth Information System), the SIM (Mortality Information System), and the RESP (Public Health Event Records), respectively. Confirmed and probable cases of CZS were those that met the criteria established by the Brazilian Ministry of Health. The information on causes of death was collected from death certificates (DCs) using the World Health Organization (WHO) DC template. We estimated proportional mortality (PM%) among children with CZS and among children with non-Zika CNS congenital anomalies (CA) by 36 months of age and proportional mortality ratio by cause (PMRc). A total of 403 children with confirmed and probable CZS who died up to 36 months of age were included in the study; 81.9% were younger than 12 months of age. Multiple congenital malformations not classified elsewhere, and septicemia unspecified, with 18 (PM = 4.5%) and 17 (PM = 4.2%) deaths, respectively, were the most attested underlying causes of death. Unspecified septicemia (29 deaths and PM = 11.2%) and newborn respiratory failure (40 deaths and PM = 12.1%) were, respectively, the predominant intermediate and immediate causes of death. Fetuses and newborns affected by the mother's infectious and parasitic diseases, unspecified cerebral palsy, and unspecified severe protein-caloric malnutrition were the underlying causes with the greatest probability of death in children with CZS (PMRc from 10.0 to 17.0) when compared to the group born with non-Zika CNS anomalies. Among the intermediate and immediate causes of death, pneumonitis due to food or vomiting and unspecified seizures (PMRc = 9.5, each) and unspecified bronchopneumonia (PMRc = 5.0) were notable. As contributing causes, fetus and newborn affected by the mother's infectious and parasitic diseases (PMRc = 7.3), unspecified cerebral palsy, and newborn seizures (PMRc = 4.5, each) were more likely to lead to death in children with CZS than in the comparison group. The main limitations of this study were the use of a secondary database without additional clinical information and potential misclassification of cases and controls. Conclusion: The sequence of causes and circumstances involved in the deaths of the children with CZS highlights the greater vulnerability of these children to infectious and respiratory conditions compared to children with abnormalities of the CNS not related to Zika.

PMID: 36827251

## 19. Exploring the unmet needs of adults with cerebral palsy living in urban South Africa Roshaan Salie, Sharon Kleintjes, Maaike M Eken, Kirsten A Donald, A Graham Fieggen, Nelleke G Langerak

Disabil Rehabil. 2023 Feb 22;1-9. doi: 10.1080/09638288.2023.2177358. Online ahead of print.

Purpose: The investigators aimed to understand the unmet needs of adults with cerebral palsy (CP) living in urban South Africa and to ascertain similarities or differences to typically developing (TD) adults in the same community. Materials and methods: Participants were interviewed with an adapted version of the Southampton Needs Assessment Questionnaire (SNAQ). Non-parametric statistical analysis was utilised for quantitative data and qualitative data were analysed using free coding to identify themes. Results: Thirty adults with CP (median age 34.8 years; GMFCS levels I/II/III/IV/V: n = 6/6/5/7/6; socio-economic status (SES) low/average/high: n = 8/17/5) were matched for gender, age, and SES. Adults with CP reported a higher unemployment rate and lower level of satisfaction with access to health services than TD peers. Core themes identified by the participants with CP that made community participation more difficult were physical capacity, poor access to accommodation, transport and health services, lack of socialising opportunities, poor universal design, and lack of financial independence. Conclusions: Adults with CP reported experiencing many challenges in their communities. Improved access to health care services and transport, and the universal design of housing and community buildings to accommodate individuals with a disability should be made a priority. Implications for rehabilitation: Adults with cerebral palsy (CP) reported that their disability had an impact on their social life, home life, and work life. Accessibility issues have been identified as a major factor affecting adults with CP in a variety of areas, including access to and use of health services, housing, transportation, and community buildings. Adults with CP reported the need for support during the transition to adulthood, especially with

developing life skills that will promote living independently in the community as adults with disabilities.

PMID: 36814408

#### 20. Prevalence and incidence of chronic conditions among adults with cerebral palsy: A systematic review and metaanalysis

Jennifer M Ryan, Fatemah Albairami, Thomas Hamilton, Nigel Cope, Noor Amirah Amirmudin, Manjula Manikandan, Cherry Kilbride, Valerie L Stevenson, Emma Livingstone, Jennifer Fortune

Review Dev Med Child Neurol. 2023 Feb 20. doi: 10.1111/dmcn.15526. Online ahead of print.

Aim: To assess the prevalence and incidence of chronic conditions among adults with cerebral palsy (CP) and compare them to the prevalence and incidence among adults without CP. Method: We searched MEDLINE and Embase for studies reporting the prevalence or incidence of one or more chronic conditions among adults with CP. Two independent reviewers screened titles, abstracts, and full-text articles. Two independent reviewers extracted data relating to prevalence and incidence and appraised study quality. We performed random-effects meta-analyses to pool prevalence and incidence. Results: We identified 69 studies; 65 reported the prevalence of 53 conditions and 13 reported the incidence of 21 conditions. At least 20% of adults had the following conditions: depression (21%); anxiety (21%); mood affective disorders (23%); asthma (24%); hypertension (26%); epilepsy (28%); urinary incontinence (32%); malnutrition (38%); and scoliosis (46%). Adults with CP were more likely to have type 2 diabetes, anxiety, bipolar disorder, depression, schizophrenia, hypertension, ischaemic heart disease, stroke, cerebrovascular disease, asthma, liver disease, osteoarthritis, osteoporosis, underweight, and chronic kidney disease than adults without CP. Interpretation: These data from 18 countries, which provide an international perspective, may be used to promote awareness, identify targets for intervention, and inform the development of appropriate supports for adults with CP.

PMID: 36807150

#### 21. Two-year outcomes following a randomised platelet transfusion trial in preterm infants

Carmel Maria Moore, Angela D'Amore, Suzanne Fustolo-Gunnink, Cara Hudson, Alice Newton, Beatriz Lopez Santamaria, Alison Deary, Renate Hodge, Valerie Hopkins, Ana Mora, Charlotte Llewelyn, Vidheya Venkatesh, Rizwan Khan, Karen Willoughby, Wes Onland, Karin Fijnvandraat, Helen V New, Paul Clarke, Enrico Lopriore, Timothy Watts, Simon Stanworth, Anna Curley; PlaNeT2 MATISSE

Arch Dis Child Fetal Neonatal Ed. 2023 Feb 21; fetalneonatal-2022-324915. doi: 10.1136/archdischild-2022-324915. Online ahead of print.

Objective: Assess mortality and neurodevelopmental outcomes at 2 years of corrected age in children who participated in the PlaNeT-2/MATISSE (Platelets for Neonatal Transfusion - 2/Management of Thrombocytopenia in Special Subgroup) study, which reported that a higher platelet transfusion threshold was associated with significantly increased mortality or major bleeding compared to a lower one. Design: Randomised clinical trial, enrolling from June 2011 to August 2017. Follow-up was complete by January 2020. Caregivers were not blinded; however, outcome assessors were blinded to treatment group. Setting: 43 level II/III/IV neonatal intensive care units (NICUs) across UK, Netherlands and Ireland. Patients: 660 infants born at less than 34 weeks' gestation with platelet counts less than 50×109/L. Interventions: Infants were randomised to undergo a platelet transfusion at platelet count thresholds of 50×109/L (higher threshold group) or 25×109/L (lower threshold group). Main outcomes measures: Our prespecified long-term follow-up outcome was a composite of death or neurodevelopmental impairment (developmental delay, cerebral palsy, seizure disorder, profound hearing or vision loss) at 2 years of corrected age. Results: Follow-up data were available for 601 of 653 (92%) eligible participants. Of the 296 infants assigned to the higher threshold group, 147 (50%) died or survived with neurodevelopmental impairment, as compared with 120 (39%) of 305 infants assigned to the lower threshold group (OR 1.54, 95% CI 1.09 to 2.17, p=0.017). Conclusions: Infants randomised to a higher platelet transfusion threshold of 50×109/L compared with 25×109/L had a higher rate of death or significant neurodevelopmental impairment at a corrected age of 2 years. This further supports evidence of harm caused by high prophylactic platelet transfusion thresholds in preterm infants. Trial registration number: ISRCTN87736839.

#### 22. Assigning F-words as ingredients of interventions for children with cerebral palsy functioning at GMFCS IV and V: A scoping review protocol

Egmar Longo, Rayane Monteiro, Álvaro Hidalgo-Robles, Ginny Paleg, Claire Shrader, Ana Carolina De Campos

Front. Rehabil. Sci. 2023 Jan 21;4: 1110552. doi: 10.3389/fresc.2023.1110552

Introduction: Children with Cerebral Palsy (CP) functioning at Gross Motor Function Classification System (GMFCS) levels IV and V require "on time" identification and intervention. Interventions offered continue to be a challenge, in high-, but even more so in middle-, and low-income countries. Aim: To describe the methods developed to explore the ingredients of published studies on early interventions in young children with cerebral palsy (CP) at highest risk of being non-ambulant based on the "F-words for child development framework" and the design of a scoping review exploring these ingredients. Method: An operational procedure was developed through expert panels to identify ingredients of published interventions and related F-words. After sufficient agreement among researchers was reached, a scoping review was designed. The review is registered in the Open Science Framework database. The "Population, Concept and Context" framework was used. Population: young children (0–5 years with CP and at highest risk for being non-ambulant (GMFCS levels IV or V); Concept: non-surgical and non-pharmacological early intervention services measuring outcomes from any ICF domain; Context: studies published from 2001 to 2021. After duplicated screening and selection, data will be extracted and quality will be assessed with the American Academy for Cerebral Palsy and Developmental Medicine (AACPDM) and Mixed Methods Appraisal (MMAT) tools. Results: We present the protocol to identify the explicit (directly measured outcomes and respective ICF domains) and implicit (intervention features not explicitly intended or measured) ingredients. Conclusion: Findings will support the implementation of the F-words in interventions for young children with non-ambulant CP.

#### Full text available

#### 23. Relative contribution of sensory and motor impairments to mobility limitations in children with cerebral palsy: an observational study

Hsiu-Ching Chiu, Louise Ada, Rong-Ju Cherng, Chiehfeng Chen

Sci Rep. 2023 Feb 24;13(1):3229. doi: 10.1038/s41598-023-30293-9.

The purpose of this study was to determine the relative contribution of sensory and motor impairments to mobility limitations in cerebral palsy. An observational study was carried out in 83 children with all types of cerebral palsy with a mean age of 10.8 years (SD 1.2). Five impairments (coordination, strength, spasticity, contracture, proprioception) and three aspects of mobility (standing up from a chair, short and long distance walking) were measured. Standard multiple regression was used to determine the relative contribution of impairments to mobility as well as the relative contribution of strength of individual muscle groups (dorsiflexors, plantarflexors, knee extensors, hip abductors and hip extensors) to mobility. Five impairments accounted for 48% of the variance in overall mobility (p < 0.001): coordination independently accounted for 9%, contracture for 4% and strength for 3% of the variance. Five muscle groups accounted for 53% of the variance in overall mobility (p < 0.001): hip extensors independently accounted for 9%, knee extensors for 4%, dorsiflexors for 4% and plantarflexors for 3% of the variance. Our findings demonstrate that the impairments making a significant independent contribution to mobility in pre-adolescent cerebral palsy were loss of coordination, loss of strength and contracture.

PMID: 36828863

#### 24. Cardiometabolic Risk and Its Relationship With Visceral Adiposity in Children With Cerebral Palsy Trevor Batson, Junsoo Lee, Joseph M Kindler, Norman K Pollock, Mary F Barbe, Christopher M Modlesky

J Endocr Soc. 2023 Feb 2;7(4):bvad014. doi: 10.1210/jendso/bvad014. eCollection 2023 Feb 9.

Context: Adults with cerebral palsy (CP) display a higher prevalence of cardiometabolic disease compared with the general population. Studies examining cardiometabolic disease risk in children with CP are limited. Objective: The purpose of this study was to determine if children with CP exhibit higher cardiometabolic risk than typically developing children, and to examine its relationship with visceral adiposity and physical activity. Methods: Thirty ambulatory children with CP and 30 age, sex-, and race-matched typically developing control children were tested for blood lipids, glucose, and the homeostatic model

assessment of insulin resistance (HOMA-IR). Visceral fat was assessed using dual-energy x-ray absorptiometry. Physical activity was assessed using accelerometer-based monitors. Results: Children with CP had higher total cholesterol, low-density lipoprotein cholesterol, and non-high-density lipoprotein cholesterol (non-HDL-C), glucose, prevalence of dyslipidemia, prevalence of prediabetes, and visceral fat mass index (VFMI) and lower physical activity than controls (all P < .05). In the groups combined, non-HDL-C and glucose were positively related to VFMI (r = 0.337 and 0.313, respectively, P < .05), and non-HDL-C and HOMA-IR were negatively related to physical activity (r = -0.411 and -0.368, respectively, P < .05). HOMA-IR was positively related to VFMI in children with CP (r = 0.698, P < .05), but not in controls. Glucose was not related to physical activity in children with CP, but it was negatively related in controls (r = -0.454, P < .05). Conclusion: Children with CP demonstrate early signs of cardiometabolic disease, which are more closely related to increased visceral adiposity than decreased physical activity.

PMID: 36819461

## 25. Seasonal variations in vitamin D do not change the musculoskeletal health of physically active ambulatory men with cerebral palsy: a longitudinal cross-sectional comparison study

Christina Kate Langley, Gladys Leopoldine Onambélé-Pearson, David Thomas Sims, Ayser Hussain, Reece Kumar Mohindra, Bethany Louise Kershaw, Christopher Ian Morse

Nutr Res. 2022 Nov 29;111:24-33. doi: 10.1016/j.nutres.2022.11.005. Online ahead of print.

Increased levels of vitamin D in the summer months from natural seasonal variations in sun exposure have been linked to improvements in musculoskeletal health and function in UK populations; however, studies have shown that differences in lifestyles because of disability can inhibit the natural vitamin D increase in these populations. We hypothesized that men with cerebral palsy (CP) will experience smaller increases in 25-hydroxyvitamin D (25(OH)D) from winter to summer and men with CP will not experience any improvements in musculoskeletal health and function during the summer. A longitudinal observational study in 16 ambulant men with CP aged  $21.0 \pm 1.3$  years and 16 healthy, physical activity matched, typically developed controls aged  $25.4 \pm 2.6$  years, completed assessments of serum 25(OH)D and parathyroid hormone during winter and summer. Neuromuscular outcomes included vastus lateralis size, knee extensor strength, 10-m sprint, vertical jumps, and grip strength. Bone ultrasounds were performed to obtain radius and tibia T and Z scores. Men with CP and typically developed controls showed a 70.5% and 85.7% increase in serum 25(OH)D from winter to summer months, respectively. Neither group showed seasonal effect on neuromuscular outcomes muscle strength, size, vertical jump, or tibia and radius T and Z scores. A seasonal interaction effect was seen in the tibia T and Z scores (P < .05). In conclusion, there were similar seasonal increases in 25(OH)D observed in men with CP and typically developed controls, but serum 25(OH)D levels were still considered insufficient to improve bone or neuromuscular outcomes.

PMID: 36812881

# **26.** [Efficacy and mechanism of scalp acupuncture for spastic cerebral palsy][Article in Chinese] Jin-Bo Xu, Guang-Lei Tong

Randomized Controlled Trial Zhongguo Zhen Jiu. 2023 Feb 12;43(2):163-9. doi: 10.13703/j.0255-2930.20220408-0001.

Objective: To observe the clinical efficacy of scalp acupuncture for spastic cerebral palsy (CP), and to explore its possible mechanism based on brain white matter fiber bundles, nerve growth related proteins and inflammatory cytokines. Methods: A total of 90 children with spastic CP were randomly divided into a scalp acupuncture group and a sham scalp acupuncture group, 45 cases in each group. The children in the two groups were treated with conventional comprehensive rehabilitation treatment. The children in the scalp acupuncture group were treated with scalp acupuncture at the parietal temporal anterior oblique line, parietal temporal posterior oblique line on the affected side, and parietal midline. The children in the sham scalp acupuncture group were treated with scalp acupuncture at 1 cun next to the above point lines. The needles were kept for 30 min, once a day, 5 days a week, for 12 weeks. Before and after treatment, the diffusion tensor imaging (DTI) indexes of magnetic resonance (FA values of corticospinal tract [CST], anterior limb of internal capsule [ICAL], posterior limb of internal capsule [ICPL], genu of internal capsule [ICGL], genu of corpus callosum [GCC], body of corpus callosum [BCC] and splenium of corpus callosum [SCC]), serum levels of nerve growth related proteins (neuron-specific enolase [NSE], glial fibrillary acidic protein [GFAP], myelin basic protein [MBP], ubiquitin carboxy terminal hydrolase-L1 [UCH-L1]) and inflammatory cytokines (interleukin 33 [IL-33], tumor necrosis factor α [TNF-α]), cerebral hemodynamic indexes (mean blood flow velocity [Vm], systolic peak flow velocity [Vs] and resistance index [RI], pulsatility index [PI] of cerebral artery), surface

electromyography (SEMG) signal indexes (root mean square [RMS] values of rectus femoris, hamstring muscles, gastrocnemius muscles, tibialis anterior muscles), gross motor function measure-88 (GMFM-88) score, modified Ashworth scale (MAS) score, ability of daily living (ADL) score were observed in the two groups. The clinical effect of the two groups was compared. Results: After treatment, the FA value of each fiber bundle, Vm, Vs, GMFM-88 scores and ADL scores in the two groups were higher than those before treatment (P<0.05), and the above indexes in the scalp acupuncture group were higher than those in the sham scalp acupuncture group (P<0.05). After treatment, the serum levels of NSE, GFAP, MBP, UCH-L1, IL-33, TNF- $\alpha$  as well as RI, PI, MAS scores and RMS values of each muscle were lower than those before treatment (P<0.05), and the above indexes in the scalp acupuncture group were lower than those in the sham scalp acupuncture group (P<0.05). The total effective rate was 95.6% (43/45) in the scalp acupuncture group, which was higher than 82.2% (37/45) in the sham scalp acupuncture group (P<0.05). Conclusion: Scalp acupuncture could effectively treat spastic CP, improve the cerebral hemodynamics and gross motor function, reduce muscle tension and spasticity, and improve the ability of daily life. The mechanism may be related to repairing the white matter fiber bundles and regulating the levels of nerve growth related proteins and inflammatory cytokines.