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Interventions and Management

1. Linking corticospinal tract activation and upper-limb motor control in adults with cerebral palsy

Saihari S Dukkipati, Sarah J Walker, Michael P Trevarrow, Morgan T Busboom, Katie L Schlieker, Max J Kurz

Dev Med Child Neurol. 2023 Sep 7. doi: 10.1111/dmcn.15750. Online ahead of print.

Aim: To quantify the cervicomedullary motor evoked potentials (CMEPs) at the cervical spinal level in adults with cerebral palsy (CP) and determine if altered CMEPs are linked with upper-extremity motor function in this population. **Method:** This cross-sectional study consisted of a cohort of adults with CP (n = 15; mean age = 33 years 5 months [SD = 11 years 8 months]); Manual Ability Classification System levels I-IV) and neurotypical controls (n = 18; mean age = 30 years 10 months [SD = 10 years 4 months]), who were recruited to participate at an academic medical center. Adults with CP and typical adults (controls) were stimulated at the cervicomedullary junction to assess CMEPs at the cervical spinal cord level. Upper-extremity motor function was quantified using the Box and Blocks and Purdue Pegboard tests, self-reported upper-extremity function (UEF), and assessments of selective motor control. **Results:** At higher stimulation levels, the contralateral CMEP responses of adults with CP were different from typical adults (p = 0.032). Reduced CMEP was correlated with reduced upper-limb function, including worse performance on the Box and Blocks (rho = 0.625, p = 0.025) and Purdue Pegboard tests (rho = 0.701, p = 0.010), lower self-reported UEF (rho = 0.761, p = 0.009), and overall selective motor control (rho = 0.731, p = 0.007). **Interpretation:** Changes in the activation of spinal motoneurons through corticospinal pathways may have an important role in the altered upper-extremity motor function of individuals with CP.

PMID: [37679938](#)

2. Reliability of an observation-based scoring grid to assess bimanual performance during unstandardized tasks in adults living with cerebral palsy

Léandre Gagné-Pelletier, Isabelle Poitras, Véronique H Flamand, Catherine Mercier

Disabil Rehabil. 2023 Sep 8;1-6. doi: 10.1080/09638288.2023.2254700. Online ahead of print.

Purpose: Most activities of daily living (ADLs) require the use of both upper extremities. However, few assessments exist to assess bimanual performance, especially among adults living with cerebral palsy (CP). The aim of this preliminary study is to assess the interrater reliability and convergent validity of the Assisting Hand Assessment (AHA) scoring grid applied to unstandardized ADLs. **Materials and methods:** For this validation study, nineteen adults living with spastic unilateral CP were videotaped performing seven bimanual ADLs. Three raters assessed the videos independently using the 20-item grid of the AHA. Gwet's AC2 was used to assess interrater reliability. Kendall's Tau-b correlation was used between the observation-based scoring grid and Jebsen-Taylor Hand Function Test (JTHFT) scores to assess convergent validity. **Results:** Interrater reliability was good (0.84, SD = 0.02). The correlation with the JTHFT was high (tau = -0.74; p < 0.001). **Conclusion:** The results show the potential of using an observation-based scoring grid with unstandardized ADLs to assess bimanual performance in adults living with CP, but further research on psychometric properties is needed. This method allows for an assessment that is occupation-oriented, ecological, and meaningful.

PMID: [37684745](#)

3. A modified angled plate for fixation of proximal femoral varus osteotomy in neuromuscular hip dislocation: Mechanical and clinical study

Ibrahim El Sayed Abdellatif Abuomira, Barakat El-Alfy, Mahmoud Seddik, Khamis Mohammed Ahmed, Ahmed Sayed Khashaba, Amer Al-Kot

Orthop Traumatol Surg Res. 2023 Sep 2;103674. doi: 10.1016/j.otsr.2023.103674. Online ahead of print.

Introduction: Proximal femoral osteotomy is an important step in the management of paralytic hip dislocation. Fixation by the angled plate is demanding and carries the risk of many complications. In this study, we made certain modifications for the angled plate. Does this plate provide a stable fixation for proximal femoral varus osteotomy? The main objective of this study was to assess the results of the modified plate in fixation of proximal femoral varus osteotomy in patients with neuromuscular hip dislocation. **Hypothesis:** This new system would offer significant advantages over the existing systems in terms of easy application and stable fixation. **Material and methods:** Twenty patients with paralytic hip dislocation were included in this study. The ages ranged from 5 to 15 years with a mean of 8.88 ± 2.92 years. There were 12 boys and 8 girls. Seventeen patients had cerebral palsy and 3 had meningocele disease. Pre-operative radiographs were done, and the migration percentage (MP), acetabular index (AI), and neck-shaft angle (NSA) were measured. All patients were treated with open reduction, pelvic osteotomy, and proximal femoral varus osteotomy. The femoral osteotomy was fixed by the modified angled plate in all cases. **Results:** The osteotomy sites united in all patients and the mean time of union was 2.9 ± 0.65 months. The acetabular index, migration percentage, and neck-shaft angle were reduced postoperatively. This reduction was statistically significant. The hips remained stable throughout the period of follow-up in all patients. No cases were complicated by nonunion or implant failure. **Conclusion:** The modified angled plate (canulated interlocking blade plate 90°) is a good method for the fixation of proximal femoral varus osteotomy in the management of neuromuscular hip dislocation. It provides a stable fixation. Level of evidence: IV; case series.

PMID: [37666326](#)

4. Subthreshold electrical noise alters walking balance control in individuals with cerebral palsy

Ashwini Sansare, Hendrik Reimann, Jeremy Crenshaw, Maelyn Arcodia, Khushboo Verma, Samuel C K Lee

Gait Posture. 2023 Aug 19;106:47-52. doi: 10.1016/j.gaitpost.2023.08.008. Online ahead of print.

Background: Sensory deficits in individuals with cerebral palsy (CP) play a critical role in balance control. However, there is a lack of effective interventions that address sensory facilitation to improve walking balance. Stochastic Resonance (SR) stimulation involves delivering sub threshold noise to improve balance in patients with sensory deficits by enhancing the detection of sensory input. **Research question:** To investigate the immediate effects of SR on walking balance in individuals with and without CP. **Methods:** Thirty-four participants (17 CP, 17 age- and sex-matched typically developing controls or TD) between 8 and 24 years of age were recruited. SR stimulation was applied to the muscles and ligaments of ankle and hip joint. An optimal SR intensity during walking was determined for each subject. Participants walked on a self-paced treadmill for three trials of two minutes each using a random order of SR stimulation (SR) and no stimulation (noSR) control conditions. Our primary outcome measure was minimum lateral margin of stability (MOS). Secondary outcome measures include anterior MOS before heelstrike and spatiotemporal gait parameters. We performed two-way mixed ANOVAs with group (CP, TD) as between-subject and condition (noSR, SR) as within subject factors. **Results:** Compared to walking without SR, there was a small but significant increase in the lateral and anterior MOS with SR stimulation, implying that a larger impulse was needed to become unstable, in turn implying higher stability. Step width and step length decreased with SR for the CP group with SR stimulation. There were no significant effects for other spatiotemporal variables. **Significance:** Sub threshold electrical noise can slightly improve walking balance control in individuals with CP. SR stimulation, through enhanced proprioception, may have improved the CP group's awareness of body motion during walking, thus leading them to adopt a more conservative stability strategy to prevent a potential fall.

PMID: [37659222](#)

5. Nonmetallic Anterior Hemiepiphyseodesis of the Distal Femur with a Low-Profile, Pretensioned Implant: A Case Report

Daniel Weltsch, Nakul S Talathi, Rachel M Thompson

JBJS Case Connect. 2023 Sep 8;13(3). doi: 10.2106/JBJS.CC.23.00106. eCollection 2023 Jul 1.

Case: A 14-year-old adolescent boy with left-sided spastic hemiplegic cerebral palsy presented with a 14° left knee flexion contracture and resultant gait disturbance in the setting of an open distal femoral physis. He underwent subsequent anterior distal femur hemiepiphyseodesis with a suture anchor-based, nonmetallic implant. He achieved full correction at the 1-year

follow-up and underwent uncomplicated implant removal. Conclusion: A low-profile, suture-based implant used for pediatric knee flexion deformity may allow surgeons to control growth in a reversible fashion by tensioning the physis while possibly avoiding some of the complications associated with currently used implants.

PMID: [37683076](#)

6. More than just having fun! Understanding the experience of involvement in physical activity of adolescents living with cerebral palsy

Gaela Kilgour, Ngaire Susan Stott, Michael Steele, Brooke Adair, Amy Hogan, Christine Imms

Disabil Rehabil. 2023 Sep 7;1-12. doi: 10.1080/09638288.2023.2251395. Online ahead of print.

Purpose: To explore the experiences of involvement of adolescents living with cerebral palsy, and their parents, while participating in physical activity. Understanding involvement in physical activity may be used to guide future participation. **Methods:** Eight adolescents (mean age 13 years 11 months, SD 1 year 6 months) with cerebral palsy participated in a New Zealand-based high-level mobility programme (HLMP) focused on running skills, twice per week for 12 weeks. The adolescents and 12 parents were interviewed before, after the 12 weeks and 9-months following the HLMP. Guided by interpretative description, 38 interviews were coded, analysed, and interpreted. **Results:** Four themes were: "Turning up is not enough" ("There's no point being there if you're not involved"); "In it all the way", "Changes on a dime", and "What works for me." Perceptions of involvement varied between adolescents and parents. Being "very involved" related to high levels of focus, concentration, effort; but not always enjoyment. **Conclusions:** Focusing on enjoyment as the key experience of involvement understates the complexity and dynamic nature of involvement. "Being involved" is not always easy and may not mean the absence of discomfort or effort. Optimising the individuals' involvement continuum during physical activity may be essential to promote lifelong participation. **IMPLICATIONS FOR REHABILITATION** Adolescents living with cerebral palsy and their parents have differing perspective of involvement and utilise different strategies to encourage being and staying active. Teaching adolescents living with cerebral palsy about their involvement continuum and optimal level of involvement for each activity, context and environment could promote sustained participation. To ensure adolescents are "being involved" in physical activity, opportunities for engagement, motivation and persistence are important; enjoyment is a possible, but not essential attribute of involvement. Encouraging involvement in physical activity can be a source of family conflict from a young age therefore clinicians have a role as an essential supporter, motivator and educator.

PMID: [37675880](#)

7. Exploring Adaptive Cycling Interventions for Young People with Disability: An Online Survey of Providers in Australia

John J Carey, Rachel Toovey, Alicia J Spittle, Christine Imms, Nora Shields

J Clin Med. 2023 Aug 25;12(17):5523. doi: 10.3390/jcm12175523.

Adapted cycles offer young people with disability a fun way to participate in over-ground cycling, but little is known about current practices to train and sustain cycling in this group. This study aimed to describe interventions used to introduce adaptive cycling to young people with disability and explore barriers and facilitators to adapted cycle use. A cross-sectional online survey was distributed among Australian allied health, education and recreation providers through targeted advertising and snowball methods. Data were analysed using mixed methods and reporting was guided by the CHERRIES and CROSS checklists. There were 107 respondents with n = 90 (84.1%) who fully completed the survey. Respondents worked with riders who had cerebral palsy, neurodevelopmental disabilities and movement impairments. Adaptive cycling interventions were customized according to a rider's goals, needs and resourcing. The training of cycling skills included "an eclectic mix" of experiential learning, individual goals, task-specific training and holistic practice models. Diverse factors impacted cycling participation, with opportunities reliant on access to a supportive environment, including a suitable adapted cycle. This study found that providers viewed adaptive cycling as a therapeutic or active leisure experience within protected traffic-free environments. Strategies to extend adaptive cycling opportunities into the community are required.

PMID: [37685591](#)

8. Resting energy expenditure in children and adolescents with cerebral palsy: accuracy of available prediction formulas and development of population-specific methods

Barbara Borsani, Giacomo Biganzoli, Francesca Penagini, Alessandra Bosetti, Erica Pendezza, Veronica Perico, Elia Biganzoli, Elvira Verduci, Gian Vincenzo Zuccotti

Front Pediatr. 2023 Aug 23;11:1097152. doi: 10.3389/fped.2023.1097152. eCollection 2023.

Introduction: Energy requirements are difficult to estimate in children with cerebral palsy (CP). Resting energy expenditure (REE), necessary to implement personalized nutritional interventions, is most commonly estimated using prediction formulae since indirect calorimetry, the reference method, is not available in all nutrition units. The aims of the present study were: (1) to evaluate the accuracy of the most commonly used REE prediction formulae developed for healthy children, in children with CP; (2) to assess the accuracy of the REE population-specific formula for CP children proposed in our preliminary report; (3) to develop new population-specific methods. **Methods:** REE was measured by indirect calorimetry in 100 children and adolescents with spastic quadriplegic cerebral palsy (SQCP) and estimated on the basis of predictive formulas selected by the clinicians [World Health Organization (WHO), Harris-Benedict, Schofield weight, Schofield weight & height, Oxford, Mifflin formulae and a population-specific formula for CP children developed in our preliminary report]. **Results:** 100 children with SQCP (35 girls, 35%) classified as level V according to gross motor function classification system (GMFCS-V); 64% with oral nutrition, 29% total enteral nutrition (nasogastric tube feeding, percutaneous endoscopic gastrostomy, percutaneous endoscopic transgastric jejunostomy) and 7% mixed nutrition. The median (IQR) REE was 41.96 (17.5) kcal/kg/day. Statistical analysis highlighted a proportional bias between the indirect calorimetry and all considered predictive formulae for REE determination. By studying the relationship between the bias and the mean values of REE, specific conversion equations were obtained. With a pre-specified model having as predictors the variable weight and the variable Triceps Skinfold (TSF) and, as response the variable REE measured by indirect calorimetry, a predictive nomogram was developed to estimate the REE in this population of children. **Conclusions:** We suggest using predictive formulae for healthy children with caution, and where possible carrying out indirect calorimetry to assess REE in children with CP. However, we propose a new tool which could be developed to become an additional help for assessment of REE in the clinical practice. Future objectives will be to obtain a larger sample size, in a multicenter perspective study, to build a specific predictive model for the REE of the studied population.

PMID: [37681200](#)

9. Gabapentin as part of a multimodal pain protocol for selective dorsal rhizotomy does not impact percentage of rootlets transected

Mary E Lynch, David J Daniels, Joline E Brandenburg

Childs Nerv Syst. 2023 Sep 7. doi: 10.1007/s00381-023-06124-7. Online ahead of print.

Purpose: We aim to determine whether preoperatively initiated gabapentin for pain control impacts the percentage of rootlets cut during monitored, limited laminectomy selective dorsal rhizotomy (SDR) procedure. **Methods:** This retrospective cohort study includes participants with cerebral palsy who had SDR for treatment of spasticity between 2010 and 2019 at a single-institution tertiary care center. One-level laminectomy SDR aimed to evaluate the cauda equina roots from levels L2-S1 with EMG monitoring. Gabapentin titration began 3 weeks prior to SDR. Data was analyzed using simple linear regression. Thirty-one individuals met inclusion criteria. Mean age was 7 years, 4 months. Eighteen participants (58%) identified as male, 12 (39%) female, and one (3%) non-binary. Thirty (97%) had bilateral CP. Sixteen (52%) were GMFCS II, four (13%) GMFCS III, five (16%) GMFCS IV, and six (19%) GMFCS V. **Results:** Mean percentage of rootlets transected was 50.75% (SD 6.00, range 36.36-60.87). There was no relationship between the dose of gabapentin at time of SDR and percentage of rootlets cut with a linear regression slope of - 0.090 and an R² of 0.012 (P = 0.56). **Conclusion:** Results indicate that preoperative initiation of gabapentin did not impact the percentage of rootlets transected. Thus, gabapentin can be initiated prior to SDR at moderate dosages without impacting SDR surgical outcomes.

PMID: [37676296](#)

10. Evaluation of the effects of robot-assisted gait training on bowel function in children with cerebral palsy and the caregiver burden: A pilot study

Damla Cankurtaran, Nihan Abidin, Ece Ünlü Akyüz, Nihal Tezel, Özgür Zeliha Karaahmet

Turk J Phys Med Rehabil. 2022 Dec 1;69(2):153-160. doi: 10.5606/tftrd.2023.10351. eCollection 2023 Jun.

Objectives: The aim of this study was to investigate the effects of robot-assisted gait training (RAGT) on bowel function by measuring the frequency of evacuation, stool consistency, and severity of constipation in children with cerebral palsy (CP) and determining caregiver burden. **Patients and methods:** This retrospective pilot study was conducted with 30 children (16 males, 14 females; mean age 8.8±3.2 years; range, 6 to 11 years) with CP between January 2019 and July 2019. Patients were equally divided into two groups: the RAGT group and the control group. Both groups underwent conventional physical therapy. The RAGT group underwent RAGT in addition to physical therapy. The results of the Bristol Stool Scale, the Constipation Assessment Scale, and the frequency of defecation before and after the study were recorded. Caregivers of children in both groups were asked to answer five questions regarding their burden at the beginning of the study and the end of the study. **Results:** While a significant improvement was found in defecation frequency in the RAGT group (p=0.01), defecation frequency was not significantly improved in the control group (p>0.999). Bristol Stool Scale scores changed significantly within both groups (p<0.05). Constipation Assessment Scale scores significantly changed only in the RAGT group (p=0.01). A significant positive change in caregiver burden was observed in the RAGT group (p<0.05). **Conclusion:** Robot-assisted gait training has positive effects on the frequency of defecation, stool consistency, and constipation severity in children with CP and

caregiver burden.

PMID: [37671370](#)

11. Telehealth in paediatric physical therapy education: Strategies and perceptions of interns and caregivers of children with disabilities in Brazil

Isabella Pessóta Sudati, Rayane Félix Lôbo Monteiro, Ana Beatriz Nasser, Nelci Adriana Cicuto Ferreira Rocha, Ana Carolina de Campos

Clin Teach. 2023 Sep 7;e13653. doi: 10.1111/tct.13653. Online ahead of print.

Aims: To describe the implementation of paediatric rehabilitation telehealth at a physical therapy (PT) unit in Brazil during the COVID-19 pandemic and to describe the perception about this modality by two groups: (1) undergraduate PT students using telehealth during their clinical rotations in this unit and (2) the caregivers of children with disabilities receiving the services. **Methods:** Twenty-one PT interns (19 females; 25 ± 2 years of age) and seven caregivers (seven females; 40 ± 6 years of age) of seven children with disabilities (five females; 10 ± 4 years of age; five children diagnosed with cerebral palsy) responded to an online questionnaire about their experience with the telehealth programme. Participant attendance and frequency of objective responses were reported descriptively; open-ended responses were analysed qualitatively and grouped according to broad themes. **Results:** 71.4% of interns rated telehealth as an excellent or good experience, and 28.6% did not appreciate it. In addition, 28.6% of them thought that telehealth should be part of the mandatory internship. Regarding caregivers, 85.8% judged the telehealth programme as excellent or good. Both interns and caregivers cited pros and cons related to technology, professional resources, communication skills and caregiver-related aspects, among others. **Conclusions:** Specific teaching strategies had to be utilised for implementation of telehealth. Despite being a novel modality for interns and caregivers, telehealth was well accepted.

PMID: [37679054](#)

12. Mortality and Causes of Death in Children With Cerebral Palsy With Scoliosis Treated With and Without Surgery

Matti Ahonen, Ilkka Helenius, Mika Gissler, Ira Jeglinsky-Kankainen

Neurology. 2023 Sep 7;10.1212/WNL.000000000207796. doi: 10.1212/WNL.000000000207796. Online ahead of print.

Objectives: To compare mortality and causes of death in scoliotic children with Cerebral palsy (CP) with and without scoliosis surgery. **Methods:** National population-based registries were searched for children with CP and scoliosis with and without surgery for scoliosis and were analyzed for comorbidities, mortality, and causes of death. **Results:** Two hundred and thirty-six had not been operated and 238 had been operated for scoliosis during the median follow-up of 17.8 (IQR 11.7-25.7) and 23.0 (IQR 18.4-28.2) years, respectively. Both groups had similar comorbidities. During the follow-up mortality was higher in the non-surgically treated group than in the surgically treated group ($n=38/236$, 16% and 8.7 per 1000 follow-up years vs. $n=29/238$, 12% and 5.3 per 1000 follow-up years, $p=0.047$). In patients with non-surgical treatment cause of death was respiratory in 76.3% (29/38) and 37.9% (11/29) in patients with surgical treatment of scoliosis (6.6 and 2.0 per 1000 follow-up years, $p=0.002$). Neurological causes of death were more common in surgically treated patients than in non-surgically treated patients, 44.8% (13/29) and 15.8% (6/38), respectively (3.0 and 1.1 per 1000 follow-up years, $p=0.009$). **Discussion:** Surgical treatment of scoliosis associates to reduced mortality due to respiratory causes in children with cerebral palsy and scoliosis. **Classification of evidence:** This study provides Class IV evidence of the effects of spinal fusion on mortality of children with severe scoliosis due to CP.

PMID: [37679048](#)

13. The impact of life of a child with cerebral palsy on the quality of life of mothers: Tuzla Canton/Bosnia and Herzegovina

Alma Glinac, Selma Sinanovic, Lejla Glinac, Lejla Matovic

Sudan J Paediatr. 2023;23(1):60-67. doi: 10.24911/SJP.106-1600718620.

The aim of the study was to examine the impact of the quality of life of children with cerebral palsy (CP) on the quality of life of mothers. A total of 122 subjects participated in the study. The general quality of life assessment of paediatric subjects PedsQLTM 4.0 Generic Scale and the specific PedsQLTM 3.0 Module Cerebral Palsy Version 3.0 were used to assess the quality of life of children with CP, and the quality of life of mothers was assessed with the PedsQLTM 2.0 Family Impact Mode Questionnaire. In the present study, the quality of life of mothers is influenced by the physical and social functioning of the child, while the impact of emotional functioning has not been proven. The specific difficulties faced by children with CP, which have a statistically significant effect on the overall quality of life of the mother, are present in the domains: daily

activities, mobility and balance and nutrition. The assessment of the quality of life of mothers and children with CP should be an integral part of the clinical assessment, as this will enable professionals to participate more successfully in providing professional assistance in the form of services, therapeutic approaches and prevention programs.

PMID: [37663105](#)

14. The Difficulty Detecting Tuberculosis in a Child with Post-COVID-19 and Cerebral Palsy

Andjelka Stojkovic, Irena Ilic, Andrijana Kostic, Katerina Dajic, Zorica Raskovic, Jelena Nestorovic, Milena Ilic

Diagnostics (Basel). 2023 Aug 31;13(17):2826. doi: 10.3390/diagnostics13172826.

When hypostatic pneumonia is present at the same time as COVID-19 pneumonia, the clinical course is almost always prolonged (prolonged-COVID-19) due to persistent inflammation, long-term anti-inflammatory syndrome, followed by immune exhaustion, i.e., by immunosuppression and catabolic syndrome. In the immunosuppression phase, viral reactivation can be accompanied by a secondary infection, which, in this case, is pulmonary tuberculosis. Pulmonary tuberculosis in post-COVID-19 patients and in patients with spastic quadriplegic cerebral palsy does not have a typical clinical course nor laboratory, radiological, immunological, microbiological, or fiberbronchoscopic pathohistological confirmation. Due to this, the treatment of pulmonary tuberculosis was not carried out on time, postponed after the unsuccessful treatment of sepsis, post-COVID-19, and other accompanying viral (adenovirus, RSV) and bacterial (streptococcus viridans) infections. The treatment of pulmonary tuberculosis was possible only "ex juvantibus" (trial) post-COVID-19. It becomes imperative to search for a new, more precise and reliable diagnostic test for the detection of tuberculosis bacillus.

PMID: [37685364](#)

15. Long-term outcomes of offspring from multiple gestations: a two-sample Mendelian randomization study on multi-system diseases using UK Biobank and FinnGen databases

Yi Jiang, Yuanyuan Du, Rui Su, Xuan Zhou, Lijie Wei, Jingyi Zhang, Shenglan Zhu, Huiting Zhang, Chenyun Fang, Yuting Chen, Peng Gao, Liangnan Zhang, Shaoshuai Wang, Jun Yu, Mengzhou He, Wencheng Ding, Ling Feng

J Transl Med. 2023 Sep 8;21(1):608. doi: 10.1186/s12967-023-04423-w.

Background: Assisted reproductive technologies (ART) have increased the incidence of multiple births, which can have a negative impact on maternal and offspring health. The study aimed to investigate the association between genetically predicted multiple birth and the risk of 42 common diseases of the nervous, psychiatric, cardiovascular, respiratory, digestive, and endocrine systems. Methods: The study utilized two-sample Mendelian randomization (MR) analysis to explore the potential causal relationship between genetically predicted multiple birth and the genetically predicted risk of diseases. The study used the FinnGen and UK Biobank datasets for analysis. Results: The study found no significant causal relationship between multiple birth and psychiatric disorders. However, the lower limits of the 95% confidence intervals for bipolar affective disorder and anxiety disorders were not robust, indicating a need for further investigation. The study found that multiple birth may be a strong risk factor for infantile cerebral palsy, and caution is necessary in both natural and ART multiple births. The study revealed a potential causal relationship between multiple birth and coronary heart disease, ischemic heart disease, and deep vein thrombosis, which may be related to abnormal intrauterine environments in multiple pregnancies. Surprisingly, multiple birth appears to have a protective effect against some respiratory diseases, such as chronic obstructive pulmonary disease and asthma. Conclusions: The study highlights the need for caution regarding the risk of infantile cerebral palsy, cardiovascular diseases, and psychiatric disorders in multiple birth. Our study can lead to the development of preventive strategies and improved clinical management for affected infants.

PMID: [37684631](#)

16. De novo TRPM3 missense variant associated with neurodevelopmental delay and manifestations of cerebral palsy

Jagadish Chandrabose Sundaramurthi, Anita M Bagley, Hannah Blau, Leigh Carmody, Amy Crandall, Daniel Danis, Michael Gargano, Anxhela Gjyshi Gustafson, Ellen M Raney, Mallory Shingle, Jon R Davids, Peter N Robinson

Cold Spring Harb Mol Case Stud. 2023 Sep 8;mcs.a006293. doi: 10.1101/mcs.a006293. Online ahead of print.

We identified a de novo heterozygous TRPM3 missense variant, p.(Asn1126Asp), in a patient with developmental delay and manifestations of cerebral palsy using phenotype-driven prioritization analysis of whole genome sequencing data with Exomiser. The variant is localized in the functionally important ion transport domain of the TRPM3 protein and predicted to destabilize the protein structure. Our report adds TRPM3 to the list of Mendelian disease-associated genes that can be associated with cerebral palsy and confirms the pathogenicity of the variant p.(Asn1126Asp).

PMID: [37684057](#)

17. Research trends in the orthopedic surgical management of cerebral palsy: a cross-analytical study of publications in the past decade

Maher Ghandour, Matthias Klotz, Axel Horsch

Review Front Neurol. 2023 Aug 22;14:1200893. doi: 10.3389/fneur.2023.1200893. eCollection 2023.

Little is known about the trends in orthopedic surgical management of cerebral palsy (CP). In this cross-analytical study we examined alterations in research publications in this field in the past 10 years through four databases. Thus, we divided publications into old (2012-2017) and recent (2018-2022). To determine if the focus of research in this field has changed, we compared both periods based on publication's (authors' number, journal, country, design), patients' (number, gender, age, CP type), and surgery-related (indication, number, category, type) characteristics. Publications showed a positive trend over the past 10 years with a peak in 2020. The number of publications was similar between old and recent ones (47.58% vs. 52.42%). Most research outputs were from the United States and Germany. Differences were noted between recent and old publications regarding journals ($p = 0.0001$), journal category ($p = 0.023$), authors' number ($p = 0.006$), and patients' age ($p = 0.02$). The impact factor was also different ($p = 0.0001$). However, no differences were noted regarding other characteristics ($p > 0.05$). The research output regarding surgical orthopedic management in CP has increased in the past decade with no difference between 2012-2017 and 2018-2022. Except for the number of authors, journal name, and patients' age, no significant differences were noted between both periods.

PMID: [37681012](#)

18. A follow up on the feasibility after national implementation of magnesium sulfate for neuroprotection prior to preterm birth

Sara Hellström, Andrea Jonsdotter, Maria Jonsson, Karin Pettersson, Sissel Saltvedt, Andreas Herbst, Johan Ågren, Ulrika Ådén, Magnus Domellöf, Henrik Hagberg, Ylva Carlsson

Acta Obstet Gynecol Scand. 2023 Sep 8. doi: 10.1111/aogs.14673. Online ahead of print.

Introduction: The risk for brain injury manifested as cerebral palsy is higher in very preterm born children than in term. Prenatal administration of magnesium sulfate (MgSO₄) has been shown to be neuroprotective and reduces the proportion of very preterm born children later diagnosed with cerebral palsy. A Swedish national clinical practice guideline was implemented in March 2020, stipulating the administration of a single intravenous dose of 6 g MgSO₄ 1-24 h prior to delivery before gestational age 32+0, aiming for 90% treatment coverage. The aim of this study was to evaluate the feasibility of this new clinical practice guideline in the first year of its implementation. **Material and methods:** Data on MgSO₄ treatment were collected by reviewing the medical charts of women who gave birth to live born children in gestational age 22+0-31+6 during the period of March 1, 2020 to February 28, 2021, at five Swedish university hospitals. Women with pre-eclampsia, eclampsia, or high elevated liver enzymes low platelets (HELLP) were excluded. **Results:** A total of 388 women were eligible and 79% received treatment with MgSO₄. Of the 21% not receiving treatment, 9% did not receive treatment due to lack of knowledge about the clinical practice guideline, 9% were not possible to treat and 3% had missing data. The proportion treated increased from 72% to 87% from the first to the last 3 months. Of those treated, 81% received the drug within the stipulated timeframe (mean 8.7 h, median 3.4 h). **Conclusions:** There was a positive trend over time in the proportion of women receiving MgSO₄ treatment, but the a priori target of 90% was not reached during the first year of implementation. Our findings indicate that this target could be reached with additional information to clinicians.

PMID: [37680134](#)

19. Predictors of poor neurodevelopmental outcomes of very preterm and very low birth weight infants

Rita Pissarra, Bárbara Pereira-Neto, Pedro Miragaia, Sara Almeida, Filipa Flor-DE-Lima, Paulo Soares

Minerva Pediatr (Torino). 2023 Sep 6. doi: 10.23736/S2724-5276.23.07360-3. Online ahead of print.

Background: Despite recent improvements, premature infants remain at high risk for long-term morbidity and poorer neurodevelopment, particularly very preterm (VP) and very low birth weight (VLBW). The aim of this study was to describe neurodevelopmental outcomes at two years and identify potential predictors of worse performance. **Methods:** In a retrospective cohort, a two-years' neurodevelopmental evaluation was analyzed. Multivariable regressions were used to study the association of perinatal history with neurodevelopmental outcomes. Subjects included VP and/or VLBW born at a Portuguese III-level perinatal center between 2011-2017. Milestones outcomes were assessed using the Griffiths' Mental Development Scales. **Results:** One hundred seventy-seven infants were included. Two-years milestones were not achieved in 18.6% in language domain and 7.3% in motor function, 4.5% wore glasses and 1.1% auditory prosthesis/cochlear implant. Almost 30% needed

intervention, 18.6% occupational therapy, 16.4% physiotherapy and 13.6% speech therapy. Griffiths' Mental Development Scales was performed in 139, with a mean global quotient of 98.3 and hearing/speech as the least quoted scale. Global development delay (GDD) was present in 14.8% and cerebral palsy in 2.8%. Multivariate analysis by logistic regression adjusted to gestational age, birth weight and confounding variables, revealed a statistically significant association between GDD and hydrocephalus with shunt/reservoir (OR:19.01), retinopathy of prematurity stage ≥ 2 (OR:7.86) and neonatal sepsis (OR:3.34). Conclusions: Consistent with recent studies, preterm are at increased risk of neurodevelopmental impairment, mainly due to GDD and language delay, rather than cerebral palsy. In this population, hydrocephalus, retinopathy of prematurity and neonatal sepsis were strongly associated with poorer outcomes. Insight into these factors is essential to refer patients for specific early intervention programs.

PMID: [37672234](#)

20. Effectiveness of virtual reality on activities of daily living in children with cerebral palsy: a systematic review and meta-analysis

YongGu Han, SunWook Park

Meta-Analysis PeerJ. 2023 Aug 31;11:e15964. doi: 10.7717/peerj.15964. eCollection 2023.

Background: No meta-analysis has been conducted on the effect of specific virtual reality (VR) treatment modes on activities of daily living (ADL) in children with cerebral palsy (CP). Therefore, this study aimed to confirm whether VR therapy is effective in improving ADL in children with CP according to subgroups. Methodology: Literature published in the Cumulated Index to Nursing and Allied Health Literature (CINAHL), Embase, the Physiotherapy Evidence Database (PEDro), and PubMed was reviewed, and Risk of Bias 2.0 (RoB 2) was used to evaluate the quality of the literature. A funnel plot was visually observed to confirm publication bias, supplemented with Egger's regression test. Data analysis was performed using R version 4.2.1. Subgroup analysis was performed according to the Gross Motor Function Classification System (GMFCS), the Manual Ability Classification System (MACS), treatment minutes per week, treatment period, age, and RoB. Results: Eleven of 2,978 studies were included, and the overall effect size was 0.37 (95% confidence interval = 0.17-0.57). Regarding GMFCS, effect sizes of 0.41 and 0.33 was observed for the low- and high-function groups, respectively. For MACS, 0.27 and 0.43 were observed for the low and high-function groups. Regarding treatment minutes per week, the values were 0.22, 0.44, and 0.27 in the 1-100, 101-200, and 201-300 min groups, respectively. In the classification according to age, 0.29 was observed for school-age children and 0.98 for preschool children. Lastly, in the classification according to the RoB, 0.52, -0.01, and 0.23 indicated studies with low risk, some concern, and high risk, respectively. Conclusions: The highest effect was observed when VR was applied within 6 weeks of 101-200 per week. Therefore, it is suggested that if the results of this review are applied to children with cerebral palsy in the community, it will be an effective intervention method.

PMID: [37667752](#)

21. Acupuncture and Tuina Treatment for Gross Motor Function in Children with Spastic Cerebral Palsy: A Monocentric Clinical Study

Xing Wang, Siew Hoon Teh, Xiao-Gang Du, Xing-Hua Wang

Clinical Trial Neuropsychiatr Dis Treat. 2023 Aug 30;19:1875-1886. doi: 10.2147/NDT.S424102. eCollection 2023.

Objective: Cerebral palsy (CP) is a condition characterized by abnormal pronunciation, posture, and movement, particularly spastic CP, which involves Gross motor dysfunction due to increased muscle tone and stiffness. This monocentric clinical study aims to evaluate the effectiveness of acupuncture and tuina (AT) in improving gross motor function and alleviating associated symptoms in children diagnosed with spastic CP. Methods: A total of 83 eligible patients received AT treatment, while 85 patients received conventional rehabilitation treatment. Both groups underwent a 12-week treatment period following the research protocol. Pre- and post-treatment assessments included the Modified Ashworth Muscle Tension Scale (MAS), Gross Motor Function Measure (GMFM-D and GMFM-E), 6-min walking distance measurement (6MWD), and Modified Children's Functional Independence Rating Scale (WeeFIM). Results: After 12 weeks of treatment, when compared with baseline, the scores of MAS in both AT group and control group are decreased ($p < 0.01$, $p < 0.01$), the scores of GMFM-D, GMFME, 6MWD, WeeFIM in both group are increased ($p < 0.01$ in all indicators). When compared with control group, AT group had significantly lower MAS scores compared to the control group ($p < 0.01$), indicating reduced muscle tension. Moreover, AT group showed significantly higher scores in GMFM-D, GMFM-E, 6MWD, and WeeFIM compared to the control group ($p < 0.01$ in all indicators), indicating improved gross motor function and functional independence. The study also revealed an inverse correlation between the children's age and treatment efficacy ($r = -0.496$, $p < 0.01$ in AT group, $r = -0.540$, $p < 0.01$ in control group), highlighting the importance of early intervention in the management of CP in children. Conclusion: These findings suggest that AT may effectively enhance gross motor function and alleviate associated symptoms in children diagnosed with spastic CP. Moreover, early initiation of treatment is crucial to maximize therapeutic efficacy in children with spastic CP.

PMID: [37667737](#)

22. Targeting the metabolic profile of amino acids to identify the key metabolic characteristics in cerebral palsy

Dan Wang, Juan Song, Ye Cheng, Yiran Xu, Lili Song, Yimeng Qiao, Bingbing Li, Lei Xia, Ming Li, Jin Zhang, Yu Su, Ting Wang, Jian Ding, Xiaoyang Wang, Sujuan Wang, Changlian Zhu, Qinghe Xing

Front Mol Neurosci. 2023 Aug 17;16:1237745. doi: 10.3389/fnmol.2023.1237745. eCollection 2023.

Background: Cerebral palsy (CP) is a neurodevelopmental disorder characterized by motor impairment. In this study, we aimed to describe the characteristics of amino acids (AA) in the plasma of children with CP and identify AA that could play a potential role in the auxiliary diagnosis and treatment of CP. **Methods:** Using high performance liquid chromatography, we performed metabolomics analysis of AA in plasma from 62 CP children and 60 healthy controls. Univariate and multivariate analyses were then applied to characterize different AA. AA markers associated with CP were then identified by machine learning based on the Lasso regression model for the validation of intra-sample interactions. Next, we calculated a discriminant formula and generated a receiver operating characteristic (ROC) curve based on the marker combination in the discriminant diagnostic model. **Results:** A total of 33 AA were detected in the plasma of CP children and controls. Compared with controls, 5, 7, and 10 different AA were identified in total participants, premature infants, and full-term infants, respectively. Of these, β -amino-isobutyric acid [$p = 2.9 \times 10^{-4}$], Fold change (FC) = 0.76, Variable importance of protection (VIP) = 1.75], tryptophan [$p = 5.4 \times 10^{-4}$, FC = 0.87, VIP = 2.22], and asparagine [$p = 3.6 \times 10^{-3}$, FC = 0.82, VIP = 1.64], were significantly lower in the three groups of CP patients than that in controls. The combination of β -amino-isobutyric acid, tryptophan, and taurine, provided high levels of diagnostic classification and risk prediction efficacy for preterm children with an area under the curve (AUC) value of 0.8741 [95% confidence interval (CI): 0.7322-1.000]. The discriminant diagnostic formula for preterm infant with CP based on the potential marker combination was defined by $p = 1/(1 + e^{-(8.295 - 0.3848 \times \text{BAIBA} - 0.1120 \times \text{Trp} + 0.0108 \times \text{Tau})})$. **Conclusion:** Full-spectrum analysis of amino acid metabolomics revealed a distinct profile in CP, including reductions in the levels of β -amino-isobutyric acid, tryptophan, and taurine. Our findings shed new light on the pathogenesis and diagnosis of premature infants with CP.

PMID: [37664242](#)

23. Association between gestational levels of toxic metals and essential elements and cerebral palsy in children

Kjell Vegard F Weyde, Adriano Winterton, Pål Surén, Guro L Andersen, Torstein Vik, Guido Biele, Helle K Knutsen, Cathrine Thomsen, Helle M Meltzer, Thea S Skogheim, Stephanie M Engel, Heidi Aase, Gro D Villanger

Front Neurol. 2023 Aug 17;14:1124943. doi: 10.3389/fneur.2023.1124943. eCollection 2023.

Introduction: Cerebral palsy (CP) is the most common motor disability in childhood, but its causes are only partly known. Early-life exposure to toxic metals and inadequate or excess amounts of essential elements can adversely affect brain and nervous system development. However, little is still known about these as perinatal risk factors for CP. This study aims to investigate the associations between second trimester maternal blood levels of toxic metals, essential elements, and mixtures thereof, with CP diagnoses in children. **Methods:** In a large, population-based prospective birth cohort (The Norwegian Mother, Father, and Child Cohort Study), children with CP diagnoses were identified through The Norwegian Patient Registry and Cerebral Palsy Registry of Norway. One hundred forty-four children with CP and 1,082 controls were included. The relationship between maternal blood concentrations of five toxic metals and six essential elements and CP diagnoses were investigated using mixture approaches: elastic net with stability selection to identify important metals/elements in the mixture in relation to CP; then logistic regressions of the selected metals/elements to estimate odds ratio (OR) of CP and two-way interactions among metals/elements and with child sex and maternal education. Finally, the joint effects of the mixtures on CP diagnoses were estimated using quantile-based g-computation analyses. **Results:** The essential elements manganese and copper, as well as the toxic metal Hg, were the most important in relation to CP. Elevated maternal levels of copper (OR = 1.40) and manganese (OR = 1.20) were associated with increased risk of CP, while Hg levels were, counterintuitively, inversely related to CP. Metal/element interactions that were associated with CP were observed, and that sex and maternal education influenced the relationships between metals/elements and CP. In the joint mixture approach no significant association between the mixture of metals/elements and CP (OR = 1.00, 95% CI = [0.67, 1.50]) was identified. **Conclusion:** Using mixture approaches, elevated levels of copper and manganese measured in maternal blood during the second trimester could be related to increased risk of CP in children. The inverse associations between maternal Hg and CP could reflect Hg as a marker of maternal fish intake and thus nutrients beneficial for foetal brain development.

PMID: [37662050](#)

24. Abstracts for the American Academy for Cerebral Palsy and Developmental Medicine, 10-13 September 2023

No authors listed

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No abstract available

PMID: [37661789](#)

Prevention and Cure

25. GSDMD gene knockout alleviates hyperoxia-induced hippocampal brain injury in neonatal mice

Naga Venkata Divya Challa, Shaoyi Chen, Huijun Yuan, Matthew R Duncan, William Javier Moreno, Helen Bramlett, W Dalton Dietrich, Merline Benny, Augusto F Schmidt, Karen Young, Shu Wu

J Neuroinflammation. 2023 Sep 7;20(1):205. doi: 10.1186/s12974-023-02878-8.

Background: Neonatal hyperoxia exposure is associated with brain injury and poor neurodevelopment outcomes in preterm infants. Our previous studies in neonatal rodent models have shown that hyperoxia stimulates the brain's inflammasome pathway, leading to the activation of gasdermin D (GSDMD), a key executor of pyroptotic inflammatory cell death. Moreover, we found pharmacological inhibition of caspase-1, which blocks GSDMD activation, attenuates hyperoxia-induced brain injury in neonatal mice. We hypothesized that GSDMD plays a pathogenic role in hyperoxia-induced neonatal brain injury and that GSDMD gene knockout (KO) will alleviate hyperoxia-induced brain injury. **Methods:** Newborn GSDMD knockout mice and their wildtype (WT) littermates were randomized within 24 h after birth to be exposed to room air or hyperoxia (85% O₂) from postnatal days 1 to 14. Hippocampal brain inflammatory injury was assessed in brain sections by immunohistology for allograft inflammatory factor 1 (AIF1) and CD68, markers of microglial activation. Cell proliferation was evaluated by Ki-67 staining, and cell death was determined by TUNEL assay. RNA sequencing of the hippocampus was performed to identify the transcriptional effects of hyperoxia and GSDMD-KO, and qRT-PCR was performed to confirm some of the significantly regulated genes. **Results:** Hyperoxia-exposed WT mice had increased microglia consistent with activation, which was associated with decreased cell proliferation and increased cell death in the hippocampal area. Conversely, hyperoxia-exposed GSDMD-KO mice exhibited considerable resistance to hyperoxia as O₂ exposure did not increase AIF1 + , CD68 + , or TUNEL + cell numbers or decrease cell proliferation. Hyperoxia exposure differentially regulated 258 genes in WT and only 16 in GSDMD-KO mice compared to room air-exposed WT and GSDMD-KO, respectively. Gene set enrichment analysis showed that in the WT brain, hyperoxia differentially regulated genes associated with neuronal and vascular development and differentiation, axonogenesis, glial cell differentiation, hypoxia-induced factor 1 pathway, and neuronal growth factor pathways. These changes were prevented by GSDMD-KO. **Conclusions:** GSDMD-KO alleviates hyperoxia-induced inflammatory injury, cell survival and death, and alterations of transcriptional gene expression of pathways involved in neuronal growth, development, and differentiation in the hippocampus of neonatal mice. This suggests that GSDMD plays a pathogenic role in preterm brain injury, and targeting GSDMD may be beneficial in preventing and treating brain injury and poor neurodevelopmental outcomes in preterm infants.

PMID: [37679766](#)