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Cerebral palsy research news

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CP Alliance Chair of Cerebral Palsy Research

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Interventions and Management

1. Exploring Kinetic and Kinematic Finger Individuation Capability in Children With Hemiplegic Cerebral Palsy
James V McCall, Xiaogang Hu, Derek G Kamper

Percept Mot Skills. 2022 Dec 13;315125221145220. doi: 10.1177/00315125221145220. Online ahead of print.

While fine manual dexterity develops over time, the extent to which children show independent control of their digits in each hand and the impact of perinatal brain injury on this individuation have not been well quantified. Our goal in this study was to assess and compare finger force and movement individuation in 8-14 year old children with hemiplegic cerebral palsy (hCP; n = 4) and their typically developing peers (TD; n = 10). We evaluated finger force individuation with five independent load cells and captured joint movement individuation with video tracking. We observed no significant differences in individuation indices between the dominant and non-dominant hands of TD children, but individuated force and movement were substantially reduced in the paretic versus non paretic hands of children with hCP ($p < 0.001$). In TD participants, the thumb tended to have the greatest level of independent control. This small sample of children with hCP showed substantial loss of individuation in the paretic hand and some deficits in the non-paretic hand, suggesting possible benefit from targeted training of digit independence in both hands for children with CP.

PMID: 36514237

2. Does the Addition of Intrathecal Baclofen Along with or After Soft-Tissue Hip Adductor Surgery Decrease the Need for Hip Reconstruction Compared with Soft-Tissue Surgery Alone for Children with Nonambulatory Cerebral Palsy?
Ali Asma, Armagan Can Ulusaloglu, Jason J Howard, Kenneth J Rogers, Freeman Miller, Michael Wade Shrader

Indian J Orthop. 2022 Nov 1;56(12):2176-2181. doi: 10.1007/s43465-022-00762-w. eCollection 2022 Dec.

Purpose: Intrathecal baclofen (ITB) is a well-known treatment option for cerebral palsy (CP) spasticity. The combination of soft-tissue release and ITB for spasticity is common. This study compared patients who had soft-tissue release before ITB (PRE-ITB), soft-tissue release at the same time as ITB (ST-ITB), and no ITB (NON-ITB) but had soft-tissue release at a similar age as PRE-ITB. Methods: Inclusion criteria were a spastic or mixed nonambulatory CP diagnosis, prior hip adductor surgery, no prior reconstructive surgery, and at least a five-year post-operative follow-up. Thirty hips were identified as PRE-ITB, 20 hips as ST-ITB, and 43 hips as NON-ITB. The primary outcome variables were the subsequent hip surgery during the study period and/or a migration percentage ≥ 50% at the final follow-up defined as "unsuccessful hip." Results: The mean follow-up duration was 9.0 years (SD 2.4) for PRE-ITB, 9.4 (SD 3.6) for ST-ITB, and 9.3 (SD 3) for NON-ITB. The odds of unsuccessful outcomes were not different between NON-ITB and PRE-ITB but were lower for the ST-ITB group. The need for subsequent osteotomies or revision adductor surgery was significantly higher in ST-ITB compared with PRE-ITB ($p = 0.02$) or NON-ITB ($p = 0.015$). The incidence of surgical site infection over the whole follow-up period was higher in ST-ITB

(40%) compared with PRE-ITB (13.3%, p = 0.035) and NON-ITB (0, p < 0.001). Conclusion: The addition of tone management with ITB did not reduce the need for later hip surgery but did increase the risk for surgical site infection.

PMID: 36507212

3. Letter to the Editor Regarding "Failure of Hip Reconstruction in Children With Cerebral Palsy: What Are the Risk Factors?"
Ahmet Imerci, İsmail Güler, Nevres Hürriyet Aydoğan

J Pediatr Orthop. 2022 Dec 15. doi: 10.1097/BPO.0000000000002325. Online ahead of print.

No abstract available

PMID: 36517916

4. Lumbar Plexus Nerve Blocks for Perioperative Pain Management in Cerebral Palsy Patients Undergoing Hip Reconstruction: More Effective Than General Anesthesia and Epidurals
Arianna Trionfo, Remy Zimmerman, Kelly Gillock, Ross Budziszewski, Aysha Hasan

J Pediatr Orthop. 2023 Jan 1;43(1):e54-e59. doi: 10.1097/BPO.0000000000002285. Epub 2022 Oct 26.

Background: Hip reconstruction in patients with cerebral palsy (CP) is associated with. significant postoperative pain. However, adequate analgesia can be difficult to achieve. in this population due to spasticity, communication barriers, and postoperative. spasticity. Recently, multimodal pain management techniques such as epidurals and. regional nerve blocks have been described for postoperative pain control, but it is unclear if 1 technique is more beneficial. The purpose of this study was to compare the outcomes of different perioperative pain management techniques. Methods: This study is a retrospective review of a consecutive series of children with CP over a 5-year period at a single pediatric tertiary-care hospital who underwent hip reconstruction (proximal femoral osteotomy with or without a pelvic osteotomy). Patients were subdivided based on their anesthetic protocol into the following groups: general anesthesia alone (G), general anesthesia with an epidural (E), and general anesthesia with lumbar plexus block (LPB). Our primary outcome was cumulative postoperative narcotic consumption (converted to morphine equivalents). Secondary outcomes included length of stay (LOS), average postoperative heart rate, and pain scores. analysis of variance testing was utilized to compare differences between the groups. Results: Fifty-four patients who underwent hip reconstruction were included: 19 in the G group, 18 in the E group, and 17 in the LPB group. LOS was significantly higher in the E group compared with the G and LPB groups: $F(2,51)=3.58$, $P=0.04$. The average pain score was significantly lower in the LPB group compared with the others: $F(2,51)=4.26$, $P=0.02$. The average postoperative heart rate was significantly lower in the LPB group: $F(2,51)=7.08$, $P<0.01$. Postoperative narcotic consumption was significantly lower in the LPB group: $F(2,51)=11.57$, $P<0.01$. Conclusion: The LPB patients required the least amount of narcotics compared with the other groups. This, combined with a lower perioperative heart rate and shorter LOS would suggest these patients experienced less pain over the time of their in-patient stay. In comparison to general anesthesia alone and epidural anesthesia, lumbar plexus nerve blocks are an effective pathway for postoperative pain control after hip reconstruction in a CP population. Level of evidence: Level III-Case control or retrospective comparative study.

PMID: 36509456

5. Prevalence and determinants of hip pain in non-ambulatory cerebral palsy children: a retrospective cohort study
Silvia Faccioli, Silvia Sassi, Adriano Ferrari, Elena Corradini, Francesca Toni, Shaniko Kaleci, Francesco Lombardi, Alessandro Picelli, Maria G Benedetti

Eur J Phys Rehabil Med. 2022 Dec 12. doi: 10.23736/S1973-9087.22.07725-5. Online ahead of print.

Background: Hip pain is common in cerebral palsy children, particularly at Gross-Motor Function Classification System level IV-V. It is associated to hip displacement and relates to the migration percentage. Recent literature suggested early reconstructive bone surgery, as the best approach to prevent hip luxation, then hip pain. Still, high rates of hip pain are

reported. Aim: To investigate prevalence and determinants of hip pain in an Italian cerebral palsy sample. Design: Single-center retrospective cohort study. Setting: Inpatient and outpatient. Population: Patients with spastic or dyskinetic cerebral palsy, Gross-Motor Function Classification System level IV or V, age 0-18. Methods: A chart review was implemented to report hip pain, as a dichotomous variable (pain/no pain), age, sex, cerebral palsy subtype, Gross-Motor Function level, lumbar scoliosis, migration percentage, previous orthopedic surgery, or botulinum injections, oral or intrathecal baclofen, drug-resistant epilepsy, assistive devices for standing or walking. Descriptive statistics and a multivariate logistic stepwise regression were performed. Results: A total of 504 subjects were included: 302 level V, 209 females, 432 spastics. The mean length of follow-up was 6 years. The overall prevalence of hip pain was 8.9% (6.3% were at level V) and of hip dislocation was 19% (15.9% were at level V). Just 39% of dislocated hips were painful. Children at spastic subtype and level V were predominantly affected. Botulinum and soft tissue surgery related to lower rates of hip pain, without statistical significance. Age (OR 1.19, 95%CI 1.14-1.25, P value 0.000), sex (OR 1.72, 95%CI 1.18-2.52, P value 0.005), migration percentage (OR 1.02, 95%CI 1.02-1.03, P value 0.000) and lumbar scoliosis (OR 1.32, 95%CI 0.86-2.01, P value 0.200) resulted significant independent determinants of hip pain. Conclusions: Hip pain relates with the migration percentage, but not all dislocated hips become painful. Hip pain may be transient and requires a targeted and individualized approach. Children at spastic subtype and level V were predominantly affected. Age and sex are confirmed as determinants. Specific validated measures are to be implemented to assess hip pain. Clinical rehabilitation impact: Considering severe non-ambulatory cerebral palsy patients, pain and quality of life should be considered as outcomes, in the management of hip luxation.

PMID: 36507793

6. Revising the stretch reflex threshold method to measure stretch hyperreflexia in cerebral palsy
Pedro Valadão, Lynn Bar-On, Francesco Cenni, Harri Piitulainen, Janne Avela, Taija Finni

Front Bioeng Biotechnol. 2022 Nov 23;10:897852. doi: 10.3389/fbioe.2022.897852. eCollection 2022.

Hyper-resistance is an increased resistance to passive muscle stretch, a common feature in neurological disorders. Stretch hyperreflexia, an exaggerated stretch reflex response, is the neural velocity-dependent component of hyper-resistance, and has been quantitatively measured using the stretch reflex threshold (i.e., joint angle at the stretch reflex electromyographic onset). In this study, we introduce a correction in how the stretch reflex threshold is calculated, by accounting for the stretch reflex latency (i.e., time between the stretch reflex onset at the muscle spindles and its appearance in the electromyographic signal). Furthermore, we evaluated how this correction affects the stretch reflex threshold in children and young adults with spastic cerebral palsy. A motor-driven ankle dynamometer induced passive ankle dorsiflexions at four incremental velocities in 13 children with cerebral palsy (mean age: 13.5 years, eight males). The stretch reflex threshold for soleus and medial gastrocnemius muscles was calculated as 1) the joint angle corresponding to the stretch reflex electromyographic onset (i.e., original method); and as 2) the joint angle corresponding to the electromyographic onset minus the individual Hoffmann-reflex latency (i.e., latency corrected method). The group linear regression slopes between stretch velocity and stretch reflex threshold differed in both muscles between methods ($p < 0.05$). While the original stretch reflex threshold was velocity dependent in both muscles ($p < 0.05$), the latency correction rendered it velocity independent. Thus, the effects of latency correction on the stretch reflex threshold are substantial, especially at higher stretch velocities, and should be considered in future studies.

PMID: 36507281

7. Comprehensive personalized ankle joint shape analysis of children with cerebral palsy from pediatric MRI
Yue Cheng, Rodolphe Bailly, Claire Scavinner-Dorval, Benjamin Fouquet, Bhushan Borotikar, Douraied Ben Salem, Sylvain Brochard, François Rousseau

Front Bioeng Biotechnol. 2022 Nov 25;10:1059129. doi: 10.3389/fbioe.2022.1059129. eCollection 2022.

Cerebral palsy, a common physical disability in childhood, often causes abnormal patterns of movement and posture. To better understand the pathology and improve rehabilitation of patients, a comprehensive bone shape analysis approach is proposed in this article. First, a group analysis is performed on a clinical MRI dataset using two state-of-the-art shape analysis methods: ShapeWorks and a voxel-based method relying on Advanced Normalization Tools (ANTs) registration. Second, an analysis of three bones of the ankle is done to provide a complete view of the ankle joint. Third, a bone shape analysis is carried out at subject level to highlight variability patterns for personnalized understanding of deformities.

PMID: 36507255

8. Functional Neuroplasticity and Motor Skill Change Following Gross Motor Interventions for Children With Diplegic Cerebral Palsy
Alicia J Hilderley, F Virginia Wright, Margot J Taylor, Joyce L Chen, Darcy Fehlings

Neurorehabil Neural Repair. 2022 Dec 15;15459683221143503. doi: 10.1177/15459683221143503. Online ahead of print.

Background: Gross motor intervention designs for children with diplegic cerebral palsy (DCP) require an improved understanding of the children's potential for neuroplasticity. Objective: To identify relations between functional neuroplasticity and motor skill changes following gross motor interventions for children with DCP. Methods: There were 17 participants with DCP (ages 8-16 years; 6 females; Gross Motor Function Classification System Level I [n = 9] and II [n = 8]). Each completed a 6-week gross motor intervention program that was directed toward achievement of individualized motor/physical activity goals. Outcomes were assessed pre/post and 4 to 6 months post-intervention (follow-up). An active ankle dorsiflexion task was completed during functional magnetic resonance imaging. The ratio of motor cortical activation volume in each hemisphere was calculated using a laterality index. The Challenge was the primary gross motor skill measure. Change over time and relations among outcomes were evaluated. Results: Challenge scores improved post-intervention (4.57% points [SD 4.45], P = .004) and were maintained at follow-up (0.75% [SD 6.57], P = 1.000). The laterality index for dominant ankle dorsiflexion increased (P = .033), while non-dominant change was variable (P = .534). Contralateral activation (laterality index ≥+0.75) was most common for both ankles. Challenge improvements correlated with increased ipsilateral activity (negative laterality index) during non-dominant dorsiflexion (r = -.56, P = .045). Smaller activation volume during non-dominant dorsiflexion predicted continued gross motor gains at follow-up (R2 = .30, P = .040). Conclusions: Motor cortical activation during non-dominant ankle dorsiflexion is a modest indicator of the potential for gross motor skill change. Further investigation of patterns of neuroplastic change will improve our understanding of effects. Clinicaltrials.gov registry: NCT02584491 and NCT02754128.

PMID: 36524254

9. What Do We Know about Frame Running? A Narrative Review
Lucas de Assis Voltolini, Pedro Henrique De Araújo, Diego Antunes, Gabriel Benedito Lima, Ricardo Dantas de Lucas, Gabriela Fischer

Review Curr Sports Med Rep. 2022 Dec 1;21(12):448-453. doi: 10.1249/JSR.0000000000001018.

This narrative review aims to provide a general overview of the literature about frame running, which is a recent modality of Para-Athletics. Frame running is practiced by using a tricycle without pedals called PETRA RaceRunner, by people with moderate to severe cerebral palsy and other lower limb functional limitations. Briefly, the movement pattern is very similar to walking and running. This review includes studies from scientific databases and content of official sports web sites by using the keywords "framerunning," "racerunning," and "petra racerunning." According to our search, this narrative review highlighted three themes involving the practice of frame running, namely health and quality of life, sports classification, and training and testing in the frame running context.

PMID: 36508601

10. The Relationship between Family Empowerment and Fine Motor, Gross Motor, and Cognitive Skills in Young Children with Cerebral Palsy
Samuel R Pierce, Julie Skorup, Athylia C Paremski, Laura A Prosser

Child Care Health Dev. 2022 Dec 15. doi: 10.1111/cch.13091. Online ahead of print.

Background: Family empowerment in families of young children with cerebral palsy (CP) is an important consideration because the first few years of life can be overwhelming for parents. The purpose of this research was to investigate the relationship between family empowerment, fine motor (FM), gross motor (GM), and cognitive development in children with CP who were under three years of age. Methods: Forty-one children with a mean age of 23.8 months participated in this study. The FES was completed by the participants' parents while the FM, GM, and cognitive subscales of the Bayley Scales of Infant and Toddler Development Third edition (B-III) were administered by physical therapists. Results: Statistically significant

positive correlations were found between the FES total and B-III raw scores for FM, GM, and cognitive subscales with coefficients ranging from 0.35-0.41. Significant relationships were also found between the FES Community subscale and the B-III FM, GM, and cognitive subscales. Conclusions: This study provides evidence of a relationship between family empowerment and FM, GM, and cognitive abilities in young children with CP, with a greater severity of impairments related to lower levels of caregiver empowerment.

PMID: 36519729

11. The Transformative Nature of Residential Immersive Life Skills Programs: Integrating Findings from a Five-Year Prospective Study of Program Opportunities, Youth Experiences, and Outcomes
Gillian King, Amy C McPherson, Shauna Kingsnorth, Jan Willem Gorter

Review Int J Environ Res Public Health. 2022 Nov 29;19(23):15865. doi: 10.3390/ijerph192315865.

Youth with disabilities often experience limited opportunities to acquire the life skills needed in adulthood. As a result, life skills programs are provided to support life skill development; however, little is known about the active ingredients of these programs, and the sustainability of their effects over time. Accordingly, the aim was to synthesize the findings of a five-year study examining the opportunities, experiences, and outcomes of residential immersive life skills (RILS) programs for youth with disabilities. A multi-method prospective study was conducted involving 38 youth ages 14 to 21 with disabilities (e.g., cerebral palsy, spina bifida) attending one of three RILS programs held over three summers. Program opportunities, youth experiences, and outcomes (self-determination, self-efficacy) were assessed pre- and post-program and 3 and 12 months post-program using standardized questionnaires. Pre-program, 3-month, and 12-month follow-up interviews were held with youth and parents. This research synthesis integrates the findings from nine published articles that used a variety of qualitative, quantitative, and mixed methods approaches. RILS programs provided rich opportunities for youth to experience meaningful social connections, psychological engagement, and choice and control, which were associated with changes over time in multiple domains related to personal growth and preparation for adulthood. Overall, the findings point to the transformative power of RILS programs to propel new life directions for some youth. By creating opportunities for meaningful, challenging, and supportive experiences fulfilling basic needs for relatedness, competency, and autonomy, RILS programs motivate youth to grow and change. More study is needed of program opportunities and capacity-enhancing experiences, as well as longitudinal studies of youth life outcomes. RILS programs have appreciable value in preparing youth for the transition to adult roles and responsibilities.

PMID: 36497940

12. Playfully Assessing Lower Extremity Selective Voluntary Motor Control in Children With Cerebral Palsy: Psychometric Study
Annina Fahr, Julia Balzer, Jeffrey W Keller, Hubertus J A van Hedel

JMIR Rehabil Assist Technol. 2022 Dec 16;9(4):e39687. doi: 10.2196/39687.

Background: Objective measures specifically assessing selective voluntary motor control are scarce. Therefore, we have developed an interval-scaled assessment based on accelerometers. Objective: This study provided a preliminary evaluation of the validity and reliability of this novel gamelike assessment measuring lower limb selective voluntary motor control in children with cerebral palsy (CP). Methods: Children with CP and their neurologically intact peers were recruited for this psychometric evaluation of the assessgame. The participants played the assessgame and steered an avatar by selective hip, knee, or ankle joint movements captured with accelerometers. The assessgame's scores provide information about the accuracy of the selective movement of the target joint and the amplitude and frequency of involuntary movements occurring in uninvolved joints. We established discriminative validity by comparing the assessgame scores of the children with CP with those of the neurologically intact children, concurrent validity by correlations with clinical scores and therapists' opinions, and relative and absolute test-retest reliability. Results: We included 20 children with CP (mean age 12 years and 5 months, SD 3 years and 4 months; Gross Motor Function Classification System levels I to IV) and 31 neurologically intact children (mean age 11 years and 1 month, SD 3 years and 6 months). The assessgame could distinguish between the children with CP and neurologically intact children. The correlations between the assessgame's involuntary movement score and the therapist's rating of the occurrence of involuntary movements during the game were moderate (Spearman ρ=0.56; P=.01), whereas the correlations of the assessgame outcomes with the Selective Control Assessment of the Lower Extremity and Gross Motor Function Classification System were low and not significant ($|\rho| \leq 0.39$). The intraclass correlation coefficients were >0.85 and

indicated good relative test-retest reliability. Minimal detectable changes amounted to 25% (accuracy) and 44% (involuntary movement score) of the mean total scores. The percentage of children able to improve by the minimal detectable change without reaching the maximum score was 100% (17/17) for the accuracy score and 94% (16/17) for the involuntary movement score. Conclusions: The assessgame proved reliable and showed discriminative validity in this preliminary evaluation. Concurrent validity was moderate with the therapist's opinion but relatively poor with the Selective Control Assessment of the Lower Extremity. We assume that the assessment's gamelike character demanded various other motor control aspects that are less considered in current clinical assessments. Keywords: accelerometer; assessment; avatar; cerebral palsy; child; digital health; eHealth; game; interactive computer play; joint; limb; lower extremities; lower extremity; mirror movements; motor; movement; neurorehabilitation; pediatric; physiotherapist; physiotherapy; rehabilitation; reliability; selective motor control; validity.

PMID: 36525299

13. Low-Cost Human-Machine Interface for Computer Control with Facial Landmark Detection and Voice Commands
Pablo Ramos, Mireya Zapata, Kevin Valencia, Vanessa Vargas, Carlos Ramos-Galarza

Sensors (Basel). 2022 Nov 29;22(23):9279. doi: 10.3390/s22239279.

Nowadays, daily life involves the extensive use of computers, since human beings are immersed in a technological society. Therefore, it is mandatory to interact with computers, which represents a true disadvantage for people with upper limb disabilities. In this context, this work aims to develop an interface for emulating mouse and keyboard functions (EMKEY) by applying concepts of artificial vision and voice recognition to replace the use of hands. Pointer control is achieved by head movement, whereas voice recognition is used to perform interface functionalities, including speech-to-text transcription. To evaluate the interface's usability and usefulness, two studies were carried out. The first study was performed with 30 participants without physical disabilities. Throughout this study, there were significant correlations found between the emulator's usability and aspects such as adaptability, execution time, and the participant's age. In the second study, the use of the emulator was analyzed by four participants with motor disabilities. It was found that the interface was best used by the participant with cerebral palsy, followed by the participants with upper limb paralysis, spina bifida, and muscular dystrophy. In general, the results show that the proposed interface is easy to use, practical, fairly accurate, and works on a wide range of computers.

PMID: 36501980

14. Respiratory Health Inequities among Children and Young Adults with Cerebral Palsy in Aotearoa New Zealand: A Data Linkage Study
Alexandra Sorhage, Samantha Keenan, Jimmy Chong, Cass Byrnes, Amanda Marie Blackmore, Anna Mackey, Timothy Hill, Dug Yeo Han, Ngaire Susan Stott

J Clin Med. 2022 Nov 25;11(23):6968. doi: 10.3390/jcm11236968.

(1) Background: Respiratory disease is a leading cause of morbidity, mortality, and poor quality of life in children with cerebral palsy (CP). This study describes the prevalence of CP-related respiratory disease and the non-modifiable risk factors for respiratory-related hospital admissions in the Aotearoa New Zealand population. (2) Methods: New Zealand Cerebral Palsy Register (NZCPR) participant data and de-identified data from the National Minimum Dataset and Pharmaceutical Dispensing Collections were linked to identify all respiratory-related hospital admissions and respiratory illness-related antibiotic exposure over 5 years in individuals with CP (0-26 years). (3) Results: Risk factors for respiratory-related hospital admissions included being classified Gross Motor Function Classification System (GMFCS) IV or V compared to GMFCS I [OR = 4.37 (2.90-6.58), p < 0.0001; OR = 11.8 (7.69-18.10), p < 0.0001, respectively,]; having ≥2 antibiotics dispensed per year [OR = 4.42 (3.01-6.48), p < 0.0001]; and being of Māori ethnicity [OR = 1.47 (1.13-1.93), p < 0.0047]. Māori experienced health inequities compared to non-Māori, with greater functional disability, and also experienced greater antibiotic dispensing than the general population. (4) Conclusion: Māori children and young adults have a higher risk of respiratory-related illness. Priority should be given to the screening for potentially modifiable risk factors for all children with CP from diagnosis onwards in a way that ensures Māori health equity.

PMID: 36498542

15. Measuring global activity performance in children with cerebral palsy in West Africa: validation of an adapted version of the ACTIVLIM-CP questionnaire
Emmanuel Segnon Sogbossi, Carlyne Arnould, Toussaint G Kpadonou, Charles Sebiyo Batcho, Yannick Bleyenheuft

Disabil Rehabil. 2022 Dec 10;1-10. doi: 10.1080/09638288.2022.2154083. Online ahead of print.

Purpose: To calibrate a West-African version of the ACTIVLIM-CP questionnaire (ACTIVLIM-CP-WA) for children with cerebral palsy (CP). Materials and methods: We recruited 287 children with CP of various age range: 2-6 years (n = 117, preschoolers), 6-12 years (n = 96, children) and 12-19 years (n = 74, adolescents). Caregivers of children of each age range completed the experimental version of the ACTIVLIM-CP-WA including 76 (preschoolers), 78 (children) and 76 (adolescents) global daily life activities. Responses were analyzed using the Rasch RUMM2030 software. Results: The final West-African version of ACTIVLIM-CP including 31 items (both common and age-specific items) defined a unidimensional, linear scale with well-discriminated response categories. It presented a high internal consistency (R = 0.94). Moreover, all items were locally independent and the item difficulty hierarchy was invariant regarding caregivers' education, children's age and gender, MACS and GMFCS levels. The ACTIVLIM-CP-WA measures were significantly correlated ($p < 0.05$) with Gross Motor Function Classification System ($\rho = -0.77$), Manual Ability Classification System ($\rho = -0.75$), Box and Block test (dominant hand $r = 0.51$; non-dominant hand $r = 0.49$), One-minute walking test ($r = 0.28$), and Timed up and Go test ($r = -0.40$). Conclusions: The ACTIVLIM-CP-WA questionnaire provides a valid and reliable tool that has the potential to follow children's evolution and quantify changes consecutive to neurorehabilitation in Sub-Saharan Africa. IMPLICATIONS FOR REHABILITATION: The West-African version of the ACTIVLIM-CP questionnaire (ACTIVLIM-CP-WA) measures global activities requiring a combination of lower and upper extremities in children with cerebral palsy. As a Rasch-built scale, measures are unidimensional and linear to document changes in children with cerebral palsy from 2 to 19 years in Sub-Saharan Africa. Rehabilitation professionals are encouraged to use the ACTIVLIM-CP-WA questionnaire as a psychometrically robust assessment tool measuring the global performance in daily life activities in children with cerebral palsy in Sub-Saharan Africa.

PMID: 36495153

16. Integrative Multi-Omics Research in Cerebral Palsy: Current Progress and Future Prospects
Chengqi Xin, Xin Guan, Liang Wang, Jing Liu

Review Neurochem Res. 2022 Dec 13. doi: 10.1007/s11064-022-03839-y. Online ahead of print.

Cerebral palsy (CP) describes a heterogeneous group of non-progressive neurodevelopmental disorders affecting movement and posture. The etiology and diagnostic biomarkers of CP are a hot topic in clinical research. Recent advances in omics techniques, including genomics, epigenomics, transcriptomics, metabolomics and proteomics, have offered new insights to further understand the pathophysiology of CP and have allowed for identification of diagnostic biomarkers of CP. In present study, we reviewed the latest multi-omics investigations of CP and provided an in-depth summary of current research progress in CP. This review will offer the basis and recommendations for future fundamental research on the pathogenesis of CP, identification of diagnostic biomarkers, and prevention strategies for CP.

PMID: 36512293

17. Prenatal exposure to antibiotics and risk of neurodevelopmental disorders in offspring: A systematic review and meta-analysis
Qiuji Tao, Yajun Shen, Yang Li, Huan Luo, Meng Yuan, Jing Gan

Front Neurol. 2022 Nov 25;13:1045865. doi: 10.3389/fneur.2022.1045865. eCollection 2022.

Background and purpose: A growing body of research suggests that inflammation and maternal infections may lead to an increased risk of neurodevelopmental problems such as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), cerebral palsy (CP), and epilepsy in offspring. The aim of this study was to observe the connection between prenatal antibiotic exposure and the risk of these neurodevelopmental disorders in offspring. Patients and methods: A comprehensive search was conducted in the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Google

Scholar, and Scopus databases for observational studies that looked into the link between prenatal exposure to antibiotics and the risk of neurodevelopmental problems in offspring, published from 1 January 1950 to 31 January 2022. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included studies. Data were analyzed using the STATA version 12 software, and an odds ratio (OR) with a 95% confidence interval (CI) was reported. Results: A total of 15 studies were included in the meta-analysis. Prenatal antibiotic exposure was associated with the increased risk of ADHD (OR = 1.14; 95% CI = 1.13 to 1.15; I 2 = 0%) and epilepsy (OR = 1.34; 95% CI = 1.02 to 1.66; I 2 = 96.8%). The link between prenatal antibiotic exposure and the risk of ASD [OR = 1.09; 95 % CI = 0.88 to 1.31; I 2 = 78.9%] and CP [OR = 0.99; 95% CI = 0.56 to 1.43; I 2 = 91%] was found to be non-significant. In all of the included prospective cohort studies, subgroup analysis suggested a significant association between prenatal antibiotic exposure and the incidence of ASD [OR = 1.17; 95% CI = 1.03 to 1.31; I 2 = 48.1%] and CP [OR = 1.18; 95% CI = 1.02 to 1.34; I 2 = 0%]. Conclusion: Prenatal antibiotic exposure during pregnancy is linked to a higher incidence of ADHD and epilepsy in the offspring. Further prospective studies that compare prenatal antibiotic use and are adjusted for various confounders are needed to further assess the association of prenatal antibiotic exposure and neurological disorders in offspring. Systematic review registration: https://www.crd.york.ac.uk/prospero/, identifier: CRD42022306248.

PMID: 36504646

18. Neonatal outcome of infants with umbilical cord arterial pH less than 7
So Ling Lau, Zara Lin Zau Lok, Shuk Yi Annie Hui, Genevieve Po Gee Fung, Hugh Simon Lam, Tak Yeung Leung

Acta Obstet Gynecol Scand. 2022 Dec 12. doi: 10.1111/aogs.14494. Online ahead of print.

Introduction: Umbilical arterial pH of less than 7 is often used as the threshold below which the risks of neonatal death and adverse long-term neurological outcomes are considered to be higher. Yet within the group with pH <7, the risks have not been further stratified. Here, we aimed to investigate the predictors of adverse long-term outcomes of this group of infants. Material and methods: This was a retrospective study of 248 infants born after 34 weeks of gestation in a tertiary obstetric unit, between 2003 and 2017, with cord arterial pH <7 or base excess ≤-12 mmol/L at birth. The infants were categorized into two groups: (1) intact survivors, or (2) neonatal/infant deaths or cerebral palsy or developmental delay. The umbilical arterial pH and base excess levels, Apgar scores, mode of delivery, gestational age, small for gestational age, birth in the era before the implementation of neonatal hypothermic therapy, and the presence of a known sentinel event, were compared between the groups using univariate analysis followed by multivariate analysis. Results: Among the 248 infants, there were 222 intact survivors (89.5%) and 26 infants with poor outcomes (10.5%), including eight deaths (3.2%) and 18 (7.3%) with cerebral palsy and/or developmental delay. Univariate analysis showed that infants with adverse outcomes had significantly lower cord arterial pH (6.85 vs. 6.95, with $p < 0.001$), lower cord arterial base excess (-19.95 vs. -15.90 mmol/L, $p < 0.001$), a higher proportion of having AS at 5 min <7 (65.4% vs. 13.1%, $p < 0.001$), and a higher proportion of having a sentinel event (34.6% vs. 16.7%, $p = 0.034$). Multivariate analysis confirmed cord arterial pH of <6.9 and an Apgar score at 5 min <7 as independent prognostic factors (the adjusted odds ratios were 4.64 and 6.62, respectively). The risk of adverse outcome increased from 4.3% when the arterial pH was between 6.9 and <7, to 30% when the pH was <6.9. Conclusions: Infants born with umbilical artery pH <7 still have a high chance of 89.5% to become intact survivors. A cord arterial pH of <6.9 and an Apgar score at 5 min <7 are independent prognostic factors for neonatal/infant death or adverse long-term neurological outcomes.

PMID: 36504253

19. Caffeine and cerebral palsy: A systematic review of randomized controlled trials and cohort studies
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Review Complement Ther Med. 2022 Dec 7;72:102906. doi: 10.1016/j.ctim.2022.102906. Online ahead of print.

Objective: To systematically review the effects of caffeine on the development of cerebral palsy (CP). Design: Systematic review. Setting: A search of five databases was performed to identify randomized controlled trials (RCT) or cohort studies published through May 2022. Studies conducted on newborns at risk of developing CP upon receiving caffeine in the first days of life were included as well. Two independent researchers assessed the screening, data extraction, and methodological quality assessment. Main outcome measures: Percentage of children with CP. Results: Four studies met our inclusion criteria. The only RCT found a decreased risk (approximately 40 %) of developing CP with 20 mg/kg caffeine citrate (OR 0.59, 95 % CI 0.39, 0.89). In addition, when comparing the period over which caffeine citrate was administered, one retrospective cohort study reported that infants who received caffeine up to the second day of life were also less likely to develop CP. Some

methodological issues should be highlighted: in the RCT, the differences between the groups with respect to loss to follow-up were not explored. Similarly, intention-to-treat analyses were not performed. Most cohort studies have not adequately identified the primary confounding factors. Conclusions: Caffeine could be an important intervention in preventing CP. However, few studies have assessed the effects of caffeine on the risk of CP development. Due to methodological differences, no recommendation regarding its use can be safely made. The findings suggest a positive effect of caffeine citrate in the early stages of life with approximately 20 mg/kg of weight; however, well-designed RCTs with adequate sample size and power, randomization process, outcome measurement, and data analysis are still required.

PMID: 36496206

20. Neurodevelopmental Outcome in Patients with Typical Imaging Features of Injury as a Result of Neonatal Hypoglycemia
Emek Uyur Yalçın, Hülya Maraş Genç, Asuman Bayhan, Yonca Anık, Bülent Kara

Noro Psikiyatr Ars. 2022 Nov 8;59(4):296-302. doi: 10.29399/npa.27997. eCollection 2022.

Introduction: Previous reports described a pattern of hypoglycemia-induced damage predominantly affecting the parieto-occipital regions. The long-term neurological sequelae of severe neonatal hypoglycemic encephalopathy include developmental delay, poor head growth, learning or behavioral difficulties, visual impairment, and epilepsy. This study reports neurodevelopmental outcome of children with neonatal hypoglycemia-associated parieto-occipital brain injury who were evaluated in our pediatric neurology outpatient clinic for different neurological complaints. Methods: We retrospectively reviewed patients who were followed at Kocaeli University Hospital, Pediatric Neurology Department between 2007 and 2015. Patients (n=42) with predominately parieto-occipital lesions on magnetic resonance imaging (MRI) with the typical pattern of neonatal hypoglycemia were evaluated. Patients with documented hypoglycemia (n=21) were included in this study. Patients (n=9) with recurrent episodes of hypoglycemia longer than 12 hours were evaluated as prolonged hypoglycemia. Results: Eleven patients (52.4%) experienced seizures in the neonatal period. Eighteen patients (85.7%) developed epilepsy during the follow-up. Refractory seizures were observed in 8 patients (38.1%). Nine patients (42.9%) manifested microcephaly, seven patients (33.3%) manifested cerebral palsy. Parieto-occipital involvement and the spasticity rate were statistically high in patients with prolonged hypoglycemia ($p<0.01$). Two patients had autistic features and four patients (19%) had attention deficit hyperactivity disorder. VEP studies could be performed in 18 of 21 patients. All patients had abnormal VEP results. Conclusion: We are of the opinion that most patients of neonatal hypoglycemia are not always documented. Patients under risk and patients with symptoms of hypoglycemia should be vigorously screened and treated to prevent neurologic impairments including cerebral palsy, epilepsy and visual disturbance.

PMID: 36514522

21. Predicting the brain age of children with cerebral palsy using a two-dimensional convolutional neural networks prediction model without gray and white matter segmentation
Chun-Yu Zhang, Bao-Feng Yan, Nurehemaiti Mutalifu, Ya-Wei Fu, Jiang Shao, Jun-Jie Wu, Qi Guan, Song-Hai Biedelehan, Ling-Xiao Tong, Xin-Ping Luan

Front Neurol. 2022 Nov 24;13:1040087. doi: 10.3389/fneur.2022.1040087. eCollection 2022.

Background: Abnormal brain development is common in children with cerebral palsy (CP), but there are no recent reports on the actual brain age of children with CP. Objective: Our objective is to use the brain age prediction model to explore the law of brain development in children with CP. Methods: A two-dimensional convolutional neural networks brain age prediction model was designed without segmenting the white and gray matter. Training and testing brain age prediction model using magnetic resonance images of healthy people in a public database. The brain age of children with CP aged 5-27 years old was predicted. Results: The training dataset mean absolute error (MAE) = 1.85, $r = 0.99$; test dataset MAE = 3.98, $r = 0.95$. The brain age gap estimation (BrainAGE) of the 5- to 27-year-old patients with CP was generally higher than that of healthy peers ($p < 0.0001$). The BrainAGE of male patients with CP was higher than that of female patients ($p < 0.05$). The BrainAGE of patients with bilateral spastic CP was higher than those with unilateral spastic CP ($p < 0.05$). Conclusion: A two-dimensional convolutional neural networks brain age prediction model allows for brain age prediction using routine hospital T1-weighted head MRI without segmenting the white and gray matter of the brain. At the same time, these findings suggest that brain aging occurs in patients with CP after brain damage. Female patients with CP are more likely to return to their original brain development trajectory than male patients after brain injury. In patients with spastic CP, brain aging is more serious in those with bilateral

cerebral hemisphere injury than in those with unilateral cerebral hemisphere injury.

PMID: 36504669

22. Plasma bisphenol a and phthalate levels in children with cerebral palsy: a case-control study
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Int J Environ Health Res. 2022 Dec 15;1-15. doi: 10.1080/09603123.2022.2153811. Online ahead of print.

The case-control study aimed to evaluate potential sources of exposure and the plasma concentrations of bisphenol A (BPA) and phthalates in prepubertal children having cerebral palsy (CP) and healthy control. Blood samples of 68 CP and 70 controls were analyzed for BPA, di-(2-ethylhexyl)-phthalate (DEHP), mono-(2-ethylhexyl)-phthalate (MEHP), and dibutyl phthalate (DBP). BPA and DBP levels were similar in groups. The median DEHP and MEHP levels of the children with CP were significantly lower than those of the controls ($p = 0.035$, $p < 0.001$, respectively). Exposure to plastic food containers/bags, personal care hygiene products, household cleaners, wood/coal stove heating, and city water supplies were associated with increased odds of higher BPA and phthalate levels in children with CP. In conclusion, potential exposure sources for BPA and phthalates differ in children with CP and healthy controls, and children with CP are not exposed to higher levels of BPA and phthalates.

PMID: 36519276

23. Imaging-based musculoskeletal models alter muscle and joint contact forces but do not improve the agreement with experimentally measured electromyography signals in children with cerebral palsy
Hans Kainz, Ilse Jonkers

Gait Posture. 2022 Nov 30;100:91-95. doi: 10.1016/j.gaitpost.2022.11.019. Online ahead of print.

Background: Musculoskeletal simulations are used to estimate muscle-tendon and joint contact forces (JCF). Personalizing the model's femoral geometry has been shown to improve the accuracy of JCF calculations. It is, however, unknown if the personalized geometry improves the agreement between estimated muscle activations and experimentally measured electromyography (EMG) signals. Research question: Does personalizing the musculoskeletal geometry improve the agreement between estimated muscle activations and EMG signals in terms of timing? Methods: We retrospectively analysed data from Bosmans et al. [5], which included three-dimensional motion capture data, EMG signals of eight lower limb muscles on each leg, and magnetic resonance imaging (MRI) data from seven children with cerebral palsy. For each patient we created a generic -scaled model and MRI-based model, which accounted for the subject-specific musculoskeletal geometry. We calculated muscle activations, muscle-tendon forces and JCF. Muscle activations were compared to the EMG signals using coefficient of determination and cosines similarity. Results: MRI-based models altered the magnitude of muscle activations and had a large impact on JCF but did not change the muscle activations profiles and therefore did not improve the agreement with EMG signals. Significance: MRI-based models do not alter the shape of muscle activations. Hence, if detailed muscle activations are a desired output of the simulations, EMG-informed modeling approaches should be used for musculoskeletal simulation in children with cerebral palsy. Furthermore, our study highlighted that altered JCF does not necessarily mean accurate muscle activations. To improve patient-specific simulations, future work should focus on developing methods to estimate cost functions representative for the neural control of children with cerebral palsy.

PMID: 36502666

24. Movement-related beta ERD and ERS abnormalities in neuropsychiatric disorders
Jaime Peter, Francesca Ferraioli, Dave Mathew, Shaina George, Cameron Chan, Tomisin Alalade, Sheilla A Salcedo, Shannon Saed, Elisa Tatti, Angelo Quartarone, M Felice Ghilardi

Review Front Neurosci. 2022 Nov 23;16:1045715. doi: 10.3389/fnins.2022.1045715. eCollection 2022.

Movement-related oscillations in the beta range (from 13 to 30 Hz) have been observed over sensorimotor areas with power decrease (i.e., event-related desynchronization, ERD) during motor planning and execution followed by an increase (i.e., event-related synchronization, ERS) after the movement's end. These phenomena occur during active, passive, imaged, and observed movements. Several electrophysiology studies have used beta ERD and ERS as functional indices of sensorimotor integrity, primarily in diseases affecting the motor system. Recent literature also highlights other characteristics of beta ERD and ERS, implying their role in processes not strictly related to motor function. Here we review studies about movement-related ERD and ERS in diseases characterized by motor dysfunction, including Parkinson's disease, dystonia, stroke, amyotrophic lateral sclerosis, cerebral palsy, and multiple sclerosis. We also review changes of beta ERD and ERS reported in physiological aging, Alzheimer's disease, and schizophrenia, three conditions without overt motor symptoms. The review of these works shows that ERD and ERS abnormalities are present across the spectrum of the examined pathologies as well as development and aging. They further suggest that cognition and movement are tightly related processes that may share common mechanisms regulated by beta modulation. Future studies with a multimodal approach are warranted to understand not only the specific topographical dynamics of movement-related beta modulation but also the general meaning of beta frequency changes occurring in relation to movement and cognitive processes at large. Such an approach will provide the foundation to devise and implement novel therapeutic approaches to neuropsychiatric disorders.

PMID: 36507340

25. Bowel Obstruction Secondary to Spontaneous Knot Formation of Ventriculoperitoneal Shunt
Meera R Laxman, Christopher A Gegg, Tamarah Westmoreland

Case Reports Cureus. 2022 Nov 8;14(11):e31236. doi: 10.7759/cureus.31236. eCollection 2022 Nov.

Ventriculoperitoneal (VP) shunts are frequently placed for the treatment of hydrocephalus. Shunt complications are a common occurrence typically involving infection, disconnections, or blockages. Abdominal complications involving the intraperitoneal portion of the catheter are rare. Spontaneous peritoneal knot formation involving the bowel with subsequent obstruction is even rarer. Spontaneous knot formation of a VP shunt is also not commonly seen in the adult population. In this report, we present the case of an 18-year-old male with cerebral palsy and hydrocephalus requiring VP shunt placement who developed a spontaneous knot leading to bowel obstruction requiring emergency laparoscopic surgery.

PMID: 36505173

26. Creatine supplementation to improve the peripheral and central inflammatory profile in cerebral palsy
Henrique J C B Gouveia, Raul Manhães-de-Castro, Diego Cabral Lacerda, Ana Elisa Toscano

Clin Nutr ESPEN. 2022 Dec;52:254-256. doi: 10.1016/j.clnesp.2022.11.016. Epub 2022 Nov 24.

This opinion paper presents a brief review on the potential use of Creatine (Cr) to improve the inflammatory profile in individuals with Cerebral Palsy (CP). CP is a condition that causes muscle atrophy followed by reduced strength and altered muscle tone. The prevalence of chronic diseases is higher in people with CP due to this, which are often associated with peripheral inflammation, but there are no studies that have evaluated central inflammation in this condition. Nevertheless, the anti-inflammatory action of Cr has already been observed in different types of studies. Thus, the use of experimental models of CP to evaluate the expression of the inflammatory markers, especially in the brain, as well as approaches to reduce the impairments already observed becomes essential. Results obtained in these preclinical studies may contribute to the quality of therapeutic strategies offered to children suffering from CP, the most common cause of chronic motor disability in childhood.

PMID: 36513462

Prevention and Cure

27. Cerebral palsy - brain repair with stem cells
Arne Jensen

Review J Perinat Med. 2022 Dec 12. doi: 10.1515/jpm-2022-0505. Online ahead of print.

Cerebral palsy, the most common disability in childhood, is a devastating non-progressive ailment of the infants' brain with lifelong sequelae, e.g., spastic paresis, chronic pain, inability to walk, intellectual disability, behavioral disorders, for which there is no cure at present. CP may develop after pediatric brain damage caused, e.g., by hypoxic-ischemia, periventricular leukomalacia, intracranial, hypoxic-ischemic encephalopathy, trauma, stroke, and infection. About 17 million people worldwide live with cerebral palsy as a result of pediatric brain damage. This reflects both the magnitude of the personal, medical, and socioeconomic global burden of this brain disorder and the overt unmet therapeutic needs of the pediatric population. This review will focus on recent preclinical, clinical, and regulatory developments in cell therapy for infantile cerebral palsy by transplantation of cord blood derived mononuclear cells from bench to bedside. The body of evidence suggests that cord blood cell therapy of cerebral palsy in the autologous setting is feasible, effective, and safe, however, adequately powered phase 3 trials are overdue.

PMID: 36503655