Cerebral palsy research news

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Interventions and Management

1. Looking beyond Body Structure and Function: ICF Foci and Who Is Being Assessed in Research about Adolescents and Young Adults with Cerebral Palsy-A Scoping Review

Camila Araújo Santos Santana, Peter Rosenbaum, Jet van der Kemp, Ana Carolina de Campos

Review Int J Environ Res Public Health. 2024 May 24;21(6):670. doi: 10.3390/ijerph21060670.

Purpose: The purpose of this study is to summarize the ICF foci, looking beyond body structures and function, and to analyze who has been assessed in research about adolescents and young adults (AYAs) with CP in the phase of transition to adulthood. Method: Medline, EMBASE, PsycINFO, and CINAHL databases were searched using terms related to cerebral palsy, adolescents/young adults, health development, participation, and independence. Studies including youth with CP (13-30 years old) published in English from 2014 to 2021 were considered. The methods of assessment reported in the included studies were used to identify the ICF foci and who was assessed. Results: In this study, 86 studies were reviewed. The main ICF foci are activity and participation (51% of the studies), personal factors (23%), ICF not covered (14%), ICF not defined (9%), with environmental factors being the least focused ICF component (3%). Most studies assessed AYAs directly (49% of studies). Conclusions: Activity- and participation-related constructs are the leading research focus of studies, and more attention is needed concerning environmental factors. AYAs are the main source of information, and the perspectives of other key figures are also being valued. To bridge the gap between child and adult health care, a broader view of health development and approaches to explore AYA developmental issues must be taken.

PMID: 38928917

2. High Velocity Passive Stretching Mimics Eccentric Exercise in Cerebral Palsy and May Be Used to Increase Spastic Muscle Fascicle Length

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Bioengineering (Basel). 2024 Jun 13;11(6):608. doi: 10.3390/bioengineering11060608.

Muscle fascicles are shorter and stiffer than normal in spastic Cerebral Palsy (CP). Increasing fascicle length (FL) has been attempted in CP, the outcomes of which have been unsatisfactory. In healthy muscles, FL can be increased using eccentric exercise at high velocities (ECC). Three conditions are possibly met during such ECC: muscle micro-damage, positive fascicle strain, and momentary muscle deactivation during lengthening. Participants with and without CP underwent a single bout of passive stretching at (appropriately) high velocities using isokinetic dynamometry, during which we examined muscle and fascicle behaviour. Vastus lateralis (VL) FL change was measured using ultrasonography and showed positive fascicle strain. Measures of muscle creatine kinase were used to establish whether micro-damage occurred in response to stretching, but the results did not confirm damage in either group. Vastus medialis (VM) and biceps femoris muscle activity were measured using electromyography in those with CP. Results supported momentary spastic muscle deactivation during lengthening: all participants experienced at least one epoch (60 ms) of increased activation followed by activation inhibition/

deactivation of the VM during knee flexion. We argue that high-velocity passive stretching in CP provides a movement context which mimics ECC and could be used to increase spastic FL with training.

PMID: 38927844

3. Lumbar Spondylolysis in Ambulant Children with Spastic Cerebral Palsy

Ryunosuke Fukushi, Hiroki Fujita, Yuji Yamamura, Atsushi Teramoto

Prog Rehabil Med. 2024 Jun 21:9:20240023. doi: 10.2490/prm.20240023. eCollection 2024.

Objectives: Lumbar spondylolysis is a common condition; nonetheless, its cause in patients with spastic cerebral palsy (CP) remains unknown. Furthermore, examination of children with CP may not accurately capture complaints, thus causing diseases to be overlooked. Understanding the clinical features and gait patterns of lumbar spondylolysis in CP can aid in diagnosis. This study aimed to identify the clinical features and specific gait patterns of lumbar spondylolysis in ambulatory children with CP. Methods: Seventy-three children with CP were divided into two groups according to the presence or absence of lumbar spondylolysis on X-ray and magnetic resonance imaging. Three-dimensional gait analysis (3DGA) was performed to evaluate the kinematic data of the lower limbs. Results: Eight participants (11.4%) had lumbar spondylolysis primarily affecting the L5 vertebra. The lumbar spondylolysis group had a higher body weight and Body Mass Index, along with a smaller left popliteal angle on the spastic side. In 3DGA, detailed kinematic data indicated significant group differences in the mean angles of hip internal rotation (39.6° vs. 20.2°) during an entire gait cycle. The gait profile score was 19.7° in the lumbar spondylolysis group and 14.9° in the spinal uninvolved group; the difference in gait profile score between the two groups showed a minimal clinically important difference of 2.75. Conclusions: The overall gait profile score revealed that the gait of the lumbar spondylolysis group was deteriorated. Excessive internal rotation of the hip during gait might be a contributing factor to lumbar spondylolysis in children with CP.

PMID: 38911606

4. Hip Surgery is Not More Painful Than Spine Surgery in Children With Cerebral Palsy

Abigail N Padilla, Lindsay M Andras, Michael J Heffernan, Tishya A L Wren, Noah G Tyau, Eugene Kim, Robert M Kay

J Pediatr Orthop. 2024 Jun 27. doi: 10.1097/BPO.0000000000002762. Online ahead of print.

Background: Posterior spinal fusion (PSF) and hip reconstruction are commonly indicated surgeries in children with cerebral palsy (CP), particularly those functioning at GMFCS levels IV and V. These are large and often painful procedures, and previous literature suggests that hip surgery is more painful than spine surgery in this patient population. The purpose of this study is to investigate pain scores and opioid use following hip and spine surgery in a large cohort of children with CP, including many patients who have undergone both types of surgery. Methods: A retrospective chart review was performed to identify children with CP who underwent hip reconstruction and/or PSF at a tertiary children's hospital between 2004 and 2022. Charts were reviewed for demographic data, pain scores, pain medication usage, duration of hospital stay, and complications. Results: Data were collected for 200 patients (101 male, 99 female) who met inclusion criteria. Eighty-seven patients underwent hip reconstruction, 62 spinal fusion, and 51 both hip and spine surgery asynchronously. Median (interquartile range) age at the time of surgery was significantly older for spinal fusion compared with hip surgery [13.1 (4.9) vs. 8.1 (5.7) y, $P<0.0001$]. Length of stay was significantly longer after PSF, with a median of 6 (4) days compared with 2 (1) days after hip surgery ($P<0.0001$). Both maximum and average daily pain scores were similar following hip and spine surgery, with the exception that average pain scores for hip surgery were slightly higher on postoperative day 1, hip=1.73 vs. spine=1.0 ($P<0.0001$). The amount of opioids used, expressed as morphine milligram equivalents (MME)/kg were similar in the hip and spine surgery groups; however, it was significantly lower in the hip surgery group on postoperative day 0, hip=0.06 versus spine=0.17 ($P<0.0001$). For the 51 patients who underwent both hip and spine surgery, the amount of opioids used mirrored that for the entire group (similar MME/kg, though only statistically significantly less on POD 0 and 3), and pain scores were not significantly different between the 2 groups except in 2 circumstances. The 2 exceptions in these 51 patients both demonstrated lower pain scores in patients after hip surgery, including lower maximum pain scores on POD 1 ($P=0.041$), and lower average pain scores on POD3 ($P=0.043$). Conclusions: This is the largest series to date comparing postoperative pain in children with CP after hip and spine surgery, including 51 of 200 patients who underwent both types of surgery. The results of this study demonstrate that hip surgery is not more painful than spine surgery in children with CP, and conflict with the traditional belief that hip surgery is more painful. This is important information for health care providers when counseling patients and families regarding these surgeries in children with CP.

PMID: 38934603

5. Pelvic Tilt in Adults With Cerebral Palsy and Its Relationship With Prior Hamstrings Lengthening

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Orthopedics. 2024 Jun 27:1-6. doi: 10.3928/01477447-20240619-01. Online ahead of print.

Background: Current studies assessing the change in pelvic tilt for ambulatory patients with cerebral palsy (CP) after surgical hamstring lengthening (SHL) lack a comparison cohort without prior SHL and are limited to younger patients. This study presents gait data of middle-aged adults with CP, primarily focusing on the pelvis, and compares pelvic tilt, trunk tilt, and knee flexion between those with and without prior SHL. Materials and methods: A consecutive series of 54 adults with CP, a mean age of 36±13 years, and Gross Motor Function Classification System (GMFCS) levels I-III were included. Thirty-two (59%) had SHL performed at a mean age of 8±5 years. Three-dimensional gait analysis data prospectively collected at a mean of 28±14 years postoperatively were retrospectively analyzed. Chi-square tests were used to compare demographic and surgical history data and statistical parameter mapping was used to compare knee flexion during stance and pelvic and trunk tilts during the gait cycle between SHL and SHL-naive groups. Results: Age, GMFCS level, sex, race, topography, and ethnicity were not different between the groups (P=.217-.612). Anterior pelvic tilt throughout gait was significantly greater in the SHL group compared with the SHL-naive group (63%-87%; P=.033). This difference was augmented after accounting for other surgical history and revision SHL (0%-32%, P=.019; and 46%-93%, P=.007). Conclusion: Within a cohort of adults with CP, GMFCS levels I-III, and a mean age of 36 years, those with a history of SHL, performed a mean of 28 years prior to 3-dimensional gait analysis, walked with increased anterior pelvic tilt compared with those without a history of SHL. [Orthopedics. 202x;4x(x):xx -xx.].

PMID: 38935848

6. Age related progression of lower limb coordination during gait in children with cerebral palsy without a history of surgical intervention

Damien Kiernan, Ailish Malone

J Biomech. 2024 Jun 24:171:112206. doi: 10.1016/j.jbiomech.2024.112206. Online ahead of print.

Walking requires precise movement between body segments, referred to as intersegmental coordination, which is an important factor in efficient motor performance. For children with cerebral palsy (CP), who often demonstrate an impaired neuromuscular system, intersegmental coordination has been shown to be different when compared to their typically developed (TD) peers. However, how intersegmental coordination changes over time in these children is unclear. The aim of this study was to quantify age-related changes in intersegmental coordination in children with bilateral CP without a history of surgical intervention and to compare to control groups of children with TD of similar age, weight, and height. A retrospective analysis of 162 children with bilateral CP who had a baseline and follow-up 3D gait assessment, and no history of surgical intervention, was conducted. Two age, weight, and height control groups of children with TD were included. A full 3-dimensional kinematic analysis was performed, and continuous relative phase analysis of the thigh-shank and shank-foot, while walking at a self-selected walking speed, was used to measure intersegmental coordination. Differences were present for children with CP compared to children with TD at baseline for thigh-shank intersegmental coordination. However, children with CP demonstrated a change over time with a move towards TD patterns at follow-up assessment. This study provides insights into the acquisition and stabilisation of intersegmental coordination between children with CP and TD.

PMID: 38941841

7. DE-AFO: A Robotic Ankle Foot Orthosis for Children with Cerebral Palsy Powered by Dielectric Elastomer Artificial Muscle

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Sensors (Basel). 2024 Jun 11;24(12):3787. doi: 10.3390/s24123787.

Conventional passive ankle foot orthoses (AFOs) have not seen substantial advances or functional improvements for decades,

failing to meet the demands of many stakeholders, especially the pediatric population with neurological disorders. Our objective is to develop the first comfortable and unobtrusive powered AFO for children with cerebral palsy (CP), the DE-AFO. CP is the most diagnosed neuromotor disorder in the pediatric population. The standard of care for ankle control dysfunction associated with CP, however, is an unmechanized, bulky, and uncomfortable L-shaped conventional AFO. These passive orthoses constrain the ankle's motion and often cause muscle disuse atrophy, skin damage, and adverse neural adaptations. While powered orthoses could enhance natural ankle motion, their reliance on bulky, noisy, and rigid actuators like DC motors limits their acceptability. Our innovation, the DE-AFO, emerged from insights gathered during customer discovery interviews with 185 stakeholders within the AFO ecosystem as part of the NSF I-Corps program. The DE-AFO is a biomimetic robot that employs artificial muscles made from an electro-active polymer called dielectric elastomers (DEs) to assist ankle movements in the sagittal planes. It incorporates a gait phase detection controller to synchronize the artificial muscles with natural gait cycles, mimicking the function of natural ankle muscles. This device is the first of its kind to utilize lightweight, compact, soft, and silent artificial muscles that contract longitudinally, addressing traditional actuated AFOs' limitations by enhancing the orthosis's natural feel, comfort, and acceptability. In this paper, we outline our design approach and describe the three main components of the DE-AFO: the artificial muscle technology, the finite state machine (the gait phase detection system), and its mechanical structure. To verify the feasibility of our design, we theoretically calculated if DE-AFO can provide the necessary ankle moment assistance for children with CP-aligning with moments observed in typically developing children. To this end, we calculated the ankle moment deficit in a child with CP when compared with the normative moment of seven typically developing children. Our results demonstrated that the DE-AFO can provide meaningful ankle moment assistance, providing up to 69% and 100% of the required assistive force during the pre-swing phase and swing period of gait, respectively.

PMID: 38931570

8. Research Toward Understanding the Benefits and Limitations of Orthotic Use To Improve Mobility and Balance for Individuals With Neuropathic Conditions

Bopha Chrea, Donald D Anderson, Koren Roach, Jason Wilken

Iowa Orthop J. 2024;44(1):37-45.

Background: Walking is a vital activity often compromised in individuals with neuropathic conditions. Charcot-Marie-Tooth (CMT) disease and Cerebral Palsy (CP) are two common neurodevelopmental disabilities affecting gait, predisposing to the risk of falls. With guiding scientific evidence limited, there is a critical need to better understand how surgical correction affects mobility, balance confidence, and gait compared to ankle foot orthosis (AFO) bracing. A systematic approach will enable rigorous collaborative research to advance clinical care. Methods: Key elements of this vision include 1) prospective studies in select patient cohorts to systematically compare conservative vs. surgical management, 2) objective laboratory-based evaluation of patient mobility, balance, and gait using reliable methods, and 3) use of patient-centric outcome measures related to health and mobility. Results: Valid and reliable standardized tests of physical mobility and balance confidence have been described in the literature. They include 1) the four-square step test, a widely used test of balance and agility that predicts fall risk, 2) the self-selected walking velocity, a measure of general mobility able to detect function change with orthosis use, and 3) the activity specific balance confidence scale, a survey instrument that assesses an individual's level of balance confidence during activity. Additionally, motion capture and ground reaction force data can be used to evaluate whole-body motion and loading, with discriminative biomechanical measures including toe clearance during the swing phase of gait, plantarflexion at 50% of swing, peak ankle plantarflexor moment, and peak ankle push-off power. Conclusion: The tools needed to support evidence-based practice and inform clinical decision making in these challenging patient populations are all available. Research must now be conducted to better understand the potential benefits and limitations of AFO use in the context of mobility and balance during gait for individuals with neuropathic conditions, particularly relative to those offered by surgical correction. Clinical relevance: Following this path of research will provide comparative baseline data on mobility, balance confidence, and gait that can be used to inform an objective criterion-based approach to AFO prescription and the impact of surgical intervention.

PMID: 38919344

9. Supported Standing and Supported Stepping Devices for Children with Non-Ambulant Cerebral Palsy: An Interdependence and F-Words Focus

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Int J Environ Res Public Health. 2024 May 23;21(6):669. doi: 10.3390/ijerph21060669.

Children functioning at Gross Motor Function Classification System (GMFCS) levels IV-V cannot maintain an aligned standing position or take steps without support. Upright positioning and mobility devices have psycho-social significance for these children and their families, enhancing use of vision, communication, functioning and emotional well-being. Standers and supported stepping devices facilitate opportunities for biomechanical loading, potentially helping to build and maintain muscle and bone integrity, and they promote physical development. However, families are often required to choose between these two devices for their young child. This study aims to synthesize evidence for use and benefits of both supported standing and stepping devices through the lens of two contemporary theoretical frameworks to support clinical reasoning and implementation. The F-words for childhood development (functioning, family, fitness, fun, friends, future) and the interdependence-Human Activity Assistive Technology (iHAAT) models were combined to illustrate the complex interactions between the child, family, caregivers, peers and contextual factors when implementing standing and stepping devices with children at GMFCS levels IV and V. Supported standing and stepping devices provide complementary benefits, and both may be necessary starting at 9-15 months. We propose they both be included ON-Time, along with other age-appropriate positioning and mobility devices, to promote more equitable developmental opportunities for children with non-ambulant cerebral palsy.

PMID: 38928915

10. Effects of Therapies Involving Plyometric-Jump Training on Physical Fitness of Youth with Cerebral Palsy: A Systematic Review with Meta-Analysis

Exal Garcia-Carrillo, Rodrigo Ramirez-Campillo, Mikel Izquierdo, Ragab K Elnaggar, José Afonso, Luis Peñailillo, Rodrigo Araneda, Daniela Ebner-Karestinos, Urs Granacher

Review Sports (Basel). 2024 May 29;12(6):152. doi: 10.3390/sports12060152.

The aim of this systematic review was to assess the effects of plyometric-jump training (PJT) on the physical fitness of youth with cerebral palsy (CP) compared with controls (i.e., standard therapy). The PRISMA 2020 guidelines were followed. Eligibility was assessed using the PICOS approach. Literature searches were conducted using the PubMed, Web of Science, and SCOPUS databases. Methodological study quality was assessed using the PEDro scale. Data were meta-analyzed by applying a random-effects model to calculate Hedges' g effect sizes (ES), along with 95% confidence intervals (95% CI). The impact of heterogeneity was assessed (I2 statistic), and the certainty of evidence was determined using the GRADE approach. Eight randomized-controlled studies with low-to-moderate methodological quality were included, involving male (n = 225) and female (n = 138) youth aged 9.5 to 14.6 years. PJT interventions lasted between 8 and 12 weeks with 2-4 weekly sessions. Compared with controls, PJT improved the muscle strength (ES = 0.66 [moderate], 95% CI = 0.36-0.96, $p < 0.001$, I2 = 5.4%), static (ES = 0.69 [moderate], 95% CI= 0.33-1.04, $p < 0.001$, I2 = 0.0%) and dynamic balance (ES = 0.85 [moderate], 95% CI = 0.12-1.58, $p = 0.023$, I2 = 81.6%) of youth with CP. Therefore, PJT improves muscle strength and static and dynamic balance in youth with CP compared with controls. However, more high-quality randomized-controlled trials with larger sample sizes are needed to provide a more definitive recommendation regarding the use and safety of PJT to improve measures of physical fitness.

PMID: 38921846

11. Evolving understanding of CP phenotypes: the importance of dystonia

Sara A Lewis, Bhooma Aravamuthan, Darcy Fehlings, Michael C Kruer

Pediatr Res. 2024 Jun 26. doi: 10.1038/s41390-024-03327-9. Online ahead of print.

Cerebral palsy (CP) is the core neurodevelopmental disorder affecting movement. Several distinct movement disorders can occur in people with cerebral palsy. Dystonia is a movement disorder that causes non-velocity-dependent hypertonia and/or abnormal, often repetitive, twisting movements, and/or postures. Dystonia occurs more frequently in patients with CP than has been recognized previously, and is treated differently than other aspects of CP. Dystonia is an important cause of chronic pain, hospitalization, and musculoskeletal complications. We describe recent advances in dystonia diagnosis in patients with cerebral palsy and highlight focus areas for ongoing research and clinical care. IMPACT: Dystonia is a movement disorder that is more common in people with cerebral palsy (CP) than previously thought. Dystonia contributes to hospitalization, chronic pain, and complications in CP patients. People with dystonic CP require different tools to diagnose and treat their condition. We summarize current state of the art in dystonia in CP and identify areas of focus for future work.

PMID: 38926549

12. Periodic limb movements during sleep in children with neuromuscular disease or cerebral palsy - An important potential contributor to sleep-related morbidity

Lauren C Nisbet, Margot J Davey, Gillian M Nixon

Sleep Med. 2024 Jun 22:121:58-62. doi: 10.1016/j.sleep.2024.06.017. Online ahead of print.

Objectives: Poor sleep is frequently reported in children with neuromuscular diseases (NMD) and cerebral palsy (CP) however breathing disorders during sleep are often the clinical focus. Periodic limb movements (PLMs) have an increased prevalence in adults with NMD and may contribute to sleep disturbance in this population. We assessed the prevalence of PLMs in children with NMD or CP. Methods: Retrospective review of polysomnography (PSG) with leg electromyography in children age 1-18 years with NMD (including Duchenne muscular dystrophy, myotonic dystrophy, spinal muscular atrophy) or CP performed at a paediatric sleep centre 2004-2022. Results: Leg electromyography was available in at least 1 PSG in 239 children (125 NMD, 114 CP), and in 2 PSGs in 105 children (73 NMD, 32 CP). At initial PSG, 72 (30 %) were female with a median age 9y and respiratory disturbance index 3.5/h (interquartile range 1.3-9.9/h). Elevated PLM index (PLMI; >5/h) occurred in 9.6 % of each of the CP and NMD groups, quantified by initial PSG. Overall, PLMI increased from baseline (median 0, maximum 33/h) to follow-up (median 0, maximum 55.8/h; $p < 0.05$). In those with an elevated PLMI, arousal percentage attributable to PLMs was up to 25 % (median 7.5 %). Conclusions: Elevated PLMI occurred at a higher prevalence in children with NMD and CP than reported in other clinic-referred paediatric populations. It is important that PLMs are not overlooked as identification and treatment may help improve sleep outcomes. Further research is required to understand the pathophysiology and consequences of PLMs specifically in this population.

PMID: 38924830

13. Correlation between Early Visual Functions and Cognitive Outcome in Infants at Risk for Cerebral Palsy or Other Neurodevelopmental Disorders: A Systematic Review

Olena Chorna, Giulia Corsi, Sabrina Del Secco, Ada Bancale, Andrea Guzzetta

Review Children (Basel). 2024 Jun 19;11(6):747. doi: 10.3390/children11060747.

Early key visual skills, such as tracking objects, sustaining gaze, and shifting attention, rapidly develop within the first 6 months of infant life. These abilities play a significant role in the development of cognitive functions but are frequently compromised in infants at risk of developing neurodevelopmental disorders. This systematic review evaluates the potential of early vision function in the prediction of cognition at or above 12 months. Five databases were searched for relevant articles, and their quality was assessed with the Quality Assessment of Diagnostic Accuracy Studies tool. Eight studies were suitable, including 521 preterm-born infants at varying risk of developing Cerebral Palsy (CP). Each study showed a significant correlation between vision and cognitive outcome. Predictive analysis including sensitivity and specificity was possible for three studies. Methodological quality was variable. Sensitivity ranged between 57 and 100% in the vision function assessments items, while specificity ranged from 59 to 100%. In conclusion, early vision showed strong correlation with cognition ≥ 12 months. While no single vision assessment was found to be superior, evaluation of specific functions, namely fixation and following, both at term age and between 3 and 6 months, demonstrated strong predictive validity.

PMID: 38929326

14. Investigating physiological symptoms associated with mental health symptoms in youth with cerebral palsy: An observational study

D Testani , C A McMorris, C A Clark, H Sanguino, E G Condliffe, M E Noel, D C Kopala Sibley, L K Brunton

Res Dev Disabil. 2024 Jun 25:151:104783. doi: 10.1016/j.ridd.2024.104783. Online ahead of print.

Over 50 % of children and youth with cerebral palsy (CP) experience mental health challenges, with anxiety and depression most common. Youth with CP also experience several physiological symptoms such as fatigue, pain, sedentary lifestyle, and sleep disturbances that impact their daily living; however, little is known about the impact of these symptoms on mental health outcomes in these youth. This study addressed this gap and examined the individual and cumulative impacts of physiological symptoms on anxiety and depression symptoms in youth with CP. Forty youth with CP aged 8 to 18 years, and their caregiver,

participated in this cross-sectional observational study. Pain, fatigue, anxiety, and depressive symptoms were measured using caregiver- and self-reported questionnaires and participants wore accelerometers for seven consecutive days, providing non-invasive physical activity and sleep pattern data. Youth with CP experienced substantial physiological symptoms and elevated anxiety and depression symptoms. Linear regression models determined that all physiological factors were predictive of caregiver-reported youth anxiety (R2 = 0.23) and youth depressive symptoms (R2 = 0.48). Fatigue, pain severity, sleep efficiency, and physical activity outcomes individually and cumulatively contributed to caregiver-reported youth anxiety and depression symptoms. These findings highlight the important role of physiological symptoms as potential risk factors and potential targets for intervention for mental health issues for in youth with CP.

PMID: 38924954

15. Clinical and functional characteristics of children and young adults with cerebral palsy and co-occurring attention-deficit/hyperactivity disorder

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Res Dev Disabil. 2024 Jun 25:151:104787. doi: 10.1016/j.ridd.2024.104787. Online ahead of print.

Background: There is emerging research that show children and young adults (CYAs) with cerebral palsy (CP) are at higher risk for attention-deficit/hyperactivity disorder (ADHD). However, little is known about the clinical and functional characteristics of CYAs with these co-occurring disorders. Aim: To estimate associations between a diagnosis of ADHD among CYAs with CP and clinical and functional characteristics. Methods: This retrospective, cross-sectional study used data from the electronic health records of CYAs (aged 4-26 years) with CP (n = 1145). We used bivariate and multivariable analyses to estimate associations between an ADHD diagnosis, CP type, Gross Motor Function Classification System (GMFCS) level, speech or language disorder, and intellectual disability. Results: 18.1 % of CYAs with CP had a diagnosis of ADHD. CYAs with spastic-bilateral CP had lower odds of ADHD (adjusted odds ratio [AOR] = 0.58; 95 % confidence interval [CI], 0.35-0.96). Odds of having ADHD were significantly lower for those with GMFCS levels III-V (AOR = 0.10; 95 % CI, 0.06-0.15). Conclusions: Our study found that a diagnosis of ADHD among CYAs with CP was associated with greater clinical and functional impairments compared to counterparts without ADHD. Findings highlight the need to screen for both conditions because of the high comorbidity rates in this population.

PMID: 38924957

16. Sensory Symptoms Across the Lifespan in People With Cerebral Palsy

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Pediatr Neurol. 2024 Apr 26:157:157-166. doi: 10.1016/j.pediatrneurol.2024.04.019. Online ahead of print.

Background: To estimate the prevalence of sensory symptoms in people with cerebral palsy (CP) across the lifespan. Methods: In this cross-sectional study, the self-reported Sensory Processing Scale Inventory (SPS-I) was administered via Research Electronic Data Capture (REDCap) between February 1, 2022, and August 15, 2022, to people with CP or their caregivers enrolled in the online MyCP Community Registry. We determined the association between SPS-I scores and age (Pearson correlation) and functional status as assessed using five validated functional classification systems for CP (analysis of variance [ANOVA]). We hypothesized that sensory symptoms would differ between younger and older individuals with CP. Results: Of 155 responses (28% response rate, age one to 76 years, 34% male), 97% reported at least one bothersome sensory symptom. Total sensory symptoms decreased with age (R2 = 0.12, P < 0.0001), driven by decreases in hyposensitivity symptoms (R2 = 0.32, P < 0.0001), primarily tactile hyposensitivity (R2 = 0.29, P < 0.0001). Sensory symptoms increased with greater functional impairment across all functional domains (ANOVA, P < 0.0001). However, the age-specific decrease in hyposensitivities was most pronounced in people with the greatest gross motor functional impairment (R2 = 0.70, P = 0.0004). Conclusion: Our findings suggest that hyposensitivity, primarily tactile sensitivity, decreases with age in people with CP. Future work should assess whether decreased hyposensitivity contributes to other age-related changes in CP like increased pain.

PMID: 38924827

17. Co-designing complex therapy interventions with parents as partners in the care of children with cerebral palsy: An Experience-based Co-design study in England

Jill Massey, Vicki Tsianakas, Anne Gordon, Natalie Sadler, Glenn Robert

Res Dev Disabil. 2024 Jun 25:151:104793. doi: 10.1016/j.ridd.2024.104793. Online ahead of print.

Background: Parents of children with hemiplegic cerebral palsy are increasingly involved in therapy intervention delivery. Enhancing the ways that parents are supported in delivery is key to optimising outcomes. This study aimed to refine an existing programme in England to better support parents partnering in their child's intervention delivery. Methods and procedures: Experience-based Co-design (EBCD) fostered collaboration between parents and therapists to identify shared improvement priorities and develop solutions. The study included eighteen interviews and sixteen co-design meetings involving twenty parents and eight therapists in total. Intervention development followed the MRC Framework for developing and evaluating complex interventions. Outcomes and results: Themes from parent and therapist interviews informed priority setting for the co-design work. Three key shared priorities emerged a) accessing rehabilitation; b) fostering partnership and c) parent learning. Aligned with these priorities, three mixed parent and therapist co-design teams produced a) a parent booklet; an education outline for healthcare professionals; b) partnership principles; adaptations to intervention logbooks c) an online parent education session. Conclusions and implications: Engaging parents and therapists in a structured co-design process using EBCD yielded innovative interventions supporting parents in delivering therapy for children with hemiplegia. This collaborative approach is anticipated to enhance programme implementation and effectiveness.

PMID: 38924956

18. Effect of family-centered care interventions on well-being of caregivers of children with cerebral palsy: a systematic review

Deepalaxmi Paresh Poojari, Shashikiran Umakanth, G Arun Maiya, Bhamini Krishna Rao, Sonia Khurana, Senthil Kumaran D, Radhika Attal, Marie Brien

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Background: Caring for a child with long-term functional limitations can have a negative impact on the physical and psychological well-being of the caregiver. Family-centered care (FCC) interventions have the potential to empower caregivers and contribute to their well-being. This systematic review aimed to synthesize existing evidence on the effectiveness of FCC interventions in improving the well-being of caregivers of children with cerebral palsy (CP), and identify the key components of such interventions that are most commonly practiced and deemed effective. Methods: This review systematically searched seven databases for randomized controlled trials that evaluated the effectiveness of any FCC intervention on the well-being of caregivers of children with or at risk of CP. We used the Cochrane RoB 2.0 tool to assess risk of bias and Critical Appraisal Skills Programme (CASP) checklist for critical appraisal. Due to high heterogeneity of studies, narrative synthesis was used to summarize the data. Results: The review consists of 11 studies which were categorized into five sections based on the components of FCC intervention provided in each individual study: 1. Information provision, and Enabling and partnership (n= 5); 2. Information provision, and Respectful and supportive care (n= 1); 3. Enabling and partnership (n= 2); 4. Enabling and partnership, and Respectful and supportive care (n= 2); 5. Information provision, Enabling and partnership and Respectful and supportive care (n= 1). Risk of bias was low in four studies, unclear in two studies, and high in five studies. Conclusion: FCC interventions were found to be effective in improving caregivers' satisfaction with attainment of child and caregiver goals. Evidence from multiple studies does not strongly support the effectiveness of FCC interventions on caregiver's mental health, parenting and personal outcomes. Limited evidence precludes a conclusion on the effectiveness of the components of FCC on well-being of caregivers of children with CP.

PMID: 38911944

19. Children with medical complexity receiving home healthcare devices in Japan: a retrospective cohort study

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BMJ Paediatr Open. 2024 Jun 28;8(1):e002685. doi: 10.1136/bmjpo-2024-002685.

Background: Limited evidence exists regarding children receiving home healthcare devices (HHDs). This study aimed to describe the range and type of HHD use by children with chronic medical conditions in Japan and explore factors leading to

increased use of these devices. Methods: This retrospective cohort study was conducted using data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan. Children receiving HHD aged ≤18 years between April 2011 and March 2019 were included. Children newly administered HHD between 2011 and 2013 were followed up for 5 years, and logistic regression analysis was performed to assess the relationship between increased HHD use and each selected risk factor (comorbidity or types of HHD). The models were adjusted for age category at home device introduction, sex and region. Results: Overall, 52 375 children receiving HHD were identified. The number (proportion) of children receiving HHD increased during the study period (11 556 [0.05%] in 2010 and 25 593 [0.13%] in 2018). The most commonly administered HHD was oxygen (51.0% in 2018). Among the 12 205 children receiving HHD followed up for 5 years, 70.4% and 68.3% who used oxygen or continuous positive airway pressure, respectively, were released from the devices, while only 25.8% who used mechanical ventilation were released from the device. The following diagnosis/comorbidities were associated with increased HHD use: other neurological diseases (OR): 2.85, 95% CI): 2.54-3.19), cerebral palsy (OR: 2.16, 95% CI: 1.87 to 2.49), congenital malformations of the nervous system (OR: 1.70, 95% CI: 1.34 to 2.13) and low birth weight (OR: 1.68, 95% CI: 1.41 to 2.00). Conclusions: This study provides nationwide population-based empirical data to clarify the detailed information regarding children receiving HHD in Japan. This information could assist healthcare professionals in improving the quality of life of these children and their families and help health policymakers consider measures.

PMID: 38942589

20. Caregiver perspectives on the long-lasting impact of the COVID-19 pandemic on children with cerebral palsy in Johannesburg, South Africa

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BMJ Paediatr Open. 2024 Jun 25;8(1):e002617. doi: 10.1136/bmjpo-2024-002617.

Background: The COVID-19 pandemic exacerbated challenges faced by children with cerebral palsy (CP), including limited access to therapy services, financial strain and disruptions in schooling and social activities. However, the specific long-lasting impacts of the pandemic on families of children with CP in the South African context remain underexplored. Aim: To explore the long-lasting impact of the COVID-19 pandemic on children with CP in South Africa. Method: A qualitative exploratory approach was used. 14 caregivers of 12 children with CP (aged 4-12) were recruited from various CP-specific schools and organisations in urban Johannesburg, South Africa. Individual semistructured interviews were conducted, and each interview was audio recorded, transcribed verbatim and analysed using inductive thematic analysis. Results: Children experienced significant changes to their physical and emotional well-being during the pandemic that had long-lasting effects on their added weight gain and activities of daily living. Many children experienced regressions during the lockdown due to the closure of schools and therapy centres. However, increased screen time observed among children with CP during the pandemic yielded unexpected positive outcomes, such as the improvement of technological skills and enhanced confidence through activities like vlogging. Implications: The pandemic has had long-lasting impacts on children with CP and addressing the multifaceted challenges faced by children with CP and their families in the post-COVID-19 era requires coordinated efforts from all stakeholders to ensure the holistic well-being and inclusion of this vulnerable population. Further research is warranted to assess the long-term impacts of the pandemic and evaluate the effectiveness of interventions aimed at mitigating its effects on this vulnerable population.

PMID: 38918024

21. Functioning and activity outcomes of the Akwenda Intervention Program for children and young adults with cerebral palsy in Uganda: A cluster-randomized trial

Elizabeth Asige, Gillian Saloojee, Carin Andrews, Lukia H Namaganda, Angelina Kakooza-Mwesige, Diane L Damiano, Hans Forssberg

Dev Med Child Neurol. 2024 Jun 25. doi: 10.1111/dmcn.16007. Online ahead of print.

Aim: To evaluate the efficacy of the Akwenda Intervention Program on motor, self-care, and social function of children and young people with cerebral palsy (CP). Method: This was a cluster-randomized, controlled, single-blinded, intervention study of 100 participants with CP (2-23 years; 52 males) in rural eastern Uganda. Half were allocated to the intervention program, the remainder served as waitlist controls. Gross Motor Function Measure-66 (GMFM-66) and the Ugandan version of Pediatric Evaluation of Disability Inventory (PEDI-UG) were collected before group allocation and after intervention. General linear models and t-tests were used to compare changes within and between groups. Cohen's d estimated the effect size of group differences. Change scores were evaluated by age and mobility subgroups. Results: Significant group by time interactions were

found for GMFM-66 (p =0.003) and PEDI-UG outcomes (p <0.001), except mobility, with the intervention group demonstrating greater changes. Both groups increased their scores on the GMFM-66 and child PEDI-UG, while only the intervention group had significant increases in caregiver assistance scores and across all age and mobility subgroups. Cohen's d showed large effect sizes (d >0.8) of differences for PEDI-UG outcomes except mobility. Interpretation: The Akwenda Intervention Program had a large positive impact on functioning and activity across age and mobility levels.

PMID: 38922854

22. Proprioception, Emotion and Social Responsiveness in Children with Developmental Disorders: An Exploratory Study in Autism Spectrum Disorder, Cerebral Palsy and Different Neurodevelopmental Situations

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Children (Basel). 2024 Jun 13;11(6):719. doi: 10.3390/children11060719.

Proprioception has long been linked with emotional dysregulation in neurotypical adults. Neuropediatric disorders such as autism spectrum disorder (ASD) and cerebral palsy (CP) are distinct entities and yet both present with deficits and challenges in sensory processing and the regulation of emotions. This study aimed to explore the relationship between proprioception and emotional-social performance in children and to compare proprioception and emotional-social performance in different underlying neurodevelopmental conditions. For this purpose, this cross-sectional study included 42 children with ASD, 34 children with CP and 50 typically developing peers. Proprioceptive acuity, proprioceptive reactive behavior as well as emotion regulation and social responsiveness were assessed. The results show a significant correlation between proprioceptive deficits and emotional difficulties in this pediatric sample, with distinct proprioceptive impairment patterns according to the underlying neurological disorder. Children with CP showed significant emotional knowledge deficits, while children with ASD predominantly showed challenges in social responsiveness. These data thus suggest a differentiated impact of proprioception on emotional-social performance in neurodevelopmental disorders and highlight proprioception as a potential therapeutic target for balancing emotion regulation in children with neurodevelopmental conditions.

PMID: 38929298

23. Oral Myiasis in an 11-year-old Child with Cerebral Palsy- Clinical Presentation, Microscopy, and Management

Morankar Rahul, Amolkumar Lokade, Mohammad Atif, Nishant Verma, Bijay Ranjan Mirdha, Neha Nityadarshini, Nitesh Tewari, Vijay Prakash Mathur

J Indian Assoc Pediatr Surg. 2024 May-Jun;29(3):303-304. doi: 10.4103/jiaps.jiaps_12_24. Epub 2024 May 8.

PMID: 38912011

24. Effects of pulmonary function improvement devices in the pediatric population with cerebral palsy: Systematic review and meta-analysis of randomized clinical trials

María Cayeiro-Marín, Javier Merino-Andrés, Álvaro Hidalgo-Robles, Arturo Ladriñán-Maestro, Alberto Sánchez-Sierra

Review Respir Med. 2024 Jun 20:231:107717. doi: 10.1016/j.rmed.2024.107717. Online ahead of print.

Introduction: Enhancing lung function can significantly improve daily life functionality for children with cerebral palsy, leading to increased interest in respiratory physiotherapy training devices in clinical practice. This study aims to evaluate the efficacy of devices (inspiratory muscle training and feedback devices) for improving pulmonary function through various respiratory parameters. Methods: A systematic review with meta-analysis of randomized clinical trials was conducted in seven databases up until May 2023. The included studies focused on training inspiratory muscle function using specific devices (inspiratory muscle training and feedback devices) in children with cerebral palsy. The main outcomes were maximum expiratory pressure and maximum inspiratory pressure. Secondary outcomes included forced vital capacity, forced expiratory volume in 1 s, peak expiratory flow, and the Tiffenau index. The effects of respiratory treatment were calculated through the estimation of the effect size and its 95% confidence intervals. The risk of bias in the included studies was assessed using the Cochrane Collaboration's tool for assessing the risk of bias (RoB2). Results: Nine studies were included in the systematic

review with meta-analysis, involving a total of 321 children aged between 6 and 18 years after secondary analyses were conducted. Feedback devices were found to be more effective in improving maximum expiratory pressure (effect size -0.604; confidence interval -1.368 to 0.161), peak expiratory flow, forced expiratory volume in 1 s, and forced vital capacity. Inspiratory muscle training devices yielded better effectiveness in improving maximum inspiratory pressure (effect size -0.500; confidence interval -1.259 to 0.259), the Tiffeneau index, and quality of life. Conclusion: Both devices showed potential in improving pulmonary function in children with cerebral palsy. Further high-quality clinical trials are needed to determine the optimal dosage and the most beneficial device type for each pulmonary function parameter.

PMID: 38908411

25. Effect of ultrasound-guided injection of botulinum toxin type A into shoulder joint cavity on shoulder pain in poststroke patients: study protocol for a randomized controlled trial

Peng Zheng, Yu Shi, Hang Qu, Meng Lin Han, Zhi Qiang Wang, Qing Zeng, Manxu Zheng, Tao Fan

Trials. 2024 Jun 27;25(1):418. doi: 10.1186/s13063-024-08258-8.

Background: Hemiplegic shoulder pain (HSP) is a common complication after stroke. It severely affects the recovery of upper limb motor function. Early shoulder pain in hemiplegic patients is mainly neuropathic caused by central nerve injury or neuroplasticity. Commonly used corticosteroid injections in the shoulder joint can reduce shoulder pain; however, the side effects also include soft tissue degeneration or increased tendon fragility, and the long-term effects remain controversial. Botulinum toxin injections are relatively new and are thought to block the transmission of pain receptors in the shoulder joint cavity and inhibit the production of neuropathogenic substances to reduce neurogenic inflammation. Some studies suggest that the shoulder pain of hemiplegia after stroke is caused by changes in the central system related to shoulder joint pain, and persistent pain may induce the reorganization of the cortical sensory center or motor center. However, there is no conclusive evidence as to whether or not the amelioration of pain by botulinum toxin affects brain function. In previous studies of botulinum toxin versus glucocorticoids (triamcinolone acetonide injection) in the treatment of shoulder pain, there is a lack of observation of differences in changes in brain function. As the content of previous assessments of pain improvement was predominantly subjective, objective quantitative assessment indicators were lacking. Functional near-infrared imaging (fNIRS) can remedy this problem. Methods: This study protocol is designed for a double-blind, randomized controlled clinical trial of patients with post-stroke HSP without biceps longus tenosynovitis or acromion bursitis. Seventy-eight patients will be randomly assigned to either the botulinum toxin type A or glucocorticoid group. At baseline, patients in each group will receive shoulder cavity injections of either botulinum toxin or glucocorticoids and will be followed for 1 and 4 weeks. The primary outcome is change in shoulder pain on the visual analog scale (VAS). The secondary outcome is the assessment of changes in oxyhemoglobin levels in the corresponding brain regions by fNIRS imaging, shoulder flexion, external rotation range of motion, upper extremity Fugl-Meyer, and modified Ashworth score. Discussion: Ultrasound-guided botulinum toxin type A shoulder joint cavity injections may provide evidence of pain improvement in patients with HSP. The results of this trial are also help to analyze the correlation between changes in shoulder pain and changes in cerebral hemodynamics and shoulder joint motor function. Trial registration: Chinese clinical Trial Registry, ChiCTR2300070132. Registered 03 April 2023, https://www.chictr.org.cn/showproj.html?proj=193722 .

PMID: 38937804

26. Hemiplegic (unilateral) cerebral palsy in northern Stockholm: Intellectual disability and epilepsy

Elsa Tillberg, Jonas K E Persson

Seizure. 2024 Jun 15:120:110-115. doi: 10.1016/j.seizure.2024.06.012. Online ahead of print.

Purpose: The purpose of this study was to describe intellectual disability and its association with epilepsy and brain imaging, in a population-based group of children with hemiplegic (unilateral) cerebral palsy, previously investigated and published in 2020. Materials and methods: Forty-seven children of school age in northern Stockholm, fulfilling the Surveillance of Cerebral Palsy in Europe-criteria of hemiplegic (unilateral spastic) cerebral palsy, were invited to participate in the study. Twenty-one children consented to participate. A WISC (Wechsler Intelligence Scale for Children)-test was performed by an experienced psychologist. Results: In the study population of twenty-one children, 57 % (n 12) displayed uneven cognitive profiles, 38 % (n 8) intellectual disability and 62 % (n 13) had a normal IQ. 43 % (n 9) developed epilepsy. Children with extensive brain lesions had more severe intellectual disability. Conclusions: In this study intellectual disability and/or epilepsy were associated with the type and extent of the underlying brain lesion. Intellectual disability and uneven cognitive profiles were common. We

therefore recommend individual cognitive assessment to ensure an optimal school start.

PMID: 38941801

27. The Prevalence and Risk Analysis of Cerebral Palsy and Other Neuro-Psychological Comorbidities in Children with Low Birth Weight in Taiwan: A Nationwide Population-Based Cohort Study

Hueng-Chuen Fan, Yu-Mei Chang, Jen-Yu Lee, Der-Shiun Wang, Chuan-Mu Chen, Shu-Wei Hu, Kuo-Liang Chiang, Fang-Chuan Kuo

J Clin Med. 2024 Jun 14;13(12):3480. doi: 10.3390/jcm13123480.

Background: This study evaluated early childhood comorbidities of cerebral palsy (CP) in low birth weight (LBW) children and assessed the impact of maternal bio-psychosocial factors on CP risk in preterm infants of varying birth weights (BWs). Methods: Data from 15,181 preterm infants (2009-2013) and 151,810 controls were analyzed using Taiwan's National Health Insurance Research Database. CP prevalence and LBW-associated comorbidities were examined, and odds ratios (ORs) were calculated. Results: This study confirmed increasing prematurity and LBW rates in Taiwan, with LBW infants showing higher CP prevalence. Significant maternal risk factors included age extremes (<20 and >40 years). LBW infants exhibited higher risks for respiratory, circulatory, nervous system, and psycho-developmental comorbidities compared with controls, with the lowest BW having even higher ORs. Maternal factors such as family income, the number of hospital admissions, and length of hospital stay were remarkably correlated with BW and subsequent complications. Each additional gestational week crucially reduced the risk of complications in premature infants. Conclusions: LBW infants are at a higher risk for CP and various comorbidities, with maternal bio-psychosocial factors playing a critical role. Addressing these factors in prenatal care and interventions is essential to improve outcomes for premature infants.

PMID: 38930008

28. Peripheral nerve transfers for dysfunctions in central nervous system injuries: a systematic review

Yun-Ting Xiang, Jia-Jia Wu, Jie Ma, Xiang-Xin Xing, Jun-Peng Zhang, Xu-Yun Hua, Mou-Xiong Zheng, Jian-Guang Xu

Int J Surg. 2024 Jun 1;110(6):3814-3826. doi: 10.1097/JS9.0000000000001267.

Background: The review highlights recent advancements and innovative uses of nerve transfer surgery in treating dysfunctions caused by central nervous system (CNS) injuries, with a particular focus on spinal cord injury (SCI), stroke, traumatic brain injury, and cerebral palsy. Methods: A comprehensive literature search was conducted regarding nerve transfer for restoring sensorimotor functions and bladder control following injuries of spinal cord and brain, across PubMed and Web of Science from January 1920 to May 2023. Two independent reviewers undertook article selection, data extraction, and risk of bias assessment with several appraisal tools, including the Cochrane Risk of Bias Tool, the JBI Critical Appraisal Checklist, and SYRCLE's ROB tool. The study protocol has been registered and reported following PRISMA and AMSTAR guidelines. Results: Nine hundred six articles were retrieved, of which 35 studies were included (20 on SCI and 15 on brain injury), with 371 participants included in the surgery group and 192 in the control group. These articles were mostly low-risk, with methodological concerns in study types, highlighting the complexity and diversity. For SCI, the strength of target muscle increased by 3.13 of Medical Research Council grade, and the residual urine volume reduced by more than 100 ml in 15 of 20 patients. For unilateral brain injury, the Fugl-Myer motor assessment (FMA) improved 15.14-26 score in upper extremity compared to 2.35-26 in the control group. The overall reduction in Modified Ashworth score was 0.76-2 compared to 0-1 in the control group. Range of motion (ROM) increased 18.4-80° in elbow, 20.4-110° in wrist and 18.8-130° in forearm, while ROM changed -4.03°-20° in elbow, -2.08°-10° in wrist, -2.26°-20° in forearm in the control group. The improvement of FMA in lower extremity was 9 score compared to the presurgery. Conclusion: Nerve transfer generally improves sensorimotor functions in paralyzed limbs and bladder control following CNS injury. The technique effectively creates a 'bypass' for signals and facilitates functional recovery by leveraging neural plasticity. It suggested a future of surgery, neurorehabilitation and robotic-assistants converge to improve outcomes for CNS.

PMID: 38935818

29. Feasibility and reliability of measured glomerular filtration rate with [I125]-iothalamate among young adults with

mild-to-moderate cerebral palsy
Daniel G Whitney, Andrea L Oliverio, Jodi Kreschmer, Shannen Bolde, Edward A Hurvitz, Ka Kit Wong

Front Med (Lausanne). 2024 Jun 12:11:1295104. doi: 10.3389/fmed.2024.1295104. eCollection 2024.

Objective: Despite the need, measuring glomerular filtration rate (mGFR) is not routinely performed for adults with cerebral palsy (CP), possibly due to unknown feasibility given the secondary complications of CP. This study aimed to assess the feasibility and reliability of mGFR and explore factors associated with eGFR-mGFR discordance among young adults with mild-to-moderate CP. Methods: This single-center, cross-sectional study included 18- to 40-year-olds with CP gross motor function classification system (GMFCS) I-III. The participants were excluded if they were pregnant/lactating, had cognitive impairments, or had contraindications to mGFR. A routine clinical protocol for mGFR and eGFR was used. mGFR feasibility was assessed based on the number of participants who completed testing. mGFR reliability was assessed using the coefficient of variation (CV) across the four 30 min intervals. The association between age, sex, and GMFCS and the percentage of eGFR-mGFR discordance was assessed. Results: Of the 19 participants enrolled, 18 completed the testing [mean age (SD), 29.9 (7.4) years, n = 10 female participants, n = 10/3/5 for GMFCS I/II/III] and most (n = 15) of the participants had an mGFR >90 mL/min; 14 participants (77.8%) had a CV <20%, 2 had a CV between 20 and 25%, and 2 had a CV >50%. eGFR overestimated mGFR by a median (interquartile range) of approximately 17.5% (2-38%); the full range of mis-estimation was -20.5 to 174.3%. Increasing age and GMFCS levels exhibited notable, but weak-to-modest, associations with a larger eGFR-mGFR discordance. Discussion: Obtaining mGFR was feasible and reasonably reliable within this small sample. eGFR overestimated mGFR by a notable amount, which may be associated with patient-level factors.

PMID: 38933110

30. Bibliometric Analysis on Equine-Assisted Interventions

María Amado-Fuentes, Angel Denche-Zamorano, Sabina Barrios-Fernandez, Margarita Gozalo

Review Animals (Basel). 2024 Jun 13;14(12):1776. doi: 10.3390/ani14121776.

Equine Assisted Interventions (EAIs) integrate the active participation of horses in therapeutic or educational interventions. A bibliometric analysis was carried out on this topic, using traditional bibliometric laws and recommendations. For this purpose, a search on the Web of Science (WoS) Core Collection database was carried out, obtaining 333 documents. Annual publications followed an exponentially increasing trend (R2 = 86%), pointing out that this topic is a growing interest among researchers, publishers, and journals. The USA was the most productive country worldwide and Jeong-yi Kwon and Ji Lee were the prolific co-authors. The WoS category with the highest number of papers was Rehabilitation (84 papers). The Journal of Alternative and Complementary Medicine, and Pediatric Physical Therapy were the journals with the highest number of publications. The most cited paper was "State of the Evidence Traffic Lights 2019: Systematic Review of Interventions for Preventing and Treating Children with Cerebral Palsy". The most used author keywords were rehabilitation, balance, and those related to specific populations such as Cerebral Palsy and Autism Spectrum Disorder. These results suggest that EAIs is a topic of increasing interest for researchers, editors, and professionals.

PMID: 38929395

31. Veno-venous extracorporeal membrane oxygenation in managing acute respiratory distress syndrome associated with hemolytic uremic syndrome and septic shock: a case report

Genta Kinoshita, Asami Ito-Masui, Takafumi Kato, Fumito Okuno, Kaoru Ikejiri, Ken Ishikura, Kei Suzuki

J Artif Organs. 2024 Jun 25. doi: 10.1007/s10047-024-01457-9. Online ahead of print.

Veno-venous extracorporeal membrane oxygenation (VV-ECMO) is a rescue therapy for severe respiratory failure in which conventional mechanical ventilation therapy is unsuccessful. Hemolysis during VV-ECMO support arises from multiple factors associated with organ damage and poor outcomes. Therefore, close and prompt monitoring is needed. Hemolytic uremic syndrome (HUS) is characterized by hemolysis, acute renal failure, and thrombocytopenia. Hemolytic features of the disease may complicate VV-ECMO management. A 26-year-old man with a history of cerebral palsy underwent VV-ECMO for acute respiratory distress syndrome (ARDS) due to septic shock caused by bacterial translocation during treatment for HUS. He showed features of hemolysis, with elevated lactate dehydrogenase (LDH), fragmented red blood cells, and low haptoglobin levels. Plasma free hemoglobin was measured daily throughout the whole course of ECMO with levels higher than 10 mg/dL but not exceeding 50 mg/dL. The extracorporeal membrane oxygenation (ECMO) circuit pressures were carefully monitored to

ensure the pump generated no excessive negative pressure. The patient was weaned off ECMO on the eleventh day. There have been several cases of VA-ECMO in patients with HUS; however, there is limited literature on VV-ECMO. As the days on VV-ECMO tend to be longer than those on VA-ECMO, features of hemolysis may complicate management. Although HUS did not directly influence the clinical course in the present case, features of hemolysis were continuously observed. This case highlighted the importance of standard ECMO monitoring, especially daily measurement of plasma free hemoglobin.

PMID: 38916825

32. Neurodevelopmental outcomes at 2 years in children who received sildenafil therapy in utero: The STRIDER randomised controlled trial

Andrew Sharp, Christine Cornforth, Richard Jackson, Jane Harrold, Mark A Turner, Louise C Kenny, Philip N Baker, Edward D Johnstone, Asma Khalil, Peter von Dadelszen, Aris T Papageorghiou, Zarko Alfirevic, Brigitte Vollmer; STRIDER group

BJOG. 2024 Jun 25. doi: 10.1111/1471-0528.17888. Online ahead of print.

Objective: Severe early-onset fetal growth restriction (FGR) causes stillbirth, neonatal death and neurodevelopmental impairment. Poor maternal spiral artery remodelling maintains vasoactive responsiveness but is susceptible to treatment with sildenafil, a phosphodiesterase type 5 (PDE5) inhibitor, which may improve perinatal outcomes. Design: Superiority, double-blind randomised controlled trial. Setting: A total of 20 UK fetal medicine units. Population: Pregnancies affected by FGR, defined as an abdominal circumference below the tenth centile with absent end-diastolic flow in the umbilical artery between 22+0 and 29+6 weeks of gestation. Methods: Treatment with sildenafil (25 mg three times/day) or placebo until delivery or 32 weeks of gestation. Main outcome measures: All infants alive at hospital discharge were assessed for cardiovascular function and cognitive, speech/language and neuromotor impairment at 2 years of age. The primary outcome was survival without cerebral palsy or neurosensory impairment, or a Bayley-III composite score of >85. Results: In total, 135 women were randomised between November 2014 and July 2016 (70 to sildenafil and 65 to placebo). We previously published that there was no improvement in time to delivery or perinatal outcomes with sildenafil. In all, 75 babies (55.5%) were discharged alive, with 61 infants eligible for follow-up (32 sildenafil and 29 placebo). One infant died (placebo), three mothers declined and ten mothers were uncontactable. There was no difference in neurodevelopment or blood pressure following treatment with sildenafil. Infants who received sildenafil had a larger head circumference at 2 years of age (median difference 49.2 cm, IQR 46.4-50.3, vs 47.2 cm, 95% CI 44.7-48.9 cm). Conclusions: Sildenafil therapy did not prolong pregnancy or improve perinatal outcomes and did not improve infant neurodevelopment in FGR survivors. Therefore, sildenafil should not be prescribed for this condition.

PMID: 38923115

33. Muscle satellite cells and fibro-adipogenic progenitors from muscle contractures of children with cerebral palsy have impaired regenerative capacity

Taryn Loomis, Vedant A Kulkarni, Marie Villalba, Jon R Davids, J Kent Leach, Lucas R Smith

Dev Med Child Neurol. 2024 Jun 27. doi: 10.1111/dmcn.16006. Online ahead of print.

Aim: To evaluate the mechanosensitivity of muscle satellite cells (MuSCs) and fibro-adipogenic progenitors (FAPs) in cerebral palsy (CP) and the efficacy of the drug verteporfin in restoring cells' regenerative capacity. Method: Muscle biopsies were collected from six children with CP and six typically developing children. MuSCs and FAPs were isolated and plated on collagen-coated polyacrylamide gels at stiffnesses of 0.2 kPa, 8 kPa, and 25 kPa. Cells were treated with verteporfin to block mechanosensing or with dimethyl sulfoxide as a negative control. MuSC differentiation and FAP activation into myofibroblasts were measured using immunofluorescence staining. Results: Surprisingly, MuSC differentiation was not affected by stiffness; however, stiff substrates resulted in large myonuclear clustering. Across all stiffnesses, MuSCs from children with CP had less differentiation than those of their typically developing counterparts. FAP activation into myofibroblasts was significantly higher in children with CP than their typically developing peers, but was not affected by stiffness. Verteporfin did not affect differentiation or activation in either cell population, but slightly decreased myonuclear clustering on stiff substrates. Interpretation: Cells from children with CP were less regenerative and more fibrotic compared to those of their typically developing counterparts, with MuSCs being sensitive to increases in stiffness. Therefore, the mechanosensitivity of MuSCs and FAPs may represent a new target to improve differentiation and activation in CP muscle.

PMID: 38937924

Prevention and Cure

34. Minimum effective dose of clemastine in a mouse model of preterm white matter injury

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Pediatr Res. 2024 Jun 28. doi: 10.1038/s41390-024-03326-w. Online ahead of print.

Background: Preterm white matter injury (PWMI) is the most common cause of brain injury in premature neonates. PWMI involves a differentiation arrest of oligodendrocytes, the myelinating cells of the central nervous system. Clemastine was previously shown to induce oligodendrocyte differentiation and myelination in mouse models of PWMI at a dose of 10 mg/kg/day. The minimum effective dose (MED) of clemastine is unknown. Identification of the MED is essential for maximizing safety and efficacy in neonatal clinical trials. We hypothesized that the MED in neonatal mice is lower than 10 mg/kg/day. Methods: Mouse pups were exposed to normoxia or hypoxia (10% FiO2) from postnatal day 3 (P3) through P10. Vehicle or clemastine at one of four doses (0.5, 2, 7.5 or 10 mg/kg/day) was given to hypoxia-exposed pups. Myelination was assessed at age P14 and 10 weeks to determine the MED. Clemastine pharmacokinetics were evaluated at steady-state on day 8 of treatment. Results: Clemastine rescued hypoxia-induced hypomyelination with a MED of 7.5 mg/kg/day. Pharmacokinetic analysis of the MED revealed Cmax 44.0 ng/mL, t1/2 4.6 h, and AUC24 280.1 ng*hr/mL. Conclusions: Based on these results, myelination-promoting exposures should be achievable with oral doses of clemastine in neonates with PWMI. Impact: Preterm white matter injury (PWMI) is the most common cause of brain injury and cerebral palsy in premature neonates. Clemastine, an FDA-approved antihistamine, was recently identified to strongly promote myelination in a mouse model of PWMI and is a possible treatment. The minimum effective dose in neonatal rodents is unknown and is critical for guiding dose selection and balancing efficacy with toxicity in future clinical trials. We identified the minimum effective dose of clemastine and the associated pharmacokinetics in a murine chronic hypoxia model of PWMI, paving the way for a future clinical trial in human neonates.

PMID: 38942888