Cerebral Palsy
ALLIANCE

Cerebral palsy research news

Monday 22 November 2021

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

Professor Nadia Badawi AM
CP Alliance Chair of Cerebral Palsy Research

Subscribe to CP Research News

Interventions and Management

1. The effect of modified constraint-induced movement therapy in children with hemiparetic cerebral palsy. Consecutive or intermittent days?

Sezen Tezcan, Tamer Çankaya

Disabil Rehabil. 2021 Nov 13;1-8. doi: 10.1080/09638288.2021.2002441. Online ahead of print.

Purpose: To investigate effect of modified constraint-induced movement therapy (mCIMT) administered on consecutive or intermittent days on upper limb function in children with hemiparetic cerebral palsy (CP). Materials and methods: Thirty-three children (age range 5-18 y) with hemiparetic CP separated into three groups: consecutive mCIMT group (n = 11), intermittent mCIMT group (n = 11), control group (n = 11). The outcome measures consist of Gross Motor Function Classification System (GMFCS), Manual Ability Classification System (MACS), Pediatric Balance Scale (PBS), Modified Tardieu Scale (MTS), Jebsen-Taylor Hand Function Test (JTHFT), Children's Hand Use Experience Questionnaire (CHEQ), Abilhand Kids Questionnaire, surface Electromyography (sEMG). The evaluations were made baseline, 10 days after, 5 weeks after the treatment. Results: Improvements were achieved in all groups. The use of upper extremities in daily life activities ($p < 0.01$), speed of performing the activities ($p < 0.001$), grasping efficiency ($p < 0.001$), the amount of a decrease in the children's sense of discomfort while performing activities ($p < 0.001$) on the affected side in both mCIMT groups were better than the control group. The gain levels in mCIMT groups were similar ($p > 0.05$). Conclusions: Administration of mCIMT on intermittent days facilitate the adaptation of a child, it was concluded to be a more tolerable method and could be more effective.Implications for rehabilitationmCIMT is more effective than low-dose conventional therapeutic interventions in improving paretic upper limb functions in children with hemiparetic CP.The application of mCIMT in the child's natural environment increases the motivation to participate in the treatment.The application of mCIMT on intermittent days will be more easily tolerated in paediatric individuals and will increase participation in the treatment.

PMID: 34775897

2. Early postoperative complications were common in non-ambulant paediatric patients with neuromuscular scoliosis

Marie Mostue Naume, Morten H Møller, Christina E Høi-Hansen, Alfred P Born, Ghita Brekke, Thomas B Andersen, Jesper Dirks, Mette Cathrine Ørngreen

Acta Paediatr. 2021 Nov 12. doi: 10.1111/apa.16183. Online ahead of print.

A high risk of postoperative complications has been reported after scoliosis surgery in ambulant and non-ambulant paediatric patients with neuromuscular scoliosis (NMS), including wound and respiratory infections. Low skeletal muscle mass is common in children with NMS, especially in non-ambulant patients, due to decreased mobility, malnutrition and underweight. They often rely on respiratory support and are at risk of developing hypoglycaemia during prolonged fasting. These patients are fragile and need special attention. A 33% rate of major complications has been reported in non-ambulatory children with cerebral palsy after spinal fusion.

PMID: 34767273

3. Gait status 26-35 years after selective dorsal rhizotomy: A 9 year follow up study

Nelleke G Langerak, Berendina E Veerbeek, A Graham Fieggen, Robert P Lamberts

Gait Posture. 2021 Oct 26;91:284-289. doi: 10.1016/j.gaitpost.2021.10.031. Online ahead of print.

Background: Although the short-term outcomes of selective dorsal rhizotomy (SDR) in children with cerebral palsy (CP) have been well documented, less is known about the long-term benefits of SDR, especially while aging. Research question: Does the gait of adults with CP, who underwent SDR in childhood, change during a nine-year aging follow-up period? Do associations exists between the gait deviation index (GDI) and contextual factors at follow-up? Methods: Three-dimensional motion data was captured (Vicon system) of 26 adults (10 female) with CP and spastic diplegia at baseline (17-to-26 years post-SDR) and at nine-year follow-up (26-to-35 years post-SDR), as well as 41 matched typically developed (TD) adults used for reference data. Kinematic, non-dimensional temporal distance and GDI parameters were determined, and associations with contextual factors were studied. Results: At follow-up the adults with CP had a (median [interquartile ranges]) age of 35.8 [34.2-41.2] years and classified as Gross Motor Function Classification System (GMFCS) level I ($n = 13$), level II ($n = 10$) and level III ($n = 3$). Overall no clinically relevant change in gait quality (GDI) was detected over the nine-year follow-up period. However, small changes were found in hip and knee range of motion, peak knee flexion and walking speed. In line with the baseline study, a number of gait parameters were different to TD adults. The only association found was between GDI and GMFCS at follow-up ($r = 0.64$, $p < 0.01$). Significance: The overall walking pattern of the adults with CP who underwent SDR in childhood was characterised by mild crouch gait with minimal signs of spasticity, confirming former physical examination findings. Some small changes in certain gait parameters were determined, though clinically the gait quality remained stable during the nine-year aging period. This finding supports the stability of the gait pattern during mid-life in adults with CP, who met the strict SDR selection criteria.

PMID: 34798419

4. Rehabilitation of motor function in children with cerebral palsy based on motor imagery

Jiaxin Xie, Lin Jiang, Yanan Li, Baodan Chen, Fali Li, Yuanling Jiang, Dongrui Gao, Lili Deng, XuLin Lv, XianKun Ma, Gang Yin, Dezhong Yao, Peng Xu

Cogn Neurodyn. 2021 Dec;15(6):939-948. doi: 10.1007/s11571-021-09672-3. Epub 2021 Mar 14.

To promote the rehabilitation of motor function in children with cerebral palsy (CP), we developed motor imagery (MI) based training system to assist their motor rehabilitation. Eighteen CP children, ten in short- and eight in long-term rehabilitation, participated in our study. In short-term rehabilitation, every 2 days, the MI datasets were collected; whereas the duration of two adjacency MI experiments was ten days in the long-term protocol. Meanwhile, within two adjacency experiments, CP children were requested to daily rehabilitate the motor function based on our system for 30 min. In both strategies, the promoted motor information processing was observed. In terms of the relative signal power spectra, a main effect of time was revealed, as the promoted power spectra were found for the last time of MI recording, compared to that of the first one, which first validated the effectiveness of our intervention. Moreover, as for network efficiency related to the motor information processing, compared to the first MI, the increased network properties were found for the last MI, especially in long-term rehabilitation in which CP children experienced a more obvious efficiency promotion. These findings did validate that our MI-based rehabilitation system has the potential for CP children to assist their motor rehabilitation.

PMID: 34790263

5. Strabismus Repair in Children with Varying Severity of Cerebral Palsy

Roland Seif, Ghassan Hmaimess, Hoda Eid, Ibrahim Dunya

Semin Ophthalmol. 2021 Nov 14;1-3. doi: 10.1080/08820538.2021.2003823. Online ahead of print.

Objective: To study the success rate of strabismus surgery in patients with varying levels of severity of cerebral palsy (CP). Design: A retrospective study was conducted. Participants: Sixty-four patients with varying severity of CP were included. Methods: All patients with different CP severity levels underwent strabismus surgery. Success was defined as any postoperative heterotropia outcome of less than 10 prism diopters in primary position. Statistical analysis was conducted using chi-square. Results: The mean age at the time of strabismus surgery was 3.1 years, and the mean follow-up was 6.0 years. The most common types of strabismus were infantile-onset exotropia in 36 patients (56%) and infantile-onset esotropia in 28 patients (44%). Surgical success was found to be better in patients with mild GMFCS (GMFCS levels 1-2) with 68% having less than 10 PD of eso or exotropia in primary gaze, as compared to patients with severe GMFCS (GMFCS levels 3-5) (38% with 10 PD of heterotropia) ($P < .05$; $\chi 2$). Refractive errors included myopia (27.5% in mild cases and 41.6% in severe), emmetropia (10% in mild and 8.3% in severe) and hyperopia (62.5% in mild and 50% in severe). Around 50% of the mild cases had absent binocular fusion compared to 66.6% of those with severe CP. Amblyopia was found in 62.5% of the mild cases and 54.1% of the severe cases. Nystagmus was present in 25% with mild disease and 29.1% of those with severe disease. Conclusion: Restoration of good ocular alignment in patients with CP is achievable in more than half of the cases. Patients with more severe CP have poorer outcomes than those with milder palsies. There appears to be no difference in outcomes between the different types of strabismus.

PMID: 34779343

6. Clinimetric properties of visuo-perceptual and visuo-cognitive assessment tools used for children with cerebral visual impairment and cerebral palsy or developmental delay: a systematic review

Swetha Sara Philip, Andrea Guzzetta, Glen A Gole, Roslyn N Boyd

Disabil Rehabil. 2021 Nov 17;1-13. doi: 10.1080/09638288.2021.1990421. Online ahead of print.

Purpose: The aim of this systematic review is to evaluate the psychometrics and clinical utility of visuo-perceptual and visuo-cognitive assessment tools in children with cerebral visual impairment (CVI) and cerebral palsy (CP) or neurodevelopmental delay (DD). Materials and methods: Five databases (PubMed, EMBASE, SCOPUS, CINAHL, and Cochrane Database) were comprehensively searched from 1970 till June 2021. The PRISMA checklist was utilised to report on the process of selecting eligible papers. The methodological quality of included studies was evaluated using COnsenus-based Standards for the selection of health Measurement INstrument (COSMIN) checklist. Results: Of the 26 assessment tools identified, only seven tools had psychometric evidence supporting their use. Based on COSMIN guidelines, 60% of included studies were rated as inadequate or doubtful for their methodological quality of measurement properties, with equal number being rated as indeterminate on the overall rating. Conclusions: Cerebral visual impairment due to its varied clinical presentation is often missed in children with CP and DD. There is a paucity of studies reporting on the validity and reliability of functional vision tools. Further studies are needed to conduct high-quality psychometric reporting using the updated COSMIN guidelines to identify appropriate functional vision tools for children with CP or DD. Implications for rehabilitation: There are paucity of studies evaluating the validity and reliability of existing perceptual and cognitive assessment tools in children with cerebral visual impairment (CVI) and cerebral palsy (CP).Development of age-appropriate assessment tools evaluating all aspects of functional vision will assist in providing more holistic child-centric rehabilitation programs. A combination of detailed perinatal history, direct observation, and clinical assessments of functional vision are important to recognise CVI in children with CP.

PMID: 34787029

7. Functional Communication Abilities in Youth With Cerebral Palsy: Association With Impairment Profiles and School-Based Therapy Goals

Clare Koopmans, Ashley Sakash, Jennifer Soriano, Helen L Long, Katherine C Hustad

Lang Speech Hear Serv Sch. 2021 Nov 12;1-16. doi: 10.1044/2021_LSHSS-21-00064. Online ahead of print.

Purpose: The aim of this study was to examine the relationship between functional communication skills, underlying speech, language, and cognitive impairments and school-based speech pathology services in students with cerebral palsy (CP). Method: Thirty-five participants with CP who had Individualized Education Programs (IEPs) were classified according to the Communication Function Classification System (CFCS). Participants completed laboratory assessments of speech, receptive language, executive functioning, and nonverbal cognition. Each participant's speech and language IEP goals were coded into treatment units and then categorized into seven, mutually exclusive target goal areas. Nonparametric analyses were employed to examine differences among CFCS groups in the number of deficit areas and the number of goal areas from the IEP. Descriptive analyses were used to evaluate the extent to which deficit and goal areas in the IEP co-occurred by CFCS level. Results: Those in more involved CFCS levels demonstrated more severe speech, receptive language, and cognitive impairments. However, there were no significant differences in the number of deficit areas across CFCS groups. Regardless of CFCS level, there were no differences in the number of treatment goals specified in the IEP. Literacy was the only goal area addressed across all CFCS levels. Those in the most involved CFCS levels had augmentative and alternative communication (AAC) goals, but those with more moderate restrictions in functional communication who also had markedly reduced speech intelligibility did not typically have speech or AAC goals. Interpretation: Individuals with CP across CFCS levels demonstrate variability in underlying deficit profiles, suggesting that measures of both functional communication and of underlying deficits are necessary to provide a complete picture of communication needs. Literacy goals were common across all CFCS levels, but AAC goals were limited to the most severely involved individuals, suggesting that continuing education may be necessary to support speech-language pathologists in developing treatments involving the integration of AAC and speech to foster functional communication at school. Supplemental Material https://doi.org/10.23641/asha.16968073.

PMID: 34767477

8. Development of a new tool for predicting the behavior of individuals with intellectual disability in the dental office: A pilot study

Iván Varela, Javier Fernández-Feijoo, Eliane García, Márcio Diniz-Freitas, Isabel Martínez, Javier Roca, Pedro Diz, Jacobo Limeres

Disabil Health J. 2021 Nov 9;101229. doi: 10.1016/j.dhjo.2021.101229. Online ahead of print.

Background: The dental treatment of individuals with intellectual disability can represent a considerable professional challenge. Objective: To develop a model for predicting the behavior of patients with intellectual disability in the dental office. Methods: The study group comprised 250 patients with Down syndrome (DS), autism spectrum disorder (ASD), cerebral palsy (CP), idiopathic cognitive impairment or rare disorders. We collected their demographic, medical, social and behavioral information and identified potential predictors (chi-squared test). We developed stratified models (Akaike information criterion) to anticipate the patients'behavior during intraoral examinations and to discern whether the dental treatment should be performed under general anesthesia. These models were validated in a new study group consisting of 80 patients. Goodness of fit was quantified with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under the receiver operating characteristic curve (AUC). We developed a mathematical algorithm for executing the models and developed software for its practical implementation (PREdictors of BEhavior in Dentistry, "PREBED"). Results: For patients with DS, ASD and CP, the model predicting the need for physical restraint during examination achieved a PPV of 0.90, 0.85 and 1.00, respectively, and an NPV of 0.66, 0.76 and 1.00, respectively. The model predicting the need for performing treatment under general anesthesia achieved a PPV of 0.63, 1.00 and 1.00, respectively, and an NPV of 1.00, 1.00 and 0.73, respectively. However, when validating the stratified models, the percentage of poorly classified individuals (false negatives + false positives) ranged from 24% to 46.6%. Conclusions: The results of the PREBED tool open the door to establishing new models implementing other potentially predictive variables.

PMID: 34776386

9. Game-based training of selective voluntary motor control in children and youth with upper motor neuron lesions: protocol for a multiple baseline design study

Annina Fahr, Andrina Kläy, Larissa S Coka, Hubertus J A van Hedel

BMC Pediatr. 2021 Nov 11;21(1):505. doi: 10.1186/s12887-021-02983-8.

Background: Impairments of selective control of joint movements can have consequences for many activities of daily life, but there are only a few interventions to improve selective voluntary motor control (SVMC). We have developed a treatment option to specifically enhance SVMC exploiting the advantages of interactive computer play technology. It targets SVMC by training selective activation of a muscle or a selective joint movement while it provides immediate feedback about involuntary muscle activations/movements at an (unwanted) joint. This study aims to investigate the effectiveness of this game-based intervention to enhance SVMC in children and youth with upper motor neuron lesions. Methods: We will conduct a randomized, non-concurrent, multiple baseline design study. Patients aged between 6 and 20 years with reduced SVMC due to an upper motor neuron lesion will be included. During the baseline phase of random length, participants will attend their regular intensive rehabilitation program, and in the intervention phase, they will additionally complete 10 therapy sessions (à 40 min) of the game-based SVMC training. The primary outcome will be a short SVMC assessment conducted repeatedly throughout both phases, which quantifies movement accuracy and involuntary movements. Changes in clinical SVMC measures, muscle strength, cortical excitability, motor control of the inhibited/unwanted movement, and functional independence will be assessed as secondary outcomes. We will use a mixed-effect model to determine the change in the course of the primary outcome when the intervention is introduced, and we will compare changes between phases for secondary outcomes with paired tests. Discussion: This study will provide first evidence whether SVMC can be improved with our game-based training. The single-case design takes into account the individualization required for this intervention, and it can help to address the challenges of intervention trials in our setting. Trial registration: German Clinical Trials Register: DRKS00025184 , registered on 28.04.2021.

PMID: 34763681

10. Development and Feasibility of a Kinect-Based Constraint-Induced Therapy Program in the Home Setting for Children With Unilateral Cerebral Palsy

Hao-Ling Chen, Szu-Yu Lin, Chun-Fu Yeh, Ren-Yu Chen, Hsien-Hui Tang, Shanq-Jang Ruan, Tien-Ni Wang

Front Bioeng Biotechnol. 2021 Oct 26;9:755506. doi: 10.3389/fbioe.2021.755506. eCollection 2021.

Introduction: Cerebral palsy (CP) is the leading cause of childhood-onset physical disability. Children with CP often have impaired upper limb (UL) function. Constraint-induced therapy (CIT) is one of the most effective UL interventions for children with unilateral CP. However, concerns about CIT for children have been repeatedly raised due to frustration caused by restraint of the child's less-affected UL and lack of motivation for the intensive protocol. Virtual reality (VR), which can mitigate the disadvantages of CIT, potentially can be used as an alternative mediator for implementing CIT. Therefore, we developed a VR-based CIT program for children with CP using the Kinect system. Aims: The feasibility of the Kinect-based CIT program was evaluated for children with unilateral CP using a two-phase study design. Materials and Methods: In phase 1, ten children with unilateral CP were recruited. To confirm the achievement of the motor training goals, maximal UL joint angles were evaluated during gameplay. To evaluate children's perceptions of the game, a questionnaire was used. In phase 2, eight children with unilateral CP were recruited and received an 8 weeks Kinect-based CIT intervention. Performance scores of the game and outcomes of the box and block test (BBT) were recorded weekly. Results: In phase 1, results supported that the design of the program was CIT-specific and was motivational for children with unilateral CP. In phase 2, game performance and the BBT scores began showing stable improvements in the fifth week of intervention. Conclusion: It suggested the Kinect-based CIT program was beneficial to the motor function of the affected UL for children with unilateral CP. According to the results of this feasibility study, larger and controlled effectiveness studies of the Kinect-based CIT program can be conducted to further improve its clinical utility. Clinical Trial Registration: ClinicalTrials.gov, NCT02808195; Comparative effectiveness of a Kinect-based unilateral arm training system vs. CIT for children with CP.

PMID: 34765593

11. Virtual motor training to improve the activities of daily living, hand grip, and gross motor function among children with cerebral palsy: Meta-regression analysis

Yanran Zhang, Runze Li, Xiuxin Miao, Ling Jie Cheng, Ying Lau

Review Gait Posture. 2021 Nov 5;91:297-305. doi: 10.1016/j.gaitpost.2021.10.046. Online ahead of print.

Background: Given that cerebral palsy is a lifelong condition, continuous motor training is necessary to correct abnormal posture and patterns to improve functional performance. Objective: To explore the essential features of virtual motor training and identify its effects on the activities of daily living, hand grip function, and gross motor function among children with cerebral palsy. Methods: Ten databases were systematically searched for randomized controlled trials from inception until

October 15, 2019. Studies with a randomized controlled trials design, children with cerebral palsy, comparisons of virtual motor training with other interventions, and activities of daily living, hand grip, and gross motor function outcomes were included. Subgroup analyses and meta-regression were performed. The effect size was assessed using random-effects meta-analysis and evaluated by using Hedges' g. Random effects univariate meta-regression model was used to examine the association of covariates with intervention effectiveness. Results: Seventeen randomized controlled trials with 853 participants were included. Meta-analysis indicated that the virtual motor training had significant positive effects on activities of daily living (g = 0.31, 95% confidence interval, CI = 0.10, 0.51), grip (g = 0.40, 95% CI = 0.08, 0.71), and gross motor (g = 0.71, 95% CI = 0.43, 0.99) function. Univariate random-effects meta-regression analysis indicated an increase in activities of daily living scores for motion capture systems that used depth imaging compared with those that used digital imaging. Significance: Our systematic review indicated that virtual motor function may significantly improve ADLs, hand grip, and gross motor functions among children with cerebral palsy.

PMID: 34798421

12. Efficacy assessment of virtual reality therapy for neuromotor rehabilitation in home environment: a systematic review

Vibhuti Vibhuti, Neelesh Kumar, Chitra Kataria

Disabil Rehabil Assist Technol. 2021 Nov 11;1-21. doi: 10.1080/17483107.2021.1998674. Online ahead of print.

Purpose: Neuromotor impairments can affect any part of the body. It leads to many disorders, injuries, or disabilities, conventional rehabilitation is a long, rigorous, and tedious process. There is a need to inculcate new and innovative techniques in rehabilitation processes, to increase individuals' interest and overall performance with such therapies. Virtual Reality is considered a new technology that has the potential to be a useful aid in overcoming therapeutic problems in clinical and home-based environments. However, providing home-based rehabilitation is more practicable, cost-effective, and even safer than in-hospital rehabilitation. In addition, the need for home-based rehabilitation is growing as the number of neuromotor disorders rises and the capacity of acute inpatient rehabilitation decreases. Therefore, the main objective of this study was to assess the efficacy of a home-based Virtual Reality exercise treatment to identify the areas for future rehabilitation research. Materials and methods: Data Extraction of 24,257 articles from seven databases were identified and the review is narrowed down and only 45 studies were focussed on efficacy assessment of Virtual Reality in the home environment. Results: The significant outcome of the effective home-based therapy system for the exercise improved functional ability, increasing range of motion, and motivation through Virtual reality-based rehabilitation is inferred. Conclusion: Unlike clinical settings, a home-based system provides efficacious therapy with a controlled environment. This survey facilitates bettering methods and devices for neuromotor disorders. It is a good living long-term problem-solving approach and investigates awareness, needs, and a preferred component of home-based rehabilitation services. IMPLICATIONS FOR REHABILITATION: VR-based rehabilitation in the home environment has many physical and mental benefits in persons with neuromotor disorders. The most commonly neuromotor disorders considered in the study were Stroke, Spinal Cord Injury, Parkinson's disease, and Cerebral Palsy. Assistive technologies in home environments can compensate for long-term disorders or be used in rehabilitation as an addition to conventional therapy. The study gives an overview of current interventions and how they can be of benefit for a person suffering from neuromotor disorders in the home environment.

PMID: 34761705

13. Effects of Robotic-Assisted Gait Training in Children and Adolescents with Cerebral Palsy: A Network Meta-Analysis

Raquel Olmos-Gómez, Antonia Gómez-Conesa, Inmaculada Calvo-Muñoz, José A López-López

Review J Clin Med. 2021 Oct 24;10(21):4908. doi: 10.3390/jcm10214908.

Gait disturbances are common in children and adolescents with cerebral palsy (CP). Robotic-assisted gait training (RAGT) is becoming increasingly widespread, and hence it is important to examine its effectiveness. A network meta-analysis (NMA) of clinical trials comparing treatments with RAGT vs. other physical therapy treatments was carried out. This study was conducted according to the NMA version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) guidelines and following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions. The outcome variables used were the D and E dimensions of the Gross Motor Function Measure (GMFM), gait speed, resistance, and stride length. Among 120 records, 8 trials were included. This NMA did not find statistically significant results for any of the comparisons examined in any of the outcomes studied and the magnitude of the effect size estimates was low or very low. Our NMA results should be interpreted with caution due to the high clinical heterogeneity of the studies included.

PMID: 34768427

14. The effect of patient-specific factors on responsiveness to robot-assisted gait training in patients with bilateral spastic cerebral palsy

Stanislava Klobucká, Robert Klobucký, Branislav Kollár

NeuroRehabilitation. 2021;49(3):375-389. doi: 10.3233/NRE-210130.

Background: No general recommendations are yet available for the application of robot-assisted treadmill therapy for children with cerebral palsy regarding the length and intensity of the intervention. Objective: The aim of the study was to evaluate patient-specific determinants of responsiveness to robot-assisted gait training (RAGT) in patients with bilateral spastic cerebral palsy. Method: During 12 months, the patients underwent 1-4 blocks of RAGT, representing 16-82 TUs. The following parameters were evaluated before (V0) and after each therapeutic block (V1-V4): dimension A (lying and rolling), B (sitting), C (crawling and kneeling), D (standing), E (walking, running and jumping) of the Gross Motor Function Measure (GMFM-88). We evaluated the change in motor functions in relation to the severity of disability, age, gender and number of therapeutic units. Results: Ninety-seven patients aged between 3.7 and 27 years (mean age 10.02 years (SD±5.29); Gross Motor Function Classification System level I [n = 5], II [n = 25], III [n = 48], IV [n = 19]) underwent 16-82 TUs (overall average number 34.06 TUs, SD±16.41) of RAGT. In the patient group, we recorded clinically meaningful improvement and statistically significant improvement ($p < 0.001$) in gross motor functions with gradual increase in the effect size after each therapeutic block. Using correlation and regression analysis, we found a statistically significant associations between the number of therapeutic units, severity of disability, and improvement in motor functions after RAGT. Conclusion: We have identified two determinants -the severity of disability and the number of therapeutic units -which could have a decisive and predictive character in setting rehabilitation/designing programmes. The duration of the applied RAGT period, frequency and intensity could be a crucial factor for the potential of improvement in children with BS-CP.

PMID: 34776432

15. Usability and performance validation of an ultra-lightweight and versatile untethered robotic ankle exoskeleton

Greg Orekhov, Ying Fang, Chance F Cuddeback, Zachary F Lerner

J Neuroeng Rehabil. 2021 Nov 10;18(1):163. doi: 10.1186/s12984-021-00954-9.

Background: Ankle exoskeletons can improve walking mechanics and energetics, but few untethered devices have demonstrated improved performance and usability across a wide range of users and terrains. Our goal was to design and validate a lightweight untethered ankle exoskeleton that was effective across moderate-to-high intensity ambulation in children through adults with and without walking impairment. Methods: Following benchtop validation of custom hardware, we assessed the group-level improvements in walking economy while wearing the device in a diverse unimpaired cohort (n = 6, body mass = 42-92 kg). We also conducted a maximal exertion experiment on a stair stepping machine in a small cohort of individuals with cerebral palsy (CP, n = 5, age = 11-33 years, GMFCS I-III, body mass = 40-71 kg). Device usability metrics (device don and setup times and System Usability Score) were assessed in both cohorts. Results: There was a 9.9 ± 2.6% ($p = 0.012$, range = 0-18%) reduction in metabolic power during exoskeleton-assisted inclined walking compared to no device in the unimpaired cohort. The cohort with CP was able to ascend 38.4 ± 23.6% ($p = 0.013$, range = 3-132%) more floors compared to no device without increasing metabolic power ($p = 0.49$) or perceived exertion ($p = 0.50$). Users with CP had mean device don and setup times of 3.5 ± 0.7 min and 28 ± 6 s, respectively. Unimpaired users had a mean don time of 1.5 ± 0.2 min and setup time of 14 ± 1 s. The average exoskeleton score on the System Usability Scale was 81.8 ± 8.4 ("excellent"). Conclusions: Our battery-powered ankle exoskeleton was easy to use for our participants, with initial evidence supporting effectiveness across different terrains for unimpaired adults, and children and adults with CP. Trial registration Prospectively registered at ClinicalTrials.gov (NCT04119063) on October 8, 2019.

PMID: 34758857

16. Strategies for highlighting items within visual scene displays to support augmentative and alternative communication access for those with physical impairments

Kevin M Pitt, John W McCarthy

Disabil Rehabil Assist Technol. 2021 Nov 17;1-11. doi: 10.1080/17483107.2021.2003455. Online ahead of print.

Purpose: In contrast to the traditional grid-based display, visual scene displays (VSDs) offer a new paradigm for aided communication. For individuals who cannot select items from an AAC display by direct selection due to physical impairments, AAC access can be supported via methods such as item scanning. Item scanning sequentially highlights items on a display until the individual signals for selection. How items are highlighted or scanned for AAC access can impact performance outcomes. Further, the effectiveness of a VSD interface may be enhanced through consultation with experts in visual communication. Therefore, to support AAC access for those with physical impairments, the aim of this study was to evaluate the perspectives of experts in visual communication regarding effective methods for highlighting VSD elements. Methods: Thirteen participants with expertise related to visual communication (e.g., photographers, artists) completed semi-structured interviews regarding techniques for item highlighting. Results: Study findings identified four main themes to inform how AAC items may be highlighted or scanned, including (1) use of contrast related to light and dark, (2) use of contrast as it relates to colour, (3) outline highlighting, and (4) use of scale and motion. Conclusion: By identifying how compositional techniques can be utilized to highlight VSD elements, study findings may inform current practice for scanning-based AAC access, along with other selection techniques where feedback or highlighting is used (e.g., eye-gaze, brain-computer interface). Further, avenues for just-in-time programming are discussed to support effective implementation for those with physical impairments. IMPLICATIONS FOR REHABILITATION: Findings identify multiple potential techniques to improve scanning through items in a photograph for individuals with severe motor impairments using alternative access strategies. Study findings inform current practice for scanning-based AAC access, along with other selection techniques where feedback or highlighting is used (e.g., eye-gaze, brain-computer interface). Avenues for just in time programming of AAC displays are discussed to decrease programming demands and support effective implementation of study findings.

PMID: 34788177

17. Health Conditions in Adults With Cerebral Palsy: The Association With CP Subtype and Severity of Impairments

Ulrica Jonsson, Meta N Eek, Katharina Stibrant Sunnerhagen, Kate Himmelmann

Front Neurol. 2021 Oct 28;12:732939. doi: 10.3389/fneur.2021.732939. eCollection 2021.

Aim: To determine the prevalence of common health conditions in adults with cerebral palsy (CP) and to identify associations with the CP subtype or the severity of impairments. Methods: A population-based, cross-sectional study of 153 adults with CP born from 1959 to 1978 (87 males, 66 females; median age 48 years 3 months, range 37-58 years; 41% with unilateral spastic, 36% bilateral spastic, 19% dyskinetic, and 4% with ataxic CP). Data was gathered through interviews, physical assessments, and medical record reviews. Results: The most common health conditions in adults with CP were pain 65%, upper gastrointestinal disorders 33%, dysphagia 29%, epilepsy 29%, and depression 27%. Cerebral palsy subtype was significantly associated with the presence of pain ($p = 0.029$), gastrointestinal ($p < 0.001$), and respiratory disorders ($p = 0.006$). A more severe physical impairment was associated with a higher prevalence of gastrointestinal disorders ($p < 0.001$), respiratory disorders ($p < 0.001$), and pressure ulcers ($p < 0.001$). Intellectual disability was associated with a higher prevalence of gastrointestinal disorders ($p < 0.001$), pneumonia ($p = 0.001$) epilepsy ($p = 0.001$), and pressure ulcers ($p < 0.001$), but with a lower prevalence of pain ($p < 0.004$) and hypertension ($p = 0.043$). Conclusion: The prevalence of several common health conditions is related to the CP subtype and severity of impairments, indicating that CP plays a role in the development of these health conditions. Follow-up of adults with CP needs to include not only impairments, but general health as well. Increased attention directed toward signs of gastrointestinal and respiratory disorders in individuals with either dyskinetic CP, gross motor function classification system (GMFCS) levels IV-V, or intellectual disability, is recommended.

PMID: 34777202

18. Relevance and applicability of ICF Core Sets for adults with cerebral palsy in low- and middle-income countries

Anupa Pathak, Saurab Sharma

Dev Med Child Neurol. 2021 Nov 18. doi: 10.1111/dmcn.15113. Online ahead of print.

PMID: 34796489

19. Physical Activity Levels of Adolescents and Adults With Cerebral Palsy in Urban South Africa

Roshaan Salie, Maaike M Eken, Kirsten A Donald, A Graham Fieggen, Nelleke G Langerak

Front Neurol. 2021 Oct 28;12:747361. doi: 10.3389/fneur.2021.747361. eCollection 2021.

Background: Research in high income countries shows that people with cerebral palsy (CP) are less physically active than typically developing (TD) peers, but less is known regarding physical activity (PA) in those with CP in low-to-middle income countries. The aim of this study was to determine daily step count and levels of PA in adolescents and adults with CP living in urban South Africa, compared to TD peers, and to determine associations with sex, Gross Motor Function Classification System (GMFCS) level, body mass index and socio-economic status. Materials and Methods: This case-control study included 26 adolescents and 22 adults with CP (GMFCS Level I-V) and matched TD peers (25 and 30, respectively). Participants wore an ActiGraph GT3X for 7 consecutive days to determine step count and time (minutes per hour) spent in PA levels, including sedentary (SED), low physical activity (LPA) and moderate to vigorous physical activity (MVPA). Results: The daily step count and PA levels for ambulant adolescents with CP (GMFCS level I-III) were similar to TD peers, while this was less for adolescents classified in GMFCS level IV-V. Daily step count, SED and MVPA were similar for adults classified in GMFCS level I-II compared to TD adults, while all parameters were lower for adults using assistive devices (GMFCS level III) and non-ambulant adults (GMFCS level IV-V) compared to TD peers. Daily step count and PA levels were inversely associated with GMFCS, while no other associations were found. Conclusion: People with CP who were more mobile dependent (higher GMFCS level) were less active. However, adolescents and adults with CP classified as GMFCS levels I-II living in urban South Africa recorded similar step count and PA levels as their TD peers. This was also the case for adolescents using assistive devices, though not for those in the adult group (GMFCS level III). Furthermore, it was apparent that even the ambulant individuals with CP and TD cohorts were relatively inactive. Intervention programs for CP and TD adolescents should be aimed at finding strategies to keep adolescents physically active well into adulthood, in order to promote physical health, social and emotional well-being and independence.

PMID: 34777217

20. Perceptions of family-centred care among caregivers of children with cerebral palsy in South India: An exploratory study

Deepalaxmi Paresh Poojari, Shashikiran Umakanth, G Arun Maiya, Bhamini Krishna Rao, Marie Brien, Amitesh Narayan

Child Care Health Dev. 2021 Nov 17. doi: 10.1111/cch.12929. Online ahead of print.

Background: Parental views and expectations about family-centred care (FCC) needs to be understood for its successful implementation. Knowledge of caregiver's perceptions and needs, within their social and cultural context, forms the basis for effective health care partnerships with families. The purpose of this study was to explore perceptions about FCC among caregivers of children with cerebral palsy (CP) in South India. Method: Fourteen caregivers of children with CP (aged 4-12 years) living in rural areas of the coastal region of Karnataka, India, participated in this qualitative study. Face-to-face semi-structured interviews were recorded and transcribed for analysis using the framework and hybrid approaches. Thematic mapping of the categories and themes was done to explore relationships about perceptions of FCC. Results: Caregiver's life emerged inductively as a new theme highlighting caregiver's own physical and mental health, family roles, and well-being, integrating the onus of care with household responsibilities, limited participation in personal activities, and social isolation. The qualitative findings revealed the ubiquity of respectful and trusting relationships with health professionals while expressing paucity of coordinated comprehensive care, sporadic partnerships and opportunities for shared decision-making, desire for receiving specific information related to child's progress and prognosis, and general information on community resources and the need of empowerment and support groups. Conclusion: Our study has practical implications for the implementation of FCC within the South Indian context, by recognizing unique caregiver needs and expectations in sync with cultural perspectives towards childhood disability such as societal stigma, values, and traditional beliefs; attitudes towards medical professionals, and life stressors and gender-responsibilities.

PMID: 34791682

21. Genetic Spectrum Identified by Exome Sequencing in a Chinese Pediatric Cerebral Palsy Cohort

Hongfang Mei, Lin Yang, Tiantian Xiao, Sujuan Wang, Bingbing Wu, Huijun Wang, Yulan Lu, Xinran Dong, Hong Yang, Wenhao Zhou

J Pediatr. 2021 Nov 14;S0022-3476(21)01084-2. doi: 10.1016/j.jpeds.2021.11.019. Online ahead of print.

Objective: To explore the genetic spectrum of cerebral palsy (CP) in a Chinese paediatric cohort. Study design: This was a retrospective observational study of patients with CP from the Children's Hospital of Fudan University between June 2015 and December 2019. Their clinical data and exome sequencing data were collected and analysed. Results: A total of 217 patients with CP were enrolled, and genetic variants were identified in 78 subjects (35.9%): 65 patients with single-nucleotide variants (SNVs), 12 patients with copy number variants (CNVs) and one patient with both an SNV and a CNV. The genetic diagnosis rates were significantly higher in patients without clinical risk factors than in patients with clinical risk factors ($\chi2=21.705$, P = .000) and were significantly higher in patients with a family history than in those without a family history ($\chi2=4.493$, P=0.034). Variants in genes related to neurologic disorders were the most commonly detected variants, affecting 41 patients (62.1%, 41/66). Among the patients with SNVs detected, the top 12 genes were found to cover 62.1% (41/66) of cases, and 39.4% (26/66) of patients with SNVs had medically actionable genetic findings. Conclusions: The overall genetic diagnostic rate in this study was 35.9%, and patients without any clinical risk factors or with a family history were more likely to have genetic risk factors. The top 12 genes detected in this study as well as genes related to neurologic disorders or other medically actionable disorders should be noted in the analysis of genetic testing results in patients with CP.

PMID: 34788679

22. The Effects of Preterm Birth on Musculoskeletal Health-Related Disorders

Florian Schachinger, Sebastian Farr

Review J Clin Med. 2021 Oct 29;10(21):5082. doi: 10.3390/jcm10215082.

Preterm birth is associated with various diseases and conditions which demand multidisciplinary medical care. Approximately 10% of all neonates are born prematurely with an increasing survival rate in almost all Western countries. This ongoing, yet desirable trend is creating new challenges for sufficient medical treatment regimens, which should be upheld throughout the patients' lives. Orthopedic surgeons are focused on musculoskeletal disorders and the improvement of patients' ability to cope with the challenges of everyday life. The most common conditions associated with preterm birth are cerebral palsy and a dysregulation of the calcium/phosphorus metabolism, which may lead to fractures. These diseases may vary greatly in their organic manifestation and clinical presentation. This demands multidisciplinary cooperation and parental support. Clinical management is aimed on the early enhancement of a patient's physical, as well as neurological condition, and to prevent the development of secondary musculoskeletal disorders. In this article, we give an overview of the current literature on the most common musculoskeletal disorders associated with preterm birth and critically discuss state of the art diagnostic standards and treatment algorithms.

PMID: 34768599

23. Risk Factors and Outcomes of Deep Tissue Candida Invasion in Neonates with Invasive Candidiasis

Hanin Eisi, Shohood Ibraheem, Tooba Hisham, Aziza Al-Harbi, Khalid Saidy, Ismail Ali, Islam Nour, Nehad Nasef

Mycoses. 2021 Nov 15. doi: 10.1111/myc.13395. Online ahead of print.

Background: Deep tissue Candida invasion represents a special entity among neonates with invasive candidiasis. We aimed to explore the risk factors and clinical outcomes for deep tissue Candida invasion among neonates with invasive candidiasis. Methods: A Retrospective data review of neonates admitted to NICU of Madinah maternity and children hospital, KSA from January 2012 to December 2019 was done. Data were analyzed between infants with or without deep tissue candidiasis among infants with invasive candidiasis. Invasive candidiasis was defined as positive blood or catheter collected urine culture for Candida. Deep tissue Candida invasion was defined as an infection of the central nervous system, eyes, heart, skeletal system, lungs, liver, or kidneys. Result: A total of 14 (11%) out of 130 neonates with invasive candidiasis had deep tissue Candida invasion. Persistent positive blood culture for Candida [OR 15.2, 95% CI (2.0 - 114), p = 0.01], prematurity [OR 7.6, 95% CI

(1.04 - 56.4), p = 0.04], and prolonged antibiotic duration [OR 1.3, 95% CI (1.02 - 1.6), p = 0.03] are independent risk factors for deep tissue Candida invasion. Deep tissue Candida invasion was associated with significantly higher rates of cerebral palsy, hydrocephalus, heart failure, and longer length of hospital stay compared to infants without deep tissue invasion. Conclusion: Persistent Candida growth in blood cultures, prematurity, and long-term antibiotic use are significant risk factors for deep tissue Candida invasion. Deep tissue Candida invasion is associated with prolonged hospital stay and higher neonatal morbidity.

PMID: 34780084

24. Risk Factors of Intractable Epilepsy in Children with Cerebral Palsy

Yehia Hamed Abdel Maksoud, Hany Abdelaziz Suliman, Sameh ElSAYED Abdulsamea, Naglaa Mohamed Kamal, Ashraf Hamed Al-Shokray, Asmaa Obada Ibrahim, Hatem Hamed Elshorbagy, Mohamed Gamal El Din Fathallah, Ahmed Mahmoud Attia, Akram Elshafey Elsadek

Iran J Child Neurol. Fall 2021;15(4):75-87. doi: 10.22037/ijcn.v15i3.31556.

Objectives: We aimed to investigate the risk factors predicting the development of intractable epilepsy in children with cerebral palsy (CP), with an emphasis on perinatal characteristics, seizure semiology, imaging, and EEG findings. Materials & methods: Following a descriptive, retrospective, case-control design, 106 children with CP and epilepsy from 2015 to 2020 were studied (46 children with CP and intractable epilepsy and 60 with CP and controlled epilepsy). Data were retrieved from medical records of participants (i.e., demographics, clinical characteristics, perinatal history, etiology of seizure and CP, seizure semiology, intellectual functions, therapeutic options, brain imaging, and EEG findings). Results: We established a model of the most important risk factors that can predict intractable epilepsy in children with CP. The model included the additive effect of a poor Apgar score at 5 minutes, the presence of neonatal seizures, focal epilepsy, and focal slowing on the EEG background (Area under the receiver operating characteristic of 0.810). Conclusion: The findings can be used to identify intractable epilepsy in children who suffer from CP with further support by offering early therapeutic interventions intended to reduce the burden of refractory seizures.

PMID: 34782844

25. Comparative effects of community-based family-child-centered care and conventional pediatric rehabilitation for cerebral palsy

Mikyoung Kim, Chanhee Park, Hyeseon Jeon, Woochol Joseph Choi, Sung Joshua Hyun You

NeuroRehabilitation. 2021 Nov 10. doi: 10.3233/NRE-210219. Online ahead of print.

Background: While the transdisciplinary-based rehabilitation provided ample evidence on improving impairment (body structure and functions) levels, the therapeutic effects on the international classification of functioning, disability, and health (ICF) domains are unknown in cerebral palsy (CP). Objective: To compare the effects of the community-based family-child-centered care (CFC) and conventional pediatric rehabilitation (CPR) on the physical, cognitive, sensory, and social integration domains in children and adolescents with CP. Methods: Twenty-six participants with CP (mean age = 9.37±5.24, 14 females) were assigned into either CPR or CFC groups. Clinical outcomes included gross motor function measure (GMFM-66), Pediatric Balance Scale (PBS), fine motor area of Bruininks-Oseretsky Test of Motor Proficiency-2 (BOT-2), Functional Independence Measure (FIM) cognition area, Short Sensory Profile (sSP), COPM, Pediatrics Quality of Life (PedsQL) questionnaire, Short Falls Efficacy Scale (sFES), and Dynamic Postural Instability (DPI). An analysis of variance (ANOVA) and an analysis of covariance (ANCOVA) was conducted at $P < 0.05$. Results: ANOVA revealed the superior effects of CFC in GMFM-66, PBS, BOT-2, FIM, and PedsQL compared to CPR ($P < 0.05$). ANCOVA showed the superior effects of CFC in Z-axis of DPI than CPR ($P < 0.05$). Conclusions: Our results provide novel, promising clinical evidence that CFC was more effective than CPR at improving impairment, activity, as well as participation levels in participants with CP.

PMID: 34776430

26. Need to Perform Rehabilitation Exercises at Home by Parents of Children with Neurological Diseases to Maintain Performance During COVID-19 Lockdown

Alireza Shamsoddini, Behzad Bazigar, Hamid Dalvand

Review Iran J Child Neurol. Fall 2021;15(4):9-14. doi: 10.22037/ijcn.v16i1.30019.

With the outbreak of the novel pandemic coronavirus disease 2019 worldwide, numerous pediatric rehabilitation clinics have closed to support social and physical distancing, and therapists similar to other individuals are staying at their homes. There is a common concern of parents and caregivers that how and with what quality children's rehabilitation exercises should proceed. Most children with neurological diseases have problems, such as muscle spasticity, range of motion (ROM) limitation, muscle shortening, balance loss, and mobility and movement impairments. The normalization of muscle tone, preservation of ROM, muscle stretch, and improvement of fine and gross motor skills and balance are essential activities that need to be considered. Therefore, this study aimed to summarize the necessities of a home-based rehabilitation exercise program during the quarantine period.

PMID: 34782837

27. Special Needs Insurance: More Stability for a Growing Family's Budget

David Morel

J Insur Med. 2021 Nov 1;49(s1):1-31. doi: 10.17849/insm-49-s1-1-31.1.

Objective.—: To propose an insurance product called special needs insurance. The insurance will pay parents a lump sum up to $100,000 if they have a child that is born with or develops a special needs condition such as Down syndrome, cerebral palsy or autism. Background.—: Raising a child is expensive; raising a child with a special need can be hundreds of thousands of dollars more expensive. These additional costs include direct costs that are not covered by health insurance and indirect costs such as the loss of earnings when a working parent must tend to a special needs child. Method.—: We analyze a gamut of birth and early childhood disabilities, both physical and cognitive, from the medico-actuarial perspective. We describe each condition using relevant medical literature and calculate prevalence rates from epidemiological studies (appendix A1-A15). After accounting for multiple births, we develop a final premium. Results.—: We find that physical impairments are sufficiently well understood to guarantee a fixed payout, whereas cognitive impairments such as autism are less understood, and so for these we propose a cognitive fund that does not guarantee a fixed payout. We find that an average single premium of $4,600 allows the insurer to profitably pay out the proposed benefits. Conclusions.—: Raising a special needs child can put a significant strain on the affected family's budget. We propose an insurance product that provides relief through a large lump sum payout. Although no new insurance product can be guaranteed success, our analysis of this product gives an interested insurer reasonable justification to take on this new risk.

PMID: 34788842

28. Quality of Life in Young Adults With Cerebral Palsy: A Longitudinal Analysis of the SPARCLE Study

Nicolas Vidart d'Egurbide Bagazgoïtia, Virginie Ehlinger, Carine Duffaut, Jérôme Fauconnier, Silke Schmidt-Schuchert, Ute Thyen, Kate Himmelmann, Marco Marcelli, Catherine Arnaud

Front Neurol. 2021 Nov 1;12:733978. doi: 10.3389/fneur.2021.733978. eCollection 2021.

Introduction: While most people with cerebral palsy (CP) will have a life expectancy similar to that of the general population, international research has primarily focused on childhood and adolescence; and knowledge about the quality of life (QoL) of young adults with CP, its trajectories, and associated factors remains scarce. Methods: This longitudinal study included young adults with CP living in five European regions and who had previously participated in the SPARCLE cohort as children and/or adolescents. Their QoL in the psychological well-being and social relationships domains was estimated using age-appropriate validated instruments (KIDSCREEN-52 in childhood/adolescence and WHOQOL-Bref in young adulthood). We used generalized linear mixed-effect models with random intercept to estimate long-term trajectories of QoL in both domains and to investigate whether severity of impairment, pain, and seizure influenced these trajectories. We sought to identify potentially different trajectories of QoL from childhood to adulthood using a shape-based clustering method. Results: In total, 164 young adults with CP aged 22-27 years participated in the study. Psychological well-being linearly decreased by 0.78 points (scale 0-100) per year (95% confidence interval (CI) -0.99 to -0.56) from childhood to young adulthood, whereas QoL in the social relationships domain increased (β coefficient 1.24, 95% CI 0.92-1.55). Severity of impairment was associated with reduced QoL in all life periods of the study (childhood, adolescence, and young adulthood): motor impairment with social relationships, and more nuancedly intellectual disability with psychological well-being and social relationships. At all periods, frequent pain significantly reduced psychological well-being, and seizures were associated with lower QoL in the social relationships domain. In both domains, we identified a group of individuals with CP who presented a reverse trajectory compared with the general QoL trajectory. Conclusion: Identification of QoL trajectories and their associated factors yields improved knowledge about the experience of individuals with CP until young adulthood. Further studies are needed to better understand the determinants that have the greatest influence on the different shapes of long-term trajectories of QoL.

PMID: 34790161

29. Should bone mineral content be part of the equation for assessing fracture risk in patients with cerebral palsy?
Weronika Agnieszka Szlachetka, Phyo Kyaw Myint

Dev Med Child Neurol. 2021 Nov 19. doi: 10.1111/dmcn.15118. Online ahead of print.

PMID: 34797573

30. Muscle synergies in cerebral palsy and variability: challenges and opportunities
Andrea d'Avella, Yury Ivanenko, Francesco Lacquaniti

Dev Med Child Neurol. 2021 Nov 15. doi: 10.1111/dmcn.15106. Online ahead of print.

PMID: 34780675

Prevention and Cure

31. Synergistic Effect in Neurological Recovery via Anti-Apoptotic Akt Signaling in Umbilical Cord Blood and Erythropoietin Combination Therapy for Neonatal Hypoxic-Ischemic Brain Injury
Jee In Choi, Joo-Wan Choi, Kyu-Ho Shim, Jin Seung Choung, Hyun-Jin Kim, Hye Ryeong Sim, Mi Ri Suh, Joo Eun Jung, MinYoung Kim

Int J Mol Sci. 2021 Nov 5;22(21):11995. doi: 10.3390/ijms222111995.

Our previous clinical studies demonstrated the synergistic therapeutic effect induced by co-administering recombinant human erythropoietin (rhEPO) in human umbilical cord blood (hUCB) therapy for children with cerebral palsy. However, the cellular mechanism beyond the beneficial effects in this combination therapy still needs to be elucidated. A hypoxic-ischemic encephalopathy (HIE) model of neonates, representing cerebral palsy, was prepared and randomly divided into five groups (hUCB+rhEPO combination, hUCB, and rhEPO treatments over HIE, HIE control, and sham). Seven days after, hUCB was administered intraperitoneally and the rhEPO injections were started. Neurobehavioral tests showed the best outcome in the combination therapy group, while the hUCB and rhEPO alone treatments also showed better outcomes compared with the control ($p < 0.05$). Inflammatory cytokines were downregulated by the treatments and attenuated most by the combination therapy ($p < 0.05$). The hUCB+rhEPO treatment also showed remarkable increase in phosphorylation of Akt and potentiation of anti-apoptotic responses with decreased Bax and increased Bcl-2 ($p < 0.05$). Pre-treatment of MK-2206, an Akt inhibitor, for the combination therapy depressed the anti-apoptotic effects. In conclusion, these findings suggest that the therapeutic effect of hUCB therapy might be potentiated by co-administration of rhEPO via augmentation of anti-inflammatory and anti-apoptotic responses related to the phosphorylation of Akt.

PMID: 34769434