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Interventions and Management

1. The use of virtual reality in the stimulation of manual function in children with cerebral palsy: a systematic review
Kharinni Uchôa Pereira, Michelle Zampar Silva, Luzia Iara Pfeifer

Rev Paul Pediatr. 2023 Mar 13;41:e2021283. doi: 10.1590/1984-0462/2023/41/2021283. eCollection 2023.

Objective: To identify in national and international literature the use of virtual reality to develop manual skills of children with cerebral palsy. Methods: This is a systematic review carried out in the PubMed database, Portal de Periódicos da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and the Online System for Search and Analysis of Medical Literature (Ovid Medline) using the keywords "cerebral palsy", "virtual reality", "occupational therapy", "child", "daily activities/activities of daily living", in English and in Portuguese. The selected articles had their methodological quality evaluated through the Physiotherapy Evidence Database (PEDro scale). Results: 228 studies were selected, as they included children with cerebral palsy undergoing treatment with exposure to virtual reality to improve manual function in daily activities. Studies on other themes, incomplete, and duplicated reviews were excluded. Three evaluators conducted the study selection process and included 14 articles in the analysis. Conclusions: The findings suggest that virtual reality therapy has contributed to an improvement in the manual function of children with cerebral palsy, constituting a useful resource for a supporting intervention to enhance traditional therapies.

PMID: 36921161

2. Risk factors for 90-day readmission and prolonged length of stay after hip surgery in children with cerebral palsy
Liam R Butler, Calista L Dominy, Christopher A White, Paulos Mengsteab, Elaine Lin, Abigail K Allen, Sheena C Ranade

J Orthop. 2023 Mar 2;38:14-19. doi: 10.1016/j.jor.2023.03.002. eCollection 2023 Apr.

Objective: Spastic hip dysplasia is a common complication of cerebral palsy in children, and surgical intervention is usually warranted. While current literature has primarily analyzed single institution outcomes, this study utilized a national database to describe readmission rates and factors correlated with readmission for children with cerebral palsy undergoing hip surgery in order to treat this population more effectively. Methods: This study queried the Nationwide Readmissions Database (2014-2018) for pediatric patients with cerebral palsy who underwent hip surgery. Patient demographics, pre-operative comorbidities, length of stay (LOS), treatment complications, and readmission data were collected for each patient and analyzed with inferential statistics. Results: Of the 1225 patients included, the average age was 9.3 ± 3.8 years and 42.8% were female. Approximately 26.3% patients had a prolonged LOS (≥5 days) and 14.2% patients required readmission within 90-days of surgery. Medical complications, cardiac arrhythmias, and iron deficiency anemia were all significantly associated with elongated LOS as well as 90-day readmission. Patients with Medicaid were more frequently associated with an inpatient

medical complication and the overall complication rate was 5.5%. Conclusions: While current literature has analyzed common risk factors and complications associated with hip surgery in the pediatric cerebral palsy patient, this study identifies a national readmission rate (14.2%) as well as preoperative comorbidities associated with readmission within 90-days and/or elongated LOS. Notably, complications are more frequently associated with patients using Medicaid. These results further exemplify the importance of equitable access to care and thorough selection of pediatric cerebral palsy patients appropriate for hip surgery.

PMID: 36925762

3. Intra- and inter-subject variability of femoral growth plate stresses in typically developing children and children with cerebral palsy

Willi Koller, Basílio Gonçalves, Arnold Baca, Hans Kainz

Front Bioeng Biotechnol. 2023 Feb 24;11:1140527. doi: 10.3389/fbioe.2023.1140527. eCollection 2023.

Little is known about the influence of mechanical loading on growth plate stresses and femoral growth. A multi-scale workflow based on musculoskeletal simulations and mechanobiological finite element (FE) analysis can be used to estimate growth plate loading and femoral growth trends. Personalizing the model in this workflow is time-consuming and therefore previous studies included small sample sizes (N < 4) or generic finite element models. The aim of this study was to develop a semi-automated toolbox to perform this workflow and to quantify intra-subject variability in growth plate stresses in 13 typically developing (TD) children and 12 children with cerebral palsy (CP). Additionally, we investigated the influence of the musculoskeletal model and the chosen material properties on the simulation results. Intra-subject variability in growth plate stresses was higher in cerebral palsy than in typically developing children. The highest osteogenic index (OI) was observed in the posterior region in 62% of the TD femurs while in children with CP the lateral region was the most common (50%). A representative reference osteogenic index distribution heatmap generated from data of 26 TD children's femurs showed a ring shape with low values in the center region and high values at the border of the growth plate. Our simulation results can be used as reference values for further investigations. Furthermore, the code of the developed GP-Tool ("Growth Prediction-Tool") is freely available on GitHub (https://github.com/WilliKoller/GP-Tool) to enable peers to conduct mechanobiological growth studies with larger sample sizes to improve our understanding of femoral growth and to support clinical decision making in the near future.

PMID: 36911204

4. Reliability of assessing proximal femur geometry with Rutz classification schema in patients with cerebral palsy

Maciej Kasprzyk, Aleksander Koch, Lukasz M Karbowski, Marek Jóźwiak, Unni G Narayanan

J Pediatr Orthop B. 2023 Mar 13. doi: 10.1097/BPB.0000000000001077. Online ahead of print.

Our investigation aimed to assess the reliability of the femoral head shape classification system devised by Rutz et al. and observe its application in patients with cerebral palsy (CP) at different skeletal maturity levels. Four independent observers assessed anteroposterior radiographs of the hips of 60 patients with hip dysplasia associated with non-ambulatory CP (Gross Motor Function Classification System levels IV and V) and recorded the femoral head shape radiological grading system as described by Rutz et al. Radiographs were obtained from 20 patients in each of three age groups: under 8 years, between 8 and 12 years and above 12 years old, respectively. Inter-observer reliability was assessed by comparing the measurements of four different observers. To determine the intra-observer reliability, radiographs were reassessed after a 4-week interval. Accuracy was checked by comparing these measurements with the assessment of expert consensus. Validity was checked indirectly by observing the relationship between the Rutz grade and the migration percentage. The Rutz classification system's evaluation of femoral head shape showed moderate to substantial intra- and inter-observer reliability (mean κ = 0.64 for intraobserver and mean κ = 0.5 for interobserver). Specialist assessors had slightly higher intra-observer reliability than trainee assessors. The grade of femoral head shape was significantly associated with increasing migration percentage. Rutz's classification was shown to be reliable. Once the clinical utility of this classification can be established, it has the potential for broad application for prognostication and surgical decision-making and as an essential radiographic variable in studies involving the outcomes of hip displacement in CP. Level of evidence: III.

PMID: 36913560

5. Lower extremity proprioception and its association with activity and participation in children with unilateral spastic cerebral palsy

Fulya Ipek Erdem, Mintaze Kerem Gunel, Ipek Alemdaroglu-Gurbuz

Objective: This cross-sectional study aimed to assess lower extremity proprioception and investigate its relationship to activity and participation levels in children with unilateral spastic cerebral palsy (USCP). Methods: A total of 22 children with USCP between the ages of 5 and 16 years participated in this study. Lower extremity proprioception was evaluated with a protocol that consisted of verbal and location identification, unilateral and contralateral limb matching, and static and dynamic balance tests performed with the impaired and less impaired lower extremities under eyes-open and eyes-closed conditions. Furthermore, the Functional Independence Measure (WeeFIM) and Pediatric Outcomes Data Collection Instrument (PODCI) were used to evaluate the independence levels in daily living activities and participation levels. Results: Children demonstrated proprioceptive loss, as evidenced by an increase in matching errors under the eyes-closed condition compared to the eyes-open condition ($p<0.05$). Also, the impaired extremity had greater proprioceptive loss than the less impaired extremity ($p<0.05$). The 5-6-year age group experienced greater proprioceptive deficits than did the 7-11 and 12-16 age groups ($p<0.05$). Children's lower extremity proprioceptive deficit was moderately associated with their activity and participation levels ($p<0.05$). Conclusions: Our findings suggest that treatment programs based on comprehensive assessments, including proprioception, may be more effective in these children.

6. Circus Activities as a Health Intervention for Children, Youth, and Adolescents: A Scoping Review

Free Coulston, Kate L Cameron, Kath Sellick, Madeline Cavallaro, Alicia Spittle, Rachel Toovey

Circus activities are emerging as an engaging and unique health intervention. This scoping review summarises the evidence on this topic for children and young people aged up to 24 years to map (a) participant characteristics, (b) intervention characteristics, (c) health and wellbeing outcomes, and (d) to identify evidence gaps. Using scoping review methodology, a systematic search of five databases and Google Scholar was conducted up to August 2022 for peer-reviewed and grey literature. Fifty-seven of 897 sources of evidence were included (42 unique interventions). Most interventions were undertaken with school-aged participants; however, four studies included participants with age ranges over 15 years. Interventions targeted both general populations and those with defined biopsychosocial challenges (e.g., cerebral palsy, mental illness, or homelessness). Most interventions utilised three or more circus disciplines and were undertaken in naturalistic leisure settings. Dosage could be calculated for 15 of the 42 interventions (range one-96 h). Improvements in physical and/or social-emotional outcomes were reported for all studies. There is emerging evidence of positive health outcomes resulting from circus activities used in general populations and those with defined biopsychosocial challenges. Future research should focus on detailed reporting of intervention elements and increasing the evidence base in preschool-aged children and within populations with the greatest need.

7. Changes in Sprint Force-Velocity Profile in International Para Footballers

Iván Peña-González, Alejandro Javaloyes, Jose Manuel Sarabia, Manuel Moya-Ramón

Purpose: Force production is crucial in football, and it is the main limitation of people with cerebral palsy (CP). This study aimed to describe the changes in sprint force-velocity (Fv) profile after a period of 25 weeks of regular training in international football players with CP. Methods: The sprint Fv profile and other physical performance variables (ie, linear sprint, vertical jump, change of direction, and intermittent endurance) of 14 international players from the Spanish national team were assessed during 2 consecutive training camps. Pretesting and posttesting sessions were carried out 1 week before and after the 25-week intervention period. The intervention consisted of 2 strength sessions per week added to the usual football training.

Results: The repeated-measures analysis of variance showed changes in players' physical performance (linear sprint: F = 18.05, P < .01; change of direction: F = 16.71, P < .01; and endurance: F = 31.45, P < .01) and in some variables of the sprint Fv profile (maximal horizontal force, maximal power, slope, maximal ratio of force, and decrease of ratio of force; F = 14.28-37.81; P < .01), whereas players' maximal velocity (theoretical and actual) did not change (F = 0.13 and 0.01; P = .72 and .98, respectively). Conclusions: This study showed that the implementation of 2 strength-training sessions per week, for 25 weeks, is effective to improve CP football players' physical performance. The main finding of this study is the improvement of force application in the acceleration phase (sprint Fv profile), which is the main attribute in many physical performance tests and is the main limitation of the CP population.

PMID: 36927998

8. Increased physical activity, higher educational attainment, and the use of mobility aid are associated with self-esteem in people with physical disabilities
Majed M Alhumaid, Mohamed Ahmed Said

Front Psychol. 2023 Feb 23;14:1072709. doi: 10.3389/fpsyg.2023.1072709. eCollection 2023.

Background: High self-esteem can help people with disabilities overcome barriers and improve their mental health and well-being. This study sought to examine self-esteem levels among Saudis with physical disabilities based on socio-economic factors. It also aimed to determine the minimum weekly duration of physical activity performed by participants and examine its effects, along with those of other socio-economic factors, on participants' self-esteem. Methods: A participant sample (N = 582) consisting of Saudi individuals aged 33.78 ± 9.81 years with physical disabilities (males, n = 289; females, n = 293) was recruited to participate in this study. Levels of self-esteem were measured using the Arabic version of the Rosenberg Self-Esteem Scale. Results: Compared to women, men demonstrated significantly higher levels of overall self-esteem, positive feelings, and negative feelings (p < 0.01). The respondents' average levels of overall self-esteem (p < 0.001), positive feelings (p < 0.01), and negative feelings (p < 0.001) also varied by type of physical disability. Wheelchair-using participants had the highest values for self-esteem and positive feelings; cane-using participants or those who did not use mobility aids had the lowest values. Weighted least squares regression showed that weekly physical activity was the factor that most affected self-esteem (β = 0.002), followed by education level (β = 0.115), then type of mobility device used (β = -0.07). Conclusion: Increased weekly physical activity, higher education levels, and the use of mobility aids were the factors likely to improve the self-esteem of Saudis with physical disabilities.

PMID: 36910798

9. The Lower the Physical Function, the Higher the Quality of Life in Japanese Adolescents with Cerebral Palsy
Masako Kato, Hiroshi Arai, Koyu Komatsu, Kiyomi Tateyama, Takashi Nishikawa

Phys Occup Ther Pediatr. 2023 Mar 17;1-12. doi: 10.1080/01942638.2023.2186197. Online ahead of print.

Aims: To investigate the factors that contribute to subjective quality of life (QOL) in adolescents with cerebral palsy (CP). Methods: We evaluated the subjective QOL in 51 adolescents with CP through interviews using the Japanese version of KIDSCREEN-27 (J-KIDSCREEN-27) and compared the scores with those of 60 typically developing adolescents. Correlations of subjective QOL with age, sex, the levels of functions (gross motor, manipulation, and communication), intelligence, the level of activity of daily living (ADL), and the type of educational support were examined. Thereafter, we investigated the predictors of the subjective QOL by multiple regression analysis. Results: The total QOL scores and individual J-KIDSCREEN-27 domains were not significantly different from those of typically developing adolescents. Sex, manipulation and communication functions, and intelligence had no relationship with subjective QOL. Gross motor function and ADL level negatively correlated with satisfaction with the school environment. Multiple regression analysis revealed that higher age predicts lower psychological well-being, lower gross motor function predicts higher satisfaction with the school environment, and attending schools or classes for special needs predicts higher physical well-being. Conclusions: Seeking adequate support for mildly affected adolescents attending regular classes will be the key to further improving subjective QOL in adolescents with CP.

PMID: 36927329

10. Social support as a mediator between anxiety and quality of sleep among Chinese parents of special children
Junda Xu, Jiliang Tang

Objective: The psychological problems among Chinese parents of special children (mental retardation, limb disorder, hearing impairment, autism, cerebral palsy and other types) should be paid more attention. The aim of this study was to investigate the association between anxiety, social support, coping style and sleep quality among Chinese parents of special children during the early COVID-19 epidemic, so as to provide more help for the mental health of parents of special children scientifically and effectively. Method: A total of 305 Chinese parents of special children were invited to accomplish four questionnaires. Anxiety was measured by the Self-Rating Anxiety Scale, social support was evaluated by the Perceived Social Support Scale, sleep quality was assessed by the Pittsburgh Sleep Quality Index, and coping style was measured by the Simplified Coping Style Questionnaire. Results: This study revealed that anxiety was positively correlated with sleep quality ($p < 0.01$) and negatively correlated with social support ($p < 0.01$) and coping style ($p < 0.01$). Sleep quality was negatively correlated with social support ($p < 0.01$), but not significantly correlated with coping style ($p > 0.05$). Social support was positively correlated with coping style ($p < 0.01$). The study confirmed that social support had a partial mediating effect on the relationship between anxiety and sleep quality. Conclusion: The anxiety of parents of special children not only directly affects sleep quality, but also indirectly affects sleep quality through social support. Social support can alleviate the impact of anxiety on sleep quality through the mediating role.

PMID: 36910806

11. Parental Stress in Raising a Child with Developmental Disabilities in a Rural Community in South Africa
Nontokozo Lilian Mbatha, Kebogile Elizabeth Mokwena

Although acceptable levels of parental stress are experienced by all parents who raise children, this stress is substantially higher among parents who raise children with developmental disabilities. Sociodemographic determinants further exacerbate parental stress among parents in rural communities, which are disadvantaged in many ways. This study aimed to quantify parental stress among mothers and female caregivers of children with developmental disorders and investigate factors associated with such stress in rural Kwa-Zulu Natal, South Africa. A cross-sectional quantitative survey was used, in which the Parenting Stress Index-Short Form (PSI-SF) and a sociodemographic questionnaire was administered to mothers and caregivers who were raising children aged 1 to 12 years old who were living with developmental disabilities. The PSI-SF scores were used, where a total score of ≤84 percentile was categorised as normal/no parenting stress, 85-89 percentile was categorised as high parental stress, and scores of ≥90 were classified as clinically significant. The sample of 335 participants consisted of 270 (80.6%) mothers and 65 (19.4%) caregivers. Their ages ranged from 19 to 65 years, with a mean of 33.9 (±7.8) years. The children were mostly diagnosed with delayed developmental milestones, communication difficulties, epilepsy, cerebral palsy, autism, ADHD, cognitive impairment, sensory impairments, and learning difficulties. The majority (52.2%) of the participants reported very high-clinically significant stress levels (≥85%ile). The four factors that independently and significantly predicted high parental stress were the advanced age of mothers and caregivers ($p = 0.002$, OR 2.3, 95% CI 1.34-3.95), caring for a child with multiple diagnoses ($p = 0.013$, OR 2.0, 95% CI 1.16-3.50), non-school enrolment of the child ($p = 0.017$, OR 1.9, 95% CI 1.13-3.46), and frequent hospital visits ($p = 0.025$, OR 1.9, 95% CI 1.09-3.44). At the subscale level, child non-enrolment in a school was found to independently predict parent distress (PD) and parent-child dysfunctional interaction (P-CDI). Frequent hospital visits were statistically and significantly associated with the difficult child (DC) and P-CDI subscales. The study established high parental stress in mothers and caregivers raising children with developmental disabilities. Lack of access to school was an independent factor that consistently increased parental stress. There is a need for support and directed intervention programs aimed at supporting mothers and caregivers of children with developmental disabilities, which will enhance their parenting abilities.

PMID: 36900985

12. Prevalence, severity, and predictors of malnutrition in Indian children with cerebral palsy and their impact on health-related quality of life

Indar Kumar Sharawat, Aparna Ramachandran, Prateek Kumar Panda, Vinod Kumar, Nowneet Kumar Bhat

Although several studies have shown that undernutrition is frequent in children with cerebral palsy (CP), studies determining predictors of undernutrition and its impact on health-related quality of life (HRQoL) are scarce. This study aimed to assess the prevalence, severity, and predictors of malnutrition in children with CP and its impact on quality of life. This prospective study was performed between August 2019 and December 2021 in children with a clinical diagnosis of CP aged 2-18 years. We also intended to determine the socio-demographic and clinical predictors of undernutrition in these children and its impact on HRQoL, measured by the cerebral palsy quality of life (CPQoL)-Primary Caregiver reported version. Out of 569 (5.4 ± 2.8 years of age, 74% boys) children with CP, 71%, 44%, and 72% children were underweight, wasted, and stunted respectively, whereas 22%, 11%, and 21% were severely underweight, wasted and stunted respectively. Lower socioeconomic status, higher Gross Motor Function Classification System, and Manual Ability Classification System level were found to be significantly associated with the severity of stunting and underweight ($p < 0.05$), but not with wasting. CPQoL score in children with CP aged > 4 years was lower in patients with severe wasting, stunting, and underweight, as compared to their rest of the counterparts when adjusted for socio-demographic and other clinical variables ($p < 0.05$). Conclusion: Chronic undernutrition is more common than severe acute malnutrition in children with CP. The severity of undernutrition is an important predictor of impaired HRQoL in children with CP. What is Known: • Several studies have shown that undernutrition is frequent in children with cerebral palsy; however, studies determining predictors of undernutrition and its impact on health-related quality of life are scarce. What is New: • Our study identifies that lower socioeconomic status, higher Gross Motor Function Classification System, and Manual Ability Classification System level are significantly associated with the severity of stunting and being underweight. • Chronic undernutrition is more common than severe acute malnutrition in children with cerebral palsy. Its severity is an important predictor of impaired health-related quality of life in children with cerebral palsy.

PMID: 36917290

13. Electronic health record and patterns of care for children with cerebral palsy

No authors listed

No abstract available

PMID: 36917689

14. Systemic corticosteroid regimens for prevention of bronchopulmonary dysplasia in preterm infants

Wes Onland, Moniek van de Loo, Martin Offringa, Anton van Kaam

Background: Systematic reviews showed that systemic postnatal corticosteroids reduce the risk of bronchopulmonary dysplasia (BPD) in preterm infants. However, corticosteroids have also been associated with an increased risk of neurodevelopmental impairment. It is unknown whether these beneficial and adverse effects are modulated by differences in corticosteroid treatment regimens related to type of steroid, timing of treatment initiation, duration, pulse versus continuous delivery, and cumulative dose. Objectives: To assess the effects of different corticosteroid treatment regimens on mortality, pulmonary morbidity, and neurodevelopmental outcome in very low birth weight infants. Search methods: We conducted searches in September 2022 of MEDLINE, the Cochrane Library, Embase, and two trial registries, without date, language or publication-type limits. Other search methods included checking the reference lists of included studies for randomized controlled trials (RCTs) and quasi-randomized trials. Selection criteria: We included RCTs comparing two or more different treatment regimens of systemic postnatal corticosteroids in preterm infants at risk for BPD, as defined by the original trialists. The following comparisons of intervention were eligible: alternative corticosteroid (e.g. hydrocortisone) versus another corticosteroid (e.g. dexamethasone); lower (experimental arm) versus higher dosage (control arm); later (experimental arm) versus earlier (control

arm) initiation of therapy; a pulse-dosage (experimental arm) versus continuous-dosage regimen (control arm); and individually -tailored regimens (experimental arm) based on the pulmonary response versus a standardized (predetermined administered to every infant) regimen (control arm). We excluded placebo-controlled and inhalation corticosteroid studies. Data collection and analysis: Two authors independently assessed eligibility and risk of bias of trials, and extracted data on study design, participant characteristics and the relevant outcomes. We asked the original investigators to verify if data extraction was correct and, if possible, to provide any missing data. We assessed the following primary outcome: the composite outcome mortality or BPD at 36 weeks' postmenstrual age (PMA). Secondary outcomes were: the components of the composite outcome; in-hospital morbidities and pulmonary outcomes, and long-term neurodevelopmental sequelae. We analyzed data using Review Manager 5 and used the GRADE approach to assess the certainty of the evidence. Main results: We included 16 studies in this review; of these, 15 were included in the quantitative synthesis. Two trials investigated multiple regimens, and were therefore included in more than one comparison. Only RCTs investigating dexamethasone were identified. Eight studies enrolling a total of 306 participants investigated the cumulative dosage administered; these trials were categorized according to the cumulative dosage investigated, 'low' being < 2 mg/kg, 'moderate' being between 2 and 4 mg/kg, and 'high' > 4 mg/kg; three studies contrasted a high versus a moderate cumulative dose, and five studies a moderate versus a low cumulative dexamethasone dose. We graded the certainty of the evidence low to very low because of the small number of events, and the risk of selection, attrition and reporting bias. Overall analysis of the studies investigating a higher dose versus a lower dosage regimen showed no differences in the outcomes BPD, the composite outcome death or BPD at 36 weeks' PMA, or abnormal neurodevelopmental outcome in survivors assessed. Although there was no evidence of a subgroup difference for the higher versus lower dosage regimens comparisons (Chi2 = 2.91, df = 1 (P = 0.09), I2 = 65.7%), a larger effect was seen in the subgroup analysis of moderate-dosage regimens versus high-dosage regimens for the outcome cerebral palsy in survivors. In this subgroup analysis, there was an increased risk of cerebral palsy (RR 6.85, 95% CI 1.29 to 36.36; RD 0.23, 95% CI 0.08 to 0.37; P = 0.02; I² = 0%; NNTH 5, 95% CI 2.6 to 12.7; 2 studies, 74 infants). There was evidence of subgroup differences for higher versus lower dosage regimens comparisons for the combined outcomes death or cerebral palsy, and death and abnormal neurodevelopmental outcomes (Chi2 = 4.25, df = 1 (P = 0.04), I2 = 76.5%; and Chi2 = 7.11, df = 1 (P = 0.008), I2 = 85.9%, respectively). In the subgroup analysis comparing a high dosage regimen of dexamethasone versus a moderate cumulative-dosage regimen, there was an increased risk of death or cerebral palsy (RR 3.20, 95% CI 1.35 to 7.58; RD 0.25, 95% CI 0.09 to 0.41; P = 0.002; I² = 0%; NNTH 5, 95% CI 2.4 to 13.6; 2 studies, 84 infants; moderate-certainty evidence), and death or abnormal neurodevelopmental outcome (RR 3.41, 95% CI 1.44 to 8.07; RD 0.28, 95% CI 0.11 to 0.44; P = 0.0009; I² = 0%; NNTH 4, 95% CI 2.2 to 10.4; 2 studies, 84 infants; moderate-certainty evidence). There were no differences in outcomes between a moderate- and a low-dosage regimen. Five studies enrolling 797 infants investigated early initiation of dexamethasone therapy versus a moderately early or delayed initiation, and showed no significant differences in the overall analyses for the primary outcomes. The two RCTs investigating a continuous versus a pulse dexamethasone regimen showed an increased risk of the combined outcome death or BPD when using the pulse therapy. Finally, three trials investigating a standard regimen versus a participant-individualized course of dexamethasone showed no difference in the primary outcome and long-term neurodevelopmental outcomes. We assessed the GRADE certainty of evidence for all comparisons discussed above as moderate to very low, because the validity of all comparisons is hampered by unclear or high risk of bias, small samples of randomized infants, heterogeneity in study population and design, non-protocolized use of 'rescue' corticosteroids and lack of long-term neurodevelopmental data in most studies. Authors' conclusions: The evidence is very uncertain about the effects of different corticosteroid regimens on the outcomes mortality, pulmonary morbidity, and long term neurodevelopmental impairment. Despite the fact that the studies investigating higher versus lower dosage regimens showed that higher-dosage regimens may reduce the incidence of death or neurodevelopmental impairment, we cannot conclude what the optimal type, dosage, or timing of initiation is for the prevention of BPD in preterm infants, based on current level of evidence. Further high quality trials would be needed to establish the optimal systemic postnatal corticosteroid dosage regimen.

PMID: 36912887

15. Intraventricular Hemorrhage in Very Preterm Children: Mortality and Neurodevelopment at Age 5

Ludovic Tréluyer, Marie Chevallier, Pierre-Henri Jarreau, Olivier Baud, Valérie Benhammou, Catherine Gire, Laetitia Marchand-Martin, Stéphane Marret, Véronique Pierrat, Pierre-Yves Ancel, Héloïse Torchin

Objectives: The objectives were to describe mortality and causes of death in children with intraventricular hemorrhage (IVH) and to study neurodevelopmental outcomes. Methods: The study was a secondary analysis of the French national prospective and population-based cohort EPIPAGE-2. Children were recruited in 2011. A standardized assessment was conducted at age 5. Children born before 32 weeks' gestation and admitted to a NICU were eligible. Exposure was IVH defined by the Papile classification. Main outcomes were mortality, causes of death, and neurodevelopmental outcomes at age 5. Results: Among the 3468 children included, 578 (16.7%) had grade 1 IVH, 424 (12.2%) grade 2 IVH, and 114 (3.3%) grade 3 IVH; 144 (4.1%) had intraparenchymal hemorrhage (IPH). Mortality was 29.7% (36 of 114) for children with grade 3 IVH and 74.4% (109 of 144) for those with IPH; 67.6% (21 of 31) and 88.7% (86 of 97) of deaths, respectively, were because of withholding and withdrawing of life-sustaining treatment. As compared with no IVH, low-grade IVH was not associated with measured

neurodevelopmental disabilities at age 5. High-grade IVH was associated with moderate and severe neurodevelopmental disabilities, reduced full-scale IQ, and cerebral palsy. Conclusions: Rates of neurodevelopmental disabilities at age 5 did not differ between children without IVH and those with low-grade IVH. For high-grade IVH, mortality rate was high, mostly because of withholding and withdrawal of life-sustaining treatment, and we found a strong association with overall neurodevelopmental disabilities in survivors.

PMID: 36919442

16. Locomotor learning in infants at high risk for cerebral palsy: A study protocol

Laura A Prosser, Julie Skorup, Samuel R Pierce, Abbas F Jawad, Andrew H Fagg, Thubi H A Kolobe, Beth A Smith

Front Pediatr. 2023 Feb 23;11:891633. doi: 10.3389/fped.2023.891633. eCollection 2023.

Background: Physical disability in individuals with cerebral palsy (CP) creates lifelong mobility challenges and healthcare costs. Despite this, very little is known about how infants at high risk for CP learn to move and acquire early locomotor skills, which set the foundation for lifelong mobility. The objective of this project is to characterize the evolution of locomotor learning over the first 18 months of life in infants at high risk for CP. To characterize how locomotor skill is learned, we will use robotic and sensor technology to provide intervention and longitudinally study infant movement across three stages of the development of human motor control: early spontaneous movement, prone locomotion (crawling), and upright locomotion (walking). Study design: This longitudinal observational/intervention cohort study (ClinicalTrials.gov Identifier: NCT04561232) will enroll sixty participants who are at risk for CP due to a brain injury by one month post-term age. Study participation will be completed by 18 months of age. Early spontaneous leg movements will be measured monthly from 1 to 4 months of age using inertial sensors worn on the ankles for two full days each month. Infants who remain at high risk for CP at 4 months of age, as determined from clinical assessments of motor function and movement quality, will continue through two locomotor training phases. Prone locomotor training will be delivered from 5 to 9 months of age using a robotic crawl training device that responds to infant behavior in real-time. Upright locomotor training will be delivered from 9 to 18 months of age using a dynamic weight support system to allow participants to practice skills beyond their current level of function. Repeated assessments of locomotor skill, training characteristics (such as movement error, variability, movement time and postural control), and variables that may mediate locomotor learning will be collected every two months during prone training and every three months during upright training. Discussion: This study will develop predictive models of locomotor skill acquisition over time. We hypothesize that experiencing and correcting movement errors is critical to skill acquisition in infants at risk for CP and that locomotor learning is mediated by neurobehavioral factors outside of training.Project Number 1R01HD098364-01A1.ClinicalTrials.gov Identifier: NCT04561232.

PMID: 36911033

17. Study protocol: peer delivered early intervention (Learning through Everyday Activities with Parents for Infants at risk of Cerebral Palsy: LEAP-CP) for First Nation Australian infants at high risk of cerebral palsy - an RCT study

Katherine Benfer, Roslyn N Boyd, Yvette Roe, Ruth Fagan, Carly Luke, Leeann Mick-Ramsamy, Koa Whittingham, Iona Novak, Margot Bosanquet, Lynda McNamara, Gulam Khandaker, Lucy Fogarty, Yvonne Cadet-James, Alan Ruben, Tracy Comans, Anthony Smith, Robert S Ware

BMJ Open. 2023 Mar 13;13(3):e059531. doi: 10.1136/bmjopen-2021-059531.

Introduction: Cerebral palsy (CP) is the most common childhood physical disability with rates approximately 50% higher in First Nations Australian children. This study aims to evaluate a culturally-adapted parent-delivered early intervention programme for First Nations Australian infants at high risk of CP (Learning through Everyday Activities with Parents for infants with CP; LEAP-CP). Methods and analysis: This study is a randomised assessor masked controlled trial. Infants with birth/postnatal risk factors will be eligible for screening. Infants at high risk of CP ('absent fidgety' on General Movements Assessment, and/or 'suboptimal score' on the Hammersmith Infant Neurological Examination) aged 12-52 weeks corrected age will be recruited. Infants and their caregivers will be randomised to receive LEAP-CP (intervention) or health advice (comparator). LEAP-CP is a culturally-adapted programme of 30 home visits delivered by a peer trainer (First Nations Community Health Worker); and includes goal-directed active motor/cognitive strategies, CP learning games and caregiver educational modules. The control arm receives a monthly health advice visit, based on the Key Family Practices, WHO. All infants continue to receive standard (mainstream) Care as Usual. Dual child primary outcomes are Peabody Developmental Motor Scales-2 (PDMS-2) and Bayley Scales of Infant Development-III. The primary caregiver outcome is the Depression,

Anxiety and Stress Scale. Secondary outcomes include function, goal attainment, vision, nutritional status and emotional availability. Sample size: total of 86 children (43/group) will enable an effect size of 0.65 on the PDMS-2 to be detected (80% power, α=0.05; 10% attrition). Ethics and dissemination: Ethics approval through Queensland ethics committees and Aboriginal Controlled Community Health Organisation Research Governance Groups, with families providing written informed consent. Findings will be disseminated with guidance from the Participatory Action Research, in collaboration with First Nations communities; peer-reviewed journal publications and national/international conference presentations. Trial registration number: ACTRN12619000969167p.

PMID: 36914182

18. Cultural adaptation and reliability assessment of the Hammersmith neonatal neurological examination for Brazilian newborns at risk of cerebral palsy

Mayara Thais Correr, Luzia Iara Pfeifer

Background: Reliable instruments that lead to early diagnosis for CP are extremely important so that these children are referred for early stimulation, benefiting their development. Objective: To perform a cross-cultural adaptation and reliability assessment of a Brazilian version of the Hammersmith Neonatal Neurological Examination (HNNE), expanded and summarized. Methods: A methodological, cross-sectional, nonexperimental quantitative analysis was conducted in two phases as follows: cultural adaptation of the HNNE, expanded and summarized, and reliability assessment of the Brazilian version of the HNNE. Phase one was developed in five stages (initial translation, synthesis of the translation, a committee of experts, backtranslation, and submission to the author), with the semantic questions, content, and face validity being evaluated. Phase two included 143 newborns and we analyzed the internal consistency, stability, and equivalence (intra- and interexaminer) of the instrument. Internal consistency was calculated using Cronbach's alpha, and intra- and interexaminer reliability and reproducibility assessed through test-retest were calculated using the intraclass correlation coefficient RESULTS: Although internal consistency, assessed using Cronbach's alpha, showed unsatisfactory results, the results of inter-and intraexaminer equivalence showed a high agreement between the evaluations in all domains. The test-retest also showed excellent agreement between the domains. Conclusions: The Brazilian HNNE expanded and summarized versions can be considered to be adapted and reliable for the neurological assessment of Brazilian newborns to identify changes in neurological development and early referral to the stimulation or early rehabilitation units and as a promising option to be used in the context of primary care in Brazil.

PMID: 36918007

19. Overview of Cochrane systematic reviews for rehabilitation interventions in individuals with cerebral palsy: A mapping synthesis

Sara Liguori, Vanessa M Young, Chiara Arienti, Elisa Pollini, Michele Patrini, Francesca Gimigliano, Stefano Negrini, Carlotte Kiekens

Aim: This overview of Cochrane systematic reviews (CSRs) reports on current evidence on the effectiveness of rehabilitation interventions for individuals with cerebral palsy (CP) and the quality of the evidence. Method: Following the inclusion criteria defined by the World Health Organization, all CSRs tagged in the Cochrane Rehabilitation database that were relevant for individuals with CP were included. A mapping synthesis was used to group outcomes and comparisons of included CSRs indicating the effect of rehabilitation interventions and the certainty of evidence. Results: A total of eight CSRs were included in the evidence map. The effect of interventions varied across comparisons and the certainty of evidence was inconsistent, ranging from high to very low. The best evidence was found for botulinum neurotoxin A (BoNT-A) combined with occupational therapy in the management of spasticity. However, the effect of BoNT-A on drooling and salivation remains unclear. A paucity of randomized controlled trials studying treatments for both dystonia and postural deformities was noted. Interpretation: This review emphasizes the need to further investigate the effectiveness and cost-benefit of rehabilitation interventions for individuals with CP.

PMID: 36908077

20. Measurement properties of the Gross Motor Function Classification System, Gross Motor Function Classification System-Expanded & Revised, Manual Ability Classification System, and Communication Function Classification System in cerebral palsy: A systematic review with meta-analysis
No authors listed

Dev Med Child Neurol. 2023 Mar 16. doi: 10.1111/dmcn.15580. Online ahead of print.

No abstract available

PMID: 36929504

21. Pharmacological and neurosurgical interventions for individuals with cerebral palsy and dystonia: a systematic review update and meta-analysis
No authors listed

Dev Med Child Neurol. 2023 Mar 16. doi: 10.1111/dmcn.15579. Online ahead of print.

No abstract available

PMID: 36929103

22. The role of the gut-microbiome-brain axis in metabolic remodeling amongst children with cerebral palsy and epilepsy
Ye Peng, Annie T G Chiu, Vivien W Y Li, Xi Zhang, Wai L Yeung, Sophelia H S Chan, Hein M Tun

Front Neurol. 2023 Feb 27;14:1109469. doi: 10.3389/fneur.2023.1109469. eCollection 2023.

Background: Epilepsy-associated dysbiosis in gut microbiota has been previously described, but the mechanistic roles of the gut microbiome in epileptogenesis among children with cerebral palsy (CP) have yet to be illustrated. Methods: Using shotgun metagenomic sequencing coupled with untargeted metabolomics analysis, this observational study compared the gut microbiome and metabolome of eight children with non-epileptic cerebral palsy (NECP) to those of 13 children with cerebral palsy with epilepsy (CPE). Among children with CPE, 8 had drug-sensitive epilepsy (DSE) and five had drug-resistant epilepsy (DRE). Characteristics at enrollment, medication history, and 7-day dietary intake were compared between groups. Results: At the species level, CPE subjects had significantly lower abundances of Bacteroides fragilis and Dialister invisus but higher abundances of Phascolarctobacterium faecium and Eubacterium limosum. By contrast, DRE subjects had a significantly higher colonization of Veillonella parvula. Regarding microbial functional pathways, CPE subjects had decreased abundances of pathways for serine degradation, quinolinic acid degradation, glutamate degradation I, glycerol degradation, sulfate reduction, and nitrate reduction but increased abundances of pathways related to ethanol production. As for metabolites, CPE subjects had higher concentrations of kynurenic acid, 2-oxindole, dopamine, 2-hydroxyphenyalanine, 3,4-dihydroxyphenylglycol, L-tartaric acid, and D-saccharic acid; DRE subjects had increased concentrations of indole and homovanilic acid. Conclusions: In this study, we found evidence of gut dysbiosis amongst children with cerebral palsy and epilepsy in terms of gut microbiota species, functional pathways, and metabolites. The combined metagenomic and metabolomic analyses have shed insights on the potential roles of B. fragilis and D. invisus in neuroprotection. The combined analyses have also provided evidence for the involvement of GMBA in the epilepsy-related dysbiosis of kynurenine, serotonin, and dopamine pathways and their complex interplay with neuroimmune and neuroendocrinological pathways.

PMID: 36923492

Prevention and Cure

23. Umbilical Cord Blood-Derived Cell Therapy for Perinatal Brain Injury: A Systematic Review & Meta-Analysis of Preclinical Studies

Timothy Nguyen, Elisha Purcell, Madeleine J Smith, Tayla R Penny, Madison C B Paton, Lindsay Zhou, Graham Jenkin, Suzanne L Miller, Courtney A McDonald, Atul Malhotra

Review Int J Mol Sci. 2023 Feb 22;24(5):4351. doi: 10.3390/ijms24054351.

Perinatal brain injury is a major contributor to long-term adverse neurodevelopment. There is mounting preclinical evidence for use of umbilical cord blood (UCB)-derived cell therapy as potential treatment. To systematically review and analyse effects of UCB-derived cell therapy on brain outcomes in preclinical models of perinatal brain injury. MEDLINE and Embase databases were searched for relevant studies. Brain injury outcomes were extracted for meta-analysis to calculate standard mean difference (SMD) with 95% confidence interval (CI), using an inverse variance, random effects model. Outcomes were separated based on grey matter (GM) and white matter (WM) regions where applicable. Risk of bias was assessed using SYRCLE, and GRADE was used to summarise certainty of evidence. Fifty-five eligible studies were included (7 large, 48 small animal models). UCB-derived cell therapy significantly improved outcomes across multiple domains, including decreased infarct size (SMD 0.53; 95% CI (0.32, 0.74), $p < 0.00001$), apoptosis (WM, SMD 1.59; 95%CI (0.86, 2.32), $p < 0.0001$), astrogliosis (GM, SMD 0.56; 95% CI (0.12, 1.01), $p = 0.01$), microglial activation (WM, SMD 1.03; 95% CI (0.40, 1.66), $p = 0.001$), neuroinflammation (TNF-α, SMD 0.84; 95%CI (0.44, 1.25), $p < 0.0001$); as well as improved neuron number (SMD 0.86; 95% CI (0.39, 1.33), $p = 0.0003$), oligodendrocyte number (GM, SMD 3.35; 95 %CI (1.00, 5.69), $p = 0.005$) and motor function (cylinder test, SMD 0.49; 95 %CI (0.23, 0.76), $p = 0.0003$). Risk of bias was determined as serious, and overall certainty of evidence was low. UCB-derived cell therapy is an efficacious treatment in pre-clinical models of perinatal brain injury, however findings are limited by low certainty of evidence.

PMID: 36901781