Cerebral palsy research news

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Interventions and Management

1. Efficacy of cervical perivascular sympathectomy in improving upper limb motor function in children with cerebral palsy and construction of a predictive model

Junjie Wu, Chao Bai, Mingbo Hu, Qi Guan, Jianglong Li, Xinping Luan, Baofeng Yan

Clin Neurol Neurosurg. 2024 Apr 2:240:108273. doi: 10.1016/j.clineuro.2024.108273. Online ahead of print.

Background: The effectiveness of cervical perivascular sympathectomy (CPVS) in enhancing upper limb motor function in children with cerebral palsy is unclear, and the factors that influence the effectiveness of the surgery have not been documented. Objective: To investigate the effectiveness of CPVS in enhancing upper limb motor function in children with cerebral palsy and develop a predictive chart for potential associated adverse outcomes METHODS: The study included 187 children with cerebral palsy who underwent CPVS at the Cerebral Palsy Center, Second Affiliated Hospital of Xinjiang Medical University, between January 2018 and January 2022. Patients were categorized into two groups based on prognostic outcomes: those with adverse and favorable prognoses. Demographic and laboratory data were collected and analyzed from both groups. To identify independent predictors of poor post-CPVS upper limb motor function outcomes, statistical techniques, including univariate analysis and binary logistic regression, were applied. Subsequently, these predictors were integrated to formulate a comprehensive predictive model. Results: In this cohort of 187 children with cerebral palsy undergoing CPVS, 68 (36.36%) exhibited a favorable prognosis for upper limb motor function and 119 (63.64%) demonstrated an adverse prognosis. Age, motor function, and serum albumin levels were identified as significant prognostic factors via logistic regression analysis. To develop the model, we divided the sample into a training set (70%, n = 131) and a validation set (30%, n = 56). Employing motor function, serum albumin levels, and age as variables, we crafted a predictive model. The model's performance, reflected by the area under the curve was 0.813 (0.732, 0.894) in the training set and 0.770 (0.647, 0.892) in the validation set, demonstrating its robust predictive capability for post-CPVS adverse outcomes. Furthermore, the consistency curve and Hosmer-Lemeshow test ($\chi 2 = 8.808$, $p = 0.359$) illustrated a strong concordance between the model's predictions of poor prognosis and the actual incidence rate. Conclusion: CPVS has been shown to be effective in improving upper limb motor function in patients with cerebral palsy. Independent prognostic factors identified encompass motor function, age, and serum albumin levels. The composite predictive model shows potential for clinical applications.

PMID: 38608351

2. Is more always better? Effectiveness of constraint-induced movement therapy in children with high-risk or unilateral cerebral palsy (0-6 years): Systematic review and meta-analysis

Javier Merino-Andrés, Purificación López-Muñoz, Rocío Palomo Carrión, Patricia Martín-Casas, Irene Ruiz-Becerro, Álvaro Hidalgo-Robles

Meta-Analysis Child Care Health Dev. 2024 May;50(3):e13262. doi: 10.1111/cch.13262.

Background: While constraint-induced movement therapy is strongly recommended as an intervention for infants with unilateral cerebral palsy, the optimal dosage remains undefined. This systematic review aims to identify the most effective

level of intensity of constraint-induced movement therapy to enhance manual function in infants at high risk of asymmetric brain lesions or unilateral cerebral palsy diagnosis. Methods: This systematic review with meta-analysis encompassed a comprehensive search across four electronic databases to identify articles that met the following criteria: randomised controlled trials, children aged 0-6 with at high risk or with unilateral cerebral palsy, and treatment involving constraint-induced movement therapy for upper limb function. Studies with similar outcomes were pooled by calculating the standardised mean difference score for each subgroup, and subgroups were stratified every 30 h of total intervention dosage (30-60, 61-90, >90 h). Risk of bias was assessed with Cochrane Collaboration's tool. Results: Seventeen studies were included. Meta-analyses revealed significant differences among subgroups. The 30-60 h subgroup showed a weak effect for spontaneous use of the affected upper limb during bimanual performance, grasp function, and parents' perception of how often children use their affected upper limb. Additionally, this subgroup demonstrated a moderate effect for the parents' perception of how effectively children use their affected upper limb. Conclusions: Using a dosage ranging from 30 to 60 h when applying a constraint-induced movement therapy protocol holds promise as the most age-appropriate and cost-effectiveness approach for improving upper limb functional outcomes and parent's perception.

PMID: 38606885

3. Reliability of the Clinical Measurement of Joint Motion and Muscle Length in the Upper and Lower Extremities of Children with Cerebral Palsy: A Systematic Review

Debra A Sala, Lori B Ragni

Review Dev Neurorehabil. 2024 Apr 10:1-13. doi: 10.1080/17518423.2024.2331459. Online ahead of print.

Reliability of joint motion and muscle length measurement in children with cerebral palsy was examined. Twenty-one studies of intraobserver and/or interobserver reliability were reviewed: joint motion of upper extremities in four and lower extremities in 13; muscle length of upper extremities in one and lower extremities in 15. Intraclass correlation coefficients for goniometric interobserver reliability varied widely for joint motion (range 0.38-0.92) and muscle length (range 0.20-0.95). Inclusion of an error measurement to provide clinicians with a value indicating true change was limited. Further research is required to determine intraobserver and interobserver reliability for these important pediatric clinical measurements.

PMID: 38600734

4. Pediatric Rehabilitation for Walking Difficulty and Calf Muscle Pain in a 13-Year-Old Male With Spastic Diplegic Cerebral Palsy and Clubfoot Deformity: A Case Report

Aakanksha Zade, H V Sharath, Nikita Gangwani

Case Reports Cureus. 2024 Mar 7;16(3):e55697. doi: 10.7759/cureus.55697. eCollection 2024 Mar.

Cerebral palsy (CP) manifests as atypical muscle tone, posture, and movement, and is classified into four main types: extrapyramidal (dyskinetic), spastic quadriplegia, spastic hemiplegia, and spastic diplegia. Patients with CP might move awkwardly because of this since it indicates that their muscles are tense. We report the case of a 13-year-old child who complained of soreness in his right calf muscle and trouble walking over the previous two years. His condition is recognized as spastic diplegic CP. This report aims to understand the impact of neurophysiotherapy procedures in the context of CP. Physical therapy employs various therapeutic techniques to help patients become more independent in carrying out their everyday tasks and enhance their quality of life, including stretching, proprioceptive neuromuscular facilitation, limb strengthening exercises, and gait training. Early rehabilitation aids in treating various motor functions, such as balance, posture, oral motor functioning, fine motor skills, gross motor skills, muscle control, muscle tone, reflexes, and body movement. It also helps children with CP reach their full potential for physical independence and fitness and enhances the quality of life for both the child and the family. Pediatric rehabilitation yields significant benefits in alleviating walking difficulty and calf muscle pain in individuals with spastic diplegic CP and clubfoot deformity.

PMID: 38586773

5. Correspondence between Expected, Perceived, and Measured Effects of BoNT-A Treatment in Calf Muscles among Children and Adolescents with Cerebral Palsy: A Mixed Methods Study

Rannei Sæther, Ann-Kristin Gunnes Elvrum, Siri Merete Brændvik

J Clin Med. 2024 Mar 2;13(5):1453. doi: 10.3390/jcm13051453.

(1) Background: Our study explores the relationship between expected, perceived, and measured effects of botulinum toxin A (BoNT-A) treatment and saline (placebo) in children and adolescents with cerebral palsy (CP) in the calf muscles of 20 children and adolescents with cerebral palsy (CP), aged 4-15 years, using the Gross Motor Function Classification System (GMFCS) I-II. (2) Methods: A mixed methods parallel database design was used. Quantitative and qualitative data were

collected at baseline and four weeks after treatment. The primary quantitative measure was gross energy cost (EC) during walking, obtained from a 5-Minute Walk Test (5MWT), while qualitative semi-structured interviews were performed with each parent and child/adolescent individually. (3) Results: Four weeks after treatment, we did not find any correspondence between expected, measured, and perceived effects. Interestingly, parental perceptions of treatment effects were more consistent than the measured outcomes. We also observed a connection between parental treatment expectations and perceived effects, often related to reduced energy expenditure. Children tended to view their parents as treatment experts and had fewer expectations and perceptions themselves. (4) Conclusions: These findings support the importance of child-centered care, which entails actively listening to children's expectations and perceptions during the treatment process.

PMID: 38592286

6. Demonstrating the utility of Instrumented Gait Analysis in the treatment of children with cerebral palsy

Michael H Schwartz, Andrew J Rie, Andrew G Georgiadis, Hans Kainz

PLoS One. 2024 Apr 9;19(4):e0301230. doi: 10.1371/journal.pone.0301230. eCollection 2024.

Background: Instrumented gait analysis (IGA) has been around for a long time but has never been shown to be useful for improving patient outcomes. In this study we demonstrate the potential utility of IGA by showing that machine learning models are better able to estimate treatment outcomes when they include both IGA and clinical (CLI) features compared to when they include CLI features alone. Design: We carried out a retrospective analysis of data from ambulatory children diagnosed with cerebral palsy who were seen at least twice at our gait analysis center. Individuals underwent a variety of treatments (including no treatment) between sequential gait analyses. We fit Bayesian Additive Regression Tree (BART) models that estimated outcomes for mean stance foot progression to demonstrate the approach. We built two models: one using CLI features only, and one using CLI and IGA features. We then compared the models' performance in detail. We performed similar, but less detailed, analyses for a number of other outcomes. All results were based on independent test data from a 70%/30% training/testing split. Results: The IGA model was more accurate than the CLI model for mean stance-phase foot progression outcomes (RMSEIGA = 11∘, RMSECLI = 13∘) and explained more than 1.5 × as much of the variance (R2IGA = .45, R2CLI = .28). The IGA model outperformed the CLI model for every level of treatment complexity, as measured by number of simultaneous surgeries. The IGA model also exhibited superior performance for estimating outcomes of mean stance-phase knee flexion, mean stance-phase ankle dorsiflexion, maximum swing-phase knee flexion, gait deviation index (GDI), and dimensionless speed. Interpretation: The results show that IGA has the potential to be useful in the treatment planning process for ambulatory children diagnosed with cerebral palsy. We propose that the results of machine learning outcome estimators-including estimates of uncertainty-become the primary IGA tool utilized in the clinical process, complementing the standard medical practice of conducting a through patient history and physical exam, eliciting patient goals, reviewing relevant imaging data, and so on.

PMID: 38593122

7. Back geometry and mobility function changes in cerebral palsy children after backward walking training: arandomized controlled trial

Amr Almaz Abdel-Aziem, Heba Mohamed Youssr El-Basatiny, Amira Husien Draz, Dina Ali Abdelaziz Ali Aglan

Dev Neurorehabil. 2024 Apr 10:1-9. doi: 10.1080/17518423.2024.2340461. Online ahead of print.

Aim: To compare the effects of backward (BW) and forward (FW) walking training on back geometry and mobility function in children with hemiparetic cerebral palsy (CP). Methods: Fifty-five children with hemiparetic CP participated in this study. They were randomly assigned into two groups. For 12 weeks, both groups got a conventional physical therapy program three days/week. Groups A and B got a specifically developed FW walking training (25 minutes/session) and a specially designed BW walking training (25 minutes/session), respectively. Results: The trunk imbalance, lateral deviation, pelvic tilting, pelvic torsion, surface motion, and dynamic gait index of group B improved significantly more than group A ($p < .05$). Both groups showed significant improvements in all measured variables ($p < .05$). Conclusion: BW walking training might be considered as an effective therapy modality for improving back geometry and mobility function in hemiparetic CP children compared with FW walking training combined with a typical program.

PMID: 38597393

8. Multi-segment foot kinematics during gait in children with spastic cerebral palsy

Wouter Schallig, Marjolein Piening, Loes Quirijnen, Melinda M Witbreuk, Annemieke I Buizer, Marjolein M van der Krogt

Gait Posture. 2024 Mar 28:110:144-149. doi: 10.1016/j.gaitpost.2024.03.014. Online ahead of print.

Background: Foot deformities (e.g. planovalgus and cavovarus) are very common in children with spastic cerebral palsy (CP), with the midfoot often being involved. Dynamic foot function can be assessed with 3D gait analysis including a multi-segment foot model. Incorporating a midfoot segment in such a model, allows quantification of separate Chopart and Lisfranc joint kinematics. Yet, midfoot kinematics have not previously been reported in CP. Research questions: What is the difference in multi-segment kinematics including midfoot joints between common foot deformities in CP and typically-developing feet? Methods: 103 feet of 57 children with spastic CP and related conditions were retrospectively included and compared with 15 typically-developing children. All children underwent clinical gait analysis with the Amsterdam Foot Model marker set. Multi-segment foot kinematics were calculated for three strides per foot and averaged. A k-means cluster analysis was performed to identify foot deformity groups that were present within CP data. The deformity type represented by each cluster was based on the foot posture index. Kinematic output of the clusters was compared to typically-developing data for a static standing trial and for the range of motion and kinematic waveforms during walking, using regular and SPM independent t-tests respectively. Results: A neutral, planovalgus and varus cluster were identified. Neutral feet showed mostly similar kinematics as typically-developing data. Planovalgus feet showed increased ankle valgus and Chopart dorsiflexion, eversion and abduction. Varus feet showed increased ankle varus and Chopart inversion and adduction. Significance: This study is the first to describe Chopart and Lisfranc joint kinematics in different foot deformities of children with CP. It shows that adding a midfoot segment can provide additional clinical and kinematic information. It highlights joint angles that are more distinctive between deformities, which could be helpful to optimize the use of multi-segment foot kinematics in the clinical decision making process.

PMID: 38608379

9. Validity and reliability of the Sitting Assessment Scale in cerebral palsy

Demet Gözaçan Karabulut, Ayşe Numanoğlu Akbaş

J Eval Clin Pract. 2024 Apr 8. doi: 10.1111/jep.13992. Online ahead of print.

Aim: The aim of this study was to examine the validity and reliability of the Sitting Assessment Scale (SAS) in individuals with cerebral palsy (CP). Methods: The study included 34 individuals with a diagnosis of spastic CP. Individuals were evaluated with the Gross Motor Function Classification System and the Manual Ability Classification System. SAS and Trunk Control Measurement Scale (TCMS) were applied to the participants. The intraclass correlation coefficient (ICC) was calculated to determine the intraobserver and interobserver reliability of the scale scored by three different physiotherapists at two different time intervals. Internal consistency was calculated with Cronbach's α coefficient. The fit between SAS and TCMS for criterion-dependent validity was evaluated using Pearson Correlation Analysis. Results: According to the GMFCS level, 79.41% of the children were mildly (Level I-II), 14.71% were moderately affected (level III), and 5.88% were severely affected (level IV). Intra > observer and interobserver reliability values of SAS were extremely high (ICCinterrater > 0.923, ICCintrarater > 0.930). It was observed that the internal consistency of SAS had high values (Cronbach α_{test} > 0.822, Cronbach α_{retest} > 0.804). For the criterion-dependent reliability; positive medium correlations found between SAS with Total TCMS Static Sitting Balance ($r = 0.579$, $p < 0.001$), with TCMS Selective Movement Control ($r = 0.597$, $p < 0.001$), with TCMS Dynamic Reaching ($r = 0.609$, $p < 0.001$), and with TCMS Total ($r = 0.619$, $p < 0.001$). Conclusion: SAS was found to have high validity and reliability in children with CP. In addition, the test-retest reliability of the scale was also high. SAS is a practical tool that can be used to assess sitting balance in children with CP.

PMID: 38588276

10. Relationship Between Postural Asymmetry, Balance, and Pain in Children With Spastic Cerebral Palsy

Zahra Shekari, Razieh Sadeghian Afarani, Saeid Fatorehchy, Enayatollah Bakhshi, Soheila Shahshahani, Elahe Mousavi

Pediatr Neurol. 2024 Mar 24:155:84-90. doi: 10.1016/j.pediatrneurol.2024.03.018. Online ahead of print.

Background: Primary symptoms of cerebral palsy (CP), such as spasm and weakness, can lead to secondary musculoskeletal problems. Exploring the interplay and impact of secondary symptoms is essential in CP management. Methods: A total of 56 children (32 males and 24 females) aged eight to 12 years in level I to III of Gross Motor Function Classification System (GMFCS) completed The Pediatric Balance Scale and Wong-Baker Faces Scale and the Posture and Postural Ability Scale. Relationships between the three groups were examined using the Kruskal-Wallis test, Tukey test, gamma coefficient, De Somers D, phi coefficient, Cramér V, and one-way analysis of variance. Results: There was a significant correlation between balance and postural asymmetry ($P < 0.001$), and no significant difference in balance was there between the severe and moderate asymmetry groups ($P = 0.759$) and between the mild asymmetry and no asymmetry groups ($P = 0.374$). Furthermore, there was a significant relationship between postural asymmetry and each of the variables of pain ($P < 0.001$) and gross motor function ($P = 0.002$). Although a meaningful correlation was identified between balance and gross motor function ($P < 0.001$), the relationship between postural asymmetry and balance in GMFCS levels was not found ($P = 0.052$, $P = 0.052$, $P = 0.233$). Conversely, no significant relationship was detected between pain and gross motor function ($P = 0.072$). Significance: Postural asymmetry negatively impacts balance and correlates with pain intensity. Addressing postural problems can contribute to pain management and improved balance.

PMID: 38608553

11. Cross-cultural adaptation, validity and reliability of the Japanese version of ABILHAND-kids for children with cerebral palsy using Rasch measurement model

Sayaka Katori, Nobuaki Himuro, Yukihiro Kitai, Ryo Tanabe, Hirofumi Ohnishi

Disabil Rehabil. 2024 Apr 9:1-9. doi: 10.1080/09638288.2024.2338201. Online ahead of print.

Purpose: The aim of this study was to develop the Japanese version of the ABILHAND-Kids and to examine its psychometric properties for Japanese children with cerebral palsy (CP). Methods: The experimental version of 75 items was developed using forward-backward translation method. Parents of 137 children with CP answered it. Their responses were analyzed to successive items, and psychometric properties of the final version were investigated through the Rasch measurement model. Results: The Japanese version of the ABILHAND-Kids contained 22 items. It showed valid item-patient targeting, no significant floor and ceiling effects, and no differential item functioning for demographic and clinical subgroups. All items contributed to the definition of one-dimensional measure. For internal consistency, the person separation index was 0.94. For test-retest reliability, the intraclass correlation coefficients were 0.96 (95% CI: 0.92-0.98). The minimal detectable difference was calculated with a logit score of 0.79 and a total raw score of 4.50. The logit score showed a strong correlation with the Manual Ability Classification System level (ρ= -0.70) and the Gross Motor Function Classification System level (ρ= -0.62). Conclusions: The Japanese version of the ABILHAND-Kids was found to be valid and reliable. It appears to be a good tool for assessing manual abilities in daily activities in children with CP.

PMID: 38591266

12. The influence of birthweight on mortality and severe neonatal morbidity in late preterm and term infants: an Australian cohort study

Tegan Triggs, Kylie Crawford, Jesrine Hong, Vicki Clifton, Sailesh Kumar

Lancet Reg Health West Pac. 2024 Apr 2:45:101054. doi: 10.1016/j.lanwpc.2024.101054. eCollection 2024 Apr.

Background: The aim of this study was to detail incidence rates and relative risks for severe adverse perinatal outcomes by birthweight centile categories in a large Australian cohort of late preterm and term infants. Methods: This was a retrospective cohort study of singleton infants (≥34+0 weeks gestation) between 2000 and 2018 in Queensland, Australia. Study outcomes were perinatal mortality, severe neurological morbidity, and other severe morbidity. Categorical outcomes were compared using Chi-squared tests. Continuous outcomes were compared using t-tests. Multinomial logistic regression investigated the effect of birthweight centile on study outcomes. Findings: The final cohort comprised 991,042 infants. Perinatal mortality occurred in 1944 infants (0.19%). The incidence and risk of perinatal mortality increased as birthweight decreased, peaking for infants <1st centile (perinatal mortality rate 13.2/1000 births, adjusted Relative Risk Ratio (aRRR) of 12.96 (95% CI 10.14, 16.57) for stillbirth and aRRR 7.55 (95% CI 3.78, 15.08) for neonatal death). Severe neurological morbidity occurred in 7311 infants (0.74%), with the highest rate (19.6/1000 live births) in <1st centile cohort. There were 75,243 cases of severe morbidity (7.59% livebirths), with the peak incidence occurring in the <1st centile category (12.3% livebirths). The majority of adverse outcomes occurred in infants with birthweights between 10 and 90th centile. Almost 2 in 3 stillbirths, and approximately 3 in 4 cases of neonatal death, severe neurological morbidity or other severe morbidity occurred within this birthweight range. Interpretation: Although the incidence and risk of perinatal mortality, severe neurological morbidity and severe morbidity increased at the extremes of birthweight centiles, the majority of these outcomes occurred in infants that were apparently "appropriately grown" (i.e., birthweight 10th-90th centile).

PMID: 38590781

13. Pediatric Dysphagia Risk Screening Instrument (PDRSI) in Children With Cerebral Palsy

Ebru Umay, Damla Cankurtaran, Nihal Tezel, Cuma Uz, Yasemin Tombak, Ozgur Karaahmet, Zeynep Aykin Yigman, Gulnur Celik, Ece Unlu Akyuz

Clin Pediatr (Phila). 2024 Apr 9:99228241241901. doi: 10.1177/00099228241241901. Online ahead of print.

This study aimed to evaluate whether the Pediatric Dysphagia Risk Screening Instrument (PDRSI) was a suitable test for children with cerebral palsy (CP) and assess the instrument's Turkish validity and reliability. One-hundred twenty-six children with CP participated in this study. "Cronbach's alpha (α)," "Cronbach's α when one item is deleted," "inter-item correlation," and "corrected item-to-total correlation" were used to assess internal consistency. In addition, inter-rater agreement tests (Cohen's kappa coefficient) were conducted for reliability. Construct validity was used to assess the validity. Moreover, flexible fiberoptic endoscopic evaluation of the swallowing method was used to describe the receiver operating characteristic curve analysis and calculate the sensitivity and specificity of T-PDRSI. It was found that the PDRSI had adequate validity and

reliability. The PDRSI can be used in children with CP as a valid and reliable instrument with high sensitivity and specificity.

PMID: 38591868

14. Association of cerebral palsy with autism spectrum disorder and attention-deficit/hyperactivity disorder in children: a large-scale nationwide population-based study

Qiang Chen, Mingwu Chen, Wei Bao, Lane Strathearn, Xiaodong Zang, Lun Meng, Guifeng Xu

BMJ Paediatr Open. 2024 Apr 9;8(1):e002343. doi: 10.1136/bmjpo-2023-002343.

Objective: To examine the association of cerebral palsy with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), providing evidence for interdisciplinary medical service for children with cerebral palsy. Design: A large-scale nationwide population-based study. Setting: The National Health Interview Survey (NHIS). Patients: 177 899 children aged 3-17 years among NHIS participants from 1997 to 2003 and 2008 to 2018. Results: Among the 177 899 children included in this analysis, 602 (0.33%) had cerebral palsy, 1997 (1.16%) had ASD, and 13 697 (7.91%) had ADHD. Compared with children without cerebral palsy, children with cerebral palsy had a higher prevalence of ASD (6.09% vs 1.15%; p<0.001) and ADHD (15.91% vs 7.89%; p<0.001). After adjustment for age, sex, race/ethnicity, family highest education level, family income level and geographical region, the OR among children with cerebral palsy, compared with children without cerebral palsy, was 5.07 (95% CI 3.25 to 7.91) for ASD (p<0.001) and 1.95 (95% CI 1.43 to 2.66) for ADHD (p<0.001). Furthermore, the association of cerebral palsy with ASD and ADHD remained significant in all subgroups stratified by age, sex and race. Conclusion: In a large, nationally representative sample of US children, this study shows that children with cerebral palsy are at an increased risk of ASD and ADHD.

PMID: 38594193

15. Molecular Mechanisms of Neuroprotection after the Intermittent Exposures of Hypercapnic Hypoxia

Pavel P Tregub, Vladimir P Kulikov, Irada Ibrahimli, Oksana F Tregub, Artem V Volodkin, Michael A Ignatyuk, Andrey A Kostin, Dmitrii A Atiakshin

Review Int J Mol Sci. 2024 Mar 25;25(7):3665. doi: 10.3390/ijms25073665.

The review introduces the stages of formation and experimental confirmation of the hypothesis regarding the mutual potentiation of neuroprotective effects of hypoxia and hypercapnia during their combined influence (hypercapnic hypoxia). The main focus is on the mechanisms and signaling pathways involved in the formation of ischemic tolerance in the brain during intermittent hypercapnic hypoxia. Importantly, the combined effect of hypoxia and hypercapnia exerts a more pronounced neuroprotective effect compared to their separate application. Some signaling systems are associated with the predominance of the hypoxic stimulus (HIF-1α, A1 receptors), while others (NF-κB, antioxidant activity, inhibition of apoptosis, maintenance of selective blood-brain barrier permeability) are mainly modulated by hypercapnia. Most of the molecular and cellular mechanisms involved in the formation of brain tolerance to ischemia are due to the contribution of both excess carbon dioxide and oxygen deficiency (ATP-dependent potassium channels, chaperones, endoplasmic reticulum stress, mitochondrial metabolism reprogramming). Overall, experimental studies indicate the dominance of hypercapnia in the neuroprotective effect of its combined action with hypoxia. Recent clinical studies have demonstrated the effectiveness of hypercapnic-hypoxic training in the treatment of childhood cerebral palsy and diabetic polyneuropathy in children. Combining hypercapnic hypoxia with pharmacological modulators of neuro/cardio/cytoprotection signaling pathways is likely to be promising for translating experimental research into clinical medicine.

PMID: 38612476

16. Neurodevelopmental Disruptions in Children of Preeclamptic Mothers: Pathophysiological Mechanisms and Consequences

Andrea González-Rojas, Martina Valencia-Narbona

Review Int J Mol Sci. 2024 Mar 24;25(7):3632. doi: 10.3390/ijms25073632.

Preeclampsia (PE) is a multisystem disorder characterized by elevated blood pressure in the mother, typically occurring after 20 weeks of gestation and posing risks to both maternal and fetal health. PE causes placental changes that can affect the fetus, particularly neurodevelopment. Its key pathophysiological mechanisms encompass hypoxia, vascular and angiogenic dysregulation, inflammation, neuronal and glial alterations, and disruptions in neuronal signaling. Animal models indicate that PE is correlated with neurodevelopmental alterations and cognitive dysfunctions in offspring and in humans, an association between PE and conditions such as cerebral palsy, autism spectrum disorder, attention deficit hyperactivity disorder, and sexual dimorphism has been observed. Considering the relevance for mothers and children, we conducted a narrative literature review

to describe the relationships between the pathophysiological mechanisms behind neurodevelopmental alterations in the offspring of PE mothers, along with their potential consequences. Furthermore, we emphasize aspects pertinent to the prevention/treatment of PE in pregnant mothers and alterations observed in their offspring. The present narrative review offers a current, complete, and exhaustive analysis of (i) the pathophysiological mechanisms that can affect neurodevelopment in the children of PE mothers, (ii) the relationship between PE and neurological alterations in offspring, and (iii) the prevention/ treatment of PE.

PMID: 38612445

17. Comparison of Executive Function Skills between Patients with Cerebral Palsy and Typically Developing Populations: A Systematic Review and Meta-Analysis

Nóra Zimonyi, Tamás Kói, Viktor Dombrádi, Marcell Imrei, Rita Nagy, Márk Ágoston Pulay, Zsolt Lang, Péter Hegyi, Zsofia K Takacs, Ibolya Túri

Review J Clin Med. 2024 Mar 24;13(7):1867. doi: 10.3390/jcm13071867.

Background: Children with CP show deficits in executive function compared to their typically developing peers, based on the majority of the available evidence. However, the magnitude of these deficits, as well as the proportions of the shortfalls in the three main components, have not yet been examined. This is the first meta-analysis to synthesize evidence on the magnitude of differences between patients with cerebral palsy (CP) and typically developing populations in different components of executive function skills (working memory, inhibitory control and cognitive flexibility), and thus makes recommendations on which areas of executive functioning are in greatest need of intervention. Methods: We conducted a systematic literature search of four databases for studies that measured executive functions in these two groups until 31 August 2023. We calculated the standardized mean difference (Hedges' g), an average effect size overall, and for the three components of executive function skills separately, we used several moderator analyses, including methodological differences between the primary studies. Results: Fifteen articles were included in the meta-analysis. The average mean difference in executive functioning overall was large (g+ = -0.82). Furthermore, large significant differences were found in working memory (g+ = -0.92) and inhibitory control (g+ = -0.82) and a moderate difference was identified in cognitive flexibility (g+ = -0.57). In addition, results of moderator analyses reveal the importance of a rigorous matching of control group participants and CP patients. Conclusions: The results demonstrate a severe impairment in all executive functions among CP patients compared to typically developing peers, which do not decrease over time.

PMID: 38610632

18. Are toddlers with neurosensory impairment more difficult to follow up? A secondary analysis of the hPOD follow-up study

Libby Lord, Jenny Rogers, Greg D Gamble, Jane E Harding; hPOD Follow-Up Group

Arch Dis Child Fetal Neonatal Ed. 2024 Apr 10:fetalneonatal-2023-326455. doi: 10.1136/archdischild-2023-326455. Online ahead of print.

Objective: To describe strategies used to maximise follow-up after a neonatal randomised trial, how these differed for families of different ethnicity, socioeconomic status and urban versus rural residence and investigate relationships between the difficulty of follow-up and rate of neurosensory impairment. Method: hPOD was a multicentre randomised trial assessing oral dextrose gel prophylaxis for neonatal hypoglycaemia. Follow-up at 2 years was conducted from 2017 to 2021. We analysed all recorded contacts between the research team and participants' families. Neurosensory impairment was defined as blindness, deafness, cerebral palsy, developmental delay or executive function impairment. Results: Of 1321 eligible participants, 1197 were assessed (91%) and 236/1194 (19.8%) had neurosensory impairment. Participants received a median of five contacts from the research team (range 1-23). Those from more deprived areas and specific ethnicities received more contacts, particularly home tracking visits and home assessments. Impairment was more common among participants receiving more contacts (relative risk 1.81, 95% CI 1.34 to 2.44 for ≥7 contacts vs <7 contacts), and among those assessed after the intended age (76/318, 23.9% if >25 months vs 160/876, 18.3% if ≤25 months). Conclusions: Varied contact strategies and long timeframes are required to achieve a high follow-up rate. Without these, the sociodemographics of children assessed would not have been representative of the entire cohort, and the rate of neurosensory impairment would have been underestimated. To maximise follow-up after randomised trials, substantial effort and resources are needed to ensure that data are useful for clinical decision-making.

PMID: 38604648

19. A new description of cerebral palsy: Framing, wording, and perspective

Bernard Dan

Editorial Dev Med Child Neurol. 2024 Apr 10. doi: 10.1111/dmcn.15922. Online ahead of print.

No abstract available

PMID: 38597825

20. Corticosteroids for the prevention and treatment of bronchopulmonary dysplasia: an overview of systematic reviews

Moniek van de Loo, Anton van Kaam, Martin Offringa, Lex W Doyle, Chris Cooper, Wes Onland

Review Cochrane Database Syst Rev. 2024 Apr 10;4(4):CD013271. doi: 10.1002/14651858.CD013271.pub2.

Background: Bronchopulmonary dysplasia (BPD) remains an important complication of prematurity. Pulmonary inflammation plays a central role in the pathogenesis of BPD, explaining the rationale for investigating postnatal corticosteroids. Multiple systematic reviews (SRs) have summarised the evidence from numerous randomised controlled trials (RCTs) investigating different aspects of administrating postnatal corticosteroids. Besides beneficial effects on the outcome of death or BPD, potential short- and long-term harms have been reported. Objectives: The primary objective of this overview was to summarise and appraise the evidence from SRs regarding the efficacy and safety of postnatal corticosteroids in preterm infants at risk of developing BPD. Methods: We searched the Cochrane Database of Systematic Reviews, MEDLINE, Embase, CINAHL, and Epistemonikos for SRs in April 2023. We included all SRs assessing any form of postnatal corticosteroid administration in preterm populations with the objective of ameliorating pulmonary disease. All regimens and comparisons were included. Two review authors independently checked the eligibility of the SRs comparing corticosteroids with placebo, and corticosteroids with different routes of administration and regimens. The included outcomes, considered key drivers in the decision to administer postnatal corticosteroids, were the composite outcome of death or BPD at 36 weeks' postmenstrual age (PMA), its individual components, long-term neurodevelopmental sequelae, sepsis, and gastrointestinal tract perforation. We independently assessed the methodological quality of the included SRs by using AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews) and ROBIS (Risk Of Bias In Systematic reviews) tools. We assessed the certainty of the evidence using GRADE. We provided a narrative description of the characteristics, methodological quality, and results of the included SRs. Main results: We included nine SRs (seven Cochrane, two non-Cochrane) containing 87 RCTs, 1 follow-up study, and 9419 preterm infants, investigating the effects of postnatal corticosteroids to prevent or treat BPD. The quality of the included SRs according to AMSTAR 2 varied from high to critically low. Risk of bias according to ROBIS was low. The certainty of the evidence according to GRADE ranged from very low to moderate. Early initiated systemic dexamethasone (< seven days after birth) likely has a beneficial effect on death or BPD at 36 weeks' PMA (risk ratio (RR) 0.88, 95% confidence interval (CI) 0.81 to 0.95; number needed to treat for an additional beneficial outcome (NNTB) 16, 95% CI 10 to 41; I2 = 39%; 17 studies; 2791 infants; moderate-certainty evidence) and on BPD at 36 weeks' PMA (RR 0.72, 95% CI 0.63 to 0.82; NNTB 13, 95% CI 9 to 21; I2 = 39%; 17 studies; 2791 infants; moderate-certainty evidence). Early initiated systemic hydrocortisone may also have a beneficial effect on death or BPD at 36 weeks' PMA (RR 0.90, 95% CI 0.82 to 0.99; NNTB 18, 95% CI 9 to 594; I2 = 43%; 9 studies; 1376 infants; low-certainty evidence). However, these benefits are likely accompanied by harmful effects like cerebral palsy or neurosensory disability (dexamethasone) or gastrointestinal perforation (both dexamethasone and hydrocortisone). Late initiated systemic dexamethasone (≥ seven days after birth) may have a beneficial effect on death or BPD at 36 weeks' PMA (RR 0.75, 95% CI 0.67 to 0.84; NNTB 5, 95% CI 4 to 9; I2 = 61%; 12 studies; 553 infants; low-certainty evidence), mostly contributed to by a beneficial effect on BPD at 36 weeks' PMA (RR 0.76, 95% CI 0.66 to 0.87; NNTB 6, 95% CI 4 to 13; I2 = 14%; 12 studies; 553 infants; low-certainty evidence). No harmful side effects were shown in the outcomes chosen as key drivers to the decision to start or withhold late systemic dexamethasone. No effects, either beneficial or harmful, were found in the subgroup meta-analyses of late hydrocortisone studies. Early initiated inhaled corticosteroids probably have a beneficial effect on death and BPD at 36 weeks' PMA (RR 0.86, 95% CI 0.75 to 0.99; NNTB 19, 95% CI not applicable; I2 = 0%; 6 studies; 1285 infants; moderate-certainty evidence), with no apparent adverse effects shown in the SRs. In contrast, late initiated inhaled corticosteroids do not appear to have any benefits or harms. Endotracheal instillation of corticosteroids (budesonide) with surfactant as a carrier likely has a beneficial effect on death or BPD at 36 weeks' PMA (RR 0.60, 95% CI 0.49 to 0.74; NNTB 4, 95% CI 3 to 6; I2 = 0%; 2 studies; 381 infants; moderate-certainty evidence) and on BPD at 36 weeks' PMA. No evidence of harmful effects was found. There was little evidence for effects of different starting doses or timing of systemic corticosteroids on death or BPD at 36 weeks' PMA, but potential adverse effects were observed for some comparisons. Lowering the dose might result in a more unfavourable balance of benefits and harms. Moderately early initiated systemic corticosteroids, compared with early systemic corticosteroids, may result in a higher incidence of BPD at 36 weeks' PMA. Pulse dosing instead of continuous dosing may have a negative effect on death and BPD at 36 weeks' PMA. We found no differences for the comparisons of inhaled versus systemic corticosteroids.

PMID: 38597338

21. Pediatric Outcomes Data Collection Instrument Scores Within Gross Motor Function Classification Scale Levels and Functional Mobility Scale Ratings in Individuals With Cerebral Palsy

Eva Ciccodicola, Adriana Liang, Robert M Kay, Tishya A L Wren

J Pediatr Orthop. 2024 Apr 9. doi: 10.1097/BPO.0000000000002684. Online ahead of print.

Background and objective: The Pediatric Outcomes Data Collection Instrument (PODCI) is a patient/parent-reported outcome measure used in children with cerebral palsy (CP). PODCI score variability has not been widely examined in patients of Gross Motor Function Classification System (GMFCS) level IV or using the Functional Mobility Scale (FMS). The purpose of this study is to examine the distribution of PODCI scores within patients with CP GMFCS levels I-IV and FMS levels 1-6. Methods: Retrospectively identified patients with CP whose parent/caregiver had completed the PODCI at their visit were grouped based on GMFCS and FMS level. One-way ANOVA with pairwise Bonferroni-adjusted post hoc tests was performed to compare the effect of GMFCS and FMS levels (1, 2-4, 5, or 6) on PODCI scores. Results: Three hundred sixty-seven patients were included (128 female, 11.7 years, SD 3.6). Global, Sports, Transfer, and Upper Extremity scores differed among all GMFCS levels ($P \leq 0.056$) and were significantly lower for GMFCS IV compared with all other levels. Happiness, Expectations, and Pain scores did not differ significantly among GMFCS levels including level IV ($P > 0.06$). Similar trends were seen at all FMS distances (5, 50, and 500âm). At 50âm, Global, Sports, Transfer, and Upper Extremity scores differed significantly among all FMS levels ($P < 0.001$) except that Upper Extremity Scores were similar between levels 2-4 and level 5 ($P = 1.00$). Happiness and Pain scores were not different between FMS levels ($P > 0.27$). Expectations scores differed only between FMS 1 and FMS 6 with FMS 6 being higher at the 50-m distance only ($P = 0.03$). Conclusions: Parent-reported outcome measures are important for providing patient-centered care. Providers can examine these measures alongside functional classification systems to create a more complete clinical picture of the patient. Providers should be aware of the score trends seen in our results when evaluating the PODCI for individuals with CP to improve shared decision-making and better monitor their need for future care. Level of evidence: Level III-retrospective study.

PMID: 38595088

22. Clinical-functional correlation with brain volumetry in severe perinatal asphyxia: a case report

Juan Pablo Velasquez-Minoli, Natalia Cardona-Ramirez, Hernan Felipe Garcia-Arias, Feliza Restrepo-Restrepo, Gloria Liliana Porras-Hurtado

Case Reports Ital J Pediatr. 2024 Apr 9;50(1):66. doi: 10.1186/s13052-024-01633-w.

Background: Hypoxic-ischemic encephalopathy (HIE) appears in neurological conditions where some brain areas are likely to be injured, such as deep grey matter, basal ganglia area, and white matter subcortical periventricular áreas. Moreover, modeling these brain areas in a newborn is challenging due to significant variability in the intensities associated with HIE conditions. This paper aims to evaluate functional measurements and 3D machine learning models of a given HIE case by correlating the affected brain areas with the pathophysiology and clinical neurodevelopmental. Case presentation: A comprehensive analysis of a term infant with perinatal asphyxia using longitudinal 3D brain information from Machine Learning Models is presented. The clinical analysis revealed the perinatal asphyxia diagnosis with APGAR <5 at 5 and 10 minutes, umbilical arterial pH of 7.0 BE of -21.2 mmol / L), neonatal seizures, and invasive ventilation mechanics. Therapeutic interventions: physical, occupational, and language neurodevelopmental therapies. Epilepsy treatment: vagus nerve stimulation, levetiracetam, and phenobarbital. Furthermore, the 3D analysis showed how the volume decreases due to age, exhibiting an increasing asymmetry between hemispheres. The results of the basal ganglia area showed that thalamus asymmetry, caudate, and putamen increase over time while globus pallidus decreases. Clinical outcomes: spastic cerebral palsy, microcephaly, treatment-refractory epilepsy. Conclusions: Slight changes in the basal ganglia and cerebellum require 3D volumetry for detection, as standard MRI examinations cannot fully reveal their complex shape variations. Quantifying these subtle neurodevelopmental changes helps in understanding their clinical implications. Besides, neurophysiological evaluations can boost neuroplasticity in children with neurological sequelae by stimulating new neuronal connections.

PMID: 38594715

23. Effectiveness of Extracorporeal Shock Wave Therapy in Treatment of Spasticity of Different Aetiologies: A Systematic Review and Meta-Analysis

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Review J Clin Med. 2024 Feb 26;13(5):1323. doi: 10.3390/jcm13051323.

Background: Spasticity is a motor disorder characterised by exaggerated movements of the tendons and accompanied by hyperreflexia and hypertonia. Extracorporeal shock wave therapy (ESWT) is used as a treatment for spasticity, although more evidence is needed on the effectiveness of this therapy in the treatment of spasticity. Therefore, the aim of this study was to assess the effectiveness ESWT in the treatment of upper and lower limbs spasticity in both children and adults through different aetiologies. Methods: A systematic search was performed in different databases from inception to December 2023. Random-effects meta-analysis was used to estimate the efficacy of ESWT on spasticity using the Modified Ashworth Scale. Results: Sixteen studies were included in the systematic review and meta-analysis. The effect of ESWT on spasticity measured with the Modified Ashworth Scale shows a significant decrease in spasticity in the upper limbs and in the lower limbs in adults with chronic stroke and in children with cerebral palsy, is more effective immediately after application, and maintains its effect up to 12 weeks post treatment. Conclusions: These findings are important for clinical practice since they show evidence that

ESWT is effective in reducing spasticity in both children and adults.

PMID: 38592705

24. Assessing the Effectiveness of Rehabilitation Interventions through the World Health Organization Disability Assessment Schedule 2.0 on Disability-A Systematic Review

Claudia-Gabriela Potcovaru, Teodor Salmen, Dragoș Bîgu, Miruna Ioana Săndulescu, Petruța Violeta Filip, Laura Sorina Diaconu, Corina Pop, Ileana Ciobanu, Delia Cinteză, Mihai Berteanu

Review J Clin Med. 2024 Feb 22;13(5):1252. doi: 10.3390/jcm13051252.

(1) Background: The World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) is a tool designed to measure disability in accordance with the International Classification of Functioning, Disability and Health. Measuring disability is becoming increasingly important due to its high prevalence, which continues to rise. Rehabilitation interventions can reduce disability and enhance functioning. (2) Objective: The present study aims to assess the impact of rehabilitation interventions on reducing disability, as measured by the WHODAS 2.0 questionnaire. It also seeks to identify which specific rehabilitation interventions are more effective and to explore other disability assessment questionnaires. (3) Methods: Following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) methodology, we conducted a systematic review, with the protocol registered with the identifier CRD42023495309, focused on "WHODAS" and "rehabilitation" using PubMed and Web of Science electronic databases. (4) Results: We identified 18 articles from various regions encompassing patients with various health conditions, related to stroke, the cardiovascular system (cardiovascular disease, chronic heart failure), the pulmonary system (chronic obstructive pulmonary disease), the neurologic system (Parkinson's disease, cerebral palsy, neurodegenerative disease), the musculoskeletal system (orthopaedic surgery), cancer, and chronic pain, and among frail elderly. These patients have received a wide range of rehabilitation interventions: from conventional therapy to virtual reality, robot-assisted arm training, exergaming, and telerehabilitation. (5) Discussion and Conclusions: A wide range of rehabilitation techniques can effectively improve disability with various comorbidities, offering numerous benefits. The WHODAS 2.0 questionnaire proves to be an efficient and reliable tool for measuring disability, and scores have a tendency to decrease after rehabilitation.

PMID: 38592067

25. Managing the move from assisted to independent living: an inclusive qualitative study among adults with cerebral palsy

Lori Rosenberg, Shira Zecharia, Yafit Gilboa, Anat Golos

Disabil Rehabil. 2024 Apr 9:1-8. doi: 10.1080/09638288.2024.2339535. Online ahead of print.

Purpose: To understand aspects important to adults with severe cerebral palsy (CP) as they prepare to move from assisted to independent living and to create an appropriate intervention. Materials and methods: An inclusive qualitative study was conducted together with adults with severe CP (Gross Motor Function Classification Scale 4-5) preparing to move to independent living. It included semi-structured interviews which were recorded, transcribed, and analyzed by two occupational therapists to create themes. The themes were reviewed and adjusted by the partners in a group context. Results: Seven partners aged 23-47 years (median= 35 years, standard deviation = 10; 4 female) participated. Four themes arose with sub-themes: (1) house management (finances, meals, maintenance, and housework), (2) interactions and boundaries (with a caregiver, family, friends, and romantic partners), (3) schedules (work, leisure, volunteering, education, and health management), and (4) "my way" (autonomy, independence, and self-advocacy; emotions and group power). These themes expressed the concerns of the partners and formed the basis of a group intervention before their move from assisted to independent living. Conclusions: The inclusive research revealed themes the partners raised that expressed their concerns; these became the basis for a group intervention to prepare for their move from assisted to independent living.

PMID: 38591970

26. Antibiotics for the treatment of lower respiratory tract infections in children with neurodisability: Systematic review

Rachael M Marpole, Asha C Bowen, Katherine Langdon, Andrew C Wilson, Noula Gibson

Review Acta Paediatr. 2024 Apr 9. doi: 10.1111/apa.17240. Online ahead of print.

Aim: Determine the optimal antibiotic choice for lower respiratory tract infection (LRTI) in children with neurodisability. Methods: Embase, Ovid Emcare and MEDLINE were searched for studies from inception to January 2023. All studies, except case reports, focusing on the antibiotic treatment of LRTI in children, with neurodisabilities were included. Outcomes included

length of stay, intensive care admission and mortality. Results: Nine studies met the inclusion criteria (5115 patients). All the studies were of low quality. The shortest length of stay was with anaerobic and gram-positive cover. Five studies used anaerobic, gram-positive and gram-negative cover (e.g., amoxicillin-clavulanic acid), which was frequently adequate. In one large study, it was better than gram-positive and gram-negative cover alone (e.g. ceftriaxone). Those unresponsive or more unwell at presentation improved faster on Pseudomonas aeruginosa cover (e.g., piperacillin-tazobactam). Conclusion: In this context, anaerobic, gram-positive and gram-negative cover is just as effective as P. aeruginosa cover, supporting empiric treatment with amoxicillin-clavulanic acid. If there is a failure to improve, broadening to include P. aeruginosa could be considered. This is consistent with a consensus statement on the treatment of LRTI in children with neurodisability. An accepted definition for what constitutes LRTI in this cohort is required before designing prospective randomised trials.

PMID: 38591640

27. Association of congenital heart disease and neurodevelopmental disorders: an observational and Mendelian randomization study

Zhi-Yuan Liu, Qiong-Qiong Wang, Xian-Yong Pang, Xiao-Bi Huang, Gui-Ming Yang, Sheng Zhao

Observational Study Ital J Pediatr. 2024 Apr 8;50(1):63. doi: 10.1186/s13052-024-01610-3.

Background: This study aims to thoroughly study the connection between congenital heart disease (CHD) and neurodevelopmental disorders (NDDs) through observational and Mendelian randomization (MR) designs. Methods: This observational study uses data from the National Survey of Children's Health (2020-2021). Multivariable logistic regression and propensity score matching (PSM) were performed to analyze the association. PSM was used to minimize bias for covariates such as age, race, gender, maternal age, birth weight, concussion or brain injury, preterm birth, cerebral palsy, Down syndrome, and other inherited conditions. In MR analyses, inverse variance-weighted measures, weighted median, and MR-Egger were employed to calculate causal effects. Results: A total of 85,314 children aged 0-17 were analyzed in this study. In regression analysis, CHD ($p = 0.04$), the current heart condition ($p = 0.03$), and the severity of current heart condition ($p < 0.05$) had a suggestive association with speech or language disorders. The severity of current heart condition ($p = 0.08$) has a potential statistically significant association with attention deficit hyperactivity disorder(ADHD). In PSM samples, ADHD($p = 0.003$), intellectual disability($p = 0.012$), and speech or language disorders($p < 0.001$) were all significantly associated with CHD. The severity of current heart condition ($p < 0.001$) also had a significant association with autism. MR analysis did not find causality between genetically proxied congenital cardiac malformations and the risk of NDDs. Conclusions: Our study shows that children with CHD have an increased risk of developing NDDs. Heart conditions currently and severity of current heart conditions were also significantly associated with these NDDs. In the future, we need to try more methods to clarify the causal relationship between CHD and NDDs.

PMID: 38589916

28. Children born to subfertile couples, how are they doing? Evidence from research

Nadine Iman Schottler, Alastair G Sutcliffe

Review Arch Dis Child. 2024 Apr 8:archdischild-2023-326023. doi: 10.1136/archdischild-2023-326023. Online ahead of print.

More than 10 million children have been born with assisted reproductive technology (ART) as we begin to enter the third generation of individuals conceived by ART. Here we summarise key messages from an enlarging body of literature regarding their health. Earlier research had pointed towards increases in perinatal, neonatal and neurological risks, such as preterm birth, low birth weight, congenital malformations and cerebral palsy. Many of these risks have continued to persist in most recent work but have shown reduction. Newer research proposes long-term cardiometabolic and endocrine concerns. Fortunately, most reports conclude there is little or no risk of increased childhood malignancy or abnormal neurodevelopment. Moving forward, new research may benefit from changes in comparator groups and a better understanding of infertility per se in ART, and the confounding role it probably plays in many of the known risk associations, to reliably scan the horizon for health threats for individuals born after ART.

PMID: 38589201

29. Development and validation of a predictive model for poor prognosis of communication disorders in children with cerebral palsy after cervical perivascular sympathectomy

Junjie Wu, Chao Bai, Baofeng Yan, Nurehemaiti Mutalifu, Qi Guan, Jianglong Li, Xinping Luan

Neurosurg Rev. 2024 Apr 8;47(1):142. doi: 10.1007/s10143-024-02380-6.

Cervical perivascular sympathectomy (CPVS) can improve communication disorders in children with cerebral palsy (CP);

however, there are no research reports on the factors affecting surgical efficacy. This study aimed to establish a nomogram for poor prognosis after CPVS. We collected data from 313 CP patients who underwent CPVS at the Neurosurgery Cerebral Palsy Center of the Second Affiliated Hospital of Xinjiang Medical University from January 2019 to January 2023. Among them, 70% (n = 216) formed the training cohort and 30% (n = 97) the validation cohort. The general data and laboratory examination data of both groups were analyzed. In training cohort, 82 (37.96%) showed improved postoperative communication function. Logistic analysis identified motor function, serum alkaline phosphatase, serum albumin, and prothrombin activity as the prognostic factors. Using these four factors, a prediction model was constructed with an area under the curve (AUC) of 0.807 (95% confidence interval [CI], 0.743-0.870), indicating its ability to predict adverse outcomes after CPVS. The validation cohort results showed an AUC of 0.76 (95% CI, 0.650-0.869). The consistency curve and Hosmer-Lemeshow test ($\chi 2 = 10.988$ and $p = 0.202$, respectively) demonstrated good consistency between the model-predicted incidence and the actual incidence of poor prognosis. Motor function, serum alkaline phosphatase, serum albumin, and prothrombin activity are independent risk factors associated with the prognosis of communication disorders after CPVS. The combined prediction model has a good clinical prediction effect and has promising potential to be used for early prediction of prognosis of CPVS.

PMID: 38587684

30. [Therapies, bonds and quality of life of children and adolescents with cerebral palsy: experiences and perceptions of their caregivers during the pandemic] [Article in Spanish]

Natalia Herrera Sterren, Francisco Fantini, Silvina Berra

Observational Study Andes Pediatr. 2024 Feb;95(1):61-68. doi: 10.32641/andespediatr.v95i1.4996.

The COVID-19 pandemic affected the health of children and adolescents (CA). Isolation-related conditions could have impacted not only the functionality of children and adolescents with cerebral palsy (CP) but also their social and emotional well-being, affecting their health-related quality of life (HRQoL). Objective: To analyze perceptions of impairment during the pandemic and differences in HRQoL dimensions compared with a previous registry in Argentinean children and adolescents diagnosed with CP from the perspective of their caregivers. Subjects and method: Cross-sectional observational study at two time points (2019 and 2021) where 98 caregivers participated. We used the KIDSCREEN-27 and CP-QOL questionnaires for the assessment of HRQoL and an open-ended question regarding the impact of the pandemic on the health of children and adolescents, including in 2021. We compared mean scores of the dimensions of the questionnaires in both stages (significant differences: Cohen's $d \geq 0.3$). Responses to the open-ended question were analyzed via "open" and "axial" coding. Results: The scores of the dimensions Participation, Emotional well-being, Social well-being, and School environment (CP-QOL) and Psychological well-being, Friends, School environment, and General HRQoL index (KIDSCREEN-27) were lower during the pandemic (2021) compared with 2019 ($d > 0.3$). Regarding perceived affectation during the pandemic, we identified three main recurrences: "impairment due to interruption of therapies and treatments", "deterioration of peer bonding", and "increased and positive appraisal of self-care". Conclusions: The pandemic affected the psychosocial dimensions of health. Qualitative data highlight the positive assessment of self-care.

PMID: 38587345

31. Exploring individual parent-to-parent support interventions for parents caring for children with brain-based developmental disabilities: A scoping review

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Review Child Care Health Dev. 2024 May;50(3):e13255. doi: 10.1111/cch.13255.

Background: Brain-based developmental disabilities (BBDDs) comprise a large and heterogeneous group of disorders including autism, intellectual disability, cerebral palsy or genetic and neurodevelopmental disorders. Parents caring for a child with BBDD face multiple challenges that cause increased stress and high risk of mental health problems. Peer-based support by fellow parents for a various range of patient groups has shown potential to provide emotional, psychological and practical support. Here, we aim to explore existing literature on individual peer-to-peer support (iP2PS) interventions for parents caring for children with BBDD with a view to (1) explore the impact of iP2PS interventions on parents and (2) identify challenges and facilitators of iP2PS. Method: An extensive literature search (January 2023) was performed, and a thematic analysis was conducted to synthesize findings. Results: Fourteen relevant articles revealed three major themes regarding the impact of iP2PS on parents: (1) emotional and psychological well-being, (2) quality of life and (3) practical issues. Four themes were identified describing challenges and facilitators of iP2PS: (1) benefits and burden of giving support, (2) matching parent-pairs, (3) logistic challenges and solutions and (4) training and supervision of parents providing peer support. Conclusions: This review revealed that iP2PS has a positive impact on the emotional and psychological well-being of parents, as well as the overall quality of life for families caring for a child with a BBDD. Individual P2PS offers peer-parents an opportunity to support others who are facing challenges similar to those they have experienced themselves. However, many questions still need to be addressed regarding benefits of different iP2PS styles, methods of tailoring support to individual needs and necessity of training and supervision for peer support providers. Future research should focus on defining these components and evaluating benefits to

establish effective iP2PS that can be provided as standard care practice for parents.

PMID: 38587275

32. Correction to 'The effects of neurofeedback training for children with cerebral palsy and co-occurring attention deficits: A pilot study'

No authors listed

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No abstract available

Erratum for
The effects of neurofeedback training for children with cerebral palsy and co-occurring attention deficits: A pilot study.
Chen YC, Chang WP, Liang KJ, Chen CL, Chen HY, Chen SP, Chan PS.
Child Care Health Dev. 2024 Mar;50(2):e13231. doi: 10.1111/cch.13231.
PMID: 38465844

PMID: 38587272

33. A Cross-Sectional Study Examining the Relationship Between Malnutrition and Gross Motor Function in Cerebral Palsy

Namrata Bharti, Ajeet K Dwivedi, Shikha Gupta, Abhishek K Singh, Bhoopendra Sharma, Imran Ahmed Khan

Cureus. 2024 Mar 7;16(3):e55753. doi: 10.7759/cureus.55753. eCollection 2024 Mar.

Introduction Cerebral palsy (CP) characterizes a range of permanent, nonprogressive symptoms of postural and motor dysfunction caused by an insult to the developing central nervous system in a fetus or an infant. CP manifests early in life, often within the first two to three years of age. CP is associated with poor growth, that is the deviation from the normal growth parameters. The prevalence of CP ranges from 2.0 to 3.5 per 1000 live births in high-income countries which is comparable to the estimates from low-income countries. Antenatal and perinatal insults are among the most commonly reported causes of CP; however, a large number of cases do not have an identifiable etiology of CP. The current study aims to examine the relationship between malnutrition and gross motor function in children with CP. Materials and Methods This study was conducted at the Department of Pediatrics and Neonatology, Nehru Hospital, Baba Raghav Das (BRD) Medical College, Gorakhpur (UP) over a period of one year (August 2020 to July 2021) after obtaining ethical clearance from the College Research Council. Children of age 1-15 years with CP attending the pediatric outpatient and inpatient departments were enrolled as the study participants after obtaining informed consent from a legal guardian. Assessment of motor function was done using the gross motor function classification system (GMFCS). Associations of malnutrition across levels of gross motor function were tested using Chi-square or Fisher's exact test whichever was applicable. Statistical significance was set at $p < 0.05$ as significant. Data was analyzed using IBM SPSS Statistics for Windows, Version 21 (Released 2012; IBM Corp., Armonk, New York, United States). Result We analyzed 110 children with a diagnosis of CP (median age 6.5 years, interquartile range (IQR) 4.4-9.0 years). The majority (65/110; 59%) of the patients were male, and 68 (61.8%) delivered at term gestation. The most common presenting symptom among children with CP was seizures (79/110; 72.3%), the second most common being delayed milestones among 73 (66.8%), followed by difficulty in breathing among 63 (57.5%). The association between the anthropometric index of participants and GMFCS was found to be highly significant. Conclusion Most CP patients were facing gross motor disturbances. Spastic type of CP was most frequent, and more than half of the patients experienced feeding difficulty. A statistically significant association was found between gross motor functioning and the prevalence of malnutrition and stunting.

PMID: 38586741

34. Clinical outcome prediction with an automated EEG trend, Brain State of the Newborn, after perinatal asphyxia

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Clin Neurophysiol. 2024 Mar 15:162:68-76. doi: 10.1016/j.clinph.2024.03.007. Online ahead of print.

Objective: To evaluate the utility of a fully automated deep learning -based quantitative measure of EEG background, Brain State of the Newborn (BSN), for early prediction of clinical outcome at four years of age. Methods: The EEG monitoring data from eighty consecutive newborns was analyzed using the automatically computed BSN trend. BSN levels during the first days of life (a of total 5427 hours) were compared to four clinical outcome categories: favorable, cerebral palsy (CP), CP with epilepsy, and death. The time dependent changes in BSN-based prediction for different outcomes were assessed by positive/

negative predictive value (PPV/NPV) and by estimating the area under the receiver operating characteristic curve (AUC). Results: The BSN values were closely aligned with four visually determined EEG categories ($p < 0{\cdot}001$), as well as with respect to clinical milestones of EEG recovery in perinatal Hypoxic Ischemic Encephalopathy (HIE; $p < 0{\cdot}003$). Favorable outcome was related to a rapid recovery of the BSN trend, while worse outcomes related to a slow BSN recovery. Outcome predictions with BSN were accurate from 6 to 48 hours of age: For the favorable outcome, the AUC ranged from 95 to 99% (peak at 12 hours), and for the poor outcome the AUC ranged from 96 to 99% (peak at 12 hours). The optimal BSN levels for each PPV/NPV estimate changed substantially during the first 48 hours, ranging from 20 to 80. Conclusions: We show that the BSN provides an automated, objective, and continuous measure of brain activity in newborns. Significance: The BSN trend discloses the dynamic nature that exists in both cerebral recovery and outcome prediction, supports individualized patient care, rapid stratification and early prognosis.

PMID: 38583406

35. Risk Factors for Term-Born Spastic Diplegic Cerebral Palsy: A Case-Control Study

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Background: To identify if a predetermined set of potential risk factors are associated with spastic diplegic cerebral palsy (SDCP) in term-born children. Methods: This is a case-control study with cases (n = 134) extracted from the Canadian Cerebral Palsy Registry (CCPR) and controls (n = 1950) from the Alberta Pregnancy Outcomes and Nutrition (APrON) study. Our primary variable was the SDCP phenotype in term-born children. Possible risk factors were selected a priori and include extreme maternal age (<19 or >35 years), pregnancy complications, maternal disease, substance use, perinatal infection, mode of delivery, perinatal adversity (i.e., neonatal encephalopathy presumably on the basis of intrapartum hypoxia-ischemia), sex, and birth weight. Multivariable analyses were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Results: Multivariable analysis revealed associations between term-born SDCP and pregnancy complications (OR = 4.73; 95% CI = 1.91 to 10.56), maternal disease (OR = 2.52; 95% CI = 1.57 to 3.93), substance use (OR = 3.11; 95% CI = 2.10 to 4.55), perinatal infection (OR = 2.72; 95% CI 1.32 to 5.10), Caesarean section (OR = 2.35; 95% CI = 1.62 to 3.40), and perinatal adversity (OR = 2.91; 95% CI = 1.94 to 4.50). Multiple regression analysis revealed associations between SDCP and pregnancy complications (OR = 3.28; 95% CI 1.20 to 8.15), maternal disease (OR = 2.52; 95% CI 1.50 to 4.12), substance use (OR = 3.59; 95% CI 2.37 to 5.40), perinatal infection (OR = 3.78, 95% CI 1.71 to 7.72), Caesarean section (OR = 2.72; 95% CI 1.82 to 4.03), and perinatal adversity (OR = 4.16; 95% CI 2.67 to 6.70). Interpretation: Antenatal (pregnancy complications, maternal disease, substance use) and perinatal (infections, Caesarean section, and perinatal adversity) risk factors are associated with an increased risk of SDCP in term-born children, suggesting variable interactions between risk factors to provide a clinicopathologic framework that is different from SDCP observed in preterm-born children.

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Prevention and Cure

36. Nicotinamide adenine dinucleotide treatment confers resistance to neonatal ischemia and hypoxia: effects on neurobehavioral phenotypes

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Neonatal hypoxic-ischemic brain injury is the main cause of hypoxic-ischemic encephalopathy and cerebral palsy. Currently, there are few effective clinical treatments for neonatal hypoxic-ischemic brain injury. Here, we investigated the neuroprotective and molecular mechanisms of exogenous nicotinamide adenine dinucleotide, which can protect against hypoxic injury in adulthood, in a mouse model of neonatal hypoxic-ischemic brain injury. In this study, nicotinamide adenine dinucleotide (5 mg/kg) was intraperitoneally administered 30 minutes before surgery and every 24 hours thereafter. The results showed that nicotinamide adenine dinucleotide treatment improved body weight, brain structure, adenosine triphosphate levels, oxidative damage, neurobehavioral test outcomes, and seizure threshold in experimental mice. Tandem mass tag proteomics revealed that numerous proteins were altered after nicotinamide adenine dinucleotide treatment in hypoxic-ischemic brain injury mice. Parallel reaction monitoring and western blotting confirmed changes in the expression levels of proteins including serine (or cysteine) peptidase inhibitor, clade A, member 3N, fibronectin 1, 5'-nucleotidase, cytosolic IA, microtubule associated protein 2, and complexin 2. Proteomics analyses showed that nicotinamide adenine dinucleotide ameliorated hypoxic-ischemic injury through inflammation-related signaling pathways (e.g., nuclear factor-kappa B, mitogen-activated protein kinase, and phosphatidylinositol 3 kinase/protein kinase B). These findings suggest that nicotinamide adenine dinucleotide treatment can

improve neurobehavioral phenotypes in hypoxic-ischemic brain injury mice through inflammation-related pathways.

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