Cerebral palsy research news

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Interventions and Management

1. Fast needling combined with occupational therapy for hand dysfunction of spastic cerebral palsy: a randomized controlled trial [Article in English, Chinese] [Abstract in English, Chinese]

Juanmei Wu, Linlin Yin, Xinping Huang, Fangchuan Chen, Yingying Wu, Rui Meng, Hongxiang Xie

Randomized Controlled Trial Zhongguo Zhen Jiu. 2024 Feb 12;44(2):149-152. doi: 10.13703/j.0255-2930.20230420-k0004.

Objectives: To compare the clinical effect of fast needling (without needle retaining), needle retaining acupuncture combined with occupational therapy and simple occupational therapy for hand dysfunction of spastic cerebral palsy in children. Methods: A total of 75 children with spastic cerebral palsy were randomly divided into an occupational therapy group (25 cases), a fast needling group (25 cases, 1 case dropped out) and a needle retaining group (25 cases, 1 case dropped out). The patients in the occupational therapy group were only treated with occupational therapy for 20 min each time. The patients in the fast needling group were treated with acupuncture (without needle retaining) combined with occupational therapy, and the needle retaining group was treated with acupuncture (needle retaining) combined with occupational therapy, and acupuncture was taken at Hegu (LI 4), Houxi (SI 3), Yuji (LU 10), Waiguan (SJ 5), Jianyu (LI 15) and so on. The needles were retained for 30 min in patients of the needle retaining group. All the above treatments were performed once a day, 5 times a week for 12 weeks. The scores of fine motor function measure (FMFM) and Peabody developmental motor scale 2 (PDMS-2) were observed in patients of the three groups before and after treatment, and the safety of the fast needling group and the needle retaining group was compared. Results: After treatment, the scores of FMFM and PDMS-2 in patients of the three groups were higher than those before treatment ($P<0.01$), and the scores of FMFM and PDMS-2 in the fast needling group and the needle retaining group were higher than those in the occupational therapy group ($P<0.05$, $P<0.01$). The incidence of acupuncture abnormalities in the fast needling group was 0.3% (5/1 440), which was lower than 1.4% (20/1 440) in the needle retaining group ($P<0.05$). Conclusions: Acupuncture combined with occupational therapy has better clinical effect than occupational therapy alone in improving hand dysfunction in children with spastic cerebral palsy, and there is no statistical difference in effect between fast needling acupuncture and needle retaining acupuncture, but fast needling has better safety than needle retaining acupuncture.

PMID: 38373759

2. Optimizing Epoch Length and Activity Count Threshold Parameters in Accelerometry: Enhancing Upper Extremity Use Quantification in Cerebral Palsy

Isabelle Poitras, Léandre Gagné-Pelletier, Jade Clouâtre, Véronique H Flamand, Alexandre Campeau-Lecours, Catherine Mercier

Sensors (Basel). 2024 Feb 8;24(4):1100. doi: 10.3390/s24041100.

Various accelerometry protocols have been used to quantify upper extremity (UE) activity, encompassing diverse epoch lengths and thresholding methods. However, there is no consensus on the most effective approach. The aim of this study was to delineate the optimal parameters for analyzing accelerometry data to quantify UE use in individuals with unilateral cerebral palsy (CP).

Methods: A group of adults with CP (n = 15) participated in six activities of daily living, while a group of children with CP (n = 14) underwent the Assisting Hand Assessment. Both groups performed the activities while wearing ActiGraph GT9X-BT devices on each wrist, with concurrent video recording. Use ratio (UR) derived from accelerometry and video analysis and accelerometer data were compared for different epoch lengths (1, 1.5, and 2 s) and activity count (AC) thresholds (between 2 and 150). Results: In adults, results are comparable across epoch lengths, with the best AC thresholds being ≥ 100. In children, results are similar across epoch lengths of 1 and 1.5 (optimal AC threshold = 50), while the optimal threshold is higher with an epoch length of 2 (AC = 75). Conclusions: The combination of epoch length and AC thresholds should be chosen carefully as both influence the validity of the quantification of UE use.

PMID: 38400258

3. Baby HABIT-ILE intervention: study protocol of a randomised controlled trial in infants aged 6-18 months with unilateral cerebral palsy

Astrid Carton de Tournai, Enimie Herman, Estelle Gathy, Daniela Ebner-Karestinos, Rodrigo Araneda, Laurence Dricot, Benoît Macq, Yves Vandermeeren, Yannick Bleyenheuft

BMJ Open. 2024 Feb 17;14(2):e078383. doi: 10.1136/bmjopen-2023-078383.

Introduction: Research using animal models suggests that intensive motor skill training in infants under 2 years old with cerebral palsy (CP) may significantly reduce, or even prevent, maladaptive neuroplastic changes following brain injury. However, the effects of such interventions to tentatively prevent secondary neurological damages have never been assessed in infants with CP. This study aims to determine the effect of the baby Hand and Arm Bimanual Intensive Therapy Including Lower Extremities (baby HABIT-ILE) in infants with unilateral CP, compared with a control intervention. Methods and analysis: This randomised controlled trial will include 48 infants with unilateral CP aged (corrected if preterm) 6-18 months at the first assessment. They will be paired by age and by aetiology of the CP, and randomised into two groups (immediate and delayed). Assessments will be performed at baseline and at 1 month, 3 months and 6 months after baseline. The immediate group will receive 50 hours of baby HABIT-ILE intervention over 2 weeks, between first and second assessment, while the delayed group will continue their usual activities. This last group will receive baby HABIT-ILE intervention after the 3-month assessment. Primary outcome will be the Mini-Assisting Hand Assessment. Secondary outcomes will include behavioural assessments for gross and fine motricity, visual-cognitive-language abilities as well as MRI and kinematics measures. Moreover, parents will determine and score child-relevant goals and fill out questionnaires of participation, daily activities and mobility. Ethics and dissemination: Full ethical approval has been obtained by the Comité d'éthique Hospitalo-Facultaire/ Université catholique de Louvain, Brussels (2013/01MAR/069 B403201316810g). The recommendations of the ethical board and the Belgian law of 7 May 2004 concerning human experiments will be followed. Parents will sign a written informed consent ahead of participation. Findings will be published in peer-reviewed journals and conference presentations. Trial registration number: NCT04698395. Registered on the International Clinical Trials Registry Platform (ICTRP) on 2 December 2020 and NIH Clinical Trials Registry on 6 January 2021. URL of trial registry record: https://clinicaltrials.gov/ct2/show/NCT04698395?term=bleyenheuft&draw=1&rank=7.

PMID: 38367973

4. Enhancing the Development and Growth of Infant Cerebral Palsy Rats Using Selective Spinal Manipulations

Tianlei Gao, Yuanwang Wang, Min Li, Liuying Yang, Suyu Chen, Lin Gao, Yinghua Shi, XingHe Zhang, XianTao Tai

J Vis Exp. 2024 Feb 2:(204). doi: 10.3791/65659.

Cerebral palsy (CP) is a refractory pediatric disease with a high prevalence, high disability rate, and difficult treatment. A variety of treatments are currently used for CP. The treatment involves drug and non-drug therapy. Traditional Chinese medicine external therapy is a very distinctive treatment method in non-drug therapy. As one of the external therapies of traditional Chinese medicine, massage is used in treating cerebral palsy and has good efficacy, small side effects, and strong operability. As a part of TCM external therapy, selective spinal manipulation can effectively promote the growth and development of infant rats with cerebral palsy. The operation was mainly divided into four steps: first, the rubbing method was applied to the spine and both sides of the spine for 1 min. The pressing and kneading method was applied to the spine for 5 min, and the muscles on both sides of the spine for 5 min. Second, pressing and kneading the sensitive local acupoints in the spine for 2 min were performed. Thirdly, the affected limb was treated by twisting method for 1 min. Fourth, the rubbing method was applied to a midline from the forehead to the back of the brain for 1 min. This study aimed to use selective spinal manipulation to treat infant rats with cerebral palsy. The weight, Rotarod test, Foot-fault score, and growth hormone of infant rats with cerebral palsy were detected to understand the effect of selective spinal manipulation on the growth and development of infant rats with cerebral palsy. The results showed that it can promote weight gain, improve balance ability and motor function, promote growth and development of infant cerebral palsy rats, promote growth hormone secretion, and increase the temperature of sensitive parts of the back.

PMID: 38372272

5. Optimization of Postural Control, Balance, and Mobility in Children with Cerebral Palsy: A Randomized Comparative Analysis of Independent and Integrated Effects of Pilates and Plyometrics

Ragab K Elnaggar, Rodrigo Ramirez-Campillo, Alshimaa R Azab, Saud M Alrawaili, Mshari Alghadier, Mazyad A Alotaibi, Ahmed S Alhowimel, Mohamed S Abdrabo, Mohammed F Elbanna, Ahmed M Aboeleneen, Walaa E Morsy

Children (Basel). 2024 Feb 15;11(2):243. doi: 10.3390/children11020243.

The paradigm of comprehensive treatment approaches for children with cerebral palsy has gained traction, prompting clinicians to deliberate between independent and integrated treatment delivery. However, this decision-making process is often hindered by the dearth of empirical evidence available to inform optimal therapeutic strategies. This study, therefore, sought to compare the effects of Pilates-based core strengthening (PsCS), plyometric-based muscle loading (PlyoML), and their combination on postural control, balance, and mobility in children with unilateral cerebral palsy (ULCP). Eighty-one children with ULCP (age: 12-18 years) were randomized to PsCS (n = 27), PlyoML (n = 27), or a combined intervention (n = 27; equated for total sets/repetitions) group. The three interventions were applied twice/week over 12 successive weeks. Postural control (directional and overall limits of stability-LoS), balance, and mobility (Community Balance and Mobility Scale-CB&M; Functional Walking Test-FWT; Timed Up and Down Stair test-TUDS) were assessed pre- and post-intervention. The combined group exhibited greater increases in directional LoS compared to PsCS and PlyoML including the backward ($p = 0.006$ and 0.033, respectively), forward ($p = 0.015$ and 0.036, respectively), paretic ($p = 0.017$ and 0.018, respectively), and non-paretic directions ($p = 0.006$ and 0.004, respectively)], and this was also the case for overall LoS ($p < 0.001$ versus PsCS and PlyoML). In addition, the combined group displayed greater improvements compared to the PsCS and PlyoML groups regarding CB&M ($p = 0.037$ and $p = 0.002$, respectively), FWT ($p = 0.012$ and $p = 0.038$, respectively), and TUDS ($p = 0.046$ and $p = 0.021$, respectively). In conclusion, the combined PsCS and PlyoML exercise program promotes considerably greater improvements in postural control, balance, and mobility compared to unimodal training in children with ULCP.

PMID: 38397355

6. Identifying and Evaluating Young Children with Developmental Central Hypotonia: An Overview of Systematic Reviews and Tools

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Review Healthcare (Basel). 2024 Feb 18;12(4):493. doi: 10.3390/healthcare12040493.

Children with developmental central hypotonia have reduced muscle tone secondary to non-progressive damage to the brain or brainstem. Children may have transient delays, mild or global functional impairments, and the lack of a clear understanding of this diagnosis makes evaluating appropriate interventions challenging. This overview aimed to systematically describe the best available evidence for tools to identify and evaluate children with developmental central hypotonia aged 2 months to 6 years. A systematic review of systematic reviews or syntheses was conducted with electronic searches in PubMed, Medline, CINAHL, Scopus, Cochrane Database of Systematic Reviews, Google Scholar, and PEDro and supplemented with hand-searching. Methodological quality and risk-of-bias were evaluated, and included reviews and tools were compared and contrasted. Three systematic reviews, an evidence-based clinical assessment algorithm, three measurement protocols, and two additional measurement tools were identified. For children aged 2 months to 2 years, the Hammersmith Infant Neurological Examination has the strongest measurement properties and contains a subset of items that may be useful for quantifying the severity of hypotonia. For children aged 2-6 years, a clinical algorithm and individual tools provide guidance. Further research is required to develop and validate all evaluative tools for children with developmental central hypotonia.

PMID: 38391868

7. Effect of repetitive transcranial magnetic stimulation-assisted training on lower limb motor function in children with hemiplegic cerebral palsy

Yan He, Qi Zhang, Ting-Ting Ma, Yan-Hua Liang, Rong-Rong Guo, Xiao-Song Li, Qian-Jin Liu, Tian-Yang Feng

BMC Pediatr. 2024 Feb 22;24(1):136. doi: 10.1186/s12887-024-04605-5.

Objective: To explore the effect of repetitive transcranial magnetic stimulation (rTMS)-assisted training on lower limb motor function in children with hemiplegic cerebral palsy (HCP). Method: Thirty-one children with HCP who met the inclusion criteria were selected and randomly divided into a control group (n = 16) and an experimental group (n = 15). The control group received routine rehabilitation treatment for 30 min each time, twice a day, 5 days a week for 4 weeks. Based on the control group, the experimental group received rTMS for 20 min each time, once a day, 5 days a week for 4 weeks. The outcome measures included a 10-metre walk test (10MWT), a 6-minute walk distance (6MWD) test, D- and E-zone gross motor function measurements (GMFM), the symmetry ratio of the step length and stance time and the muscle tone of the triceps surae and the hamstrings (evaluated according to the modified Ashworth scale), which were obtained in both groups of children before and after treatment. Results: After training, the 10MWT ($P < 0.05$), 6MWD ($P < 0.01$), GMFM ($P < 0.001$) and

the symmetry ratio of the step length and stance time of the two groups were significantly improved ($P < 0.05$), there was more of an improvement in the experimental group compared with the control group. There was no significant change in the muscle tone of the hamstrings between the two groups before and after treatment ($P > 0.05$). After treatment, the muscle tone of the triceps surae in the experimental group was significantly reduced ($P < 0.05$), but there was no significant change in the control group ($P > 0.05$). Conclusion: Repetitive TMS-assisted training can improve lower limb motor function in children with HCP.

PMID: 38383331

8. Sensory Stimulation of the Triceps Surae Muscle Complex Modulates Spinal Reflex Responses-A Comparison between Tapotement Massage and Repetitive Peripheral Magnetic Stimulation (rPMS)

Volker R Zschorlich, Fengxue Qi, Jörg Schorer, Dirk Büsch

Brain Sci. 2024 Jan 24;14(2):119. doi: 10.3390/brainsci14020119.

Background: The reduction of muscular hypertonia is important in the treatment of various diseases or rehabilitation. This study aims to test the efficacy of a 5 Hz mechanical muscle stimulation (tapotement massage) in comparison to a 5 Hz repetitive peripheral magnetic stimulation (rPMS) on the neuromuscular reflex response. Methods: In a randomized control trial, 15 healthy volunteers were administered with either 5 Hz rPMS, tapotement massage, or rPMS sham stimulation. The posterior tibial nerve was stimulated with rPMS and sham stimulation. The Achilles tendon was exposed to a mechanically applied high-amplitude 5 Hz repetitive tendon tapotement massage (rTTM). The tendon reflex (TR) was measured for the spinal response of the soleus muscle. Results: After rPMS, there was a reduction of the TR response (-9.8%, $p \leq 0.034$) with no significant changes after sham stimulation. Likewise, TR decreased significantly (-17.4%, $p \leq 0.002$) after Achilles tendon tapotement intervention. Conclusions: These findings support the hypothesis that both afferent 5 Hz sensory stimulations contributed to a modulation within the spinal and/or supraspinal circuits, which resulted in a reduction of the spinal reflex excitability. The effects could be beneficial for patients with muscle hypertonia and could improve the functional results of rehabilitation programs.

PMID: 38391694

9. Short-Term Effects of Botulinum Toxin-A Injection on the Medial Gastrocnemius Histological Features in Ambulant Children with Cerebral Palsy: A Longitudinal Pilot Study

Jorieke Deschrevel, Anke Andries, Karen Maes, Nathalie De Beukelaer, Marlies Corvelyn, Lauraine Staut, Hannah De Houwer, Domiziana Costamagna, Kaat Desloovere, Anja Van Campenhout, Ghislaine Gayan-Ramirez

Toxins (Basel). 2024 Jan 30;16(2):69. doi: 10.3390/toxins16020069.

Botulinum toxin-A (BoNT-A) injection is known to exert beneficial effects on muscle tone, joint mobility and gait in children with cerebral palsy (CP). However, recent animal and human studies have raised the concern that BoNT-A might be harmful to muscle integrity. In CP-children, the impact of BoNT-A on muscle structure has been poorly studied, and inconsistent results have been reported. This study was aimed at determining the time course effect of a single BoNT-A administration on medial gastrocnemius (MG) morphology in CP-children. MG microbiopsies from 12 ambulant and BoNT-A-naïve CP-children (age, 3.4 (2.3) years, ranging from 2.5 to 7.8 years; seven boys and five girls; GMFCS I = 5, II = 4 and III = 3) were collected before and 3 and 6 months after BoNT-A treatment to analyze the fiber cross-sectional area (fCSA) and proportion; capillarization; and satellite cell (SC) content. Compared with the baseline, the fCSA decreased at 3 months (-14%, NS) and increased at 6 months (+13%, NS). Fiber size variability was significantly higher at 3 months (type I: +56%, $p = 0.032$; type IIa: +37%, $p = 0.032$) and 6 months (type I: +69%, $p = 0.04$; type IIa: +121%, $p = 0.032$) compared with the baseline. The higher type I proportion seen at 3 months was still present and more pronounced at 6 months (type I: +17%, $p = 0.04$; type IIx: -65%, $p = 0.032$). The capillary fiber density was reduced at 3 months (type I: -43%, NS; type II: -44%, $p = 0.0320$) but normalized at 6 months. There was a non-significant increase in SC/100 fibers at 3 months (+75%, NS) and 6 months (+40%, NS) compared with the baseline. These preliminary data suggest that BoNT-A induced alterations in the MG of children with CP, which were still present 6 months after BoNT-A injection but with signs of muscle recovery.

PMID: 38393147

10. Does crouch alter the effects of neuromuscular impairments on gait? A simulation study

Elijah C Kuska, Katherine M Steele

J Biomech. 2024 Feb 21:165:112015. doi: 10.1016/j.jbiomech.2024.112015. Online ahead of print.

Cerebral palsy (CP) is a neurologic injury that impacts control of movement. Individuals with CP also often develop secondary impairments like weakness and contracture. Both altered motor control and secondary impairments influence how an individual

walks after neurologic injury. However, understanding the complex interactions between and relative effects of these impairments makes analyzing and improving walking capacity in CP challenging. We used a sagittal-plane musculoskeletal model and neuromuscular control framework to simulate crouch and nondisabled gait. We perturbed each simulation by varying the number of synergies controlling each leg (altered control), and imposed weakness and contracture. A Bayesian Additive Regression Trees (BART) model was also used to parse the relative effects of each impairment on the muscle activations required for each gait pattern. By using these simulations to evaluate gait-pattern specific effects of neuromuscular impairments, we identified some advantages of crouch gait. For example, crouch tolerated 13 % and 22 % more plantarflexor weakness than nondisabled gait without and with altered control, respectively. Furthermore, BART demonstrated that plantarflexor weakness had twice the effect on total muscle activity required during nondisabled gait than crouch gait. However, crouch gait was also disadvantageous in the presence of vasti weakness: crouch gait increased the effects of vasti weakness on gait without and with altered control. These simulations highlight gait-pattern specific effects and interactions between neuromuscular impairments. Utilizing computational techniques to understand these effects can elicit advantages of gait deviations, providing insight into why individuals may select their gait pattern and possible interventions to improve energetics.

PMID: 38394953

11. Efficacy of Lower Limb Orthoses in the Rehabilitation of Children Affected by Cerebral Palsy: A Systematic Review

Sandra Miccinilli, Fabio Santacaterina, Rebecca Della Rocca, Silvia Sterzi, Federica Bressi, Marco Bravi

Review Children (Basel). 2024 Feb 6;11(2):212. doi: 10.3390/children11020212.

Lower limb orthoses are frequently used in children suffering from cerebral palsy (CP) alongside rehabilitation. The aim of this study was to analyze the effectiveness of ankle-foot orthosis (AFO) and knee-ankle-foot orthosis (KAFO) in walking, balance maintenance, spasticity, and quality of life improvement during rehabilitation in children affected by CP. The hypothesis was that the use of orthoses could improve the parameters compared to non-use. A systematic review was conducted in the main databases, including English language RCTs published about the use of AFO and KAFO in combination or not with rehabilitation methods in children affected by CP and studies mentioning walking, balance, muscle length, and quality of life as outcomes. From an initial number of 1484 results, a final number of 11 RCTs were included, comprising a total number of 442 participants and showing an overall high risk of bias in 10 studies and some concerns in one study. Six studies investigated the domain of walking, four studies investigated the domain of balance, and two studies investigated how KAFO and AFO orthoses could improve and prevent muscle contractures. Using highly heterogeneous study designs, different kinds of orthoses and different assessment tools were used. Further studies conducted with higher methodological quality are needed to establish whether AFO and KAFO are useful or not in combination with rehabilitation in improving the investigated domains.

PMID: 38397324

12. Bone Deformities through the Prism of the International Classification of Functioning, Disability and Health in Ambulant Children with Cerebral Palsy: A Systematic Review

Rodolphe Bailly, Christelle Pons, Anne-Charlotte Haes, Lisa Nguyen, Matthias Thepaut, Laëtitia Houx, Mathieu Lempereur, Sylvain Brochard

Review Children (Basel). 2024 Feb 16;11(2):257. doi: 10.3390/children11020257.

(1) Aim: The aim of this study was to determine the relationship between lower limb bone deformities and body functions, activity, and participation in ambulant children with CP and whether changing bone morphology affects outcomes in these domains. (2) Methods: A systematic literature search (PROSPERO CRD42020208416) of studies reporting correlations between measures of lower limb bone deformities and measures of body function, activity or participation, or post-surgical outcomes in these domains was conducted from 1990 to 2023 in Medline, Scopus, and Cochrane Library. We assessed study quality with the Checklist for Case Series (CCS) and a quality assessment developed by Quebec University Hospital. Meta-analysis was not possible; therefore, descriptive synthesis was performed. (3) Results: A total of 12 of 3373 screened articles were included. No studies evaluated the relationships between bone deformities and activity or participation, or the effect of isolated bone surgery on these domains. Correlations between bone deformities and body functions were poor-to-moderate. Internal hip rotation during gait improved after femoral derotation osteotomy. (4) Conclusions: A shift in paradigm is urgently required for the research and management of bone deformities in children with CP to include the activity and participation domains of the ICF, as well as consider more psychological aspects such as self-image.

PMID: 38397369

13. Is the Walking Adaptability Ladder test for Kids (WAL-K) reliable and valid in ambulatory children with Cerebral Palsy?

Rosanne Kuijpers, Brenda E Groen, Ellen Smulders, Maria W G Nijhuis-van der Sanden, Vivian Weerdesteyn

Disabil Rehabil. 2024 Feb 24:1-7. doi: 10.1080/09638288.2024.2321325. Online ahead of print.

Purpose: Walking adaptability is essential for children to participate in daily life. We studied whether the Walking Adaptability Ladder test for Kids (WAL-K) is reliable and valid for assessing walking adaptability in 6-12 year old ambulatory children with Cerebral Palsy (CP). Materials and methods: Thirty-six children with CP (26 GMFCS-level I, 10 GMFCS-level II) completed the single and double run of the WAL-K. Intra- and inter-rater reliability were determined by Intraclass Correlation Coefficients (ICCs). Construct validity was determined by comparing WAL-K scores between 122 typically developing (TD) and CP children taking age into account, comparing WAL-K scores between CP children in GMFCS-levels I and II, and correlating WAL-K scores with scores of the 10 times 5 m Sprint Test (10 × 5mST). Results: ICCs for reliability varied between 0.997 and 1.000. WAL-K scores were significantly higher (i.e., worse) in CP children compared to TD children ($p < 0.001$), and in children in GMFCS-level II compared to GMFCS-level I ($p = 0.001$). Significant positive correlations were found between the WAL-K and 10 × 5 mST (single run r = .89, double run r = .84). Conclusions: The WAL-K shows to be a promising reliable, valid, and easy-to-use tool for assessing walking adaptability in children with CP. Responsiveness to change has yet to be evaluated.

PMID: 38400694

14. The Effects of Family Functioning on Gross Motor Function, Activity, and Participation in Children with Cerebral Palsy

Muhammed Samed Dalakçi, Anıl Özüdoğru, Caner Karatı

Iran J Child Neurol. 2024 Winter;18(1):119-130. doi: 10.22037/ijcn.v18i1.32271. Epub 2024 Jan 18.

Objectives: The present study aimed to investigate whether family functioning (FF) could impact gross motor function, activity, and participation in children with cerebral palsy (CP). Materials & methods: Sixty-seven children with spastic diplegic CP who were admitted to the Special Education and Rehabilitation Clinic were included in the study. The guidelines of the American Academy of Neurology were followed for the diagnosis of spastic diplegia. The type of home where the family lives, the family's average income, the child's age, gender, and number of siblings, and the age and educational level of the child's primary caregiver were recorded. The gross motor function capacity of children with CP was assessed with the Gross Motor Function Classification System (GMFCS). The Pediatric Evaluation of Disability Inventory (PEDI) was used to evaluate activity and participation performance. Results: The children living in detached houses had statistically higher PEDI mobility levels than those living in apartments ($p < 0.05$). PEDI's social function and self-care levels were higher in 12 to 18-year-old children with two siblings ($p < 0.05$). The age and educational status of the primary caregiver were found to have an important impact on the PEDI scores. According to the results, social function and self-care levels were higher in children whose primary caregivers were 30 to 65 years old and had high levels of education above high school ($p < 0.05$ The effects of family income and gender on PEDI scores were statistically non-significant ($p> 0.05$). Variables related to family functioning had no statistically significant effect on GMFCS scores ($p> 0.05$). Conclusion: These factors can enable healthcare providers to collaborate with the families to develop more comprehensive intervention plans emphasizing family strengths and supporting their needs.

PMID: 38375120

15. Predictive Value of Fidgety Movement Assessment and Magnetic Resonance Imaging for Cerebral Palsy in Infants

Hui Wang, Zhenghuan Mao, Yu Du, Haifeng Li, Huiying Jin

Pediatr Neurol. 2024 Jan 28:153:131-136. doi: 10.1016/j.pediatrneurol.2024.01.019. Online ahead of print.

Background: The early prediction of cerebral palsy (CP) could enable the follow-up of high-risk infants during the neuroplasticity period. This study aimed to explore the predictive value of fidgety movement assessment (FMA) and brain magnetic resonance imaging (MRI) for the development of CP in clinic rehabilitation setting. Methods: This retrospective observational study included infants who underwent FMA and brain MRI at age nine to 20 weeks at Children's Hospital, Zhejiang University School of Medicine, between March 2018 and September 2019. The area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and accuracy of FMA and MRI for predicting the development of CP were assessed. Results: A total of 258 infants (169 males, gestational age 37.4 ± 3.0 weeks, birth weight 2987.9 ± 757.1 g) were included. Fifteen children had CP after age two years. The diagnostic value of FMA and brain MRI combination showed 86.7% sensitivity (95% confidence interval [CI]: 58.4% to 97.7%), 98.4% specificity (95% CI: 95.6% to 99.5%), and 97.7% accuracy (95% CI: 95.0% to 99.1%); the combination diagnostic value also showed a significantly higher AUC for predicting CP after age two years than FMA alone (AUC: 0.981 vs 0.893, P = 0.013). Conclusions: The diagnostic value of FMA and brain MRI

combination during infancy showed a high predictive value for CP development in clinical rehabilitation setting.

PMID: 38382245

16. Automated identification of abnormal infant movements from smart phone videos

E Passmore, A L Kwong, S Greenstein, J E Olsen, A L Eeles, J L Y Cheong, A J Spittle, G Ball

PLOS Digit Health. 2024 Feb 22;3(2):e0000432. doi: 10.1371/journal.pdig.0000432. eCollection 2024 Feb.

Cerebral palsy (CP) is the most common cause of physical disability during childhood, occurring at a rate of 2.1 per 1000 live births. Early diagnosis is key to improving functional outcomes for children with CP. The General Movements (GMs) Assessment has high predictive validity for the detection of CP and is routinely used in high-risk infants but only 50% of infants with CP have overt risk factors when they are born. The implementation of CP screening programs represents an important endeavour, but feasibility is limited by access to trained GMs assessors. To facilitate progress towards this goal, we report a deep-learning framework for automating the GMs Assessment. We acquired 503 videos captured by parents and caregivers at home of infants aged between 12- and 18-weeks term-corrected age using a dedicated smartphone app. Using a deep learning algorithm, we automatically labelled and tracked 18 key body points in each video. We designed a custom pipeline to adjust for camera movement and infant size and trained a second machine learning algorithm to predict GMs classification from body point movement. Our automated body point labelling approach achieved human-level accuracy (mean ± SD error of 3.7 ± 5.2% of infant length) compared to gold-standard human annotation. Using body point tracking data, our prediction model achieved a cross-validated area under the curve (mean ± S.D.) of 0.80 ± 0.08 in unseen test data for predicting expert GMs classification with a sensitivity of 76% ± 15% for abnormal GMs and a negative predictive value of 94% ± 3%. This work highlights the potential for automated GMs screening programs to detect abnormal movements in infants as early as three months term-corrected age using digital technologies.

PMID: 38386627

17. The Effect of Melatonin on Sleep Disorders in Children with Cerebral Palsy A Randomized Clinical Trial

Hamid Reza Goldouzi, Javad Akhondian, Mehran Beiraghi Toosi, Hassan Mehrad Majd, Shima Shekari, Meisam Babaei

Iran J Child Neurol. 2024 Winter;18(1):51-59. doi: 10.22037/ijcn.v18i1.41949. Epub 2024 Jan 18.

Objectives: Cerebral palsy (CP) is one of the most common causes of serious physical disability in childhood and is a persistent movement disorder before the age of three. This disorder can negatively affect both the child and their family. In recent years, the use of melatonin as a safe, effective, and cheap drug has been expanding in improving the sleep disorders of these children. Therefore, this study aimed to investigate melatonin's effect on sleep disorders in children with CP. Materials & methods: This double-blind clinical trial was conducted on children aged 2 to 12 years with CP who were referred to the pediatric neurology clinic for sleep problems. The participants were included in the study by convenience sampling. After obtaining informed consent from parents, patients were divided randomly into two intervention (melatonin) and control (placebo) groups. In the intervention group, patients received oral melatonin tablets, and in the control group, patients received a placebo (3 mg oral lactose) 30 minutes before going to sleep. Results: The results of this study showed no significant relationship between age and gender with sleep disorders in children with CP ($P>0.05$). A significant effect of melatonin on sleep disorders was found in children with CP. The greatest effect of melatonin is the time required to start falling asleep. Melatonin was associated with decreased time needed to fall asleep and increased sleep duration. Conclusion: The results of the study demonstrated that sleep disorders are prevalent among children with CP. Therefore, proper and timely treatment of these children is crucial. According to the present study's findings, melatonin effectively improves the time of falling asleep and these children's sleep duration.

PMID: 38375130

18. Speech and communication classification of children with cerebral palsy: Novice rater agreement and clinical utility

Katy D Caynes, Tanya A Rose, Robert S Ware, Leanne M Johnston

Int J Speech Lang Pathol. 2024 Feb 20:1-13. doi: 10.1080/17549507.2023.2287991. Online ahead of print.

Purpose: To examine novice inter-rater agreement and clinical utility perspectives for speech and communication classification of children with cerebral palsy (CP). Method: Twenty-one clinicians (speech-language pathologists [SLPs] n = 11; physiotherapists [PTs] n = 5; occupational therapists [OTs] n = 5) novice to the Viking Speech Scale (VSS), Functional Communication Classification System (FCCS), and Communication Function Classification System (CFCS) rated eight unfamiliar children with CP (8-16 years) following classification orientation. Inter-rater agreement was examined between (a) novices, (b) novice SLPs vs. PTs and OTs, and (c) novice vs. expert (kappa statistics). Utility perceptions were scored regarding classification terminology, ease of use, assistive decision-making resources, and construct validity and were analysed

using Kruskal-Wallis H-tests. Result: Rating agreement between novices was substantial (VSS, k = 0.72, 95% CI [0.53-0.92]) to moderate (FCCS, k = 0.44, 95% CI [0.23-0.65]; CFCS, k = 0.45, 95% CI [0.18-0.71]), and almost perfect between novice and expert ratings (VSS, kw = 0.89, 95% CI [0.86-0.92]; FCCS, kw = 0.89, 95% CI [0.86-0.92]; CFCS, kw = 0.86, 95% CI [0.82-0.91]). Statistically significant differences, presented highest to lowest, were found for clinical utility: terminology (VSS, FCCS, CFCS; p = 0.02), assistive decision-making resources (FCCS, VSS, CFCS; p = 0.009), and construct validity (FCCS, CFCS, VSS; p < 0.001). Conclusion: Novice raters achieved substantial agreement for speech classification, supporting utilisation in clinical, research, and CP register activities. Orientation to communication classification constructs, content, and instructions is recommended for novice raters.

PMID: 38379211

19. The effect of selective dorsal rhizotomy on the improvement of the quality of life of children with stage GMFCS IV and V cerebral palsy: Pain, nursing, positioning, and dressing

Jeanne Meyer-Sauvage, Manel Krouma, Caroline Klovan, Philippe Bardot, Marie-Ange Rohon, Jean-Michel Viton, Christophe Boulay, Didier Scavarda

Review Childs Nerv Syst. 2024 Feb 23. doi: 10.1007/s00381-024-06321-y. Online ahead of print.

Aim: The objective of this study is to evaluate the benefit of selective dorsal rhizotomy on the quality of life of patients with severe spasticity with significant impairment of gross motor functions (GMFCS stages IV and V) according to 4 items: pain, nursing care, positioning, and dressing. Materials and methods: We conducted a monocentric retrospective cohort study including patients who underwent selective dorsal rhizotomy between March 2008 and May 2022 at the University Hospital of Marseille. Results: Seventy percent of patients showed an improvement in quality of life criteria: dressing, nursing, positioning, and pain at the last follow-up. A small proportion of patients still showed a worsening between the first 2 follow-ups and the last follow-up. Postoperatively, 27.3% of patients were free of joint spasticity treatment, and we have shown that there was a significant decrease in the number of children who received botulinum toxin postoperatively. However, there was no significant reduction in the number of drug treatments or orthopaedic procedures following RDS. For the CPCHILD© scores, an overall gain is reported for GMFCS IV and V patients in postoperative care. The gain of points is more important for GMFCS IV patients. Improvement was mainly observed in 2 domains, "comfort and emotions" and "hygiene and dressing". For the "quality of life" item, only 3 parents out of the 8 noted a positive change. Conclusion: Our study shows an improvement in nursing care, positioning, and dressing which are associated with a reduction in pain in children with a major polyhandicap GMFCS IV and V who have benefited from a selective dorsal rhizotomy.

PMID: 38393385

20. Oral feeding trajectories and neurodevelopmental outcomes at 12 and 24 month follow-up for preterm infants

L J Dietrich, A Gong, J Gelfond, C L Blanco

J Neonatal Perinatal Med. 2024 Feb 23. doi: 10.3233/NPM-230088. Online ahead of print.

Background: Few studies characterize feeding performance in the NICU when predicting neurodevelopmental outcomes. Our objective was to investigate the relationship between time to full oral feeds (FULL-PO) and neurodevelopmental and feeding outcomes in the first 2 years in preterm infants admitted to the NICU. Methods: This retrospective study included infants born between 01/01/2014-07/31/2017, gestational age < 32 weeks and/or birth weight < 1500 g. We examined feeding difficulties, cerebral palsy, and Bayley scores for those reaching FULL-PO at a post menstrual age (PMA)≤38.0 weeks (EARLY) vs.>38.0 weeks (LATE). Additionally, the oral feeding achieved at various timepoints between 36- and 42-weeks postmenstrual age (PMA) was measured to construct a timeline of oral feeding acquisition. Results: Of 192 infants, 147(77%) achieved FULL-PO EARLY and 45(23%) LATE. Comorbidities and length of stay were higher and unadjusted Bayley scores were lower at 12 months corrected age (CA) and 24 months chronological age (CH) in the LATE group. Feeding difficulties were higher in the LATE group at 24 months CH. Infants born < 27-28 weeks GA were more likely to achieve oral feeding at a later PMA. Infants with bronchopulmonary dysplasia (BPD) had significant feeding and developmental delays. Conclusions: Establishing full oral feeds by 38.0 weeks PMA may be used as a predictor for feeding difficulties at 24 months CH. Infants born < 27-28 weeks GA and those with BPD are more likely to take extended amounts of time to achieve full oral feeding and need additional feeding support. Infants with BPD are high risk for neurodevelopmental delays.

PMID: 38393924

21. A real-time, high-performance brain-computer interface for finger decoding and quadcopter control

Matthew S Willsey, Nishal P Shah, Donald T Avansino, Nick V Hahn, Ryan M Jamiolkowski, Foram B Kamdar, Leigh R Hochberg, Francis R Willett, Jaimie M Henderson

bioRxiv [Preprint]. 2024 Feb 8:2024.02.06.578107. doi: 10.1101/2024.02.06.578107.

People with paralysis express unmet needs for peer support, leisure activities, and sporting activities. Many within the general population rely on social media and massively multiplayer video games to address these needs. We developed a high-performance finger brain-computer-interface system allowing continuous control of 3 independent finger groups with 2D thumb movements. The system was tested in a human research participant over sequential trials requiring fingers to reach and hold on targets, with an average acquisition rate of 76 targets/minute and completion time of 1.58 ± 0.06 seconds. Performance compared favorably to previous animal studies, despite a 2-fold increase in the decoded degrees-of-freedom (DOF). Finger positions were then used for 4-DOF velocity control of a virtual quadcopter, demonstrating functionality over both fixed and random obstacle courses. This approach shows promise for controlling multiple-DOF end-effectors, such as robotic fingers or digital interfaces for work, entertainment, and socialization.

PMID: 38370697

22. Effectivity of Virtual Reality to Improve Balance, Motor Function, Activities of Daily Living, and Upper Limb Function in Children with Cerebral Palsy: A Systematic Review and Meta-Analysis

Maria Komariah, Shakira Amirah, Muhammad Fahd Abdurrahman, Mohammad Farrel Shaquille Handimulya, Hesti Platini, Sidik Maulana, Annisa Dewi Nugrahani, Aep Maulid Mulyana, Shurouq Ghalib Qadous, Henny Suzana Mediani, Arpit Mago

Review Ther Clin Risk Manag. 2024 Feb 14:20:95-109. doi: 10.2147/TCRM.S432249. eCollection 2024.

Background: Cerebral palsy (CP) is the most common motor disorder in childhood. CP limits movement, which can interfere with children's daily activities. As a technology that provides intensive mass practice to children, virtual reality (VR) can create an interactive and motivating environment. With the intensity set by the therapist and feedback that can be used to produce individualized therapy, VR has great potential to improve CP patients' quality of life, especially in a safe, enjoyable, and playful environment. Purpose: This systematic review and meta-analysis sought to determine the effectiveness of VR for children with CP. Methods: We conducted a comprehensive literature search based on the PRISMA guidelines through PubMed, Scopus, Embase, Wiley, and ProQuest to assess the efficacy of VR in managing children with CP up to 15 September 2022. Risk assessment of bias was performed using Cochrane RoB 2. Results: Nineteen randomized controlled trials with 467 and 427 patients with CP were included in the intervention and control groups in qualitative and quantitative analyses. Participants consisted of cerebral palsy with hemiplegia (n=7), diplegia (n=2), a combination of both (n=4), and undefined (n=13). From all studies conducted, VR showed significant results where VR could improve balance (MD: 2.71[1.95, 3.48]; $p < 0.00001$), motor function (MD: 3.73 [1.67, 5.79]; $p = 0.0004$), and activity daily living (MD: 10.05 [2.89, 17.22]. However, VR showed not effective in improving upper limb function. Conclusion: With its advantages and excellent effectiveness, VR may improve functional mobility and the quality of life of children with CP.

PMID: 38375076

23. The Promise of Endovascular Neurotechnology: A Brain-Computer Interface to Restore Autonomy to People with Motor Impairment

Thomas J Oxley

Am J Phys Med Rehabil. 2024 Feb 8. doi: 10.1097/PHM.0000000000002463. Online ahead of print.

This Joel A. DeLisa Lecture on endovascular brain-computer interfaces was presented by Dr. Thomas Oxley on February 23, 2023, at the Association of Academic Physiatrists Annual Scientific Meeting. The lecture described how brain-computer interfaces (BCIs) replace lost physiological function to enable direct communication between the brain and external digital devices such as computers, smartphones, and robotic limbs. Specifically, the potential of a novel endovascular BCI technology was discussed. The BCI uses a stent-electrode array delivered via the jugular vein and is permanently implanted in a vein adjacent to the motor cortex. In a first-in-human clinical trial, participants with upper limb paralysis who received the endovascular BCI could use the system independently and at home to operate laptop computers for various instrumental activities of daily living. An FDA-approved trial of the endovascular BCI in the United States is in progress. Future development of the system will provide recipients with continuous autonomy through digital access with minimal caregiver assistance. Physiatrists and occupational therapists will have a vital role in helping people with paralysis achieve the potential of implantable BCIs.

PMID: 38377064

24. Five-Year Survival Analysis and Causes of Late Deaths of Infants Admitted to the Tertiary Newborn Intensive Care in Latvia

Baiba Balmaka, Sandija Skribāne, Ildze Ābele, Reinis Balmaks

Medicina (Kaunas). 2024 Jan 24;60(2):202. doi: 10.3390/medicina60020202.

Background and Objectives: Studies on long-term survival following admission to neonatal intensive care units (NICUs) are scarce. The aim of this study was to analyse the epidemiology, five-year survival, and causes of late death of infants admitted to the only tertiary NICU in Latvia. Materials and Methods: The study population included all newborns admitted to the Children's Clinical University Hospital (CCUH) NICU from 1 January 2013 to 31 December 2017. The unique national identity numbers from the infants or their mothers were used to link the CCUH electronic medical records to the Medical Birth Register and the Database of Causes of Death of Inhabitants of Latvia maintained by The Centre for Disease Prevention and Control of Latvia. Results: During the study period, a total of 2022 patients were treated in the tertiary NICU. The average admission rate was 18.9 per 1000 live births per year. One hundred and four patients (5.1%) died in the tertiary NICU before hospital discharge. A total of 131 (6.5%) patients from the study cohort died before 12 months of age and 143 (7.1%) before 5 years of age. Patients with any degree of prematurity had a lower five-year mortality (0.9%, 9 out of 994 discharged alive) than term infants (3.2%, 30 out of 924 discharged alive; $p < 0.001$). Of the 39 patients who died after discharge from the NICU, the most common causes of death were congenital heart disease 35.9% (n = 14), multiple congenital malformations and chromosomal abnormalities 17.9% (n = 7), cerebral palsy 10.3% (n = 4), and viral infections 7.7% (n = 3). Conclusions: We observed increased mortality up to five years following NICU admission in both premature and term infants. These findings will help to guide the NICU follow-up programme.

PMID: 38399490

25. Racial and Ethnic Inequities in Therapeutic Hypothermia and Neonatal Hypoxic-Ischemic Encephalopathy: A Retrospective Cohort Study

Carolyn Fall, Rebecca J Baer, Laura Jelliffe-Pawlowski, Nana Matoba, Henry C Lee, Christina D Chambers, Gretchen Bandoli

J Pediatr. 2024 Feb 16:113966. doi: 10.1016/j.jpeds.2024.113966. Online ahead of print.

Objective: To investigate racial inequities in the use of therapeutic hypothermia (TH) and outcomes in infants with hypoxic ischemic encephalopathy (HIE). Study design: We queried an administrative birth cohort of mother-baby pairs in California from 2010 through 2019 using ICD codes to evaluate the association between race and ethnicity and the application of TH in infants with HIE. We identified 4,779 infants with HIE. Log-linear regression was used to calculate risk ratios (RR) for TH, adjusting for hospital transfer, rural location, gestational age between 35 and 37 weeks, and HIE severity. Risk of adverse infant outcome was calculated by race and ethnicity and stratified by TH. Results: From our identified cohort, 1338 (28.0%) neonates underwent TH. White infants were used as the reference sample and 410 (28.4%) received TH. Black infants were significantly less likely to receive TH with 74 (20.0%) with an adjusted risk ratio (aRR) of 0.7 (95% confidence interval 0.5 to 0.9). Black infants with any HIE who did not receive TH were more likely to have a hospital readmission (aRR 1.36, 95% CI 1.10 to 1.68) and a tracheostomy (aRR 3.07, 95% CI 1.19 to 7.97). Black infants with moderate/severe HIE who did not receive TH were more likely to have cerebral palsy (aRR 2.72, 95% CI 1.07 to 6.91). Conclusions: In this study cohort, Black infants with HIE were significantly less likely to receive TH. Black infants also had significantly increased risk of some adverse outcomes of HIE. Possible reasons for this inequity include systemic barriers to care and systemic bias.

PMID: 38369239

26. Editorial Comment on: "External Urethral Sphincter Botulinum Toxin Injection to Treat Pseudodyssynergia in Patients with Cerebral Palsy" (#URL-D- 01629R1)

Alex Gomelsky

Editorial Urology. 2024 Feb 16:S0090-4295(24)00070-0. doi: 10.1016/j.urology.2024.01.016. Online ahead of print.

No abstract available

PMID: 38369196

27. Slipped capital femoral epiphysis in a 5-year-old boy with cerebral palsy on valproic acid and levetiracetam for epilepsy: a case report

Osama R Aldhafian

Case Reports J Surg Case Rep. 2024 Feb 13;2024(2):rjae058. doi: 10.1093/jscr/rjae058. eCollection 2024 Feb.

This study presents a rare case of unilateral slipped capital femoral epiphysis treated surgically in a 5-year-old boy with cerebral palsy who was born at 27 weeks' gestation and developed grade III intraventricular haemorrhage and periventricular leucomalacia and was on antiepileptic drugs, including valproic acid and levetiracetam for >3 years. The patient had no history

of endocrine, renal, and significant familial diseases.

PMID: 38370596

28. Association of maternal pre-pregnancy or first trimester body mass index with neurodevelopmental impairment or death in extremely low gestational age neonates

Sanjay Chawla, Abbot R Laptook, Emily A Smith, Sylvia Tan, Girija Natarajan, Myra H Wyckoff, Rachel G Greenberg, Namasivayam Ambalavanan, Edward F Bell, Krisa P Van Meurs, Susan R Hintz, Betty R Vohr, Erika F Werner, Abhik Das, Seetha Shankaran; NICHD Neonatal Research Network

J Perinatol. 2024 Feb 23. doi: 10.1038/s41372-024-01905-7. Online ahead of print.

Objective: To compare the rates of death or survival with severe neurodevelopmental impairment (sNDI) at 2 years among extremely preterm infants in relation to pre-pregnancy or first-trimester maternal body mass index (BMI). Methods: This retrospective cohort study included extremely preterm infants (gestational age 220/7-266/7 weeks). The study was conducted at National Institute of Child Health and Human Development Neonatal Research Network sites. The primary outcome was death or sNDI at 2 years. Results: Data on the primary outcome were available for 1208 children. Death or sNDI was not different among the three groups: 54.9% in normal, 56.1% in overweight, and 53.4% in obese group (p = 0.39). There was no significant difference in mortality, sNDI, moderate/severe cerebral palsy, Bayley Scales of Infant Development (BSID)-III cognitive composite score <70, BSID-III language composite score <70 in adjusted models. Conclusion: Neurodevelopmental outcome was not significantly associated with maternal pre-pregnancy BMI among extreme preterm infants.

PMID: 38396053

29. Neurosensory, cognitive and academic outcomes at 8 years in children born 22-23 weeks' gestation compared with more mature births

India Rm Marks, Lex W Doyle, Rheanna M Mainzer, Alicia J Spittle, Marissa Clark, Rosemarie A Boland, Peter J Anderson, Jeanie Ly Cheong

Arch Dis Child Fetal Neonatal Ed. 2024 Feb 23:fetalneonatal-2023-326277. doi: 10.1136/archdischild-2023-326277. Online ahead of print.

Despite providing intensive care to more infants born <24 weeks' gestation, data on school-age outcomes, critical for counselling and decision-making, are sparse. Objective: To compare major neurosensory, cognitive and academic impairment among school-aged children born extremely preterm at 22-23 weeks' gestation (EP22-23) with those born 24-25 weeks (EP24-25), 26-27 weeks (EP26-27) and term (≥37 weeks). Design: Three prospective longitudinal cohorts. Setting: Victoria, Australia. Participants: All EP live births (22-27 weeks) and term-born controls born in 1991-1992, 1997 and 2005. Main outcome measures: At 8 years, major neurosensory disability (any of moderate/severe cerebral palsy, IQ <-2 SD relative to controls, blindness or deafness), motor, cognitive and academic impairment, executive dysfunction and poor health utility. Risk ratios (RRs) and risk differences between EP22-23 (reference) and other gestational age groups were estimated using generalised linear models, adjusted for era of birth, social risk and multiple birth. Results: The risk of major neurosensory disability was higher for EP22-23 (n=21) than more mature groups (168 EP24-25; 312 EP26-27; 576 term), with increasing magnitude of difference as the gestation increased (adjusted RR (95% CI) compared with EP24-25: 1.39 (0.70 to 2.76), p=0.35; EP26-27: 1.85 (0.95 to 3.61), p=0.07; term: 13.9 (5.75 to 33.7), p<0.001). Similar trends were seen with other outcomes. Two-thirds of EP22-23 survivors were free of major neurosensory disability. Conclusions: Although children born EP22-23 experienced higher rates of disability and impairment at 8 years than children born more maturely, many were free of major neurosensory disability. These data support providing active care to infants born EP22-23.

PMID: 38395594

30. Amyotrophic Lateral Sclerosis due to ALS2 Pathogenic Variant Masquerading as Cerebral Palsy

Vykuntaraju K Gowda, Sharath Babu, Uddhava Kinhal, Varunvenkat M Srinivasan

Indian J Pediatr. 2024 Feb 23. doi: 10.1007/s12098-024-05081-6. Online ahead of print.

No abstract available

PMID: 38393638

31. Therapeutic hypothermia after perinatal asphyxia in Vietnam: medium-term outcomes at 18 months - a prospective cohort study

Hang Thi Thanh Tran, Ha Thi Le, Dien Minh Tran, Giang Thi Huong Nguyen, Lena Hellström-Westas, Tobias Alfven, Linus Olson

BMJ Paediatr Open. 2024 Feb 21;8(1):e002208. doi: 10.1136/bmjpo-2023-002208.

Aim: To determine neurodevelopmental outcome at 18 months after therapeutic hypothermia for hypoxic-ischaemic encephalopathy (HIE) infants in Vietnam, a low-middle-income country. Method: Prospective cohort study investigating outcomes at 18 months in severely asphyxiated outborn infants who underwent therapeutic hypothermia for HIE in Hanoi, Vietnam, during the time period 2016-2019. Survivors were examined at discharge and at 6 and 18 months by a neonatologist, a neurologist and a rehabilitation physician, who were blinded to the infants' clinical severity during hospitalisation using two assessment tools: the Ages and Stages Questionnaire (ASQ) and the Hammersmith Infant Neurological Examination (HINE), to detect impairments and promote early interventions for those who require it. Results: In total, 130 neonates, 85 (65%) with moderate and 45 (35%) with severe HIE, underwent therapeutic hypothermia treatment using phase change material. Forty-three infants (33%) died during hospitalisation and in infancy. Among the 87 survivors, 69 (79%) completed follow-up until 18 months. Nineteen children developed cerebral palsy (8 diplegia, 3 hemiplegia, 8 dyskinetic), and 11 had delayed neurodevelopment. At each time point, infants with a normal or delayed neurodevelopment had significantly higher ASQ and HINE scores ($p<0.05$) than those with cerebral palsy. Conclusion: The rates of mortality and adverse neurodevelopment rate were high and comparable to recently published data from other low-middle-income settings. The ASQ and HINE were useful tools for screening and evaluation of neurodevelopment and neurological function.

PMID: 38388007

32. External Urethral Sphincter Botulinum Toxin Injection to Treat Pseudodyssynergia in Patients with Cerebral Palsy

Ryan Haggart, Christopher J Loftus, Molly DeWitt-Foy, Valencia Henry, Shawn Grove, Joseph Pariser, Sean Elliott

Urology. 2024 Feb 20:S0090-4295(24)00069-4. doi: 10.1016/j.urology.2023.11.037. Online ahead of print.

Objective: To evaluate urinary outcomes following cystoscopic external urinary sphincter onabotulinumtoxinA (BTX) injections in patients with CP. Adults with cerebral palsy (CP) can suffer from bladder outlet obstruction and urinary retention due to a spastic external urethral sphincter ("pseudodysynergia"). We have used BTX injections into the sphincter to relieve the obstruction and allow patients to maintain spontaneous voiding rather than intermittent catheterization. Methods: Patients were included in this retrospective cohort study if they had a diagnosis of CP, were at least 18 years of age, and underwent a urethral external sphincter BTX injection between 2016-2023. The procedure included 100u or 200u of BTX mixed in 4cc of saline. Primary outcomes were subjective, patient or caregiver reported changes in retention, lower urinary tract symptoms (LUTS), frequency of recurrent urinary tract infections (UTIs), and hydronephrosis or bladder stones/debris on ultrasound. Results: 50 patients were included; the majority were male (60%), lived at home with assistance (58%), and had a Gross Motor Function Classification System level of V (50%; i.e., severe CP). The most common indications for BTX were retention (96%), LUTS (48%), hydronephrosis (18%), and recurrent UTIs (22%). Post-BTX improvement was seen in 67% of those with LUTS, 65% with retention, 67% with hydronephrosis, and 73% with recurrent UTIs. Most patients underwent repeat injections (60%). There were no significant complications associated with injections. Conclusion: External urethral sphincter BTX is a safe, effective option for treating pseudodysynergia in adults with CP.

PMID: 38387511

33. Association Between Seizures and Neurodevelopmental Outcome at Two and Five Years in Asphyxiated Newborns With Therapeutic Hypothermia

Juliette F Langeslag, Wes Onland, Floris Groenendaal, Linda S de Vries, Anton H van Kaam, Timo R de Haan; PharmaCool Study Group

Pediatr Neurol. 2024 Feb 2:153:152-158. doi: 10.1016/j.pediatrneurol.2024.01.023. Online ahead of print.

Objective: To investigate the association between the presence and severity of seizures in asphyxiated newborns and their neurodevelopmental outcome at ages two and five years. Methods: Retrospective data analysis from a prospectively collected multicenter cohort of 186 term-born asphyxiated newborns undergoing therapeutic hypothermia (TH) in 11 centers in the Netherlands and Belgium. Seizures were diagnosed by amplitude-integrated electroencephalography (EEG) and raw EEG signal reading up to 48 hours after rewarming. Neurodevelopmental outcome was assessed by standardized testing at age two and five years. Primary outcome was death or long-term neurodevelopmental impairment (NDI) including cerebral palsy. Associations were calculated using univariate and multivariate logistic regression analyses adjusting for Thompson score and a validated brain magnetic resonance imaging (MRI) score. Results: Seventy infants (38%) had seizures during TH or rewarming, and 44 (63%) of these needed two or more antiseizure medications (ASMs). Overall mortality was 21%. Follow-up

data from 147 survivors were available for 137 infants (93%) at two and for 94 of 116 infants (81%) at five years. NDI was present in 26% at two and five years. Univariate analyses showed a significant association between seizures and death or NDI, but this was no longer significant after adjusting for Thompson and MRI score in the multivariate analysis; this was also true for severe seizures (need for two or more ASMs) or seizures starting during rewarming. Conclusion: The presence or severity of seizures in newborns undergoing TH for hypoxic-ischemic encephalopathy was not independently associated with death or NDI up to age five years after adjusting for several confounders.
PMID: 38387280

34. Clinical Characteristics Suggestive of a Genetic Cause in Cerebral Palsy: A Systematic Review

Anna M Janzing, Erik Eklund, Tom J De Koning, Hendriekje Eggink

Review Pediatr Neurol. 2024 Feb 2:153:144-151. doi: 10.1016/j.pediatrneurol.2024.01.025. Online ahead of print.

Background: Cerebral palsy (CP) is a clinical diagnosis and was long categorized as an acquired disorder, but more and more genetic etiologies are being identified. This review aims to identify the clinical characteristics that are associated with genetic CP to aid clinicians in selecting candidates for genetic testing. Methods: The PubMed database was systematically searched to identify genes associated with CP. The clinical characteristics accompanying these genetic forms of CP were compared with published data of large CP populations resulting in the identification of potential indicators of genetic CP. Resullts: Of 1930 articles retrieved, 134 were included. In these, 55 CP genes (described in two or more cases, n = 272) and 79 candidate genes (described in only one case) were reported. The most frequently CP-associated genes were PLP1 (21 cases), ARG1 (17 cases), and CTNNB1 (13 cases). Dyskinesia and the absence of spasticity were identified as strong potential indicators of genetic CP. Presence of intellectual disability, no preterm birth, and no unilateral distribution of symptoms were classified as moderate genetic indicators. Conclusions: Genetic causes of CP are increasingly identified. The clinical characteristics associated with genetic CP can aid clinicians regarding to which individual with CP to offer genetic testing. The identified potential genetic indicators need to be validated in large CP cohorts but can provide the first step toward a diagnostic algorithm for genetic CP.

PMID: 38382247

35. Motor imagery ability in children and adolescents with cerebral palsy: a systematic review and evidence map

José Fierro-Marrero, Alejandro Corujo-Merino, Roy La Touche, Sergio Lerma-Lara

Front Neurol. 2024 Feb 6:15:1325548. doi: 10.3389/fneur.2024.1325548. eCollection 2024.

Background: Cerebral palsy (CP) refers to a group of permanent movement and posture disorders. Motor imagery (MI) therapy is known to provide potential benefits, but data on MI ability in children and adolescents with CP is lacking. Objective: A systematic review was performed to explore MI abilities in children and adolescents with CP compared to typically developed (TD) subjects. Methods: We searched on PubMed, Web of Science (WOS), EBSCO, Google Scholar, and PEDro including observational studies. Methodological quality was assessed with the modified Newcastle-Ottawa Scale and evidence map was created to synthesize the evidence qualitatively and quantitatively. Results: Seven cross-sectional studies were selected, which included 174 patients with CP and 321 TD subjects. Three studies explored explicit MI, two MI-execution synchrony, and four implicit MI domains. Methodological quality ranged from 6 to 8 stars. Moderate evidence supported the absence of differences in vividness between the groups. As there was only limited evidence, establishing a clear direction for the results was not possible, especially for the capacity to generate MI, mental chronometry features, and MI-execution synchrony domains. Moderate evidence supported a lower efficiency in cases for hand recognition, derived from a lower accuracy rate, while reaction time remained similar between the two groups. Moderate evidence indicated that patients with CP and TD controls showed similar features on whole-body recognition. Conclusion: Moderate evidence suggests that patients with CP present a reduced ability in hand recognition, which is not observed for whole-body recognition compared to healthy controls. Severe limitations concerning sample size calculations and validity of assessment tools clearly limits establishing a direction of results, especially for explicit MI and MI-Execution synchrony domains. Further research is needed to address these limitations to enhance our comprehension of MI abilities in children, which is crucial for prescribing suitable MI-based therapies in this child population.

PMID: 38379703

36. What challenges do siblings of children with chronic disorders express to their parents? A thematic analysis of 73 sibling-parent dialogues

Amalie Schumann, Torun M Vatne, Krister W Fjermestad

J Pediatr Nurs. 2024 Feb 16:76:91-98. doi: 10.1016/j.pedn.2024.01.032. Online ahead of print.

Purpose: The study explored challenges experienced by siblings of children with chronic disorders, as expressed by siblings in

parent-child dialogues. Design and methods: Seventy-three parent-child dialogues (M duration = 28.6 min) were analyzed using qualitative thematic analysis. The dialogues took place within the SIBS group intervention for siblings and parents of children with chronic disorders. The siblings (aged 8 to 14 years) had brothers and sisters with autism spectrum disorders, ADHD, rare disorders, cerebral palsy, or severe mental health disorders. The data are from session 5 in the SIBS intervention, in which the siblings are to express their wishes about family-related challenges (e.g., desired changes) to their parents. The parents are encouraged to listen, explore, and validate the child's perspective before discussing solutions. Results: Most of the family-oriented challenges the siblings expressed were related to the diagnosis of the brother or sister with a disorder. Four main themes were identified: (1) Family life (e.g., limitations in family activities); (2) The diagnosis (e.g., concerns about the future); (3) Violence; and (4) Important relationships. Conclusion: The siblings experienced challenges and difficult emotions in interactional processes in which the diagnosis affected family life and relationships. The study adds a new dimension to the field by identifying siblings' expressed challenges based on parent-child dialogues. Practice implications: Identified themes can guide how parents should meet and address siblings' needs, how health care providers inform and support parents in doing so, and emphasize the relevance of interventions targeting family-level risk and resilience factors.

PMID: 38367476

37. Modification of the Paediatric Gastro-oesophageal Reflux Disease Symptom and Quality of Life Questionnaire (PGSQ) for children with cerebral palsy: a preliminary study

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BMJ Paediatr Open. 2024 Feb 20;8(1):e002256. doi: 10.1136/bmjpo-2023-002256.

Objective: Gastro-oesophageal reflux disease (GORD) is a common condition affecting children, characterised by the passage of gastric contents into the oesophagus causing pain, vomiting and regurgitation. Children with neurodisability (such as cerebral palsy; CP) are predisposed to more severe GORD due to coexisting gut dysmotility and exclusive/supplementary liquid diet; however, there are no existing tools or outcome measures to assess the severity of GORD in this patient group. For children without CP, the 'Paediatric Gastro-oesophageal Symptom and Quality of Life Questionnaire' (PGSQ) assesses symptoms and response to treatment, but the questions are not suitable for children with significant cognitive impairment. We aimed to adapt the existing PGSQ assessment tool to enable use in evaluating children with CP and GORD. Patients/interventions: Cognitive interviews were conducted by the research team with six parents/carers of children (aged 3-15) with CP (Gross Motor Function Classification System level V) who have current or past symptoms of reflux. They were asked to interpret the questionnaire using a 'think-aloud technique,' and offer suggestions on alterations to questions. Reasons for changing questions included confusing/difficult to understand questions, differing interpretations of questions and response choices not applying to the patient group. Results: The PGSQ was modified iteratively following each interview. Overall, parents/carers reported that it was acceptable to recall information over the past 7 days. In the final version, it was felt the questions were relevant, useful and related to symptoms that they observed. It was easy to comprehend with no uncomfortable questions. Suggestions for future work included a section specifically focusing on the school day answered by school staff and home life answered by carers who assist them in the home. Conclusions: We have adapted the PGSQ to improve relevance and acceptability for families/carers of children with symptoms of GORD and neurodisability. Further work is needed to validate the questionnaire for this patient group.

PMID: 38378669

38. Polyethylene Glycol 4000 for Fecal Disimpaction in Cerebral Palsy Children

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Iran J Child Neurol. 2024 Winter;18(1):61-69. doi: 10.22037/IJCN.v17i2.37876. Epub 2024 Jan 18.

Objectives: This study evaluated the efficacy of Polyethylene glycol 4000 for fecal disimpaction in children with cerebral palsy. Materials & methods: A randomized control trial study was conducted on children with cerebral palsy between February - March 2017 in the pediatric neurology outpatient clinic Dr. Soetomo Hospital. Children aged 2-16 years with fecal impaction randomly assigned into polyethylene glycol 4000 (PEG 4000) and saline enema group. Polyethylene glycol 4000 was given at a dosage of 0.7 g/kg and enema using normal saline 15ml/kg twelve hourly. Constipation was diagnosed using ROME IV criteria, and abdominal palpation identified fecal impaction. Efficacy was evaluated by clinical observation and adverse symptom monitoring. Data were analyzed by statistical software using an independent t-test ($p<0,05$). Results: Thirty-two children were randomized into the study. Muscle relaxant was discovered in 17/32 patients. Sex, age, and body weight were not statistically different between groups. The resolution of fecal impaction was significantly different between PEG 4000 and saline enema (21.69 hours and 39 hours respectively; $p=0.001$). Application of muscle relaxant and severity of the disease did not involve treatment efficacy. There was no adverse symptom reported during treatment. Conclusion: Polyethylene glycol 4000 results in fecal disimpaction faster than enema in constipated children with cerebral palsy.

PMID: 38375128

39. A pilot study proposing an algorithm for pubertal induction in cerebral palsy

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J Pediatr Endocrinol Metab. 2024 Feb 20. doi: 10.1515/jpem-2024-0013. Online ahead of print.

Objectives: To explore delayed puberty in cerebral palsy (CP) and to test the acceptability of an interventional puberty induction algorithm. Methods: A two phase cohort study in children and adolescents diagnosed with CP who have delayed puberty. Phase 1: Retrospective review of clinical records and interviews with patients who have been treated with sex-steroids and Phase 2: Prospective interventional trial of pubertal induction with a proposed algorithm of transdermal testosterone (males) or oestrogen (females). Phase 1 examined experiences with sex-steroid treatment. Phase 2 collected data on height adjusted bone mineral density (BMAD), fractures, adverse effects, mobility and quality of life over two years during the induction. Results: Phase 1, treatment was well tolerated in 11/20 treated with sex-steroids; phase 2, using the proposed induction algorithm, 7/10 treated reached Tanner stage 3 by nine months. One participant reached Tanner stage 5 in 24 months. Mean change in BMAD Z-scores was +0.27 % (SD 0.002) in those who could be scanned by dual-energy X-ray absorptiometry (DXA). Conclusions: Delayed puberty may be diagnosed late. Treatment was beneficial and well tolerated, suggesting all patients with severe pubertal delay or arrest should be considered for sex hormone supplementation.

PMID: 38374118

40. Unmet environmental needs and unmet healthcare needs in a population of young adults with cerebral palsy: what the SPARCLE study tells us

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Front Rehabil Sci. 2024 Feb 2:5:1294999. doi: 10.3389/fresc.2024.1294999. eCollection 2024.

Introduction: Optimizing care for young adults with cerebral palsy is crucial for their physical and psychological well-being. The inadequacy of proximal environment may play a role in the provision of health services. The aim of this study is to explore the association between unmet environmental needs in the physical, social and attitudinal domains and unmet healthcare needs in four interventions: physiotherapy, occupational therapy, speech therapy and psychological counselling. Methods: Young adults with cerebral palsy were recruited in the SPARCLE3 European multicenter cross-sectional study. Healthcare needs and coverages were assessed using the Youth Health Care, Satisfaction, Utilization and Needs questionnaire. The need and availability of environmental factors in physical, social and attitudinal domains were collected using the European Adult Environment Questionnaire. Logistic regressions were conducted separately for each intervention to measure associations between unmet environmental needs and unmet healthcare needs. Results: We studied 310 young adults with cerebral palsy, with a mean age of 24.3 years; 37.4% could not walk independently, 51.5% had an IQ below 70, 34.2% had severe communication difficulties. The most commonly expressed need was physiotherapy (81.6% of participants). Unmet healthcare needs were reported by 20.9%, 32.4%, 40.3% and 49.0% of participants requiring physiotherapy, occupational therapy, psychological counselling and speech therapy, respectively. The physical environment was never significantly associated with unmet healthcare needs. In contrast, the social environment was significantly associated with unmet healthcare needs across all interventions, with odds ratios over 2.5, depending on the number of unmet needs and the nature of intervention needed. With regard to the attitudinal environment, when at least one unmet attitudinal environmental need was reported, the odds of also reporting an unmet healthcare need were of 3.68 for speech therapy and 3.77 for physiotherapy. The latter association was significant only for individuals with severe motor impairment. Discussion: Our results highlight the importance of the social and attitudinal environment in meeting healthcare needs in young adults with cerebral palsy. The lack of correlation between unmet healthcare needs and the physical environment suggests that it can be partly compensated for by social support.

PMID: 38370854

41. Neurological outcomes and mortality after neonatal seizures with electroencephalographical verification. A systematic review

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Aim: To conduct a systematic review of post-neonatal neurological outcomes and mortality following neonatal seizures with electroencephalographical verification. Methods: The databases Medline, Embase and Web of Science were searched for eligible studies. All abstracts were screened in a blinded fashion between research team members and reports found eligible were obtained and screened in full text by two members each. From studies included, outcome results for post-neonatal epilepsy, cerebral palsy, intellectual disability, developmental delay, mortality during and after the neonatal period and composite outcomes were extracted. A quality assessment of each study was performed. Results: In total, 5518 records were screened and 260 read in full text. Subsequently, 31 studies were included, containing cohorts of either mixed or homogenous

etiologies. Follow-up time and gestational ages varied between studies. No meta-analysis could be performed due to the low number of studies with comparable outcomes and effect measures. Reported cumulative incidences of outcomes varied greatly between studies. For post-neonatal epilepsy the reported incidence was 5-84%, for cerebral palsy 9-78%, for intellectual disability 24-67%, for developmental delay 10-67% and for mortality 1-62%. Subgroup analysis had more coherent results and in cohorts with status epilepticus a higher incidence of post-neonatal epilepsy from 46 to 84% was shown. Conclusion: The large variation of reported incidences for neurological outcomes and mortality found even when restricting to cohorts with electroencephalographically verified neonatal seizures indicates selection bias as a significant confounder in existing studies. Population-based approaches are thus warranted to correctly predict outcomes in this group.

PMID: 38367369

42. Exposure to Paracetamol in Early Pregnancy and the Risk of Developing Cerebral Palsy: A Case-Control Study Using Serum Samples

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Objective: To investigate whether maternal paracetamol use in early pregnancy is associated with cerebral palsy (CP) in offspring. Study design: We conducted a registry and biobank-based case-control study with mother-child pairs. We identified CP cases (n=322) born between 1995-2014 from a nationwide CP-registry. Randomly selected controls (n=343) and extra preterm controls (n=258) were obtained from a birth registry. For each mother, a single serum sample from early pregnancy (gestation weeks 10-14) was retrieved from a biobank and analyzed for serum concentrations of paracetamol, categorized into unexposed (<1 ng/ml), mildly exposed (1-100 ng/ml), and highly exposed (>100 ng/ml), and in quartiles. Analyses were performed using logistic regression and adjusted for potential confounders. Separate analyses were conducted including only those children born preterm and only those born term. Results: Of the 923 participants, 36.8% were unexposed, 53.2% mildly exposed, and 10% highly exposed to paracetamol. Overall, prenatal exposure to paracetamol was not associated with CP. Sensitivity and subgroup analyses showed no clear associations between paracetamol and CP across strata of term/preterm birth as well as subtypes of CP. Conclusions: The present study does not support an association between intrauterine exposure to paracetamol in early pregnancy and the risk of CP. However, it is important to stress that the exposure estimate is based on a single serum sample.

PMID: 38369234

43. Antenatal Magnesium Sulfate Benefits Female Preterm Infants but Results in Poor Male Outcomes

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Magnesium sulfate (MagSul) is used clinically to prevent eclamptic seizures during pregnancy and as a tocolytic for preterm labor. More recently, it has been implicated as offering neural protection in utero for at-risk infants. However, evidence is mixed. Some studies found that MagSul reduced the incidence of cerebral palsy (CP) but did not improve other measures of neurologic function. Others did not find any improvement in outcomes. Inconsistencies in the literature may reflect the fact that sex effects are largely ignored, despite evidence that MagSul shows sex effects in animal models of neonatal brain injury. The current study used retrospective infant data to assess differences in developmental outcomes as a function of sex and MagSul treatment. We found that on 18-month neurodevelopmental cognitive and language measures, preterm males treated with MagSul ($n = 209$) had significantly worse scores than their untreated counterparts ($n = 135$; $p < 0.05$). Female preterm infants treated with MagSul ($n = 220$), on the other hand, showed a cognitive benefit relative to untreated females ($n = 123$; $p < 0.05$). No significant effects of MagSul were seen among females on language ($p > 0.05$). These results have tremendous implications for risk-benefit considerations in the ongoing use of MagSul and may explain why benefits have been hard to identify in clinical trials when sex is not considered.

PMID: 38399433

44. Neurodevelopmental Outcome after Culture-Proven or So-Called Culture-Negative Sepsis in Preterm Infants

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J Clin Med. 2024 Feb 17;13(4):1140. doi: 10.3390/jcm13041140.

(1) Background: Prematurity is a serious condition associated with long-term neurological disability. This study aimed to

compare the neurodevelopmental outcomes of preterm neonates with or without sepsis. (2) Methods: This single-center retrospective case-control study included infants with birth weight < 1500 g and/or gestational age ≤ 30 weeks. Short-term outcomes, brain MRI findings, and severe functional disability (SFD) at age 24 months were compared between infants with culture-proven or culture-negative sepsis or without sepsis. A chi-squared test or Mann-Whitney U test was used to compare the clinical and instrumental characteristics and the outcomes between cases and controls. (3) Results: Infants with sepsis (all sepsis n = 76; of which culture-proven n = 33 and culture-negative n = 43) were matched with infants without sepsis (n = 76). Compared with infants without sepsis, both all sepsis and culture-proven sepsis were associated with SFD. In multivariate logistic regression analysis, SFD was associated with intraventricular hemorrhage (OR 4.7, CI 1.7-13.1, p = 0.002) and all sepsis (OR 3.68, CI 1.2-11.2, p = 0.021). (4) Conclusions: All sepsis and culture-proven sepsis were associated with SFD. Compared with infants without sepsis, culture-negative sepsis was not associated with an increased risk of SFD. Given the association between poor outcomes and culture-proven sepsis, its prevention in the neonatal intensive care unit is a priority.

PMID: 38398453

Prevention and Cure

45. Human amniotic mesenchymal stromal cell-derived exosomes promote neuronal function by inhibiting excessive apoptosis in a hypoxia/ischemia-induced cerebral palsy model: A preclinical study

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Biomed Pharmacother. 2024 Feb 22:173:116321. doi: 10.1016/j.biopha.2024.116321. Online ahead of print.

Background: Cerebral palsy (CP) is a condition resulting from perinatal brain injury and can lead to physical disabilities. Exosomes derived from human amniotic mesenchymal stromal cells (hAMSC-Exos) hold promise as potential therapeutic options. Objective: This study aimed to investigate the impact of hAMSC-Exos on neuronal cells and their role in regulating apoptosis both in vitro and in vivo. Methods: hAMSC-Exos were isolated via ultracentrifugation and characterized via transmission electron microscopy, particle size analysis, and flow cytometry. In vitro, neuronal damage was induced by lipopolysaccharide (LPS). CP rat models were established via left common carotid artery ligation. Apoptosis levels in cells and CP rats were assessed using flow cytometry, quantitative reverse transcription polymerase chain reaction (RT-qPCR), Western blotting, and TUNEL analysis. Results: The results demonstrated successful isolation of hAMSC-Exos via ultracentrifugation, as the isolated cells were positive for CD9 (79.7%) and CD63 (80.2%). Treatment with hAMSC-Exos significantly mitigated the reduction in cell viability induced by LPS. Flow cytometry revealed that LPS-induced damage promoted apoptosis, but this effect was attenuated by treatment with hAMSC-Exos. Additionally, the expression of caspase-3 and caspase-9 and the Bcl-2/Bax ratio indicated that excessive apoptosis could be attenuated by treatment with hAMSC-Exos. Furthermore, tail vein injection of hAMSC-Exos improved the neurobehavioral function of CP rats. Histological analysis via HE and TUNEL staining showed that apoptosis-related damage was attenuated following hAMSC-Exo treatment. Conclusions: In conclusion, hAMSC-Exos effectively promote neuronal cell survival by regulating apoptosis, indicating their potential as a promising therapeutic option for CP that merits further investigation.

PMID: 38394849