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Interventions and Management

1. Association between upper limb clinical tests and accelerometry metrics for arm use in daily life in children with unilateral cerebral palsy

Jenny Hedberg-Graff, Lucian Bezuidenhout, Lena Krumlinde-Sundholm, Jenny Hallgren, David Moulaee Conradsson, Maria Hagströmer

Disabil Rehabil. 2024 Aug 27:1-7. doi: 10.1080/09638288.2024.2393801. Online ahead of print.

Purpose: To evaluate the association between upper-limb (UL) clinical tests and UL accelerometry-derived metrics in children with unilateral Cerebral Palsy (CP). Methods: In this cross-sectional study, twenty children with unilateral CP and Manual Ability Classification System level I-III were included. Outcomes of the Assisting Hand Assessment, Box and Block-Test and accelerometry metrics were collected in the clinical setting and in daily life. UL asymmetry index (i.e., the ratio between the well-functioning UL and the affected UL use) was evaluated in different physical activity levels and relative use of UL was evaluated during daily living. Spearman's correlation was used to determine the association between UL clinical tests and accelerometry metrics in a clinical setting and in daily life. Results: The strongest negative association was between the Assisting Hand Assessment units and accelerometry metrics during the sedentary time in daily life (rs = -0.64). The asymmetries between ULs were highest during the child's sedentary time (asymmetry index: 45.15) compared to when the child was in light (asymmetry index: 23.97) or higher intensity physical activity (asymmetry index: 13.39). The children used both ULs simultaneously for 44% of the time during daily life. Conclusion: Accelerometry metrics may provide additional objective information to clinical tests by quantifying the amount of UL movements and the amount of asymmetry between the upper limbs in daily life.

PMID: 39192545

2. Effect of touch screen tablet use on fine motor functions in children with hemiparetic cerebral palsy: A randomized controlled trial

Hanaa M Abd-Elfattah, Dina O Shokri M Galal, Shaima M Abdelmageed, Sobhy M Aly, Fairouz H Ameen, Asmaa O Sayed, Amira M Abd-Elmonem

Randomized Controlled Trial NeuroRehabilitation. 2024;55(1):137-146. doi: 10.3233/NRE-240134.

Background: Cerebral palsy is the most frequent condition affecting the central nervous system and causing large disability. Objective: To determine the impact of touch screen tablet upon fine motor functions in children with hemiparesis. Method: This was a randomized controlled trial involving 60 children, ranging in age from 5 to 7 years old, randomized into two groups: intervention or control group (30 children per group). Both groups were given 12 consecutive weeks of designed fine motor tasks. Additionally, for thirty minutes, the intervention group was given a fine motor exercise program on a touch screen tablet. Upper limb function, finger dexterity and pinch strength were measured pre and post the recommended treatment program using the quality of upper extremity skill test (QUEST), Nine-Hole Peg Test and Jamar hydraulic pinch gauge, respectively. Results: All outcome measures were equivalent between intervention groups at admission (P > 0.05). Significant improvements were found in all assessed variables within the two groups. Meanwhile, the intervention group had

significantly higher improvements ($P < 0.05$) in finger dexterity, pinch strength, and upper limb function when compared with the control groups. Conclusion: Including a touch screen smart tablet application with a specially designed fine motor program is an effective method that helps children with U-CP perform more effectively with their fine motor skills.

PMID: 39213101

3. Muscle Synergy Analysis as a Tool for Assessing the Effectiveness of Gait Rehabilitation Therapies: A Methodological Review and Perspective

Daniele Borzelli, Cristiano De Marchis, Angelica Quercia, Paolo De Pasquale, Antonino Casile, Angelo Quartarone, Rocco Salvatore Calabrò, Andrea d'Avella

Review Bioengineering (Basel). 2024 Aug 5;11(8):793. doi: 10.3390/bioengineering11080793.

According to the modular hypothesis for the control of movement, muscles are recruited in synergies, which capture muscle coordination in space, time, or both. In the last two decades, muscle synergy analysis has become a well-established framework in the motor control field and for the characterization of motor impairments in neurological patients. Altered modular control during a locomotion task has been often proposed as a potential quantitative metric for characterizing pathological conditions. Therefore, the purpose of this systematic review is to analyze the recent literature that used a muscle synergy analysis of neurological patients' locomotion as an indicator of motor rehabilitation therapy effectiveness, encompassing the key methodological elements to date. Searches for the relevant literature were made in Web of Science, PubMed, and Scopus. Most of the 15 full-text articles which were retrieved and included in this review identified an effect of the rehabilitation intervention on muscle synergies. However, the used experimental and methodological approaches varied across studies. Despite the scarcity of studies that investigated the effect of rehabilitation on muscle synergies, this review supports the utility of muscle synergies as a marker of the effectiveness of rehabilitative therapy and highlights the challenges and open issues that future works need to address to introduce the muscle synergies in the clinical practice and decisional process.

PMID: 39199751

4. Effect of robotic-assisted gait training program on spatiotemporal gait parameters for ambulatory children with cerebral palsy: A randomized control trial

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Randomized Controlled Trial NeuroRehabilitation. 2024;55(1):127-136. doi: 10.3233/NRE-240156.

Background: Gait training programs are commonly used to improve gait in children with cerebral palsy (CP). Objective: To compared the effects of robotic-gait assistant training (RAGT) and conventional body weight support treadmill training (CBWSTT) on gait parameters among ambulatory children with CP. Methods: The study is a randomized controlled trial of 36 children (17 in the RAGT group and 19 in the CBWSTT group) aged 5 to 14. Gait training involved 30-to 35-minute sessions three times per week over eight weeks. Results: Mixed ANCOVA showed no main effect of time or group on all gait parameters ($P > .05$). Gross motor function measure dimensions D (GMFM D) and E (GMFM E) show main effects on step width. Stride length, step length, speed, swing phase, and double support phase interacted with GMFM D and E. There was a negative correlation between motor function level and the change from baseline. Children with lower motor function show a greater change from baseline. Conclusion: There were no significant differences between CBWSTT and RAGT for children with CP; however, with gait training interventions, the level of motor function should be considered.

PMID: 39213102

5. Informing creation of the FEEDS Toolkit to support parent-delivered interventions for eating, drinking and swallowing difficulties in young children with neurodisability: intervention use by neurodevelopmental diagnosis and healthcare professional role

Emogene Shaw, Lindsay Pennington, Morag Andrew, Helen Taylor, Jill Cadwgan, Diane Sellers, Christopher Morris, Deborah Garland, Jeremy Parr

BMJ Paediatr Open. 2024 Aug 24;8(1):e002394. doi: 10.1136/bmjpo-2023-002394.

Background: The FEEDS (Focus on Early Eating, Drinking and Swallowing) study focused on interventions used to improve feeding for children with neurodisability and eating, drinking and swallowing difficulties (EDSD), and the outcomes viewed as important by healthcare professionals (HPs) and parent carers. The FEEDS Toolkit was created subsequently as an intervention decision aid to be used collaboratively by parent carers and HPs. This study aimed to inform on current intervention practices and influence toolkit design by ascertaining whether specific intervention use varied by a child's main diagnosis and by specific HP role. Methods: FEEDS survey data were grouped by child's main diagnosis and HP role. Main diagnoses included autism

spectrum disorder (ASD) n=183; Down syndrome (DS) n=69; cerebral palsy (CP) n=30). HPs included were speech and language therapists (SLT) n=131; occupational therapists (OT) n=63; physiotherapists (PT) n=57; paediatricians n=50; dieticians n=40; nurses n=32 and health visitors n=14. Results: Most interventions were used commonly across diagnoses. However, some interventions were used more commonly with specific conditions, for example, positioning (CP 85%, DS 70%, ASD 23%, strategies/programmes aimed at changing behaviour at mealtimes (ASD 52%, CP 8%, DS 11%); visual supports (ASD 58%, CP 0%, DS 21%). HPs reported using a broad range of interventions, SLTs (mean=13.9), dieticians (12.3), OTs (12.7) and paediatricians (11.1). There was overlap between intervention use and HP role, for example, positioning (100% PT, 97% SLT, 94% OT, 73% paediatricians and 69% nurses). Conclusions: Interdisciplinary working is common when managing EDSD, with all HP types using multiple interventions. A child's main diagnosis does not substantially influence intervention use, and the individual context of each child requires consideration in intervention selection. Study findings have supported development of the FEEDS Toolkit for use in feeding services.

PMID: 39181695

6. Short- medium- and long-term effects of botulinum toxin on upper limb spasticity in children with cerebral palsy: A meta-analysis of randomized controlled trials

Tingting Chen, Yin Wu, Mengru Zhong, Kaishou Xu

Review Ann Phys Rehabil Med. 2024 Aug 23;67(7):101869. doi: 10.1016/j.rehab.2024.101869. Online ahead of print.

Background: Botulinum toxin (BTX) is an effective management method for spasticity in children with cerebral palsy (CP), but the short- medium- and long-term effects remain unclear. Objective: The primary objective was to quantify the effects of BTX injections on upper limb spasticity over time in children with CP. The secondary objective was to evaluate efficacy according to the International Classification of Functioning, Disability, and Health-Children & Youth version framework. Methods: We conducted a systematic review and meta-analysis of randomized controlled trials that included control/comparison groups treated with a placebo or other treatments. We searched CINAHL, Embase, PubMed, Scopus, Web of Science, and PsycINFO from their inception to April 2024. The pooled mean difference (MD) or standard mean difference (SMD) with 95 % CI was calculated using a random effects model at the short-term (up to 3 months), medium-term (3 to 6 months), and long-term (over 6 months). Results: A total of 658 children with CP aged 1.8 to 19 years old in 12 eligible trials were involved. The primary outcome of the Melbourne Assessment percentile showed a significant increase in the medium- (MD = 2.63, 95 % CI 0.22 to 5.04, I^2 = 0 %) and long-term (MD = 4.72, 95 % CI 0.93 to 8.51, I^2 = 0 %) in favor of BTX. Pooled effects also showed that BTX significantly improved Modified Ashworth Scale scores in the short- (MD = -0.44, 95 % CI -0.88 to -0.01, I^2 = 88 %) and medium-term (MD = -0.20, 95 % CI -0.28 to -0.13, I^2 = 0 %), and individual goals and bimanual performance up to 6-months. No significantly higher risk of adverse events was observed with BTX. Conclusions and implications: BTX injections sustainably improved the quality of affected upper limb function and temporarily improved individual goals and bimanual performance in children with CP. Our findings cautiously support a time interval of 3 to 6 months between BTX injections in the upper limbs of children with CP. Trial registration: This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration ID: CRD42022323672).

PMID: 39181066

7. Repeated Transcranial Magnetic Stimulation Combined with Action Observation Training in Children with Spastic Cerebral Palsy

Taolin Fan, Huiqun Wei, Jin'e Dai, Gang You, Zhihui Lu

Randomized Controlled Trial J Vis Exp. 2024 Aug 9:(210). doi: 10.3791/66013.

This study presents the results of a randomized controlled trial utilizing a 2 x 2 factorial design, comparing the effects of repeated transcranial magnetic stimulation (rTMS) and action observation training (AOT) intervention methods on spasticity, balance function, and motor function in children with spastic cerebral palsy (SCP). The study aimed to investigate whether the combination of the two interventions produces greater improvement than either treatment alone or conventional treatment. Subject children in this study, in accordance with the random number table, were randomly divided into four groups: conventional group, rTMS group, AOT group, and combined intervention group. All the children in the four groups received conventional rehabilitation treatment, on the basis of which they were given different therapeutic programs of rehabilitation measures. The conventional group had no other treatment while the rTMS group received rTMS, the AOT group received AOT and the combined intervention group was given a combined intervention of rTMS and AOT. They were trained five days per week for 12 weeks. Changes in scores of spasticity, balance function, walking ability, and gross motor function were assessed at the onset of the training program and upon completion of 12 weeks of treatment. A total of 64 Children with SCP completed the study, and their results were analyzed. The total gross motor function efficiency of 87.50% in the experimental group was significantly higher than that of 25.00% in the conventional group, 62.50% in the rTMS group, and 68.75% in the AOT group. The preliminary results showed that combined intervention of rTMS and AOT could effectively improve the balance function and motor function of children, and the therapeutic effect of the combined intervention was better than that of conventional treatment, rTMS or AOT alone. Finally, clinical efficacy and optimal treatment parameters of the combined intervention were

clarified to provide a clinical basis for therapists to conduct lower limb function rehabilitation for children with SCP.

PMID: 39185889

8. Effects of various exercise interventions on motor function in cerebral palsy patients: a systematic review and network meta-analysis

Bingjie Wang, Hailiang Huang

Neurol Sci. 2024 Aug 27. doi: 10.1007/s10072-024-07741-z. Online ahead of print.

Purpose: A network meta-analysis was utilized to compare the rehabilitative effectiveness of different exercise interventions on motor function in cerebral palsy(CP) patients. Methods: Computer searches were conducted across 9 databases, including PubMed, Cochrane Library, Scopus, Web of Science, Embase, and others, to identify randomized controlled trials focusing on different exercise interventions aimed at enhancing motor function in CP patients. The search spanned from the inception of the databases to January 31, 2024. Results: 20 articles, encompassing 570 patients and evaluating three types of exercise interventions, were included in the analysis. Results showed that aerobic training, resistance training, and mixed training exhibited superior outcomes compared to the control group, as evidenced by improvements in Gross Motor Function Measure scores, muscle strength, gait speed, and 10-Meter Walk Test scores ($P < 0.05$). Furthermore, the network meta-analysis revealed that resistance training ranked highest in enhancing gross motor function and gait speed among CP patients, while mixed training was deemed most effective in improving muscle strength and 10-Meter Walk Test scores. Conclusion: Exercise interventions have been shown to significantly improve motor function in CP patients. Among these, resistance training and mixed training stand out for their effectiveness in enhancing walking capabilities. Resistance training is specifically aimed at improving gross motor function, while mixed training focuses on increasing muscle strength.

PMID: 39190170

9. F-words ingredients of non-invasive interventions for young ambulant children with cerebral palsy: A scoping review

Hércules Ribeiro Leite, Ricardo Rodrigues de Sousa Junior, Deisiane Oliveira Souto, Jaíza Marques Medeiros E Silva, Arthur Felipe Barroso de Lima, Carolyne de Miranda Drumond, Eliane Beatriz Cunha Policiano, Ariane Cristina Marques, Paula Silva de Carvalho Chagas, Egmar Longo

Review Dev Med Child Neurol. 2024 Aug 26. doi: 10.1111/dmcn.16074. Online ahead of print.

Aim: To map the ingredients of non-invasive interventions provided to young ambulant children with cerebral palsy. Method: Articles were screened and each study's characteristics extracted. The intervention ingredients were described in terms of the Rehabilitation Treatment Specification System and linked to the 'F-words'. Results were interpreted and validated by a patient and public involvement group. Results: Sixty-one papers were included, of which 55.5% were classified as randomized controlled trial design studies. The selected studies included a total of 2187 children (mean age range 3 months to 5 years 11 months), most from high-income countries. The included studies investigated a total of 27 interventions, which together presented ingredients representing all F-words, in the following order of frequency: 'fitness' (e.g. strength and endurance training), 'functioning' (e.g. active and repetitive practice of a task), 'family' (e.g. context-focused therapy), 'fun' (e.g. inclusion of child-friendly activities), 'friends' (e.g. group activities), and 'future' (e.g. didactic information sharing). Thus, ingredients related to the F-word 'future' were the most infrequently reported. Interpretation: Therapists and families need to be aware of the most appropriate match between the F-word goals, ingredients, and targets. Finally, 'fun', 'friends', and 'future' should be addressed as potential outcomes in future studies.

PMID: 39187986

10. Parents in the Driver's Seat-Experiences of Parent-Delivered Baby-mCIMT Coached Remotely

Katarina Svensson, Ann-Christin Eliasson, Heléne Sundelin, Kajsa Lidström Holmqvist

J Clin Med. 2024 Aug 18;13(16):4864. doi: 10.3390/jcm13164864.

Background/Objectives: Recent guidelines on early intervention in children at high risk of cerebral palsy (CP) recommend parental involvement and family-centered home-based interventions with parents as primary trainers. Therapist coaching by home visitation is resource demanding, and telerehabilitation is a viable option for remote intervention and coaching. This study aims to describe parents' experiences of engaging in Baby-mCIMT coached remotely. Their infants are at high risk of unilateral cerebral palsy and the parents have been the primary trainers in regard to home-based intervention, optimizing the use of the affected hand. Methods: A qualitative approach involving semi-structured interviews with eight parents was employed. Data were analyzed using qualitative content analysis. Results: The overarching theme "Parents in the driver's seat-learning through remote coaching to create conditions to enhance the child's motor skills" describes parents' experiences as

primary training providers. The following three underlying categories with subcategories were identified: (1) Baby-mCIMT coached remotely in an everyday context-practical and technical prerequisites; (2) the child's response and the therapists' coaching supports active parental learning; (3) capability and sense of control-strengthening and demanding aspects. Conclusions: Our findings revealed that Baby-mCIMT coached remotely empowered the parents as primary trainers, which provided them with opportunities for understanding and learning about their child and their development. The findings underscore the importance of responsive professional guidance and a strong therapist-parent relationship to succeed with the Baby-mCIMT program coached remotely and to manage the digital coaching format.

PMID: 39201006

11. The Motor Optimality Score-Revised Improves Early Detection of Unilateral Cerebral Palsy in Infants with Perinatal Cerebral Stroke

Natascia Bertoncelli, Lucia Corso, Luca Bedetti, Elisa Muttini Della Casa, Maria Federica Roversi, Greta Toni, Marisa Pugliese, Isotta Guidotti, Francesca Miselli, Laura Lucaccioni, Cecilia Rossi, Alberto Berardi, Licia Lugli

Children (Basel). 2024 Aug 4;11(8):940. doi: 10.3390/children11080940.

Background: Neonatal cerebral stroke includes a range of focal and multifocal ischemic and hemorrhagic brain lesions, occurring in about one of 3000 live births. More than 50% of children with neonatal stroke develop adverse outcomes, mainly unilateral cerebral palsy. Asymmetries in segmental movements at three months have been proven to be an early sign of CP in infants with unilateral brain damage. Recognition of additional early signs could enhance prognostic assessment and enable an early and targeted intervention. Aim: The aim of the study was to assess early signs of CP in infants with arterial cerebral stroke through the General Movements Assessment and the Motor Optimality Score-Revised (MOS-R). Method: Twenty-four infants born at term (12 females and 12 males) diagnosed with ACS, and 24 healthy infants (16 females and 8 males) were assessed. The GMs (fidgety movements) and MOS-R were assessed from videos recorded at 11-14 weeks of post-term age. Cognitive and motor outcomes were assessed at 24 months using the Griffiths III developmental quotient and Amiel-Tison neurological examination. The gross motor function classification system expanded and revised (GMFCS-E&R) was adopted to categorize CP. Results: Among infants with ACS, 21 (87.5%) developed unilateral CP. Most of them showed non-disabling CP (14 had GMFCS-E&R grade 1 [66.6%], 6 grade 2 [28.6%], and 1 grade 5 [4.8%]). Fidgety movements (FMs) were absent in 17 (70.8%), sporadic in 4 (16.7%) infants, and normal in 3 (12.5%). Segmental movement asymmetry was found in 22/24 (91.7%). According to the MOS-R, motor items (kicking, mouth movements), postural patterns (midline centered head, finger posture variability), and movement character (monotonous and stiff) were statistically different among infants with ACS and healthy infants. The MOS-R median global score was lower in the group with ACS compared to the control group (6 vs 26; $p < 0.01$). FMs, segmental movement asymmetry, and MOS-R global score were significantly correlated with abnormal outcome. MOS-R global scores less than or equal to 13 had 100% specificity and sensitivity in predicting GMFCS-E&R grade ≥ 2 CP in infants with ACS. Conclusions: The rate of CP was high among infants with ACS, but in most cases it showed low GMFCS-E&R grades. The study highlighted a significant correlation between MOS-R, together with absent FMs and unilateral CP in infants with ACS. Moreover, the MOS-R showed high sensitivity and specificity in the prediction of CP. Combined assessment of FMs and MOS-R could help to better identify infants at high risk of developing UCP in a population of infants with ACS. Early identification of precocious signs of unilateral CP is fundamental to providing an early individualized intervention.

PMID: 39201875

12. Rehabilitation Intervention Is Associated With Improved Neurodevelopment and Modulation of Inflammatory Molecules in Children With Cerebral Palsy

Rafael Coelho Magalhães, Roberta da Silva Filha, Érica Leandro Marciano Vieira, Antônio Lúcio Teixeira, Janaina Matos Moreira, Ana Cristina Simões E Silva

J Child Neurol. 2024 Aug 28:8830738241273436. doi: 10.1177/08830738241273436. Online ahead of print.

Aim: To evaluate the effects of systematic rehabilitation on both the neuropsychomotor development, and on the peripheral response from immunological and neuroplastic mediators in children with cerebral palsy. Methods: This is a prospective cohort study with 90 children with cerebral palsy at 18 months of age. Sixty children received rehabilitation for 6 months, and they were compared to 30 children that were placed in the waiting list. Peripheral biomarkers and neuropsychomotor parameters were compared between the Rehab vs the Nonrehab groups at baseline and at 6 months. Results: Results showed higher Bayley III scores in the Rehab group, with significant differences in inflammatory and neurotrophic biomarkers between groups. Rehabilitation was associated to decreased levels of IL-12p70, IL-6, IL-1β, CXCL8 IL-8, and CXCL9/MIG and increased levels of BDNF and GDNF. Nonrehab children had stable immune molecule levels but decreased BDNF levels over time. Conclusion: Rehabilitation improved neurodevelopment parameters and modulated levels of inflammatory (↓) and neurotrophic (↑) biomarkers.

PMID: 39196287

13. Real-World Observational Analysis of Clinical Characteristics and Treatment Patterns of Patients with Chronic Sialorrhea

Michael A Hast, Amanda M Kong, Jenna Abdelhadi, Rohan Shah, Andrew Szendrey, Jordan Holmes

Observational Study Toxins (Basel). 2024 Aug 17;16(8):366. doi: 10.3390/toxins16080366.

Chronic sialorrhea is a condition characterized by excessive drooling, often associated with neurological and neuromuscular disorders such as Parkinson's disease, cerebral palsy, and stroke. Despite its prevalence, it remains underdiagnosed and poorly understood, leading to a lack of comprehensive data on patient demographics, clinical characteristics, and treatment patterns. This study aimed to help fill these existing gaps by analyzing real-world data using Optum's de-identified Clinformatics® Data Mart Database. Patients were required to have a diagnosis indicative of sialorrhea plus evidence of sialorrhea treatment between 1/1/2007 and 5/31/2022. Two cohorts were analyzed: patients with evidence of newly diagnosed sialorrhea and associated treatment, and sialorrhea patients initiating incobotulinumtoxinA. Clinical characteristics, comorbidities, symptoms, and treatment utilization were described before and after diagnosis and incobotulinumtoxinA initiation. No formal statistical comparisons were performed. Patients were predominantly aged 65 or older, male, and non-Hispanic white. Parkinson's disease and cerebral palsy were the most common comorbidities among adults and children, respectively. Treatment patterns suggest that anticholinergics are more commonly used than botulinum toxin therapy. The findings offer valuable information for improving diagnosis and treatment approaches and suggest a need for further research into treatment effectiveness, safety, and disease burden.

PMID: 39195776

14. Psychometric Properties of Fine Motor Function Measure in Children With Cerebral Palsy: A Rasch Analysis

Kanglong Peng, Guixiang Liu, Jinggang Wang, Turong Chen

Clin Pediatr (Phila). 2024 Aug 25:99228241274295. doi: 10.1177/00099228241274295. Online ahead of print.

Our study utilized Rasch Analysis to examine the psychometric properties of 61-items fine motor function measure (FMFM) in children with cerebral palsy (CP). Partial credit model (PCM) was utilized to test the reliability and validity of FMFM. The response pattern of this samples displayed acceptable fitness to PCM. The analysis results supported the assumption of 1-dimensionality of FMFM. Disordered category thresholds were found in 30 items. Differential item functioning (DIF) was detected in 23 items. Participants with different CP subtypes in different age groups may perform in differently responses patterns. The Rasch analysis produces reliable evidence to support the clinical application of FMFM. Some items may produce inaccurate measurements originated from category structures. Difference in age groups and symptom topography may be associated with variation in fine motor ability among children with CP and leading to unnecessary assessment bias. Hence, FMFM items need modifications to calibrate the former item formulation.

PMID: 39183559

15. Assessing proprioception in children with upper motor neuron lesions: feasibility, validity, and reliability of the proprioception measurement tool

Petra Marsico, Lea Meier, Anke Buchmann, Andrina Kläy, Marietta L van der Linden, Thomas H Mercer, Hubertus J A van Hedel

Front Rehabil Sci. 2024 Aug 9:5:1373793. doi: 10.3389/fresc.2024.1373793. eCollection 2024.

Introduction: To investigate the feasibility, discriminative and convergent validity, and reliability of a lower limb sensor-based proprioception measure in children with upper motor neuron (UMN) lesions. Method: We assessed three proprioception modalities (joint movement, joint position, and dynamic position sense) of the lower limbs in 49 children with UMN lesions and 50 typically developing (TD) peers (5-19 years). Forty-three children with UMN lesion had a congenital and six an acquired brain lesion and 82% were able to walk without a walking aid. We evaluated the feasibility, compared the test results between children with UMN lesions and TD peers, and calculated Spearman correlations (rs) between the modalities. We quantified relative reliability with Intra-Class Correlation Coefficients (ICC) and absolute reliability with Smallest Detectable Changes (SDC). Results: Most children with UMN lesions (>88%) found the tests easy to perform. The children with UMN lesions had significantly ($p < 0.001$) lower proprioceptive function than the TD children. The correlation between the three proprioceptive modalities was moderate to high ($0.50 \leq rs \leq 0.79$). The relative reliability for test-retest and the inter-rater reliability was moderate to high (ICCs = 0.65-0.97), and SDC was between 2° and 15°. Discussion: The three tests are feasible, and discriminative and convergent validity and reliability were confirmed. Further studies should investigate the influence on motor function and performance in children with UMN lesions.

PMID: 39185005

16. Neural Correlates of Mobility in Children with Cerebral Palsy: A Systematic Review

Isabella Pessóta Sudati, Diane Damiano, Gabriela Rovai, Ana Carolina de Campos

Review Int J Environ Res Public Health. 2024 Aug 7;21(8):1039. doi: 10.3390/ijerph21081039.

Recent advances in brain mapping tools have enabled the study of brain activity during functional tasks, revealing neuroplasticity after early brain injuries and resulting from rehabilitation. Understanding the neural correlates of mobility limitations is crucial for treating individuals with cerebral palsy (CP). The aim is to summarize the neural correlates of mobility in children with CP and to describe the brain mapping methods that have been utilized in the existing literature. This systematic review was conducted based on PRISMA guidelines and was registered on PROSPERO (n° CRD42021240296). The literature search was conducted in the PubMed and Embase databases. Observational studies involving participants with CP, with a mean age of up to 18 years, that utilized brain mapping techniques and correlated these with mobility outcomes were included. The results were analyzed in terms of sample characteristics, brain mapping methods, mobility measures, and main results. The risk of bias was evaluated using a checklist previously created by our research group, based on STROBE guidelines, the Cochrane Handbook, and the Critical Appraisal Skills Programme (CASP). A total of 15 studies comprising 313 children with CP and 229 with typical development using both static and mobile techniques met the inclusion criteria. The studies indicate that children"with'CP have increased cerebral activity and higher variability in brain reorganization during mobility activities, such as gait, quiet standing, cycling, and gross motor tasks when compared with children with typical development. Altered brain activity and reorganization underline the importance of conducting more studies to investigate the neural correlates during mobility activities in children with CP. Such information could guide neurorehabilitation strategies targeting brain neuroplasticity for functional gains.

PMID: 39200649

17. Comparing the effectiveness of robotic plantarflexion resistance and biofeedback between overground and treadmill walking

Collin D Bowersock, Zachary F Lerner

J Biomech. 2024 Aug 16:175:112282. doi: 10.1016/j.jbiomech.2024.112282. Online ahead of print.

Individuals with diminished walking performance caused by neuromuscular impairments often lack plantar flexion muscle activity. Robotic devices have been developed to address these issues and increase walking performance. While these devices have shown promise in their ability to increase musculature engagement of the lower limbs when used on a treadmill, most have not been developed or validated for overground walking and community use. Overground walking may limit the effectiveness of robotic devices due to differences in gait characteristics between walking terrains and reduced user engagement. The purpose of this study was to validate our multimodal robotic gait training system for overground walking in individuals with neuromuscular gait impairments. This untethered wearable robotic device can provide an ankle resistive torque proportional to the users' biological ankle torque. The device can also provide audio biofeedback based on users' plantar pressure intending to increase ankle power and muscle activity of the plantar flexors. Seven individuals with cerebral palsy participated. Participants walked overground and on a treadmill with our robotic gait training system in a single testing session. Results showed all seven participants to increase peak plantar flexor muscle activity, 10.3% on average, when walking with the gait trainer overground compared to treadmill. When compared to typical baseline overground walking, overground gait trainer use caused individuals to have slightly less knee joint excursion (3°) and moderately more ankle joint excursion (7°). This work supports our vision of using the wearable robotic device as a gait aid and rehabilitation tool in the home and community settings.

PMID: 39182263

18. Functional Electrical Stimulation and Brain-Machine Interfaces for Simultaneous Control of Wrist and Finger Flexion

Matthew J Mender, Ayobami L Ward, Luis H Cubillos, Madison M Kelberman, Joseph T Costello, Hisham Temmar, Dylan M Wallace, Edanjen T Lin, Jordan L W Lam, Matthew S Willsey, Nishant Ganesh Kumar, Theodore A Kung, Parag G Patil, Cynthia A Chestek

bioRxiv [Preprint]. 2024 Aug 12:2024.08.11.607263. doi: 10.1101/2024.08.11.607263.

Brain-machine interface (BMI) controlled functional electrical stimulation (FES) is a promising treatment to restore hand movements to people with cervical spinal cord injury. Recent intracortical BMIs have shown unprecedented successes in decoding user intentions, however the hand movements restored by FES have largely been limited to predetermined grasps. Restoring dexterous hand movements will require continuous control of many biomechanically linked degrees-of-freedom in the hand, such as wrist and finger flexion, that would form the basis of those movements. Here we investigate the ability to restore simultaneous wrist and finger flexion, which would enable grasping with a controlled hand posture and assist in

manipulating objects once grasped. We demonstrate that intramuscular FES can enable monkeys with temporarily paralyzed hands to move their fingers and wrist across a functional range of motion, spanning an average 88.6 degrees at the metacarpophalangeal joint flexion and 71.3 degrees of wrist flexion, and intramuscular FES can control both joints simultaneously in a real-time task. Additionally, we demonstrate a monkey using an intracortical BMI to control the wrist and finger flexion in a virtual hand, both before and after the hand is temporarily paralyzed, even achieving success rates and acquisition times equivalent to able-bodied control with BMI control after temporary paralysis in two sessions. Together, this outlines a method using an artificial brain-to-body interface that could restore continuous wrist and finger movements after spinal cord injury.

PMID: 39211094

19. Automatic two-dimensional & three-dimensional video analysis with deep learning for movement disorders: A systematic review

Wei Tang, Peter M A van Ooijen, Deborah A Sival, Natasha M Maurits

Review Artif Intell Med. 2024 Aug 14:156:102952. doi: 10.1016/j.artmed.2024.102952. Online ahead of print.

The advent of computer vision technology and increased usage of video cameras in clinical settings have facilitated advancements in movement disorder analysis. This review investigated these advancements in terms of providing practical, low-cost solutions for the diagnosis and analysis of movement disorders, such as Parkinson's disease, ataxia, dyskinesia, and Tourette syndrome. Traditional diagnostic methods for movement disorders are typically reliant on the subjective assessment of motor symptoms, which poses inherent challenges. Furthermore, early symptoms are often overlooked, and overlapping symptoms across diseases can complicate early diagnosis. Consequently, deep learning has been used for the objective video-based analysis of movement disorders. This study systematically reviewed the latest advancements in automatic two-dimensional & three-dimensional video analysis using deep learning for movement disorders. We comprehensively analyzed the literature published until September 2023 by searching the Web of Science, PubMed, Scopus, and Embase databases. We identified 68 relevant studies and extracted information on their objectives, datasets, modalities, and methodologies. The study aimed to identify, catalogue, and present the most significant advancements, offering a consolidated knowledge base on the role of video analysis and deep learning in movement disorder analysis. First, the objectives, including specific PD symptom quantification, ataxia assessment, cerebral palsy assessment, gait disorder analysis, tremor assessment, tic detection (in the context of Tourette syndrome), dystonia assessment, and abnormal movement recognition were discussed. Thereafter, the datasets used in the study were examined. Subsequently, video modalities and deep learning methodologies related to the topic were investigated. Finally, the challenges and opportunities in terms of datasets, interpretability, evaluation methods, and home/remote monitoring were discussed.

PMID: 39180925

20. Uncovering early predictors of cerebral palsy through the application of machine learning: a case-control study

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BMJ Paediatr Open. 2024 Aug 30;8(1):e002800. doi: 10.1136/bmjpo-2024-002800.

Objective: Cerebral palsy (CP) is a group of neurological disorders with profound implications for children's development. The identification of perinatal risk factors for CP may lead to improved preventive and therapeutic strategies. This study aimed to identify the early predictors of CP using machine learning (ML). Design: This is a retrospective case-control study, using data from the two population-based databases, the Slovenian National Perinatal Information System and the Slovenian Registry of Cerebral Palsy. Multiple ML algorithms were evaluated to identify the best model for predicting CP. Setting: This is a population-based study of CP and control subjects born into one of Slovenia's 14 maternity wards. Participants: A total of 382 CP cases, born between 2002 and 2017, were identified. Controls were selected at a control-to-case ratio of 3:1, with matched gestational age and birth multiplicity. CP cases with congenital anomalies (n=44) were excluded from the analysis. A total of 338 CP cases and 1014 controls were included in the study. Exposure: 135 variables relating to perinatal and maternal factors. Main outcome measures: Receiver operating characteristic (ROC), sensitivity and specificity. Results: The stochastic gradient boosting ML model (271 cases and 812 controls) demonstrated the highest mean ROC value of 0.81 (mean sensitivity=0.46 and mean specificity=0.95). Using this model with the validation dataset (67 cases and 202 controls) resulted in an area under the ROC curve of 0.77 (mean sensitivity=0.27 and mean specificity=0.94). Conclusions: Our final ML model using early perinatal factors could not reliably predict CP in our cohort. Future studies should evaluate models with additional factors, such as genetic and neuroimaging data.

PMID: 39214549

21. Prolonged oligohydramnios and the adverse composite outcome of death or severe neurodevelopmental impairment at 3 years of age in infants born at 22-29 gestational weeks

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Early Hum Dev. 2024 Aug 15:197:106100. doi: 10.1016/j.earlhumdev.2024.106100. Online ahead of print.

Objective: To investigate the association between prolonged oligohydramnios and a composite outcome of death or severe neurodevelopmental impairment (NDI) at 3 years of age. Methods: This single-center retrospective cohort study enrolled infants born at 22-29 weeks of gestational age without major congenital anomalies. The patients were classified into three groups depending on the existence and duration of oligohydramnios: no/non-prolonged oligohydramnios (no or 0-7 days of oligohydramnios), prolonged oligohydramnios (8-14 days), and very prolonged oligohydramnios (> 14 days). The primary outcome was a composite of death or severe NDI, which was defined as severe cerebral palsy, developmental delay, severe visual impairment, or deafness at age 3. Results: Out of the 843 patients, 784 (93 %), 30 (3.6 %), and 29 (3.4 %) were classified into the no/non-prolonged, prolonged, and very prolonged oligohydramnios groups, respectively. After excluding patients lost to follow-up, the adverse composite outcome at 3 years of age was observed in 194/662 (29 %), 7/26 (27 %), and 8/23 (35 %) in the corresponding groups. The composite outcome showed no significant trend with the duration of oligohydramnios (P = 0.70). In a logistic regression model controlling the known predictors of gestational age, birth weight, small-for-gestational-age, male sex, multiple pregnancy, hypertensive disorders of pregnancy, antenatal corticosteroids, and the number of family-social risk factors, the duration of oligohydramnios was not independently associated with the composite outcome; odds ratio 1.3 (95 % confidence interval, 0.78-2.0). Conclusion: Prolonged oligohydramnios was not associated with the composite outcome of death or severe NDI at 3 years of age.

PMID: 39180798

22. Early neurodevelopmental outcomes of preterm infants with intraventricular haemorrhage and periventricular leukomalacia

Nicole Sc Ng, Abdul Razak, Preethi Chandrasekharan, Glenda McLean, Vathana Sackett, Lindsay Zhou, Pramod Pharande, Atul Malhotra

J Paediatr Child Health. 2024 Aug 26. doi: 10.1111/jpc.16654. Online ahead of print.

Aim: Intraventricular haemorrhage (IVH) and periventricular leukomalacia (PVL) in preterm infants are associated with an increased risk of long-term neurodevelopmental impairments (NDI) and cerebral palsy (CP). However, little is known about their impact on early neurodevelopmental outcomes despite increasing evidence highlighting the feasibility and importance of early NDI/CP diagnosis. We aimed to determine the early neurodevelopmental outcomes of preterm infants with IVH and PVL. Methods: This was a retrospective single-centre cohort study of preterm infants born at <29 weeks gestation or <1000 g birth weight who attended an Early Neurodevelopment Clinic at 3 to 4 months of corrected age. Primary outcomes of early NDI and CP/high-risk CP diagnoses based on Prechtl's General Movements Assessment and the Hammersmith Infant Neurological Examination were compared between infants without IVH and infants with mild IVH (grades I-II), severe IVH (grades III-IV), and severe brain injury (SBI; severe IVH or cystic PVL). Results: Of 313 infants, 52.1% (n = 163), 41.2% (n = 129), 6.7% (n = 21) and 8.6% (n = 27) had no IVH, mild IVH, severe IVH and SBI, respectively. The adjusted odds of early CP/high-risk CP diagnosis were significantly higher in infants with severe IVH (aOR 6.07, 95% CI 1.50-24.50) and SBI (aOR 15.28, 95% CI 3.70-63), but not in those with mild IVH (aOR 1.24, 95% CI 0.49-3.10). However, the adjusted odds of any early NDI were similar across groups. Conclusion: Preterm infants with severe IVH and SBI are at increased risk of early CP/high-risk of CP diagnosis at 3 to 4 months of corrected age.

PMID: 39183581

23. The Genetic Puzzle of Cerebral Palsy: Results of a Monocentric Study

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Pediatr Neurol. 2024 Aug 5:161:1-8. doi: 10.1016/j.pediatrneurol.2024.07.019. Online ahead of print.

Background: Cerebral palsy (CP) is the most frequent cause of motor impairment in children. Although perinatal asphyxia was long considered to be the leading cause of CP, recent studies demonstrate its causation in only around one in 10 individuals with CP. Instead, genetic causes are increasingly demonstrated. We systematically performed clinical phenotyping and genetic investigations in a monocentric CP cohort, aiming to gain insight into the contribution of genetic variants in CP and its different subtypes. Methods: Chromosomal microarray and/or trio exome sequencing were systematically performed in 337 individuals with CP between September 2017 and August 2022. Deep phenotyping was performed through clinical multidisciplinary evaluation and review of medical files. Results: Genetic analyses resulted in an overall diagnostic yield of

38.3% (129 of 337). In cases with one or more comorbidities (intellectual disability, epilepsy, autism spectrum disorder), the yield increased to almost 50%. Functional enrichment analysis showed over-representation of the following pathways: genetic imprinting, DNA modification, liposaccharide metabolic process, neuron projection guidance, and axon development. Conclusions: Genetic analyses in our CP cohort, the largest monocentric study to date, demonstrated a diagnostic yield of 38.3%, highlighting the importance of genetic testing in CP. The diagnosis of a genetic disorder is essential for prognosis and clinical follow-up, as well as for family counseling. Pathway analysis points to dysregulation of general developmental and metabolic processes as well as neuronal development and function. Unraveling the role of these pathways in CP pathogenesis is instrumental for the identification of CP candidate genes as well as potential therapeutic targets.

PMID: 39213953

24. Combined generalized and focal epilepsy with reflex features in Adaptor protein complex 4-associated hereditary spastic paraplegias: A cohort observational study

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Seizure. 2024 Aug 24:121:186-193. doi: 10.1016/j.seizure.2024.08.009. Online ahead of print.

Background: Patients with genetic deficiency of the adaptor protein complex 4 (AP-4) exhibit earlyonset developmental delay, spastic diplegia, intellectual disability, speech impairment. The phenotype overlaps with other hereditary spastic paraplegias and cerebral palsies. Febrile seizures are common at onset. Epilepsy has been described in more than half of cases, arising in early infancy often with status epilepticus, but no typical seizure semiology or electroencephalographic features have been identified thus far. Purpose: We aimed to specifically investigate the epileptological characteristics of the syndrome to unveil possible biomarkers of seizure development and prognosis in AP-4 deficiency. Methods: Observational cohort study on patients with bi-allelic pathogenic variants in AP-4 subunits and epilepsy. We focused on the seizure semiology, electroencephalographic characteristics and response to antiseizure medications. Results: Patients harboured pathogenic variants in AP4S1 (n = 5) or AP4M1 (n = 1). The phenotype included spastic paraparesis, intellectual disability, speech/ language impairment, microcephaly, and MRI evidence of hypoplasia of the corpus callosum. In 66 % of the patients, febrile seizures preceded the onset of epilepsy, which spanned from infancy to adolescence (range=14 months-13 years). Absences (66 %) and focal motor seizures (50 %) were common. No patient met the criteria for drug-resistance. Peculiar electroencephalographic features arose after the epilepsy onset and persisted at long-term follow-up: bilateral and asynchronous focal discharges combined with independent diffuse spike-wave-discharges (100 %) and reflex abnormalities (66 %). Conclusion: In AP-4 complex disease, epilepsy could arise beyond early infancy, until adolescence, with variable combination of generalized and focal seizures. The prognosis was favourable. We observed a common electroencephalographic signature - combined focal/generalized and reflex abnormalities - which may constitute a biomarker of AP-4 deficiency with epilepsy, applicable to inform genetic testing and disentangle the differential diagnosis.

PMID: 39208719

25. Genetic investigations in cerebral palsy

Anna P Basu, Karen Low, Thiloka Ratnaike, David Rowitch

Review Dev Med Child Neurol. 2024 Aug 29. doi: 10.1111/dmcn.16080. Online ahead of print.

The original description of cerebral palsy (CP) contained case histories suggesting that perinatal environmental stressors resulted in brain injury and neurodevelopmental disability. While there are clear associations between environmental impact on brain development and CP, recent studies indicate an 11% to 40% incidence of monogenic conditions in patients given a diagnosis of CP. A genetic diagnosis supports the delivery of personalized medicine. In this review, we describe how the Wnt pathway exemplifies our understanding of pathophysiology related to a gene variant (CTNNB1) found in some children diagnosed with CP. We cover studies undertaken to establish the baseline prevalence of monogenic conditions in populations attending CP clinics. We list factors indicating increased likelihood of a genomic diagnosis; and we highlight the need for a comprehensive, accurate, genotype-phenotype reference data set to aid variant interpretation in CP cohorts. We also consider the wider societal implications of genomic management of CP including significance of the diagnostic label, benefits and pitfalls of a genetic diagnosis, logistics, and cost.

PMID: 39208295

26. PLEKHG1: New Potential Candidate Gene for Periventricular White Matter Abnormalities

Francesco Calì, Mirella Vinci, Simone Treccarichi, Carla Papa, Angelo Gloria, Antonino Musumeci, Concetta Federico, Girolamo Aurelio Vitello, Antonio Gennaro Nicotera, Gabriella Di Rosa, Luigi Vetri, Salvatore Saccone, Maurizio Elia

Case Reports Genes (Basel). 2024 Aug 20;15(8):1096. doi: 10.3390/genes15081096.

Hypoxic-ischemic brain damage presents a significant neurological challenge, often manifesting during the perinatal period. Specifically, periventricular leukomalacia (PVL) is emerging as a notable contributor to cerebral palsy and intellectual disabilities. It compromises cerebral microcirculation, resulting in insufficient oxygen or blood flow to the periventricular region of the brain. As widely documented, these pathological conditions can be caused by several factors encompassing preterm birth (4-5% of the total cases), as well single cotwin abortion and genetic variants such as those associated with GTPase pathways. Whole exome sequencing (WES) analysis identified a de novo causative variant within the pleckstrin homology domain-containing family G member 1 (PLEKHG1) gene in a patient presenting with PVL. The PLEKHG1 gene is ubiquitously expressed, showing high expression patterns in brain tissues. PLEKHG1 is part of a family of Rho guanine nucleotide exchange factors, and the protein is essential for cell division control protein 42 (CDC42) activation in the GTPase pathway. CDC42 is a key small GTPase of the Rho-subfamily, regulating various cellular functions such as cell morphology, migration, endocytosis, and cell cycle progression. The molecular mechanism involving PLEKHG1 and CDC42 has an intriguing role in the reorientation of cells in the vascular endothelium, thus suggesting that disruption responses to mechanical stress in endothelial cells may be involved in the formation of white matter lesions. Significantly, CDC42 association with white matter abnormalities is underscored by its MIM phenotype number. In contrast, although PLEKHG1 has been recently associated with patients showing white matter hyperintensities, it currently lacks a MIM phenotype number. Additionally, in silico analyses classified the identified variant as pathogenic. Although the patient was born prematurely and subsequently to dichorionic gestation, during which its cotwin died, we suggest that the variant described can strongly contribute to PVL. The aim of the current study is to establish a plausible association between the PLEKHG1 gene and PVL.

PMID: 39202455

27. Uncertainties Regarding Cerebral Palsy Diagnosis: Opportunities to Clarify the Consensus Definition

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Neurol Clin Pract. 2024 Dec;14(6):e200353. doi: 10.1212/CPJ.0000000000200353. Epub 2024 Aug 16.

Background and objectives: We have established that physicians, including neurologists, variably diagnose cerebral palsy (CP) when using the most recent CP definition from 2006. We also know that child neurologists and neurodevelopmentalists view themselves to be optimally suited to diagnose CP based on their training backgrounds. Therefore, to reduce variability in CP diagnosis, our objective was to elucidate uncertainties child neurologists and neurodevelopmentalists may have regarding practical application of the 2006 definition. Methods: We conducted a cross-sectional survey of child neurologists and neurodevelopmentalists built into a discussion seminar at the 2022 Child Neurology Society (CNS) Annual Meeting, the largest professional meeting of these specialists in North America. Seminar attendees were provided the 2006 definition and asked whether they had any uncertainties about the practical application of the definition across 4 hypothetical clinical vignettes. A group of national and international CP leaders then processed these data through iterative discussions to develop recommendations for clarifying the 2006 definition. Results: The seminar was attended by 50% of all conference attendees claiming CME (202/401). Of the 164 closing survey respondents, 145 (88%) expressed uncertainty regarding the clinical application of the 2006 definition. These uncertainties focused on 1) age, both regarding the minimum and maximum ages of brain disturbance or motor symptom onset (67/164, 41%), and 2) interpretation of the term "nonprogressive" (48/164, 29%). Almost all respondents (157/164, 96%) felt that we should revise the 2006 consensus definition of CP. Discussion: To address the most common CP diagnostic uncertainties we identified, we collectively propose 4 points of clarification to the 2006 definition: 1) motor symptoms/signs should be present by 2 years old; 2) CP can and should be diagnosed as early as possible; 3) the clinical motor disability phenotype should be nonprogressive through 5 years old; and 4) a CP diagnosis should be re-evaluated if motor disability is progressive or absent by 5 years old. We anticipate that clarifying the 2006 definition of CP in this manner could address the uncertainties we identified among child neurologists and neurodevelopmentalists and reduce the diagnostic variability that currently exists.

PMID: 39193394

28. The overlapping diagnosis of congenital Zika syndrome and cerebral palsy

Colleen Peyton, Sarah B Mulkey

Pediatr Res. 2024 Aug 28. doi: 10.1038/s41390-024-03501-z. Online ahead of print.

No abstract available

PMID: 39198588

29. Regional Disparities in Growth Patterns of Children with Cerebral Palsy: A Comparative Analysis of Saudi Arabian, UK, and US Data

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Children (Basel). 2024 Jul 25;11(8):891. doi: 10.3390/children11080891.

Aim: In order to understand the global variations in the growth trajectories of cerebral palsy patients, this study aimed to compare the growth patterns of cerebral palsy patients in Saudi Arabi with United States and United Kingdom counterparts. Method: Anthropometric data from 107 participants with cerebral palsy in Saudi Arabia were collected, including age, gender, cerebral palsy type, Gross Motor Function Classification System level, birth weight, weight at assessment, height at assessment, body mass index, and head circumference at assessment. Results: This study found discrepancies between the growth patterns of Saudi Arabian children with cerebral palsy and United Kingdom and the United States growth charts, particularly among those with severe cerebral palsy. Significant differences were observed in weight, height, and body mass index z-scores when comparing Saudi Arabian data with the United Kingdom and United States reference data. Interpretation: These findings emphasize the importance of validating growth charts across different populations to ensure accurate monitoring and clinical management of children with cerebral palsy. Additionally, this study highlights the need for region-specific growth references to better address the diverse needs of individuals with cerebral palsy worldwide.

PMID: 39201827

30. Prevalence and Regional Differences in Migrated Hips in Danish Children with Cerebral Palsy from 2008 to 2021-A Comparison of Ambulant vs. Non-Ambulant Children

Muhammed Bakhtiyar, Afrim Iljazi, Michael Mørk Petersen, Anders Odgaard, Christian Wong

Children (Basel). 2024 Aug 10;11(8):964. doi: 10.3390/children11080964.

Purpose: This study aims to assess the incidence of hip displacement and dislocation (denominated as hip migration) among ambulant and non-ambulant Danish children with cerebral palsy (CP) by estimating their cumulative incidence of migrated hips. A secondary objective is to compare the prevalence across different Danish regions. Methods: Data were obtained from the Danish Cerebral Palsy Follow-Up Program (CPOP) from the years 2008 to 2021. This population-based cohort study included 1388 children with CP (58% male; 42% female) as subjects; aged 0-15 years; with an average age of 5.4 years at their last follow-up. The children were categorized according to their Gross Motor Function Classification System (GMFCS) level into ambulators (GMFCS I-III) and non-ambulators (GMFCS IV-V). The Kaplan-Meier estimator was employed to calculate the cumulative incidence of migrated hips from birth until the date of their last radiographic follow-up. Differences between ambulatory and non-ambulatory children and regional differences were assessed with the Log-rank test. Results: Median radiological follow-up for ambulators was 51 months and 94 months for non-ambulators. The cumulative incidence of hip dislocation was 0.3% (95% CI: 0-0.8%) and 22.0% (95% CI: 9.2-34.8%) for ambulators and non-ambulators, respectively ($p < 0.0001$), whereas the incidence of hip displacement was 21.1% (95% CI: 16.3-25.9%) and 76.7% (95% CI: 68.6-84.7%) for ambulators and non-ambulators, respectively ($p < 0.0001$). There were no significant regional differences in the incidence of hip dislocation among ambulators, but there were significant differences for non-ambulators. Moreover, significant regional differences were detected in hip displacement for both ambulators and non-ambulators. Conclusions: The prevalence of hip migration in Danish children with CP is significantly higher among non-ambulators, who are at an increased risk of hip migration compared to their ambulant counterparts. However, the low frequency of radiographic follow-up for ambulators might cause the incidence of hip migration to be underestimated. This study highlights the necessity of continued targeted surveillance and interventions in Danish non-ambulators.

PMID: 39201899

31. Outcomes of COVID-19 and Influenza in Cerebral Palsy Patients Hospitalized in the United States: Comparative Study of a Nationwide Database

Mohammed A Quazi, Muhammad Hassan Shakir, Zohaa Faiz, Ibrahim Quraishi, Adeel Nasrullah, Hafiz Abdullah Ikram, Amir H Sohail, Sulaiman Sultan, Abu Baker Sheikh

Comparative Study Viruses. 2024 Aug 12;16(8):1284. doi: 10.3390/v16081284.

Patients with cerebral palsy (CP) are particularly vulnerable to respiratory infections, yet comparative outcomes between COVID-19 and influenza in this population remain underexplored. Using the National Inpatient Sample from 2020-2021, we performed a retrospective analysis of hospital data for adults with CP diagnosed with either COVID-19 or influenza. The study aimed to compare the outcomes of these infections to provide insights into their impact on this vulnerable population. We assessed in-hospital mortality, complications, length of stay (LOS), hospitalization costs, and discharge dispositions. Multivariable logistic regression and propensity score matching were used to adjust for confounders, enhancing the analytical rigor of our study. The study cohort comprised 12,025 patients-10,560 with COVID-19 and 1465 with influenza. COVID-19

patients with CP had a higher in-hospital mortality rate (10.8% vs. 3.1%, p = 0.001), with an adjusted odds ratio of 3.2 (95% CI: 1.6-6.4). They also experienced an extended LOS by an average of 2.7 days. COVID-19 substantially increases the health burden for hospitalized CP patients compared to influenza, as evidenced by higher mortality rates, longer hospital stays, and increased costs. These findings highlight the urgent need for tailored strategies to effectively manage and reduce the impact of COVID-19 on this high-risk group.

PMID: 39205258

32. Neglect of Psychological Care for Children with Cerebral Palsy and Their Families and Its Impact on Their Occupational Engagement in Saudi Arabia

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Medicina (Kaunas). 2024 Jul 27;60(8):1216. doi: 10.3390/medicina60081216.

Background and Objectives: Many children with (CP) and their families in Saudi Arabia struggle emotionally. Unfortunately, there have not been many studies conducted on how to help them with these challenges. This research aims to bring attention to this gap and to explore how a lack of proper mental health care might affect these children's ability to participate in everyday activities. Materials and Methods: In this cross-sectional descriptive study, a survey was conducted between August and October 2023. A total of 300 parents of CP children from Saudi Arabia participated in the study. The impact of psychological care negligence on the occupational engagement of CP children and their families was assessed by designing a valid questionnaire. Results: A total of 300 parents of children with CP participated in this study. The majority of the sample, 71% of parents, said that their children did not receive any psychological care, and 59.7% of the participants said that their children did not even receive a referral to a psychologist. However, 60.3% of parents of children noticed a significant decline in the occupational performance of their children, and 65.7% predicted an improvement in their children's performance with future psychological care. Conclusions: It is clear that there is a lack of awareness about the importance of mental health care for children with CP in Saudi Arabia. This lack of care hinders these children and their families' occupational engagement and social participation.

PMID: 39202497

33. Standardized clinical data capture to describe cerebral palsy

Susie Kim, Kelsey Steffen, Lauren Gottschalk-Henneberry, Jennifer Miros, Katie Leger, Amy Robichaux-Viehoever, Karen Taca, Bhooma Aravamuthan

medRxiv [Preprint]. 2024 Aug 9:2024.08.09.24311474. doi: 10.1101/2024.08.09.24311474.

Objective: To describe a standardized methodology for capturing clinically valuable information on young people with cerebral palsy (CP) from caregivers and clinicians during routine clinical care. Methods: We developed a caregiver-facing intake form and clinician-facing standardized note template and integrated both into routine clinical care at a tertiary care CP center (https://bit.ly/CP-Intake-Methodology). We extracted this caregiver and clinician-entered data on people with an ICD10 diagnosis of CP seen between 3/22/23 and 12/28/23. We used this data to describe how CP manifests in this group and which medical features affected the odds of walking, oral feeding, and speech by age 5. Results: Of 686 visits, 663 (97%) had caregiver- and clinician-entered data and 633 had a clinician-confirmed CP diagnosis (mean age 9.1, 53.4% Male, 78.5% White). It was common to have quadriplegia (288/613, 47.0%), both spasticity and dystonia (257/632, 40.7%), walk independently (368/633, 58.1%), eat all food and drink safely by mouth (288/578, 55.9%), and produce understandable speech (249/584, 42.6%). Cortical grey matter injury and duration of initial critical care unit stay affected the odds of walking, oral feeding, and speech (binary logistic regression, p<0.001). Conclusions: We comprehensively captured caregiver and clinician-entered data on 97% of people seen in a tertiary care CP Center and used this data to determine medical features affecting the odds of three functional outcomes. By sharing our methodology, we aim to facilitate replication of this dataset at other sites and grow our understanding of how CP manifests in the US. Article summary: Using caregiver and clinician-entered data on people seen in a tertiary-care CP center, we determined medical features affecting the odds of three functional outcomes. What's known on this subject: Detailed CP characterization can be limited if using population-based registries and retrospective chart review alone, including limited data on recently validated functional classification systems for CP. What this study adds: We comprehensively captured caregiver and clinician-entered data on 97% of people seen in our CP Center to describe how CP manifests and show that cortical injury and initial ICU stay duration affect the odds of walking, oral feeding, and speech. Contributors statement: Susie Kim helped design the study, aggregated data, carried out data analyses, and critically reviewed and revised the manuscript.Kelsey Steffen helped conceptualize and design the study and critically reviewed and revised the manuscript.Lauren Gottschalk, Jennifer Miros, Katie Leger, Amy Viehoever, and Karen Taca helped design the study and critically reviewed and revised the manuscript.Bhooma Aravamuthan conceptualized and designed the study, supervised data collection and analysis, drafted the initial manuscript, and critically reviewed and revised the manuscript.

PMID: 39211855

34. Employing Siamese Networks as Quantitative Biomarker for Assessing the Effect of Dolphin-Assisted Therapy on Pediatric Cerebral Palsy

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Brain Sci. 2024 Jul 31;14(8):778. doi: 10.3390/brainsci14080778.

This study explores the potential of using a Siamese Network as a biomarker for assessing the effectiveness of Dolphin-Assisted Therapy (DAT) in children with Spastic Cerebral Palsy (SCP). The problem statement revolves around the need for objective measures to evaluate the impact of DAT on patients with SCP, considering the subjective nature of traditional assessment methods. The methodology involves training a Siamese network, a type of neural network designed to compare similarities between inputs, using data collected from SCP patients undergoing DAT sessions. The study employed Event-Related Potential (ERP) and Fast Fourier Transform (FFT) analyses to examine cerebral activity and brain rhythms, proposing the use of SNN to compare electroencephalographic (EEG) signals of children with cerebral palsy before and after Dolphin-Assisted Therapy. Testing on samples from four children yielded a high average similarity index of 0.9150, indicating consistent similarity metrics before and after therapy. The network is trained to learn patterns and similarities between pre- and post-therapy evaluations, in order to identify biomarkers indicative of therapy effectiveness. Notably, the Siamese Network's architecture ensures that comparisons are made within the same feature space, allowing for more accurate assessments. The results of the study demonstrate promising findings, indicating different patterns in the output of the Siamese Network that correlate with improvements in symptoms of SCP post-DAT. Confirming these observations will require large, longitudinal studies but such findings would suggest that the Siamese Network could have utility as a biomarker in monitoring treatment responses for children with SCP who undergo DAT and offer them more objective as well as quantifiable manners of assessing therapeutic interventions. Great discrepancies in neuronal voltage perturbations, 7.9825 dB on average at the specific samples compared to the whole dataset (6.2838 dB), imply a noted deviation from resting activity. These findings indicate that Dolphin-Assisted Therapy activates particular brain regions specifically during the intervention.

PMID: 39199471

35. Neonatal therapy principles during transition from neonatal intensive care unit to home: A modified Delphi study

Kerry Miller, Sandra Willett, Dana Mccarty, Stacey C Dusing

Dev Med Child Neurol. 2024 Aug 26. doi: 10.1111/dmcn.16075. Online ahead of print.

Aim: To establish expert consensus on key principles for therapist-supported interventions supporting infants born preterm and their families during the transition from neonatal intensive care unit (NICU) to home in the USA. Method: A diverse, interdisciplinary panel of experts evaluated the use of key intervention principles. A modified Delphi technique was used to seek opinions from independent and relevant interdisciplinary experts on the clarity of terminology, efficacy, and feasibility of implementing these intervention principles during the NICU-to-home transition. Results: After our team consensus, one round of surveys was required to reach expert consensus. Twenty-four experts, representing a variety of disciplines, responded to the survey. Results showed strong consensus on four key therapist-supported interventions: building caregiver-child relationships; optimizing infant development; education and knowledge sharing; and enriched environments. Interpretation: This research provides valuable insights into key therapist-supported interventions that may be used during the NICU-to-home transition to address the needs of high-risk infants and the well-being of their families. Findings will inform the development of streamlined and effective interventions, improving child and family outcomes during this critical transition period.

PMID: 39187953

Prevention and Cure

36. Progesterone improves motor coordination impairments caused by postnatal hypoxic-ischemic brain insult in neonatal male rats

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Background: Hypoxic-ischemic (HI) insult in infants induces brain injury and results in motor coordination impairments associated with cerebral palsy; however, preventive measures for HI brain injury in preterm infants remain unclear. We investigated the impact of progesterone (P4) in a rat HI insult model that mimics HI brain injury in preterm infants. Methods:

Neonatal male rats with their right common carotid artery coagulated were exposed to a 1-h hypoxia (6% oxygen) on postnatal day (PND) 3. P4 (0.2 mg) was subcutaneously administered daily from PND4-12. Motor coordination function and muscular strength were evaluated on PND50 using rotarod and grip strength tests, respectively. Brain histology was evaluated via immunohistochemistry using anti-NeuN, anti-Olig2, and anti-IbaI antibodies on PND15 and PND50. Results: In male rats, P4 significantly improved the latency-to-fall off on the rotarod test in the insult rats to the levels of the sham-operation rats. Neither the insult nor P4 administration impacted the grip strength results. No significant differences were observed in the number of neurons, oligodendrocyte progenitor cells (OPCs), and microglia in the motor and somatosensory area of the cortex between the insult and insult followed by P4-administered rats on PND50. The number of OPCs in the corpus callosum was significantly increased in the ipsilateral side compared with the contralateral side of the insult in the P4-administered rats, indicating that P4 facilitates recruitment of OPCs to the corpus callosum. HI insult accelerated neuronal differentiation in rats on PND15, which was abrogated in the P4-administerd group, suggesting that P4 suppresses transient neuronal differentiation caused by the insult. Conclusion: P4 administration restored motor coordination impairments caused by postnatal HI insult in male rats. The insult timing corresponds to that of human preterm infants, indicating P4's potential for protecting HI brain injury in preterm male infants.

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37. Human neural stem cells transplanted during the sequelae phase alleviate motor deficits in a rat model of cerebral palsy

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Aims: Cerebral palsy (CP) is the most common physical disability in children, yet lacks an ideal animal model or effective treatment. This study aimed to develop a reliable CP model in neonatal rats and explore the effectiveness and underlying mechanisms of human neural stem cells (hNSCs) transplantation during the sequelae phase of CP. Methods: Vasoconstrictor endothelin-1 (ET-1) was administered intracranially to the motor cortex and striatum of rats on postnatal day 5 to establish a CP model. hNSCs (5 × 105/5 μL) pretreated with hypoxia (5% O2 for 24 h) were transplanted near the infarct 3 weeks after ET -1 injury (the sequelae phase). The distribution and differentiation of hNSCs were observed after transplantation. Changes in neurotrophic factors, neurogenesis, angiogenesis, axonal plasticity, and motor function were analyzed. Results: Neurobehavioral tests showed poor muscle strength and postural control in young ET-1 rats. Motor deficits of the left forelimb and gait abnormalities persisted into adulthood. Histopathological findings and MRI indicated the atrophy of the cortex, striatum, and adjacent corpus callosum in ET-1 rats. At 56 days after transplantation, hNSCs were widely distributed in the ipsilateral hemisphere, and differentiated into neurons, oligodendrocytes and astrocytes. Transplantation of hNSCs increased BDNF and VEGF expression, EdU+ cell number in the SVZ area, RECA-1+ vessel density and GAP-43 intensity around the lesion in ET-1 rats. The cylinder test revealed a significant increase in the left forelimb motor function from 28 days after transplantation, and the staircase and CatWalk tests showed improvements in fine motor function and gait parameters. Conclusions: Intracerebral injection of ET-1 modelled key functional and histopathological features of CP. hNSCs transplanted during the sequelae phase of CP resulted in long-term improvement in motor performance, possibly attributed to its capacity to stimulate neurotrophic factors, facilitate neurogenesis, angiogenesis, and promote axonal plasticity.

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38. Role of Microglial Modulation in Therapies for Perinatal Brain Injuries Leading to Neurodevelopmental Disorders

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Neurodevelopmental disorders (NDDs) encompass various conditions stemming from changes during brain development, typically diagnosed early in life. Examples include autism spectrum disorder, intellectual disability, cerebral palsy, seizures, dyslexia, and attention deficit hyperactivity disorder. Many NDDs are linked to perinatal events like infections, oxygen disturbances, or insults in combination. This chapter outlines the causes and effects of perinatal brain injury as they relate to microglia, along with efforts to prevent or treat such damage. We primarily discuss therapies targeting microglia modulation, focusing on those either clinically used or in advanced development, often tested in large animal models such as sheep, non-human primates, and piglets-standard translational models in perinatal medicine. Additionally, it touches on experimental studies showcasing advancements in the field.

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