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Interventions and Management

1. The effect of botulinum toxin-A on neural and non-neural components of wrist hyper-resistance in adults with stroke or cerebral palsy

Aukje Andringa, Erwin van Wegen, Ingrid van de Port, Lisette Guit, Wojtek Polomski, Gert Kwakkel, Carel Meskers

PM R. 2021 Apr 2. doi: 10.1002/pmrj.12602.

Introduction: Botulinum toxin-A (BoNT) is widely used to manage focal upper limb spasticity and is effective in reducing resistance to passive movement, as measured with the modified Ashworth scale. Discrimination and quantification of the underlying neural and non-neural components of hyper-resistance may further improve understanding of the effect of BoNT. Objective: To explore the effects of BoNT on neural (NC), non-neural elastic (EC) and viscous (VC) components of resistance to passive wrist extension in adults with stroke or cerebral palsy, and the association between the effects on wrist hyper-resistance components and clinical spasticity, pain and motor function scales. Design: Pre-experimental study with pre- and post-intervention measurements at 6 and 12 weeks. Setting: An outpatient clinic of a hospital. Participants: Adults with chronic stroke or cerebral palsy indicated for BoNT treatment for hyper-resistance in the wrist (N = 18). Interventions: BoNT injections in the wrist and/or finger flexor muscles. Main outcome measures: Wrist hyper-resistance components, using the NeuroFlexor, and clinical scales (modified Ashworth scale, Tardieu scale, passive wrist extension, pain, Fugl-Meyer motor assessment of the upper extremity, and action research arm test). Results: NC was significantly reduced 6 and 12 weeks post-intervention (median -11.96 Newton, $p < 0.001$ and median -9.34 Newton, $p = 0.001$, respectively); non-neural EC and VC showed no change. NC reduction 6 weeks post-intervention correlated significantly with BoNT dose (Pearson correlation coefficient $r_p = -0.56$). No significant correlations were found between change scores in wrist hyper-resistance components and clinical scales. Conclusions: BoNT affected the neural component of resistance to passive wrist extension, while leaving the non-neural elastic and viscous components unaffected. This instrumented approach to quantify the effects of BoNT in the wrist and finger flexor muscles on the components of wrist hyper-resistance may have an added value for BoNT treatment evaluation in clinical practice. This article is protected by copyright. All rights reserved.

PMID: [33811454](https://pubmed.ncbi.nlm.nih.gov/33811454/)

2. Impaired postural control of axial segments in children with cerebral palsy

Jonathan Pierret, Sébastien Caudron, Jean Paysant, Christian Beyaert

Gait Posture. 2021 Mar 8;86:266-272. doi: 10.1016/j.gaitpost.2021.03.012.

Background: Sensorimotor control of axial segments, which develops during childhood and is not mature until adolescence, is essential for the development of balance control during motor activities. Children with cerebral palsy (CP) have deficits in postural control when standing or walking, including less stabilization of the head and trunk which could affect postural control. Research question: Is dynamic stabilization of axial segments during an unstable sitting task deficient in children with CP compared to typically developing children? Is this deficit correlated with the deficit of postural control during standing? Method: Seventeen children with CP (GMFCS I-II) and 17 typically-developing children from 6 to 12 years old were rated on the Trunk Control Measurement Scale (TCMS). In addition, posturography was evaluated in participants while they maintained their balance in stable sitting, unstable sitting, and quiet standing, under "eyes open" and "eyes closed" conditions. In sitting tasks, the participants had to remain stable while being prevented from using the lower and upper limbs (i.e. to ensure the involvement of axial segments alone). Results: Children with CP compared to TD children had significantly larger surface area, mean velocity and RMS values of CoP displacements measured during the unstable sitting task and the standing task, under both "eyes open" and "eyes closed" conditions. No significant group effects were observed during the stable sitting task. The TCMS total score was significantly lower, indicating trunk postural deficit, in the CP group than in the TD group and was significantly correlated with postural variables in the sitting and standing tasks. Significance: Children with CP indeed have a specific impairment in the postural control of axial segments. Since the postural control of axial segments is important for standing and walking, its impairment should be taken into account in rehabilitation programs for children with CP.

PMID: [33819768](#)

3. Clinical Implications of the General Movement Optimality Score: Beyond the Classes of Rasch Analysis

Vanessa Maziero Barbosa, Christa Einspieler, Everett Smith, Arend F Bos, Giovanni Cioni, Fabrizio Ferrari, Hong Yang, Berndt Urlesberger, Peter B Marschik, Dajie Zhang

J Clin Med. 2021 Mar 4;10(5):1069. doi: 10.3390/jcm10051069.

This article explores the clinical implications of the three different classes drawn from a Rasch analysis of the general movements optimality scores (GMOS) of 383 infants. Parametric analysis of the class membership examines four variables: age of assessment, brain injury presence, general movement patterns, and 2-year-old outcomes. GMOS separated infants with typical (class 3) from atypical development, and further separated cerebral palsy (class 2) from other neurodevelopmental disorders (class 1). Each class is unique regarding its quantitative and qualitative representations on the four variables. The GMOS has strong psychometric properties and provides a quantitative measure of early motor functions. The GMOS can be confidently used to assist with early diagnosis and predict distinct classes of developmental outcomes, grade motor behaviors, and provide a solid base to study individual general movement developmental trajectories.

PMID: [33806626](#)

4. Outcomes of Vertical Expandable Prosthetic Titanium Ribs in Children With Early-Onset Scoliosis Secondary to Cerebral Palsy

Randa Elmallah, Travis Fortin, Josny Thimothee, Hamdi Sukkarieh, Patrick B Wright, M Wade Shrader, Jaysson Brooks

Cureus. 2021 Mar 4;13(3):e13690. doi: 10.7759/cureus.13690.

Purpose: Patients who have neuromuscular scoliosis, such as cerebral palsy (CP), often develop spinal deformities that negatively impact quality of life. The vertical expandable prosthetic titanium rib (VEPTR) was designed for thoracic insufficiency syndrome (TIS), but it has also been utilized in patients with CP with restrictive lung disease and spine deformity. Few studies report on VEPTRs in neuromuscular scoliosis; however, none reports on their utilization specifically in patients with CP. Our purpose was to assess if VEPTRs can improve spinal deformity and TIS in these patients. **Methods** A retrospective chart review was performed of all patients with CP and scoliosis treated with a VEPTR between 2008 and 2017. Eight patients were eligible for this study. The mean follow-up was four years. Outcomes evaluated were Cobb angle, pelvic obliquity, space available for lung ratio (SAL), T1-S1 height, and complication rates. A p-value of less than 0.05 was used for statistical significance. **Results** There were significant postoperative improvements in Cobb angle, pelvic obliquity, and T1-S1 height, but no statistical difference in SAL. Prior to final fusion, the mean number of VEPTR lengthening procedures was 3. The mean time from index surgery to final fusion was 3.7 years. The most common complications were infection (62.5%) and wound dehiscence (25%). Only 25% of patients did not have a complication. **Conclusion** VEPTRs demonstrated significant improvement in almost all parameters and may be valuable in improving TIS in patients with CP. The complication and reoperation rates were similar to those of VEPTRs used for other pathological conditions.

PMID: [33833914](#)

5. Pseudomonas aeruginosa infection in respiratory samples in children with neurodisability-to treat or not to treat?

Elizabeth Gregson, Lowri Thomas, Heather E Elphick

Eur J Pediatr. 2021 Apr 6. doi: 10.1007/s00431-021-04025-y.

The objective was to investigate the prevalence of *Pseudomonas aeruginosa* (PA) in patients with complex neurodisability and current treatment practice in our centre in order to inform future guidelines. A retrospective case note review was undertaken at a tertiary children's hospital. One hundred sixty-two patients (mean age 11.7 years) with a primary diagnosis of neuromuscular disease (NMD) or severe cerebral palsy (CP) and a respiratory sample sent for analysis during the study period were studied. Associations between PA in respiratory samples and diagnosis, long-term ventilation, presence of a gastrostomy or a tracheostomy, antibiotic choice, clinical deterioration and adverse events were analysed. Twenty-five (15%) had one or more PA isolate in respiratory samples. There was a significant association between PA in respiratory samples and tracheostomy ($p < 0.05$). In 52% samples, multiple pathogens co-existed. There was no significant association between choice of antibiotic and clinical outcome but when antibiotics were changed to specific PA antibiotics during the course of the illness, all resulted in clinical improvement. Twenty-six episodes involving 8 patients with recurrent admissions involved PA organisms that were resistant to one or more antibiotics. **Conclusions:** A larger prospective study may establish clearer criteria for guideline development. Techniques such as point-of-care testing to identify virulent strains of PA may improve patient outcomes and prevent the development of antibiotic resistance in the future. **What is Known:** •Children with complex neurodisability are at increased risk of respiratory morbidity and of infection with gram-negative organisms such as *Pseudomonas aeruginosa*. •There are currently no guidelines to inform treatment choices in this group of vulnerable children. **What is New:** •15% children in this study population had *Pseudomonas aeruginosa* in respiratory samples during a 12-month period, the majority of whom did not require critical care treatment. Thirteen of these children had a tracheostomy in situ and 12 did not. •In those that deteriorated clinically or developed antibiotic resistant organisms, earlier detection and targeted treatment of *Pseudomonas aeruginosa* may have prevented deterioration.

PMID: [33822245](#)

6. Unusual mechanical failures of intrathecal baclofen pump systems: symptoms, signs, and trouble shooting

Janina Gburek-Augustat, Matthias Krause, Matthias Bernhard, Ina Sorge, Daniel Gräfe, Manuela Siekmeyer, Ulf Nestler, Andreas Merckenschlager

Childs Nerv Syst. 2021 Apr 8. doi: 10.1007/s00381-021-05154-3.

Introduction: Although intrathecal baclofen (ITB) therapy is an effective treatment for spasticity, it has several disadvantages and a risk of complications. **Methods:** We present six pediatric patients who suffered from unusual mechanical failures of intrathecal baclofen pump systems. **Results:** With these case-vignettes, we provide a systematic approach on how to interpret the symptoms of ITB complications and an advice which further diagnostic and therapeutic steps to follow. We underline the seriousness of baclofen overdose, underdosing or withdrawal.

PMID: [33834279](#)

7. Why the Hips Remain Stable When the Spine Strays: A Deeper Analysis of the Relationship Between Hip Displacement and Severe Scoliosis in Patients With Cerebral Palsy

Matthew J Hadad, Amy L Xu, Barry R Bryant, Nicholas S Andrade, Alexander H Hoon Jr, Paul D Sponseller

J Pediatr Orthop. 2021 May-Jun 01;41(5):261-266. doi: 10.1097/BPO.0000000000001765.

Background: Many patients with spastic quadriplegic cerebral palsy (CP) and severe scoliosis develop hip displacement, whereas others do not. We investigated demographic characteristics, risk factors for CP, and imaging findings associated with nondisplaced hips in patients with CP and severe scoliosis. **Methods:** We retrospectively analyzed records of 229 patients with spastic quadriplegic CP and severe scoliosis who presented for treatment at our US academic tertiary care hospital between August 2005 and September 2015. Demographic characteristics, risk factors for CP, and brain magnetic resonance imaging (MRI) findings were documented. Patients were classified as Gross Motor Function Classification System (GMFCS) level 4 or higher, with 58% at GMFCS level 5.3. Displaced hips (n=181 patients) were defined as a migration percentage of $\geq 30\%$ or previous surgery for hip displacement/adductor contractures. Patients who did not meet these criteria were classified as nondisplaced (n=48 patients). We used univariate analysis and multivariate logistic regression to determine associations between patient factors and hip displacement ($\alpha=0.05$). **Results:** Patients born at term (≥ 37 wk) had 2.5 times the odds [95% confidence interval (CI): 1.3-5.0] of having nondisplaced hips compared with patients born prematurely. Females had 2.0 times the odds (95% CI: 1.0-3.9) of having nondisplaced hips compared with males. Patients with normal brain MRI findings had 9.6 times the odds (95% CI: 2.3-41) of having nondisplaced hips compared with patients with abnormal findings. Hip displacement was not associated with race ($P>0.05$). **Conclusions:** Gestational age 37 weeks or above, female sex, and normal brain MRI findings are independently associated with nondisplaced hips in patients with spastic quadriplegic CP and severe scoliosis. These findings direct attention to characteristics that may place patients at greater risk of displacement. Future work may influence preventative screening practices and improve patient counseling regarding the risk of hip displacement.

PMID: [33825716](#)

8. Effect of performing daily activities while standing on the quantity and quality of the thigh muscles in adults with severe cerebral palsy: a cross-sectional study

Soma Endo, Toshikazu Soyama, Hitoshi Asai, Pleiades Tiharu Inaoka, Hiroyuki Sasaki, Issei Nomura, Keisuke Sakurakichi

J Phys Ther Sci. 2021 Mar;33(3):288-294. doi: 10.1589/jpts.33.288. Epub 2021 Mar 17.

[Purpose] To observe the effect of daily standing, as indicated by gross motor function, on the quantity and quality of the thigh muscles in adults with severe cerebral palsy and to obtain data to determine an appropriate intervention that will improve their quality of life. [Participants and Methods] Thirty-three adults with severe cerebral palsy participated in the study. We assessed the gross motor function using the GMFM-66-IS. We then evaluated the quadriceps muscle thickness and the rectus femoris muscle echo intensity using ultrasonography. We divided the participants into the standing and non-standing groups and then examined the correlations of the GMFM-66-IS score to muscle thickness and echo intensity. We calculated the difference in mean muscle thickness and echo intensity between the two groups using an independent t-test. [Results] Significant positive correlations were found between the GMFM-66-IS score and muscle thickness and echo intensity. In the group-specific analysis, no significant correlation was found between echo intensity and the GMFM-66-IS score in either group. Muscle thickness and echo intensity were greater in the participants of the standing group. [Conclusion] Daily standing, as indicated by gross motor function, affected muscle thickness and echo intensity. Quantitative and qualitative data might need to be evaluated when assessing the muscles of adults with severe cerebral palsy using ultrasonography.

PMID: [33814718](#)

9. Recurrence of knee flexion contracture after surgical correction in children with cerebral palsy Supitchakarn Cheewasukanon, Phatcharapa Osateerakun, Noppachart Limpaphayom

Int Orthop. 2021 Apr 6. doi: 10.1007/s00264-021-05035-z.

Purpose: Knee flexion contracture (FC) and crouch gait are challenging to treat in children with cerebral palsy (CCP), and recurrent knee FC after surgery is a severe complication. The aim was to identify factors associated with recurrent knee FC after surgery. **Methods:** The records of 62 CCP (age 10.6±2.6 years) who underwent surgery and were followed for > six months were reviewed. Knee FC was treated by hamstring lengthening, posterior knee capsulotomy, and femoral shortening/extension osteotomy until full extension was obtained. Kaplan-Meier analysis was used to estimate the probability of the correction being maintained. Cox proportional hazard modeling was used to compare parameters between patients with and without recurrent knee FC, with the time to recurrence as the endpoint. Potential confounding factors were included in the multivariate analysis. **Results:** In total, the procedure was performed on 122 knees. The average weight-for-age z score was -1.3±1.2. The average follow-up period was 5.4±4.2 years. Knee FC recurrence was observed in 37 knees (30%). The average recurrence-free time was 4.9 years, with most cases of recurrence (33 knees) occurring within six years after surgery. The factors associated with recurrence were age (HR, 1.19) and a required posterior knee capsulotomy procedure (HR, 4.53). **Conclusion:** Recurrent knee FC after correction is associated with CCP who are older at the time of operation and when posterior knee capsulotomy is performed. The age at operation should be optimized. The sequence of procedures should be performed only as necessary to minimize the chance of post-operative muscle weakness and recurrence.

PMID: [33822275](#)

10. Combination of Quantitative MRI Fat Fraction and Texture Analysis to Evaluate Spastic Muscles of Children With Cerebral Palsy

Tugba Akinci D'Antonoli, Francesco Santini, Xenia Deligianni, Meritxell Garcia Alzamora, Erich Rutz, Oliver Bieri, Reinald Brunner, Claudia Weidensteiner

Front Neurol. 2021 Mar 22;12:633808. doi: 10.3389/fneur.2021.633808. eCollection 2021.

Background: Cerebral palsy (CP) is the most common cause of physical disability in childhood. Muscle pathologies occur due to spasticity and contractures; therefore, diagnostic imaging to detect pathologies is often required. Imaging has been used to assess torsion or estimate muscle volume, but additional methods for characterizing muscle composition have not thoroughly been investigated. MRI fat fraction

(FF) measurement can quantify muscle fat and is often a part of standard imaging in neuromuscular dystrophies. To date, FF has been used to quantify muscle fat and assess function in CP. In this study, we aimed to utilize a radiomics and FF analysis along with the combination of both methods to differentiate affected muscles from healthy ones. **Materials and Methods:** A total of 9 patients (age range 8-15 years) with CP and 12 healthy controls (age range 9-16 years) were prospectively enrolled (2018-2020) after ethics committee approval. Multi-echo Dixon acquisition of the calf muscles was used for FF calculation. The images of the second echo (TE = 2.87 ms) were used for feature extraction from the soleus, gastrocnemius medialis, and gastrocnemius lateralis muscles. The least absolute shrinkage and selection operator (LASSO) regression was employed for feature selection. RM, FF model (FFM), and combined model (CM) were built for each calf muscle. The receiver operating characteristic (ROC) curve and their respective area under the curve (AUC) values were used to evaluate model performance. **Results:** In total, the affected legs of 9 CP patients and the dominant legs of 12 healthy controls were analyzed. The performance of RM for soleus, gastrocnemius medialis, and gastrocnemius lateralis (AUC 0.92, 0.92, 0.82, respectively) was better than the FFM (AUC 0.88, 0.85, 0.69, respectively). The combination of both models always had a better performance than RM or FFM (AUC 0.95, 0.93, 0.83). FF was higher in the patient group (FFS 9.1%, FFGM 8.5%, and FFGL 10.2%) than control group (FFS 3.3%, FFGM 4.1%, FFGL 6.6%). **Conclusion:** The combination of MRI quantitative fat fraction analysis and texture analysis of muscles is a promising tool to evaluate muscle pathologies due to CP in a non-invasive manner.

PMID: [33828520](https://pubmed.ncbi.nlm.nih.gov/33828520/)

11. Development of Lower Extremity Strength in Ambulatory Children With Bilateral Spastic Cerebral Palsy in Comparison With Typically Developing Controls Using Absolute and Normalized to Body Weight Force Values

Nicolaos Darras, Eirini Nikaina, Magda Tziomaki, Georgios Gkrimas, Antigone Papavasiliou, Dimitrios Pasparakis

Front Neurol. 2021 Mar 19;12:617971. doi: 10.3389/fneur.2021.617971. eCollection 2021.

This cross-sectional study aimed to examine the development of lower limb voluntary strength in 160 ambulatory patients with bilateral spastic cerebral palsy (CP) (106 diplegics/54 quadriplegics) and 86 typically developing (TD) controls, aged 7-16 years. Handheld dynamometry was used to measure isometric strength of seven muscle groups (hip adductors and abductors, hip extensors and flexors, knee extensors and flexors, and ankle dorsiflexors); absolute force (AF) values in pounds were collected, which were then normalized to body weight (NF). AF values increased with increasing age ($p < 0.001$ for all muscle groups), whereas NF values decreased through adolescence ($p < 0.001$ for all muscle groups except for hip abduction where $p = 0.022$), indicating that increases in weight through adolescence led to decreases in relative force. Both AF and NF values were significantly greater in TD subjects when compared with children with CP in all muscle and all age groups ($p < 0.001$). Diplegics and quadriplegics demonstrated consistently lower force values than TD subjects for all muscle groups, except for the hip extensors where TD children had similar values with diplegics ($p = 0.726$) but higher than quadriplegics ($p = 0.001$). Diplegic patients also exhibited higher values than quadriplegics in all muscles, except for the knee extensors where their difference was only indicative ($p = 0.056$). The conversion of CP subjects' force values as a percentage of the TD subjects' mean value revealed a pattern of significant muscle strength imbalance between the CP antagonist muscles, documented from the following deficit differences for the CP muscle couples: (hip extensors 13%) / (hip flexors 32%), (adductors 27%) / (abductors 52%), and (knee extensors 37%) / (knee flexors 53%). This pattern was evident in all age groups. Similarly, significant force deficiencies were identified in GMFCS III/IV patients when compared with TD children and GMFCS I/II patients. In this study, we demonstrated that children and adolescents with bilateral CP exhibited lower strength values in lower limb muscles when compared with their TD counterparts. This difference was more prevalent in quadriplegic patients and those with a more severe impairment. An important pattern of muscle strength imbalance between the antagonist muscles of the CP subjects was revealed.

PMID: [33815249](#)

12. Factors related to better outcomes after single-event multilevel surgery (SEMLS) in patients with cerebral palsy

Kamila Moreira de Freitas Guardini, Cátia M Kawamura, José Augusto F Lopes, Marcelo H Fujino, Francesco C Blumetti, Mauro C de Moraes Filho

Gait Posture. 2021 Mar 27;86:260-265. doi: 10.1016/j.gaitpost.2021.03.032.

Background: Good outcomes have been described after single-event multilevel surgery (SEMLS) in cerebral palsy (CP); however, there is limited evidence regarding factors influencing them. **Research question:** What were the factors related to kinematic outcomes after SEMLS in the present study? **Methods:** Two hundred and fifty-eight patients with spastic diplegic CP, GMFCS I-III, who underwent SEMLS and had done pre and post-operative gait analyses were included in the SEMLS Group (SEMLS-G). A second search was performed in the same database looking for patients to compose the Control Group (CG), and 88 subjects, with at least two gait analyses and with no surgical intervention between tests, were identified. Demographic data, GDI and GPS (Gait Profile Score) were analyzed in both groups, and the results compared. A second evaluation was performed in the SEMLS-G in order to identify the influence of age, gender, follow-up time, pre-operative GDI, GMFCS and gait velocity on results. **Results:** The GDI (51.3-58.4) and GPS (2.5°) improvement occurred only in SEMLS-G ($p < 0.001$). On sagittal plane, there was an improvement at the knee and ankle levels in SEMLS-G, whereas the pelvic alignment improved in the CG. In SEMLS-G, patients with improvement on GDI > 10 points had lower pre-operative GDI (46.15) than other groups ($p < 0.001$). In addition, patients with reduction on GDI after intervention had lower pre-operative gait velocity than subjects with improvement > 10 points ($p = 0.01$). The increase on GDI after SEMLS was greater in patients GMFCS I and II than GMFCS III ($p = 0.003$). There was a negative effect of GMFCS III on GDI improvement after intervention ($p = 0.014$). **Significance:** Lower pre-operative GDI, higher baseline gait velocity and GMFCS levels I and II were related to better outcomes after SEMLS in the present study. On the other hand, patients GMFCS III were more susceptible to deteriorate after SEMLS.

PMID: [33813186](#)

13. Coordination of the upper and lower extremities during walking in children with cerebral palsy

Alexis Sidiropoulos, Richard Magill, Andrew Gordon

Review Gait Posture. 2021 Mar 24;86:251-255. doi: 10.1016/j.gaitpost.2021.03.028.

Background: Children with cerebral palsy indicate poor continuous gait inter-limb coordination compared to typically developing children. Limited research exists in the understanding of the coordinative relationship between the arms and legs of these children and if the phasing relationships between limbs can be improved. **Research question:** Which motor control factors impact coordination in children with cerebral palsy and can coordination improve with intervention? **Methods:** This literature review provides a comprehensive overview of the current knowledge of continuous coordination in a pediatric, pathologic population with an emphasis on inter-limb coordination. Peer-reviewed research articles related to inter-limb coordination, with a focus on gait, were reviewed to identify relevant research and any gaps in the literature which could inform future study design. Consideration of the most appropriate analysis for evaluation of such movement is also presented. **Results:** The coordinative difficulties experienced by children with cerebral palsy may originate from the deficits in motor control, muscle tone, and weakness caused by damage to the central nervous system, which is vital in motor control of inter-limb coordination. Continuous inter-limb coordination in children with cerebral palsy may be improved with enhanced function of the upper extremities through intensive motor-learning based rehabilitation or botulinum toxin injection of the more-affected arm. Importantly, analysis of limb movements should include continuous measures of relative phase, as it provides a more detailed description of coordination

compared to discrete measures. Significance: Improved upper extremity function may produce a positive change in the phasing relationship between the arms and legs. This type of coordination should be analyzed using relative phase analysis, as this type of analysis can provide more information compared to traditional spatiotemporal parameters. However, more research is required to fully understand the connection between improved upper extremity function and its positive impact on gait coordination in children with cerebral palsy.

PMID: [33812293](#)

14. A comparison of leg stiffness in running between typically developing children and children with cerebral palsy

A Chappell, G T Allison, N Gibson, G Williams, S Morris

Clin Biomech (Bristol, Avon). 2021 Mar 23;84:105337. doi: 10.1016/j.clinbiomech.2021.105337.

Background: Leg stiffness is important during running to increase velocity and maximise efficiency by facilitating use of the stretch-shortening cycle. Children with cerebral palsy who have neuromuscular impairments may have altered leg stiffness. The aim of this study was to describe leg stiffness during running in typically developing children and those with cerebral palsy in Gross Motor Function Classification Scale levels I and II at a range of speeds. **Methods:** This cross-sectional study examined kinematic data collected from typically developing children (n = 21) and children with cerebral palsy (Gross Motor Function Classification Scale level I n = 25, Gross Motor Function Classification Scale level II n = 13) during jogging, running and sprinting. Derived variables were resultant ground reaction force, change in leg length and three-dimensional leg stiffness. Linear mixed models were developed for statistical analysis. **Findings:** Children with cerebral palsy had reduced stiffness when jogging (Gross Motor Function Classification Scale level I affected t = 3.81 p < 0.01; non-affected t = 2.19 p = 0.03; Gross Motor Function Classification Scale level II affected t = 2.04 p = 0.04) and running (Gross Motor Function Classification Scale level I affected t = 3.23 p < 0.01) compared to typically developing children. Affected legs were less stiff than non-affected legs only in Gross Motor Function Classification Scale level I during running (t = 2.26 p = 0.03) and sprinting (t = 2.95 p < 0.01). **Interpretation:** Children with cerebral palsy have atypical leg stiffness profiles which differ according to functional classification.

PMID: [33812200](#)

15. Musculoskeletal Pathology in Cerebral Palsy: A Classification System and Reliability Study

H Kerr Graham, Pam Thomason, Kate Willoughby, Tandy Hastings-Ison, Renee Van Stralen, Benan Dala -Ali, Peter Wong, Erich Rutz

Children (Basel). 2021 Mar 23;8(3):252. doi: 10.3390/children8030252.

This article presents a classification of lower limb musculoskeletal pathology (MSP) for ambulant children with cerebral palsy (CP) to identify key features from infancy to adulthood. The classification aims to improve communication, and to guide referral for interventions, which if timed appropriately, may optimise long-term musculoskeletal health and function. Consensus was achieved by discussion between staff in a Motion Analysis Laboratory (MAL). A four-stage classification system was developed: Stage 1: Hypertonia: Abnormal postures are dynamic. Stage 2: Contracture: Fixed shortening of one or more muscle-tendon units. Stage 3: Bone and joint deformity: Torsional deformities and/or joint instability (e.g., hip displacement or pes valgus), usually accompanied by contractures. Stage 4: Decompensation: Severe pathology where restoration of optimal joint and muscle-tendon function is not possible. Reliability of the classification was tested using the presentation of 16 clinical cases to a group of experienced observers, on two occasions, two weeks apart. Reliability was found to be very good to excellent, with mean Fleiss' kappa ranging from 0.72 to 0.84. Four-stages are proposed to classify lower limb MSP in children with CP. The classification was reliable in a group of clinicians who work together. We emphasise the features of decompensated MSP in the lower limb, which may not always benefit from

reconstructive surgery and which can be avoided by timely intervention.

PMID: [33807084](#)

16. Kinect V2-Based Gait Analysis for Children with Cerebral Palsy: Validity and Reliability of Spatial Margin of Stability and Spatiotemporal Variables

Yunru Ma, Kumar Mithraratne, Nichola Wilson, Yanxin Zhang, Xiangbin Wang

Sensors (Basel). 2021 Mar 17;21(6):2104. doi: 10.3390/s21062104.

Children with cerebral palsy (CP) have high risks of falling. It is necessary to evaluate gait stability for children with CP. In comparison to traditional motion capture techniques, the Kinect has the potential to be utilised as a cost-effective gait stability assessment tool, ensuring frequent and uninterrupted gait monitoring. To evaluate the validity and reliability of this measurement, in this study, ten children with CP performed two testing sessions, of which gait data were recorded by a Kinect V2 sensor and a referential Motion Analysis system. The margin of stability (MOS) and gait spatiotemporal metrics were examined. For the spatiotemporal parameters, intraclass correlation coefficient (ICC2,k) values were from 0.83 to 0.99 between two devices and from 0.78 to 0.88 between two testing sessions. For the MOS outcomes, ICC2,k values ranged from 0.42 to 0.99 between two devices and 0.28 to 0.69 between two test sessions. The Kinect V2 was able to provide valid and reliable spatiotemporal gait parameters, and it could also offer accurate outcome measures for the minimum MOS. The reliability of the Kinect V2 when assessing time-specific MOS variables was limited. The Kinect V2 shows the potential to be used as a cost-effective tool for CP gait stability assessment.

PMID: [33802731](#)

17. Early intervention evidence for infants with or at risk for cerebral palsy: an overview of systematic reviews

Diane L Damiano, Egmar Longo

Review Dev Med Child Neurol. 2021 Apr 6. doi: 10.1111/dmcn.14855.

Aim: To perform an overview of systematic reviews and more recent randomized controlled trials (RCTs) on early motor interventions in infants aged 0 to 3 years with or at risk of cerebral palsy to inform current clinical and research efforts and provide a benchmark to assess future interventions ideally initiated within the first 6 months. **Method:** Standardized searches of the PubMed, Embase, Scopus, and Web of Science databases were conducted for systematic reviews (2009-2020) and RCTs (2015-2020). **Results:** From 840 unique records, 31 full texts were reviewed, yielding three systematic reviews encompassing 46 studies, 16 with comparison groups, and six additional RCTs that met the criteria. Two enrichment- and activity-based approaches had medium effect sizes on motor development, only one with low risk of bias; two others had large task-specific effect sizes but some bias concerns; and three enriched environment studies with some bias concerns had medium effect sizes on cognitive development. Most had small or no effect sizes, bias concerns, and uncertain diagnostic determinations. **Interpretation:** Data synthesis revealed limited data quantity and quality, and suggest, although not yet confirmed, greater benefit from early versus later intervention. Research efforts with greater early diagnostic precision and earlier intervention are accelerating, which may transform future outcomes and practices.

PMID: [33825199](#)

18. Early intervention for infants at high risk for cerebral palsy: evidently important, but where's the evidence?

Anna Purna Basu

Dev Med Child Neurol. 2021 Apr 6. doi: 10.1111/dmcn.14875.

PMID: [33825191](#)

19. Acupuncture for drooling in children with cerebral palsy: A protocol for systematic review

Wei Xiong, Ling Cheng, Genhua Tang, Xinju Hou, Manhua Zhu, Lunbin Lu, Zhiying Zhong

Medicine (Baltimore). 2021 Apr 9;100(14):e25393. doi: 10.1097/MD.00000000000025393.

Background: The aim of this study is to provide the methods used to evaluate the effectiveness and safety of acupuncture therapy for treating drooling in children with cerebral palsy. **Methods and analysis:** A comprehensive search of Pubmed, Embase, Cochrane Central Register of Controlled Trials, Web of Science, 4 Chinese databases (China National Knowledge Infrastructure, Chinese Biomedical Literatures database, Wan-Fang Database and Chinese Science and Technology Periodicals) will be conducted to identify randomized controlled trials of acupuncture for treating children with cerebral palsy salivation with no restriction on time or language. The primary outcome of this systematic review will be the effective rate. The risk of bias will be implemented according to Cochrane Handbook for Systematic Reviews of Interventions. We will conduct the meta-analysis to synthesize the evidence for each outcome, if possible. The heterogeneity will be evaluated statistically using the χ^2 test and the I² statistic. The random-effect model will be used to provide more conservative results, if significant heterogeneity is identified (I² > 50% or P < .10). **Ethics/dissemination:** Our findings will be disseminated in a peer-reviewed journal and at conference meetings. It is not necessary for formal ethical approval as no primary data are collected.

PMID: [33832131](#)

20. The relationship between breast milk intake and speech in children with cerebral palsy

Gül Demet Kaya Özçora

Turk J Med Sci. 2021 Apr 6. doi: 10.3906/sag-2011-43.

Purpose: To assess the relationship between breast milk intake and speech functions in children with cerebral palsy. **Methods:** We performed a cross-sectional, observational study of children with cerebral palsy aged over 4 years. The clinical features and the variables regarding breast milk intake were abstracted from medical records and mothers' reviews. The Gross Motor Function Classification System (GMFCS) and the Viking Speech Scale (VSS) were used to categorize children based on motor and speech functions. **Results:** A total of 251 children with cerebral palsy were included. The mean duration of exclusive breast milk intake was 56.9 (range, 0-180) days. The mean duration of total breast milk intake was 7.4 (range, 0-36) months. Forty-three children (17%) received no breast milk. There was a weak positive correlation between birth weight and the level of VSS, indicating better speech function in children with lower birth weight. The preterm-born children presented significantly lower levels of VSS than term-born children. There was a negative moderate correlation between the duration of exclusive breast milk intake and the total duration of breast milk intake with the level of VSS. **Conclusion:** We found that the duration of breast milk intake might reflect motor function and predict speech performance in children with cerebral palsy.

PMID: [33819974](#)

21. "Capturing the magic": identifying the active ingredients of a physical activity participation intervention for children and youth with disabilities

Claire Willis, Catherine Elliott, Siobhan Reid, Astrid Nyquist, Reidun Jahnsen, Sven Bölte, Michael Rosenberg, Sonya Girdler

Disabil Rehabil. 2021 Apr 5;1-10. doi: 10.1080/09638288.2021.1907458.

Purpose: This study aimed to define the active ingredients of a participation-focused physical activity intervention for children and youth with disabilities. **Materials and methods:** An ethnographic approach was employed, triangulating participant observation, interviews and focus groups. Participant recruitment occurred through purposive sampling of staff employed at Beitostolen Healthsports Centre (BHC), and paediatric service providers visiting the centre. Interviews were transcribed verbatim and coded together with observation data. Secondary coding linked data to corresponding categories of the International Classification of Functioning, Disability and Health: Child and Youth version. **Results:** Thirteen staff from BHC and 7 paediatric service providers participated in the study. Fourteen active ingredients were identified and were characterised at the level of the intervention ($k = 8$), the organisation ($k = 4$), and the individual ($k = 2$). Within the ingredients, 53 unique ICF-CY categories were identified. Twenty-six categories belonged to the ICF-CY component of "environment," and 26 categories to "activities and participation." No categories related to "body functions" or "body structures." **Conclusions:** The role of the environment, and specifically support and relationships, may be an essential consideration for enabling physical activity participation. Outcomes may guide program design and implementation to promote and sustain physical activity behaviours for children and youth with disabilities. **Implications for rehabilitation:** The active ingredients identified in this study may guide the design and implementation of programs to promote and sustain physical activity behaviours of children and youth with disabilities. Leadership qualities and strength-based attitudes may be key characteristics of organisational practice that optimise outcomes for children and families. A "relationship-centred" approach, i.e., a network of children, families, health professionals, peers, mentors, and services in the community, may support children and young people with disabilities to achieve their physical activity participation goals.

PMID: [33820452](#)

22. Constraint-induced intervention as an emergent phenomenon from synaptic competition in biological systems

Won J Sohn, Terence D Sanger

J Comput Neurosci. 2021 Apr 6. doi: 10.1007/s10827-021-00782-9.

The principle of constraint-induced therapy is widely practiced in rehabilitation. In hemiplegic cerebral palsy (CP) with impaired contralateral corticospinal projection due to unilateral injury, function improves after imposing a temporary constraint on limbs from the less affected hemisphere. This type of partially-reversible impairment in motor control by early brain injury bears a resemblance to the experience-dependent plastic acquisition and modification of neuronal response selectivity in the visual cortex. Previously, such mechanism was modeled within the framework of BCM (Bienenstock-Cooper-Munro) theory, a rate-based synaptic modification theory. Here, we demonstrate a minimally complex yet sufficient neural network model which provides a fundamental explanation for inter-hemispheric competition using a simplified spike-based model of information transmission and plasticity. We emulate the restoration of function in hemiplegic CP by simulating the competition between cells of the ipsilateral and contralateral corticospinal tracts. We use a high-speed hardware neural simulation to provide realistic numbers of spikes and realistic magnitudes of synaptic modification. We demonstrate that the phenomenon of constraint-induced partial reversal of hemiplegia can be modeled by simplified neural descending tracts with 2 layers of spiking neurons and synapses with spike-timing-dependent plasticity (STDP). We further demonstrate that persistent hemiplegia following unilateral cortical inactivation or deprivation is predicted by the STDP-based model but is inconsistent with BCM model. Although our model is a highly simplified and limited representation of the corticospinal system, it offers an explanation of how constraint as an intervention can help the system to escape from a suboptimal solution. This is a display of an emergent phenomenon from the synaptic competition.

PMID: [33825082](#)

23. Integration of Motor Learning Principles Into Virtual Reality Interventions for Individuals With Cerebral Palsy: Systematic Review

Marika Demers, Karen Fung, Sandeep K Subramanian, Martin Lemay, Maxime T Robert

JMIR Serious Games. 2021 Apr 7;9(2):e23822. doi: 10.2196/23822.

Background: Increasing evidence supports the use of virtual reality systems to improve upper limb motor functions in individuals with cerebral palsy. While virtual reality offers the possibility to include key components to promote motor learning, it remains unclear if and how motor learning principles are incorporated into the development of rehabilitation interventions using virtual reality. **Objective:** The objective of this study was to determine the extent to which motor learning principles are integrated into virtual reality interventions targeting upper limb function in individuals with cerebral palsy. **Methods:** A systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The search was performed in 10 databases using a combination of keywords related to cerebral palsy, virtual reality, video games, and rehabilitation. Studies were divided into 2 categories: commercial video game platforms and devices and custom virtual reality systems. Study quality was assessed using the modified Downs and Black checklist. **Results:** The initial search yielded 1497 publications. A total of 26 studies from 30 publications were included, with most studies classified as "fair" according to the modified Downs and Black checklist. The majority of studies provided enhanced feedback and variable practice and used functionally relevant and motivating virtual tasks. The dosage varied greatly (total training time ranged from 300 to 3360 minutes), with only 6 studies reporting the number of movement repetitions per session. The difficulty progression and the assessment of skills retention and transfer were poorly incorporated, especially for the commercial video games. **Conclusions:** Motor learning principles should be better integrated into the development of future virtual reality systems for optimal upper limb motor recovery in individuals with cerebral palsy.

PMID: [33825690](https://pubmed.ncbi.nlm.nih.gov/33825690/)

24. Overground Robot-Assisted Gait Training for Pediatric Cerebral Palsy

Seung Ki Kim, Dongho Park, Beomki Yoo, Dain Shim, Joong-On Choi, Tae Young Choi, Eun Sook Park

Sensors (Basel). 2021 Mar 16;21(6):2087. doi: 10.3390/s21062087.

The untethered exoskeletal robot provides patients with the freest and realistic walking experience by assisting them based on their intended movement. However, few previous studies have reported the effect of robot-assisted gait training (RAGT) using wearable exoskeleton in children with cerebral palsy (CP). This pilot study evaluated the effect of overground RAGT using an untethered torque-assisted exoskeletal wearable robot for children with CP. Three children with bilateral spastic CP were recruited. The robot generates assistive torques according to gait phases automatically detected by force sensors: flexion torque during the swing phase and extension torque during the stance phase at hip and knee joints. The overground RAGT was conducted for 17~20 sessions (60 min per session) in each child. The evaluation was performed without wearing a robot before and after the training to measure (1) the motor functions using the gross motor function measure and the pediatric balance scale and (2) the gait performance using instrumented gait analysis, the 6-min walk test, and oxygen consumption measurement. All three participants showed improvement in gross motor function measure after training. Spatiotemporal parameters of gait analysis improved in participant P1 (9-year-old girl, GMFCS II) and participant P2 (13-year-old boy, GMFCS III). In addition, they walked faster and farther with lower oxygen consumption during the 6-min walk test after the training. Although participant P3 (16-year-old girl, GMFCS IV) needed the continuous help of a therapist for stepping at baseline, she was able to walk with the platform walker independently after the training. Overground RAGT using a torque-assisted exoskeletal wearable robot seems to be promising for improving gross motor function, walking speed, gait endurance, and gait efficiency in children with CP. In addition, it was safe and feasible even for children with severe motor impairment (GMFCS IV).

PMID: [33809758](#)

25. Leap Motion Controller Video Game-Based Therapy for Upper Extremity Motor Recovery in Patients with Central Nervous System Diseases. A Systematic Review with Meta-Analysis

Irene Cortés-Pérez, Noelia Zagalaz-Anula, Desirée Montoro-Cárdenas, Rafael Lomas-Vega, Esteban Obrero-Gaitán, María Catalina Osuna-Pérez

Review Sensors (Basel). 2021 Mar 15;21(6):2065. doi: 10.3390/s21062065.

Leap Motion Controller (LMC) is a virtual reality device that can be used in the rehabilitation of central nervous system disease (CNSD) motor impairments. This review aimed to evaluate the effect of video game-based therapy with LMC on the recovery of upper extremity (UE) motor function in patients with CNSD. A systematic review with meta-analysis was performed in PubMed Medline, Web of Science, Scopus, CINAHL, and PEDro. We included five randomized controlled trials (RCTs) of patients with CNSD in which LMC was used as experimental therapy compared to conventional therapy (CT) to restore UE motor function. Pooled effects were estimated with Cohen's standardized mean difference (SMD) and its 95% confidence interval (95% CI). At first, in patients with stroke, LMC showed low-quality evidence of a large effect on UE mobility (SMD = 0.96; 95% CI = 0.47, 1.45). In combination with CT, LMC showed very low-quality evidence of a large effect on UE mobility (SMD = 1.34; 95% CI = 0.49, 2.19) and the UE mobility-oriented task (SMD = 1.26; 95% CI = 0.42, 2.10). Second, in patients with non-acute CNSD (cerebral palsy, multiple sclerosis, and Parkinson's disease), LMC showed low-quality evidence of a medium effect on grip strength (GS) (SMD = 0.47; 95% CI = 0.03, 0.90) and on gross motor dexterity (GMD) (SMD = 0.73; 95% CI = 0.28, 1.17) in the most affected UE. In combination with CT, LMC showed very low-quality evidence of a high effect in the most affected UE on GMD (SMD = 0.80; 95% CI = 0.06, 1.15) and fine motor dexterity (FMD) (SMD = 0.82; 95% CI = 0.07, 1.57). In stroke, LMC improved UE mobility and UE mobility-oriented tasks, and in non-acute CNSD, LMC improved the GS and GMD of the most affected UE and FMD when it was used with CT.

PMID: [33804247](#)

26. Benefits of a Low-Cost Walking Device in Children with Cerebral Palsy: A Qualitative Study

Isabel Rodríguez-Costa, Irene De la Cruz-López, Ignacio Fernández-Zárate, Saturnino Maldonado-Bascón, Sergio Lafuente-Arroyo, Susana Nunez-Nagy

Int J Environ Res Public Health. 2021 Mar 10;18(6):2808. doi: 10.3390/ijerph18062808.

Children with Cerebral Palsy (CP) participate less regularly in physical and social activities. Support walkers allow mobility for infants who need aid. The aim of this study is to explore the benefits of a low-cost walking device in children with CP. A qualitative study using semi-structured, face-to-face interviews was conducted. Eight participants (two parents, two educational professionals, and four physical therapists) who live or work with children with CP that use a low-cost walking device were questioned to examine the benefits of the practice. Thematic analysis denoted three key factors about the benefits: emotional welfare, physical wellbeing, and social enjoyment. To conclude, the use of a support walker in children with CP makes them feel happier, improves their self-confidence and autonomy, and promotes participation.

PMID: [33801985](#)

27. Neurodevelopmental Outcomes of Preterm Infants Conceived by Assisted Reproductive Technology

Smita Roychoudhury, Abhay Lodha, Anne Synnes, Ayman Abou Mehrem, Roderick Canning, Rudaina Banihani, Marc Beltempo, Katherine Theriault, Junmin Yang, Prakesh S Shah, Amuchou S Soraisham, Canadian Neonatal Network (CNN), Canadian Preterm Birth Network (CPTBN), and Canadian Neonatal Follow-Up Network (CNFUN) Investigators

Am J Obstet Gynecol. 2021 Mar 30;S0002-9378(21)00207-6. doi: 10.1016/j.ajog.2021.03.027.

Background: There have been concerns about potential adverse consequences of assisted reproductive technology on the development of children conceived in this way. Despite multiple studies investigating the outcomes of assisted conception, data focusing specifically on the neurodevelopmental outcomes of infants conceived with assisted reproductive technology and born preterm are limited. **Objective:** To evaluate and compare the neurodevelopmental outcomes at 18 to 24 months' corrected age of preterm infants born <29 weeks' gestational age who were conceived by assisted reproductive technology and those who were conceived naturally. **Study design:** This retrospective cohort study included inborn, non-anomalous infants, born at <29 weeks' gestation between January 1, 2010 and December 31, 2016, who had a neurodevelopmental assessment at 18 to 24 months' corrected age at any of 10 Canadian Neonatal Follow-Up Network clinics. The primary outcome was neurodevelopmental impairment at 18 to 24 months, defined as the presence of any of the following: cerebral palsy; Bayley-III cognitive, motor, or language composite score of <85; sensorineural or mixed hearing loss; and unilateral or bilateral visual impairment. Secondary outcomes included mortality, composite of mortality or neurodevelopmental impairment, significant neurodevelopmental impairment, and each component of the primary outcome. We compared outcomes between infants conceived by assisted reproductive technology and those conceived naturally, using bivariate and multivariable analyses after adjustment. **Results:** Of the 4863 eligible neonates, 651 (13.4%) were conceived using assisted reproductive technology. Maternal age; education level; and rates of diabetes, receipt of antenatal corticosteroids, and cesarean section were higher in the assisted reproduction group compared to the natural conception group. Neonatal morbidity and death rates were similar except for intraventricular hemorrhage, which was lower in the assisted reproduction group [181/546 (33%) vs 1284/3318(39%)], $P = 0.01$). Of the 4176 surviving infants, 3386 (81%) had follow up outcome at 18 to 24 months' corrected age. Multivariable logistic regression adjusting for gestational age, antenatal steroids, sex, small for gestational age, multiple gestations, mode of delivery, maternal age, maternal education, pregnancy-induced hypertension, maternal diabetes, and smoking showed that infants conceived through assisted reproduction was associated with lower odds of neurodevelopmental impairment (adjusted odds ratio, 0.67; 95% confidence interval, 0.52-0.86) and the composite of death or neurodevelopmental impairment (adjusted odds ratio, 0.67; 95% confidence interval, 0.54-0.84). Being conceived through assisted reproductive technology was associated with decreased odds of a Bayley-III composite cognitive score <85 (adjusted odds ratio, 0.68; 95% confidence interval, 0.48-0.99), and composite language score <85 (adjusted odds ratio, 0.67; 95% confidence interval, 0.50-0.88). **Conclusions:** Compared with natural conception, assisted conception was associated with lower odds of adverse neurodevelopmental outcomes, especially cognitive and language outcomes, at 18 to 24 months' corrected age among preterm infants born <29 weeks' gestation. Longer-term follow up studies are required to assess the risks of learning disabilities and development of complex visual-spatial and processing skills in these children as they reach school age.

PMID: [33798481](#)

28. The effects of exergames on muscle strength: A systematic review and meta-analysis

Ricardo Borges Viana, Vinnycius Nunes de Oliveira, Scott J Dankel, Jeremy P Loenneke, Takashi Abe, Wellington Fernando da Silva, Naiane Silva Morais, Rodrigo Luiz Vancini, Marília Santos Andrade, Claudio Andre Barbosa de Lira

Review Scand J Med Sci Sports. 2021 Apr 2. doi: 10.1111/sms.13964.

This systematic review and meta-analysis examined studies on the chronic effects of exergames on muscle strength in humans. PubMed, Scopus, CENTRAL, Web of Science, SciELO, Biblioteca Virtual em Saúde, and Google Scholar were searched, and manual searches of the reference lists of included studies and hand-searches on Physiotherapy Evidence Database and ResearchGate were conducted from inception to August 10, 2020. Randomized and non-randomized exergame intervention studies with or without a non-exercise group and/or a "usual care intervention group" (any other intervention that did not

incorporate exergames), which evaluated muscle strength through direct measurements, were included. Forty-seven and 25 studies were included in the qualitative review and meta-analysis, respectively. The between-groups meta-analyses showed no significant differences between exergames and non-exercise control groups for handgrip strength in healthy/unhealthy middle-aged/older adults or knee extension maximum voluntary isometric contraction (MVIC) in healthy older adults. However, exergames provided a greater increase in handgrip strength, knee flexion MVIC, and elbow extension MVIC, but not knee extension MVIC or elbow flexion MVIC, in individuals with different health statuses when compared to usual care interventions. Also, there was a greater increase in handgrip strength in children with hemiplegic cerebral palsy favouring usual care plus exergames compared to usual care interventions. These results suggest that exergames may improve upper and lower limb muscle strength in individuals with different health statuses compared to usual care interventions, but not muscle strength in middle age/older adults after accounting for random error. Also, exergames appear to be a useful tool for improving handgrip strength in children with hemiplegic cerebral palsy when added to usual care. However, as the exergame interventions were applied in different populations and there currently are many different approaches to perform exergames, future randomized controlled trials with high methodological quality and large sample sizes are needed to provide more compelling evidence in favour of a specific exergame protocol, or to elucidate exergame protocol design principles that appear to strongly influence outcomes.

PMID: [33797115](#)

29. Pattern of comorbidities in school-aged children with cerebral palsy in Cross River State, Nigeria

Roseline E Duke, Chimaeze Torty, Uche Okorie, Min J Kim, Nnena Eneli, Ukam Edadi, Kathryn Burton, Cally Tann, Richard Bowman

BMC Pediatr. 2021 Apr 8;21(1):165. doi: 10.1186/s12887-021-02637-9.

Background: To describe the pattern of comorbidities in school-aged children with cerebral palsy (CP) and to identify which, if any, were associated with poor school attendance. A cross-sectional study, using the key informant methodology, between December 2017 and July 2018 was conducted in Cross River State, Nigeria. Assessments, confirmation of CP and identification of systemic comorbidities using standard tools and questionnaires were performed. Children confirmed to have CP between the ages 4 to 15 years were included. **Results:** Three hundred and eighty-eight children were confirmed to have CP, 59% males. The mean age was 9.2 years \pm SD 4.0; 28% were non-ambulatory (gross motor function classification system (GMFCS) level IV-V) and spastic CP was seen in 70%. Comorbidities included Speech impairment 85%, feeding difficulties 86%, and swallowing difficulties 77%, learning difficulties 88%, abnormal behaviour 62%, visual acuity impairment 54%, objective perceptual visual disorders 46%, communication difficulties 45%, epilepsy 35%, hearing impairment 12% and malnutrition 51%. Learning difficulties (OR 10.1, $p < 0.001$; CI: 3.6-28.1), visual acuity impairment (OR 2.8, $p = 0.002$; CI: 1.5-5.3), epilepsy (OR 2.3, $p = 0.009$; CI:1.2-4.3) manual ability classification scale 4-5 (OR 4.7, $p = 0.049$; CI:1.0-22.2) and CP severity (GMFCS V-VI) OR 6.9 $p = 0.002$, CI: 2.0-24.0.) were seen as increasing the likelihood of poor school attendance. **Conclusion:** Comorbidities were common, and some were associated with limited school attendance. A multidisciplinary tailored approach to care, with application of available therapeutic interventions for comorbidities is suggested. This may be useful in reducing barriers to school attendance.

PMID: [33832457](#)

30. Providing Home-Based Support for Children with Chronic Conditions in an Urban Slum: Experiences from a Community-Based Palliative Care Program in Bangladesh

Mostofa Kamal Chowdhury, Khadija Shopna, Anisha Lynch-Godrei, Mehr Jain, Nadia Farheen, Noorjahan Begum, Nezamuddin Ahmad, Megan Doherty

Glob Pediatr Health. 2021 Mar 24;8:2333794X21999155. doi: 10.1177/2333794X21999155. eCollection

2021.

We describe the palliative care needs of children with chronic conditions and their caregivers in an urban slum in Bangladesh. In this cross-sectional study, we interviewed 25 caregivers whose children receive support from a community-based program lead by community health workers, that provides medication, medical supplies, food, caregiver training, and psychological support free of charge. The chronic conditions of children in the program included cerebral palsy (80%), congenital heart disease (8%), neurodegenerative conditions (4%), cancer (4%), and intellectual disabilities (4%). Common symptoms included cough or breathing problems (64%), fever (56%), and pain (56%). Most caregivers (96%) reported they were unable to do any paid work due to their child's needs and in all families, the child's condition had a significant impact on their financial situation. Community-based palliative care programs can be developed to support children with chronic conditions who may not access care from acute care facilities.

PMID: [33816710](#)

31. Evaluation of the effects of the COVID-19 pandemic on children with cerebral palsy, caregivers' quality of life, and caregivers' fear of COVID-19 with telemedicine

Damla Cankurtaran, Nihal Tezel, Sadik Yigit Yildiz, Gulnur Celik, Ece Unlu Akyuz

Ir J Med Sci. 2021 Apr 9;1-8. doi: 10.1007/s11845-021-02622-2.

Background: The sudden and unexpected pandemic changed the daily routine of the children with cerebral palsy (CP) and their caregivers. **Aims:** This study aimed to investigate the impact of the novel coronavirus (COVID-19) pandemic on the utilization of health and rehabilitation services and the general health and physical status of children with CP. In addition, the second aim of the study was to examine the effects of the COVID-19 pandemic on caregivers' quality of life (QOL) and their fear of COVID-19. **Methods:** The utilization of children health and rehabilitation services during the pandemic, the general health and physical status of the children during the pandemic, and the children and caregivers' history of COVID-19 infections were questioned. Furthermore, the caregivers' level of fear of COVID-19 and their QOL were examined. **Results:** One hundred twenty caregivers were contacted by phone, and 94 (78.33%) caregivers agreed to participate in the study. Sixty-three of 94 children (67.1%) did not attend their routine control check-up during the pandemic. Twelve children (12.8%) discontinued their physical therapy sessions during the pandemic. Caregivers physical and mental QOL significantly decreased during the pandemic ($p < 0.05$). The median of caregivers' Fear of COVID-19 scale (FCV-19S) was 17.5 (7-35). **Conclusion:** We think that more attention should be given to telerehabilitation and telemedicine services of the clinicians who deal with the children with CP, and their caregivers in order to prevent the negative effects of future pandemic periods.

PMID: [33834363](#)

32. Positive perception of stem cells for neurological conditions: results from an Australian public forum

Megan Finch-Edmondson, Madison Cb Paton, Claire Galea, Genevieve Cowie, Nadia Badawi, Rob White, Iona Novak

Regen Med. 2021 Apr 9. doi: 10.2217/rme-2020-0184.

Background: Stem cells offer great hope and promise as a potential treatment for human diseases. The aim of this study was to gain insight into the public perception of stem cells for neurological conditions. **Materials & methods:** A paper-based questionnaire was administered to all attendees of a free, public stem cell forum. **Results:** Of 203 respondents, >95% believe that stem cells have the potential to treat neurological conditions. There was also high support (92%) for the use of embryonic/fetally-derived cells, and 67% of respondents indicated a high likelihood to participate in a clinical trial of stem

cell treatment/s, indicating overall support for research and translation. **Conclusion:** Our data demonstrates a positive perception of stem cell treatments for neurological conditions in our cohort.

PMID: [33834843](#)

33. "It Should Have Been Given Sooner, and We Should Not Have to Fight for It": A Mixed-Methods Study of the Experience of Diagnosis and Early Management of Cerebral Palsy

Sian A Williams, Woroud Alzاهر, Anna Mackey, Amy Hogan, Malcolm Battin, Alexandra Sorhage, N Susan Stott

J Clin Med. 2021 Mar 31;10(7):1398. doi: 10.3390/jcm10071398.

Listening to the family experience is integral to identifying areas of strength and for improvement in health service delivery around diagnosis and early management of cerebral palsy (CP). Families of children with a diagnosis of CP were invited to complete a purpose-developed electronic survey that included items around the timing of diagnosis, their experiences and satisfaction. It also allowed families to expand on their experiences through free text. Of the 57 families responding, 49% of children functioned at Gross Motor Function Classification System (GMFCS) levels I or II, 8% at GMFCS level III and 23% at GMFCS levels IV or V. 51% of participants were satisfied or very satisfied with the diagnosis experience, 18% were neutral about the experience and 31% were dissatisfied or very dissatisfied. Though the findings of this study may be subject to selection bias, perceived delays in the receipt of diagnosis of CP appeared common with 60% of participants indicating concerns about their child by <6 months of age but only 21% provided with a diagnosis of CP <6 months of age. Approximately 18% of families experienced a delay of more than 12 months. Thirty-four (61%) participants noted a delay between referrals to a service and receipt of service management/therapy. Common themes impacting on families' experience in the diagnosis and health service delivery journey related to provision of information, and the style of communication, with both direct and ongoing communication styles common for greater family satisfaction. Overall, families desired the diagnosis experience to be informative and timely, with early follow up support and assistance with health sector navigation.

PMID: [33807393](#)

34. Atypical Presentation of Cerebral Palsy and Seizures: A Case Report on Rasmussen's Encephalitis in an Adolescent

Naveed S Noordin, Logan J Deyo, Connor W Ryon, Willie T Anderson

Case Reports Cureus. 2021 Mar 4;13(3):e13705. doi: 10.7759/cureus.13705.

Rasmussen's encephalitis is a rare neurological disease first described in 1958 that is characterized by medico-refractory seizures, focal unilateral cerebral inflammation, and deficits such as hemiparesis. While we still do not have a full understanding of this disease, proposed theories behind its etiology include auto-immune manifestations, immune attack by T cells, and malfunctioned alterations in genetic expression. It is classically considered a rare childhood malady with a median age of onset of six years, and cases in adolescents and adults are even rarer, representing up to 10% of all cases to date. In this report, we would like to share a rare case of Rasmussen's encephalitis that occurred in an adolescent. Our 17-year-old male patient presented with signs and symptoms beginning at age 14 and was initially diagnosed with cerebral palsy only to later present with additional symptoms and characteristic EEG and MRI findings that ultimately led to a diagnosis of Rasmussen's encephalitis. Thus, with this case report, our intent is twofold: to shed light on an atypical presentation of an already rare disease, even rarer in adolescents and adults, and to underscore the importance of keeping a broad differential when it comes to evaluating a patient with seizures.

PMID: [33824839](#)

35. Botulinum Toxin A and Osteosarcopenia in Experimental Animals: A Scoping Review

Min Jia Tang, H Kerr Graham, Kelsey E Davidson

Review Toxins (Basel). 2021 Mar 14;13(3):213. doi: 10.3390/toxins13030213.

We conducted a scoping review to investigate the effects of intramuscular injection of Botulinum Toxin A (BoNT-A) on bone morphology. We investigated if the muscle atrophy associated with Injection of BoNT-A had effects on the neighboring bone. We used the search terms: osteopenia, bone atrophy, Botulinum Toxin A, Micro-CT, mice or rat. The following databases were searched: Medline, Embase, PubMed and the Cochrane Library, between 1990 and 2020. After removal of duplicates, 228 abstracts were identified of which 49 studies satisfied our inclusion and exclusion criteria. The majority of studies (41/49) reported a quantitative reduction in at least one measure of bone architecture based on Micro-CT. The reduction in the ratio of bone volume to tissue volume varied from 11% to 81% (mean 43%) according to the experimental set up and study time points. While longer term studies showed muscle recovery, no study showed complete recovery of all bone properties at the termination of the study. In experimental animals, intramuscular injection of BoNT-A resulted in acute muscle atrophy and acute degradation of the neighboring bone segment. These findings may have implications for clinical protocols in the use of Botulinum Toxin in children with cerebral palsy, with restraint recommended in injection protocols and consideration for monitoring bone density. Clinical studies in children with cerebral palsy receiving injections of Botulinum are indicated.

PMID: [33799488](#)

36. [Rule of point selection in treatment of cerebral palsy in children with acupuncture based on data mining of 1584 electronic medical records] [Article in Chinese]

Zi-Jun Mou, Li-Yun He, Hu-Jie Song, Qiu Cheng, Bao-Yan Liu

Zhongguo Zhen Jiu. 2021 Mar 12;41(3):355-8. doi: 10.13703/j.0255-2930.20200410-k0006.

Objective: To explore the rule of point selection in treatment of cerebral palsy with acupuncture in preschool children. Methods: Based on the electronic medical records of Xi'an Encephalopathy Hospital of TCM, through structuring medical record text, acupuncture prescriptions were extracted. Using the data mining tools of the ancient and modern medical record cloud platform V2.2.3 and the clinical effective prescription and molecular mechanism analysis system of traditional Chinese medicine V2.0, the cluster analysis and complex network analysis were conducted on acupuncture prescriptions. Results: Of 1584 acupuncture prescriptions for cerebral palsy in children, there were 84 acupoints and stimulating areas of scalp acupuncture, of which, foot-motor-sensory area, balance area and Sanyinjiao (SP 6) were the top 3 acupoints with the highest use rate. With cluster analysis, 5 groups of common supplementary acupoints and stimulating areas were found, named, Weizhong (BL 40) and Waiguan (TE 5), Shousanli (LI 10), Xingjian (LR 2), Xuanzhong (GB 39) and Chengfu (BL 36), foot-motor-sensory area, balance area and Sanyinjiao (SP 6), Xuehai (SP 10) and Fenglong (ST 40), Pishu (BL 20), motor area and Yanglingquan (GB 34). With complex network analysis on core prescriptions, 13 core acupoints and stimulating areas of scalp acupuncture were obtained, including 3 core main points, i.e. Sanyinjiao (SP 6), balance area and foot-motor-sensory area and 10 sub-core points, i.e. Taichong (LR 3), motor area, Xuehai (SP 10), Ganshu (BL 18), Pishu (BL 20), Yanglingquan (GB 34), Sishencong (EX-HN 1), Baihui (GV 20), Fengchi (GB 20) and Shenshu (BL 23). Conclusion: In treatment of acupuncture for cerebral palsy in preschool children, the core prescriptions reveal the simultaneous treatment of exterior and interior, the mutual regulation of yin and yang and the combination of acupoints with stimulating areas of scalp acupuncture for both encephalopathy and paralysis.

PMID: [33798325](#)

37. Modelling extracellular matrix and cellular contributions to whole muscle mechanics

Ryan N Konno, Nilima Nigam, James M Wakeling

PLoS One. 2021 Apr 2;16(4):e0249601. doi: 10.1371/journal.pone.0249601. eCollection 2021.

Skeletal muscle tissue has a highly complex and heterogeneous structure comprising several physical length scales. In the simplest model of muscle tissue, it can be represented as a one dimensional nonlinear spring in the direction of muscle fibres. However, at the finest level, muscle tissue includes a complex network of collagen fibres, actin and myosin proteins, and other cellular materials. This study shall derive an intermediate physical model which encapsulates the major contributions of the muscle components to the elastic response apart from activation-related along-fibre responses. The micro-mechanical factors in skeletal muscle tissue (eg. connective tissue, fluid, and fibres) can be homogenized into one material aggregate that will capture the behaviour of the combination of material components. In order to do this, the corresponding volume fractions for each type of material need to be determined by comparing the stress-strain relationship for a volume containing each material. This results in a model that accounts for the micro-mechanical features found in muscle and can therefore be used to analyze effects of neuro-muscular diseases such as cerebral palsy or muscular dystrophies. The purpose of this study is to construct a model of muscle tissue that, through choosing the correct material parameters based on experimental data, will accurately capture the mechanical behaviour of whole muscle. This model is then used to look at the impacts of the bulk modulus and material parameters on muscle deformation and strain energy-density distributions.

PMID: [33798249](#)

38. Transitional milestones and developmental challenges for adults with cerebral palsy

Reuben Escorpizo

Dev Med Child Neurol. 2021 Apr 8. doi: 10.1111/dmcn.14894.

PMID: [33834496](#)

39. The Whitney Comorbidity Index for adults with cerebral palsy: a challenge for practice

Dev Med Child Neurol. 2021 Apr 8. doi: 10.1111/dmcn.14890.

Sander R Hilberink

PMID: [33834477](#)

40. Whitney Comorbidity Index to monitor health status for adults with cerebral palsy: validation and thresholds to assist clinical decision making

Daniel G Whitney, Tanima Basu

Dev Med Child Neurol. 2021 Apr 7. doi: 10.1111/dmcn.14879.

Aim: To validate the Whitney Comorbidity Index (WCI), which was recently developed to monitor disease status for adults with cerebral palsy (CP), and to identify WCI scores associated with an increased mortality risk using a representative sample of adults with CP. **Method:** Data from 2016 to 2018 were used from a random 20% sample from the fee-for-service Medicare database for this retrospective cohort study. The WCI was examined as unweighted (WCI_{unw}) and weighted (WCI_w) among adults at least 18 years old with CP. Cox regression models were developed with mortality as the outcome after adjusting for demographics. A concordance statistic (C-statistic) of at least 0.70 was considered as showing sufficient validity. The hazard ratio of mortality for each WCI score was estimated. Secondary analyses were performed for subgroups with co-occurring epilepsy and/or intellectual disabilities. **Results:** For the entire group (n=16 728) and subgroups, the WCI showed sufficient validity (C-statistic 0.73-0.81). For the entire group, the mortality rate was elevated for a score of 1 compared with 0 from the WCI_{unw} (hazard ratio 3.06; 95% confidence interval [CI] 1.52-6.17) and WCI_w (hazard ratio 4.08; 95% CI 1.69-9.85), and

became larger with each WCI score. Results were similar for the subgroups. Interpretation: The WCI is a valid marker for health/disease status for adults with CP. Several WCI score thresholds were identified to assist in clinical decision making for preventive medicine and intervention implementation.

PMID: [33829504](#)

41. Hammersmith Infant Neurological Examination and long-term cognitive outcome in children born very preterm

Karoliina Uusitalo, Leena Haataja, Anna Nyman, Tuomo Lehtonen, Sirkku Setänen, PIPARI Study Group
Dev Med Child Neurol. 2021 Apr 8. doi: 10.1111/dmcn.14873.

Aim: To study the association between the Hammersmith Infant Neurological Examination (HINE) at age 2 years and neurocognition at age 11 years in children born very preterm. We hypothesized that the HINE at 2 years would be associated with neurocognition, that is, neurological, motor, and cognitive outcomes at 11 years. **Method:** A total of 174 children (mean gestational age 29.0wks, SD 2.7; minimum 23.0, maximum 35.9; 95 [55%] males, 79 [45%] females) born very preterm (birthweight \leq 1500g/gestational age <32wks), were included in a prospective cohort recruited from 2001 to 2006 in Turku, Finland. The HINE was performed at 2 years' corrected age. Neurocognition at 11 years was assessed with the Touwen Infant Neurological Examination (TINE), Movement Assessment Battery for Children, Second Edition (MABC-2), and full-scale IQ (Wechsler Intelligence Scale for Children, Fourth Edition). **Results:** The HINE global score was associated with the results of the TINE (odds ratio [OR]=0.9, 95% confidence interval [CI] 0.8-0.9, $p=0.001$), MABC-2 ($\beta=1.4$, 95% CI 0.7-2.2, $p<0.001$), and full-scale IQ ($\beta=1.2$, 95% CI 0.8-1.7, $p<0.001$), even when adjusted. When children with cerebral palsy (CP) were excluded, the HINE was still associated with full-scale IQ (unadjusted $\beta=1.2$, 95% CI 0.3-2.1, $p=0.01$). **Interpretation:** A higher HINE global score at 2 years was associated with better general intelligence at 11 years even in children without CP. The HINE may be a useful tool to detect children at risk for later cognitive impairment.

PMID: [33834473](#)

42. Prognostic value of brain abnormalities for cognitive functioning in cerebral palsy: A prospective cohort study

Irene Moll, Jeanine M Voorman, Marjolijn Ketelaar, Petra E van Schie, Jan Willem Gorter, Maarten H Lequin, Linda S de Vries, R Jeroen Vermeulen

Eur J Paediatr Neurol. 2021 Mar 16;32:56-65. doi: 10.1016/j.ejpn.2021.03.010.

Introduction: Brain abnormalities in cerebral palsy (CP) are known to relate to motor outcome; however, their association with cognitive functioning is less clear. **Aim of the study:** 1) To investigate the prognostic value of brain abnormalities for cognitive functioning; 2) To explore the added value of prognostic variables across ICF domains: motor function, epilepsy, gestational age, birthweight and educational level of the parents. **Methods:** We retrospectively analyzed brain MRI scans of 75 children with CP (GMFCS level I-V, 36% born preterm), as part of a longitudinal study. **MRI classification:** qualitative classification of brain abnormality pattern and semi-quantitative grading of the extent of damage. Cognitive functioning, measured as non-verbal intelligent quotient (IQ), was dichotomized into 'impaired cognition' (IQ \leq 70) and 'normal' (IQ > 70). Multivariable logistic regression produced odds ratios (OR) with 95% confidence interval (C.I.) of risk factors for impaired cognition. **Results:** Overall, 27% of the tested participants had a non-verbal IQ below 70 and 36% of the participants was classified as 'having impaired cognition'. At a young age, a higher degree of white matter damage (OR 1.6, 95% C.I. 0.97-2.67) and a more severe GMFCS level (OR 3.2, 95% C.I. 1.70-5.98) are risk factors for impaired cognition at school-age (4-7 years of age). This model correctly predicts 89% of the cases. Brain damage alone predicts the presence of impaired cognition in 71% of the cases. **Interpretation:** Brain MRI characteristics and GMFCS level at a young age can each help identify children with CP at risk for impaired cognition at school age and together have a strong predictive value.

PMID: [33819831](#)

43. Germinal Matrix-Intraventricular Hemorrhage: A Tale of Preterm Infants

Walufu Ivan Egesa, Simon Odoch, Richard Justin Odong, Gloria Nakalema, Daniel Asimwe, Eddymond Ekuk, Sabinah Twesigemukama, Munanura Turyasiima, Rachel Kwambele Lokengama, William Mugowa Waibi, Said Abdirashid, Dickson Kajoba, Patrick Kumbowi Kumbakulu
 Review Int J Pediatr. 2021 Mar 16;2021:6622598. doi: 10.1155/2021/6622598. eCollection 2021.
 Germinal matrix-intraventricular hemorrhage (GM-IVH) is a common intracranial complication in preterm infants, especially those born before 32 weeks of gestation and very-low-birth-weight infants. Hemorrhage originates in the fragile capillary network of the subependymal germinal matrix of the developing brain and may disrupt the ependymal lining and progress into the lateral cerebral ventricle. GM-IVH is associated with increased mortality and abnormal neurodevelopmental outcomes such as posthemorrhagic hydrocephalus, cerebral palsy, epilepsy, severe cognitive impairment, and visual and hearing impairment. Most affected neonates are asymptomatic, and thus, diagnosis is usually made using real-time transfontanellar ultrasound. The present review provides a synopsis of the pathogenesis, grading, incidence, risk factors, and diagnosis of GM-IVH in preterm neonates. We explore brief literature related to outcomes, management interventions, and pharmacological and nonpharmacological prevention strategies for GM-IVH and posthemorrhagic hydrocephalus.

PMID: [33815512](#)

44. Intrapartum opioid analgesia and childhood neurodevelopmental outcomes among infants born preterm

Lindsay S Robbins, William M Perez, Brian M Casey, Ms Christina T Blanchard, Alan T Tita, Lorie M Harper

Am J Obstet Gynecol MFM. 2021 Apr 5;100372. doi: 10.1016/j.ajogmf.2021.100372. Online ahead of print.

Background: There are concerns regarding neurobehavioral changes in infants exposed to parenteral opioids during labor, yet long-term neurodevelopment remains unstudied. **Objective:** We aimed to examine the association between parenteral opioids for labor analgesia and perinatal outcomes and childhood neurodevelopment until two years of age among infants born preterm. We hypothesized that intrapartum exposure to parenteral opioids is associated with impaired neurodevelopment and adverse perinatal outcomes. **Study design:** Secondary analysis of a multicenter randomized controlled trial assessing magnesium for prevention of cerebral palsy in infants at risk for preterm birth. Women delivering a singleton, non-anomalous, live infant prior to 37 weeks gestation were considered for inclusion. Women were excluded if they were missing exposure or primary outcome data, were exposed to general anesthesia, or reported use of heroin or unspecified illicit drugs. Women reporting use of non-opioid illicit drugs such as cocaine and marijuana were not excluded. Groups were compared based on exposure or non-exposure to parenteral opioids (intravenous or intramuscular) for labor analgesia. The primary outcome was any psychomotor or mental developmental delay at 24 months by Bayley Scales of Infant Development II. Secondary outcomes were BSID subdomains and adverse perinatal outcomes. Multivariable logistic regression models were performed and adjusted odds ratios with 95% confidence intervals were estimated. **Results:** Of 1,404 women included, 535 (38%) received parenteral opioids for labor analgesia. Women receiving parenteral opioids were more likely to be younger, Hispanic, and present with cervical dilation ≥ 4 cm. Parenteral opioid recipients had lower rates of illicit non-opioid drug or tobacco use, a lower rate of cesarean delivery, lower educational achievement, and were less likely to be undergoing induction. Women receiving parenteral opioids who underwent cesarean delivery were less likely to do so due to non-reassuring fetal status. In unadjusted and adjusted analyses, there were no significant differences in the primary outcome of psychomotor or mental developmental delay at two years of age (aOR 0.96, CI 0.76-1.20). The only significant difference in secondary outcomes was a shorter oxygen requirement duration in the parenteral opioid group (2 vs. 4 days, $p=0.002$). **Conclusion:**

Among a population of preterm infants vulnerable to neurologic impairment, intrapartum exposure to parenteral opioids was not associated with an increased risk of neurodevelopmental delay up to two years of age, nor did these infants have worse perinatal outcomes.

PMID: [33831589](#)

45. New Ethical Issues in Cerebral Palsy

Bernard Dan

Review Front Neurol. 2021 Mar 19;12:650653. doi: 10.3389/fneur.2021.650653. eCollection 2021.

Current societal and technological changes have added to the ethical issues faced by people with cerebral palsy. These include new representations of disability, and the current International Classification of Functioning, Disability, and Health, changes in legislation and international conventions, as well as applications of possibilities offered by robotics, brain-computer interface devices, muscles and brain stimulation techniques, wearable sensors, artificial intelligence, genetics, and more for diagnostic, therapeutic, or other purposes. These developments have changed the way we approach diagnosis, set goals for intervention, and create new opportunities. This review examines those influences on clinical practice from an ethical perspective and highlights how a principled approach to clinical bioethics can help the clinician to address ethical dilemmas that occur in practice. It also points to implications of those changes on research priorities.

PMID: [33815261](#)

46. Effects of three kinds of head acupuncture therapies on regulation of brain microenvironment and rehabilitation of nerve function in rats with cerebral palsy

Zixuan Wang, Xiangwei Fan, Kaiyun Chen, Xuefeng Yu, Jing Gao

J Tradit Chin Med. 2021 Apr;41(2):276-283.

Objective: To compare and observe the effects of three kinds of cephalic acupuncture therapies commonly used in the clinic on promoting nerve function rehabilitation in the brain microenvironment of rats with cerebral palsy. **Methods:** A negative control group, positive control group, and three cephalic acupuncture groups based on the administration of three cephalic acupuncture therapies were established. Ten experimental rats were selected from each group at 1, 2, and 3 weeks after modeling. Neuromotor function after treatment was rated according to the Basso, Beattie, and Bresnahan method. White matter fiber bundles were evaluated by head diffusion tensor imaging. The expression levels of neuron-specific enolase, microtubule-associated protein 2, and myelin basic protein in the brain tissue extract were detected by Western blot analysis and the activities of ATPases were determined using a fixed phosphorus method. **Results:** The pathological changes in brain tissue were restored and motor function scores were increased in the mice in each cephalic acupuncture group, and the expression of neuronal growth-related proteins in the brain tissue extract was significantly increased. Additionally, the activities of ATPases in the lesion area were significant enhanced ($P < 0.05$). Diffusion tensor imaging revealed that the white matter fiber bundles of mice in each cephalic acupuncture group gradually increased and recovered. The nervous system structure was significantly improved. **Conclusions:** All three acupuncture methods promoted the rehabilitation of nerve function damaged by cerebral palsy. These effects are likely related to the improved expression of nerve growth-related proteins, enhancement of ATPase activities, and regulation of the brain microenvironment.

PMID: [33825408](#)

47. [Acupuncture combined with Heixiaoyao powder for children with cerebral palsy and its effect on serum immune indexes and nerve growth related protein][Article in Chinese]

Dong-Mei Yang, Xi-Zhen Wang, Ji-Qiang Dong, Zhen-Zhen Liu, Qing Shang

Randomized Controlled Trial *Zhongguo Zhen Jiu*. 2021 Mar 12;41(3):288-92. doi: 10.13703/j.0255-2930.20200301-0002.

Objective: To observe the efficacy of acupuncture combined with Heixiaoyao powder for children with cerebral palsy (liver-qi stagnation, spleen-kidney deficiency syndrome) and its effect on serum immune indexes and nerve growth related protein. **Methods:** A total of 180 children with cerebral palsy were randomly divided into a combined group (60 cases, 2 cases dropped off), an acupuncture group (60 cases, 4 cases dropped off) and a Chinese medication group (60 cases, 5 cases dropped off). On the basis of conventional treatment, the children in the combined group were treated with acupuncture [Baihui (GV 20), Sishencong (EX-HN 1), Shenting (GV 24), Benshen (GB 13), 30 min each time, twice a day] and Heixiaoyao powder; the children in the acupuncture group were treated with acupuncture, and the children in the Chinese medication group were treated with Heixiaoyao powder, the treatment was same with the combined group. All the children were treated for 6 consecutive days and rest for 1 day, totaling for 8 weeks. The Gesell developmental schedules (GDS) and TCM symptom scores were recorded before treatment, after treatment and at 3-month, 6-month and 12-month follow-up visit; the serum immune indexes (IgA, IgG and IgM) and nerve growth related protein [myelin basic protein (MBP), high mobility group box-1 (HMGB1), neuronspecific enolase (NSE)] were detected before and after treatment. The clinical efficacy of each group was evaluated. **Results:** The total effective rate was 91.4% (53/58) in the combined group, which was higher than 80.4% (45/56) in the acupuncture group and 78.2% (43/55) in the Chinese medication group ($P<0.05$). Compared before treatment, the GDS scores in the three groups were increased and the TCM symptom scores were reduced after treatment and at 3-month, 6-month and 12-month follow-up visit ($P<0.05$). The GDS score in the combined group was higher than that in the acupuncture group and the Chinese medication group, and the TCM symptom score was lower than that in the acupuncture group and Chinese medication group ($P<0.05$). After treatment, the serum levels of IgA, IgG and IgM in the combined group were increased ($P<0.05$), and the serum levels of MBP, HMGB1 and NSE were decreased ($P<0.05$), and the improvements were superior to those in the acupuncture group and the Chinese medication group ($P<0.05$). **Conclusion:** Acupuncture combined with Heixiaoyao powder could effectively improve the development quotient in children with cerebral palsy (liver-qi stagnation, spleen-kidney deficiency syndrome), regulate the serum immune indexes and nerve growth related protein levels.

PMID: [33798312](#)

Prevention and Cure

48. Nutraceuticals in the Prevention of Neonatal Hypoxia-Ischemia: A Comprehensive Review of their Neuroprotective Properties, Mechanisms of Action and Future Directions

Marta Reyes-Corral, Noelia Sola-Idígora, Rocío de la Puerta, Joan Montaner, Patricia Ybot-González

Review *Int J Mol Sci*. 2021 Mar 3;22(5):2524. doi: 10.3390/ijms22052524.

Neonatal hypoxia-ischemia (HI) is a brain injury caused by oxygen deprivation to the brain due to birth asphyxia or reduced cerebral blood perfusion, and it often leads to lifelong limiting sequelae such as cerebral palsy, seizures, or mental retardation. HI remains one of the leading causes of neonatal mortality and morbidity worldwide, and current therapies are limited. Hypothermia has been successful in reducing mortality and some disabilities, but it is only applied to a subset of newborns that meet strict inclusion criteria. Given the unpredictable nature of the obstetric complications that contribute to neonatal HI, prophylactic treatments that prevent, rather than rescue, HI brain injury are emerging as a therapeutic alternative. Nutraceuticals are natural compounds present in the diet or used as dietary supplements that have antioxidant, anti-inflammatory, or antiapoptotic properties. This review summarizes the preclinical in vivo studies, mostly conducted on rodent models, that have investigated the neuroprotective properties

of nutraceuticals in preventing and reducing HI-induced brain damage and cognitive impairments. The natural products reviewed include polyphenols, omega-3 fatty acids, vitamins, plant-derived compounds (tanshinones, sulforaphane, and capsaicin), and endogenous compounds (melatonin, carnitine, creatine, and lactate). These nutraceuticals were administered before the damage occurred, either to the mothers as a dietary supplement during pregnancy and/or lactation or to the pups prior to HI induction. To date, very few of these nutritional interventions have been investigated in humans, but we refer to those that have been successful in reducing ischemic stroke in adults. Overall, there is a robust body of preclinical evidence that supports the neuroprotective properties of nutraceuticals, and these may represent a safe and inexpensive nutritional strategy for the prevention of neonatal HI encephalopathy.

PMID: [33802413](#)

49. Generation of GPM knockout human embryonic stem cell line SYSUe-008-A using CRISPR/Cas9

Chuanbo Sun, Bing Li, Miaomiao Yang, Ruirui Guo, Simin Yuan, Jichang Wang, Hao Hu

Stem Cell Res. 2021 Mar 19;53:102303. doi: 10.1016/j.scr.2021.102303.

GPAM (glycerol-3-phosphateacyltransferase1) is a mitochondrial enzyme that catalyze an essential step in glycerolphospholipids and triacylglycerol biosynthesis process. Loss-of-function mutation of GPAM has been shown to lead to hypomyelination of corticospinal tract in cerebral palsy patient. To model this rare disease with human brain organoid, we generated a GPAM knockout human embryonic stem cell line SYSUe-008-A by CRISPR/cas9. The GPAM knockout cell line maintains a normal karyotype and shows comparable level of pluripotent stem cell marker expression and differentiation potential as wild-type human embryonic stem cells.

PMID: [33831647](#)