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## Interventions and Management

### 1. Muscle Selection and Dosing in a Phase 3, Pivotal Study of AbobotulinumtoxinA Injection in Upper Limb Muscles in Children With Cerebral Palsy

Joyce Oleszek, Ann Tilton, Jorge Carranza Del Rio, Nigar Dursun, Marcin Bonikowski, Edward Dabrowski, Simon Page, Benjamin Regnault, Catherine Thompson, Mauricio R Delgado

Front Neurol. 2021 Oct 29;12:728615. doi: 10.3389/fneur.2021.728615. eCollection 2021.

**Background:** Guidelines recommend botulinum toxin-A in pediatric upper limb spasticity as part of routine practice. Appropriate dosing is a prerequisite for treatment success and it is important that injectors have an understanding on how to tailor dosing within a safe and effective range. We report upper limb dosing data from a phase 3 study of abobotulinumtoxinA injections in children with cerebral palsy. **Methods:** This was a double-blind, repeat-treatment study (NCT02106351). In Cycle 1, children were randomized to abobotulinumtoxinA at 2 U/kg control dose or clinically relevant 8 U/kg or 16 U/kg doses. Doses were divided between the primary target muscle group (PTMG, wrist or elbow flexors) and additional muscles tailored to clinical presentation. During Cycles 2-4, children received doses of 8 U/kg or 16 U/kg and investigators could change the PTMG and other muscles to be injected. Injection of muscles in the other upper limb and lower limbs was also permitted in cycles 2-4, with the total body dose not to exceed 30 U/kg or 1,000 U (whichever was lower) in the case of upper and lower limb treatment. **Results:** 212 children were randomized, of which 210 received  $\geq 1$  abobotulinumtoxinA injection. Per protocol, the elbow and wrist flexors were the most commonly injected upper limb muscles. Across all 4 cycles, the brachialis was injected in 89.5% of children (dose range 0.8-6 U/kg), the brachioradialis in 83.8% (0.4-3 U/kg), the flexor carpi ulnaris in 82.4% (0.5-3 U/kg) and the flexor carpi radialis in 79.5% (0.5-4 U/kg). Other frequently injected upper limb muscles were the pronator teres (70.0%, 0.3-3 U/kg), adductor pollicis (54.3%, 0.3-1 U/kg), pronator quadratus (44.8%, 0.1-2 U/kg), flexor digitorum superficialis (39.0%, 0.5-4 U/kg), flexor digitorum profundus (28.6%, 0.5-2 U), flexor pollicis brevis/opponens pollicis (27.6%, 0.3-1 U/kg) and biceps (27.1%, 0.5-6 U/kg). AbobotulinumtoxinA was well-tolerated at these doses; muscular weakness was reported in 4.3% of children in the 8 U/kg group and 5.7% in the 16 U/kg group. **Conclusions:** These data provide information on the pattern of injected muscles and dose ranges used in this study, which were well-tolerated. Per protocol, most children received injections into the elbow and wrist flexors. However, there was a wide variety of other upper limb muscles injected as physicians tailored injection patterns to clinical need.

PMID: [34803878](https://pubmed.ncbi.nlm.nih.gov/34803878/)

### 2. Percutaneous hamstring lengthening in cerebral palsy: Technique and gait outcomes based on GMFCS level

Kristan Pierz, Michael Brimacombe, Sylvia Öunpuu

Gait Posture. 2021 Oct 29;91:318-325. doi: 10.1016/j.gaitpost.2021.10.035. Online ahead of print.

**Background:** Increased knee flexion at initial contact and in stance is a common problem for children with cerebral palsy. Surgical correction with percutaneous hamstring lengthening is an alternative to open hamstring lengthening; however, outcomes are less well documented, and there is concern about increasing anterior pelvic tilt. The purpose of this study was to evaluate the short-term outcomes of percutaneous hamstring lengthenings in children with cerebral palsy using comprehensive gait analysis techniques. **Research question:** Does percutaneous hamstring lengthening improve knee function, and do knee and anterior pelvic tilt outcomes vary by GMFCS level? **Methods:** A convenience sample of 52 patients with both pre and post-surgical gait analyses was evaluated retrospectively for changes in gait function in terms of temporal-spatial parameters, kinematics and kinetics. Patients were divided into two GMFCS subgroups: GMFCS level I/II and III. **Results:** The percutaneous hamstring lengthening results in statistically significant improvements in knee function during gait with increased knee extension at initial contact (mean 32° SD 13° to mean 21° SD 11°,  $p = 0.000$ ) and improved mean knee flexion in stance (mean 23° SD 12° to mean 16° SD 11°,  $p = 0.000$ ) for the total study cohort. Beneficial changes were found for knee function in both GMFCS level subgroups; however, there was an increase in pelvic tilt pre to post-surgery in the GMFCS level III subgroup (mean 21° SD 8° to mean 26° SD 6°,  $p = 0.012$ ) but not the GMFCS level I/II subgroup (mean 18° SD 7° to mean 20° SD 8°,  $p = 0.427$ ). **Significance:** Percutaneous hamstring lengthening can improve knee function for all patients; however, the impact on anterior pelvic tilt varies by GMFCS level, with increasing anterior tilt for GMFCS level III only. This study highlights the importance of understanding differences in surgical outcomes by GMFCS level to better predict post-surgical function.

PMID: [34823200](#)

### **3. Relationship between 3D lower limb bone morphology and 3D gait variables in children with uni and bilateral Cerebral Palsy**

Bailly Rodolphe, Lempereur Mathieu, Thepaut Matthias, Pons Christelle, Houx Laetitia, Brochard Sylvain

Gait Posture. 2021 Nov 16;92:51-59. doi: 10.1016/j.gaitpost.2021.11.011. Online ahead of print.

**Background:** Medical and surgical interventions to prevent or reduce bone deformities and improve gait in children with cerebral palsy (CP) are based on empirical evidence that there is a relationship between bone deformities and gait deviations. **Research question:** What is the relationship between tibial-femoral bone morphology and kinematic gait variables in ambulant children with CP? **Methods:** A retrospective analysis was conducted on data from 121 children with uni- ( $n = 64$ , mean age 9.9 (SD 3.4) years) and bi- lateral ( $n = 57$ , mean age 10.4 (SD 3.6) years) CP who had undergone 3D gait analysis and biplanar X-rays (EOS® system). The limbs were split as DIP (the more impaired limb of children with bilateral CP), HEMI (the impaired limb of unilateral CP) and REF (the unimpaired limb of unilateral CP). Multi-variable Linear Regressions were performed between 23 kinematic variables, the Gait Deviation Index (GDI) and a model composed of nine 3D bone variables for each limb type. **Results:** When the whole sample was pooled, 72% of R2 values were poor, 16% were fair, and 12% were moderate. Lower limb bone morphology models explained less than 1% of GDI variability. Correlations between tibial-femoral rotational parameters and hip rotation were mostly poor. Mean foot progression angle was the only kinematic parameter that was fairly to moderately correlated with bone variables in the 3 limb types. A tibial-femoral bone model explained 48% of the variability of mean foot progression angle in the REF limbs, 31% in the HEMI limbs and 25% in the DIP limbs. **Significance:** Tibial-femoral bone morphology was only weakly related to kinematic gait variables, in contrast with common clinical assumptions. These results suggest that factors other than bone morphology influence gait quality and thus a thorough clinical examination and gait analysis is required prior to making treatment decisions.

PMID: [34826693](#)

### **4. An effect of spinal and ankle-foot orthoses on gait of spastic diplegic child: A case report**

Jurgita Ziziene, Kristina Daunoraviciene, Giedre Juskeniene, Jolanta Pauk

Technol Health Care. 2021 Nov 12. doi: 10.3233/THC-219009. Online ahead of print.

**Background:** In children with spastic cerebral palsy (CP), the most common motor dysfunction is pathological gait. **Objective:** To evaluate the effectiveness of measures for an individual CP case. **Methods:** The case of one spastic diplegia child has been analyzed. Both lower extremities and spine were examined under three gait conditions: 1) barefoot, 2) with ankle-foot orthoses (AFOs) and thoracolumbosacral spinal orthosis (TLSO), and 3) with TLSO only. Spatiotemporal gait and kinematic parameters of the pelvic, hip, knee, ankle joints, and spine were obtained using Vicon Plug-in-Gait model. The difference ( $\Delta$ ) between the measured values and normative ranges was calculated to determine the efficiency of the orthoses. **Results:** Significant

differences were found in kinematic and spatiotemporal parameters comparing results between conditions and body sides. The effectiveness of the measures was confirmed by the smallest  $\Delta$  values in the double and single support time with the AFOs/TLSO and in the stride and stance time with TLSO. Conclusions: Based on the study results, the best stability of the spine, ankle plantarflexion, and knee hyperextension is achieved with the AFOs/TLSO; therefore, this combination of measures was considered the most effective. However, not only quantitative parameters should be taken into account, but also the child's willingness and comfort.

PMID: [34806639](#)

### **5. Combination taping technique versus ankle foot orthosis on improving gait parameters in spastic cerebral palsy: A controlled randomized study**

Mohamed A Abdel Ghafar, Osama R Abdelraouf, Amr A Abdel-Aziem, Gihan Samir Mousa, Ali O Selim, Mariam E Mohamed

J Rehabil Med. 2021 Nov 23. doi: 10.2340/jrm.v53.900. Online ahead of print.

Background: One of the important goals in the treatment of spastic cerebral palsy is to maintain efficient and effective walking in order to be independent in activities and participate in society. Objective: To compare the efficacy of foot combination taping of kinesio tape and athletic tape vs ankle foot orthosis in correcting spatiotemporal gait parameters in children with spastic diplegia. Methods: Thirty-six children with spastic diplegia were randomly assigned into 3 groups; control, combination taping, and ankle foot orthosis groups. Children in the control group, in addition to those in both experimental groups, continued with conventional physical therapy, 1 h, 3 times per week for 4 weeks. Spatiotemporal gait parameters were assessed with the GAITRite system before and after the application of interventions. Results: Significant increases in walking velocity, step length, stride length, right single support duration, and left single support duration of the ankle foot orthosis and combination taping groups than pre-intervention values. [AQ9] Moreover, the post-intervention values of the double support duration of the ankle foot orthosis and combination taping groups were significantly lower than pre-intervention values. There were no significant differences between the post-intervention values of the ankle foot orthosis and combination taping groups for all parameters. Conclusion: The results demonstrated that combination taping is an effective alternative technique to ankle foot orthosis to improve spatiotemporal parameters in children with spastic diplegic in combination with conventional physiotherapy.

PMID: [34812472](#)

### **6. Surgical Management of Foot and Ankle Deformities in Cerebral Palsy**

Tamir Bloom, Sanjeev Sabharwal

Review Clin Podiatr Med Surg. 2022 Jan;39(1):37-55. doi: 10.1016/j.cpm.2021.09.001.

Children with cerebral palsy (CP) are at a high risk of developing foot and ankle deformities that can impact function, brace/shoe fit, and seating. The 3 commonly observed foot and ankle segmental malalignment patterns include equinus, planovalgus, and equinovarus. Assessment of foot deformities is multifaceted, requiring the collection and integration of data from a combination of sources that include the clinical history, standardized physical examination, observational and quantitative gait analysis, GMFCS classification, and radiographic findings. Surgical procedures are determined by identifying all segmental malalignments and assessing the contribution of dynamic or flexible soft-tissue imbalance, fixed soft-tissue imbalance, and skeletal deformities.

PMID: [34809794](#)

### **7. Neurologic Disorders Affecting the Foot and Ankle**

William R Yorns Jr

Review Clin Podiatr Med Surg. 2022 Jan;39(1):15-35. doi: 10.1016/j.cpm.2021.08.005.

The neurologic causes of foot and leg dysfunction are reviewed. Disorders causing foot and ankle pain, weakness, or other sensorimotor disturbances often cause difficulty with ambulation and prompt patients to seek medical evaluation. Physical signs and symptoms along with targeted diagnostic testing are needed to come to the correct diagnosis and treatment plan. An overview of peripheral nerve, muscle, and central nervous system disorders affecting the foot and leg are discussed.

PMID: [34809793](#)

### **8. Evaluation of an intensive voice treatment to reduce anterior drooling in children with cerebral palsy: Protocol for a concurrent multiple-baseline, single case experimental design study**

Michelle McInerney, Christine Imms, Paul N Carding, Dinah S Reddihough

Contemp Clin Trials Commun. 2021 Nov 17;24:100872. doi: 10.1016/j.conctc.2021.100872. eCollection 2021 Dec.

Anterior drooling is common in children with cerebral palsy (CP) and poses significant risks to the child's health. Causes of drooling include oro-motor dysfunction, inefficient swallowing and reduced sensation in the orofacial musculature. Behavioural interventions are frequently recommended to reduce drooling; however, this is in the absence of high-quality research evidence. This paper describes a protocol for evaluating the effectiveness of the Lee Silverman Voice Treatment LOUD (LSVT LOUD®) in reducing drooling; and optimising speech and swallowing in a group of children with CP. A structured and systematic visual analysis supplemented with statistical analyses will be used to analyse the data. The risk of bias in n-of-1 trials (RoBiNT) Scale [1] guided the design and implementation of the study.

PMID: [34825105](#)

### **9. Dental procedures cause stress in children with cerebral palsy?**

Maria de Fátima-Monteiro Tomasin, Giselle-Rodrigues de Sant'Anna, Adriano-Tomio Hoshi, Danilo-Antônio Duarte

J Clin Exp Dent. 2021 Nov 1;13(11):e1112-e1117. doi: 10.4317/jced.58392. eCollection 2021 Nov.

Background: To evaluate the level of stress during dental care in children and preadolescents with cerebral palsy through biological and psychological parameters. Material and methods: A total of 38 children aged 7 to 12 years were divided into two groups: one with 18 children with cerebral palsy and the other with 20 healthy children (control group). Saliva was noninvasively collected before and after dental care to analyze salivary biomarkers. The Frankl Behavior Scale and the Facial Image Scale were applied. Results: After the dental procedure, cortisol levels were significantly higher ( $p = 0.02$ ) in the cerebral palsy group than in the control group. Salivary alpha-amylase was not significantly different between groups. Regarding psychological parameters, anxiety was significantly higher ( $p = 0.00012$ ) in the cerebral palsy group than in the control group. Conclusions: There was a change in physiological parameters (salivary cortisol and salivary alpha-amylase) and in psychological parameters (Frankl Behavioral Scale and Facial Image Scale) in patients with cerebral palsy, who exhibited higher stress and anxiety levels than did children without cerebral palsy.

PMID: [34824697](#)

### **10. Computer-Aided Diagnosis of Children with Cerebral Palsy under Deep Learning Convolutional Neural Network Image Segmentation Model Combined with Three-Dimensional Cranial Magnetic Resonance Imaging**

Rui Yang, Haoran Zuo, Shusheng Han, Xiaoping Zhang, Qian Zhang

J Healthc Eng. 2021 Nov 10;2021:1822776. doi: 10.1155/2021/1822776. eCollection 2021.

In this paper, we analyzed the application value and effect of deep learn-based image segmentation model of convolutional neural network (CNN) algorithm combined with 3D brain magnetic resonance imaging (MRI) in diagnosis of cerebral palsy in children. 3D brain model was segmented based on CNN algorithm to obtain the segmented MRI images of brain tissue, and the

validity was verified. Then, 70 children with cerebral palsy were rolled into the observation group ( $n = 35$ ), which received MRI for diagnosis after segmentation of brain tissue, and control group ( $n = 35$ ), which were diagnosed by computed tomography (CT). The diagnosis results of the two groups were compared. The validity experiment verified that the image segmentation method based on CNN algorithm can obtain effective style graphics. In clinical trials, the diagnostic accuracy of 88.6% in the observation group was evidently superior to that of 80% in the control group ( $P < 0.05$ ). In the observation group, one patient was diagnosed as normal, four patients had white matter lesions, 17 patients had corpus callosum lesions, and five patients had basal ganglia softening foci. In the control group, two patients were diagnosed as normal, two patients had white matter lesions, 19 patients had corpus callosum lesions, and four patients had basal ganglia softening foci. No notable difference was found between the two groups ( $P > 0.05$ ). According to the research results, in the diagnosis of cerebral palsy in children, the image segmentation of brain 3D model based on CNN to obtain the MRI image of segmented brain tissue can effectively improve the detection accuracy. Moreover, the specific symptoms can be diagnosed clearly. It can provide the corresponding diagnostic basis for clinical diagnosis and treatment and was worthy of clinical promotion.

PMID: [34804446](#)

### 11. Prevalence of knee contractures is high in children with cerebral palsy in Denmark

André Nis Klenø, Martin Bækgaard Stisen, Claes Høgh Cubel, Inger Mechlenburg, Kirsten Nordbye-Nielsen

Physiother Theory Pract. 2021 Nov 22;1-8. doi: 10.1080/09593985.2021.2007558. Online ahead of print.

**Introduction:** Cerebral palsy (CP) is a neurological disease occurring in children at early gestation, often resulting in pronounced functional limitations. A Swedish cross-sectional study (Cloodt, et al., 2018) discovered that 22% of children with CP had a knee contracture, which was associated with higher levels of Gross Motor Function Classification System (GMFCS), higher age, and higher levels of spasticity measured by the Modified Ashworth Scale (MAS). The current study investigated these associations in a Danish population. **Methods:** This is a cross-sectional study including 1,163 children with CP aged 0-15 years, registered in the Danish National Cerebral Palsy Registry between 2017 and 2019. Prevalence of knee contracture was estimated, and logistic regression analysis was applied with results presented as odds ratio (OR) with 95% confidence intervals (CI). **Results:** A total of 511 children with CP had knee contracture resulting in a prevalence of 44%. Age groups 4-6 years (OR: 1.73, CI: 1.19; 2.52), 7-9 years (OR: 1.85, CI: 1.29; 2.66) and 10-12 years (OR: 2.12, CI: 1.39; 3.24) were significantly associated with a higher prevalence of knee contractures compared to age group 0-3 years. Knee contractures were significantly more frequent at GMFCS levels IV (OR: 1.9, CI: 1.21; 2.97) and V (OR: 3.62, CI: 2.36; 5.55) compared to level I. Knee contractures were not associated with higher levels of MAS. **Conclusions:** Knee contractures are highly prevalent and significantly associated with high levels of GMFCS and increased age until 12 years, but not with high levels of spasticity in children with CP in Denmark.

PMID: [34809532](#)

### 12. ICF Core Sets for the assessment of functioning of adults with cerebral palsy

Suzie Noten, Melissa Selb, Lorenzo A A Troenosemito, Deborah E Thorpe, Elisabet Rodby-Bousquet, Wilma M A van der Slot, Marij E Roebroek, ICF Core Set for Adults with CP Consensus Group

Dev Med Child Neurol. 2021 Nov 20. doi: 10.1111/dmcn.15104. Online ahead of print.

**Aim:** To report on the results of the online international consensus process to develop the comprehensive and brief International Classification of Functioning, Disability and Health (ICF) Core Sets for adults with cerebral palsy (CP). **Method:** An online iterative decision-making and consensus process involved 25 experts, including clinicians and researchers working with adults with CP, an adult with CP, and the parents of adults with CP from all six regions of the World Health Organization. The most relevant categories were selected from a list of 154 unique second-level candidate categories to develop the ICF Core Sets for adults with CP. This list resulted from evidence gathered during four preparatory studies, that is, a systematic literature review, a qualitative study, an expert survey, and an empirical study. **Results:** The consensus process resulted in the comprehensive ICF Core Set containing 120 second-level ICF categories: 33 body functions; eight body structures; 50 activities and participation; and 29 environmental factors, from which the most essential categories, 33 in total, were selected for the brief ICF Core Set. For body functions, most of the categories were mental functions and neuromusculoskeletal and movement-related functions. Body structures were mostly related to movement. All the chapters of the activities and participation component were represented, with mobility and self-care as the most frequently covered chapters. For environmental factors, most of the categories addressed products and technology and services, systems, and policies.

Interpretation: The comprehensive and brief ICF Core Sets for adults with CP were created using a new online version of an established ICF Core Set consensus process. These Core Sets complement the age-specific ICF Core Sets for children and young people with CP and will promote standardized data collection worldwide.

PMID: [34800032](#)

### **13. Neurovascular Unit Alterations in the Growth-Restricted Newborn Are Improved Following Ibuprofen Treatment**

Kirat K Chand, Stephanie M Miller, Gary J Cowin, Lipsa Mohanty, Jany Pienaar, Paul B Colditz, Stella Tracey Bjorkman, Julie A Wixey

Mol Neurobiol. 2021 Nov 26. doi: 10.1007/s12035-021-02654-w. Online ahead of print.

The developing brain is particularly vulnerable to foetal growth restriction (FGR) and abnormal neurodevelopment is common in the FGR infant ranging from behavioural and learning disorders to cerebral palsy. No treatment exists to protect the FGR newborn brain. Recent evidence suggests inflammation may play a key role in the mechanism responsible for the progression of brain impairment in the FGR newborn, including disruption to the neurovascular unit (NVU). We explored whether ibuprofen, an anti-inflammatory drug, could reduce NVU disruption and brain impairment in the FGR newborn. Using a preclinical FGR piglet model, ibuprofen was orally administered for 3 days from birth. FGR brains demonstrated a proinflammatory state, with changes to glial morphology (astrocytes and microglia), and blood-brain barrier disruption, assessed by IgG and albumin leakage into the brain parenchyma and a decrease in blood vessel density. Loss of interaction between astrocytic end-feet and blood vessels was evident where plasma protein leakage was present, suggestive of structural deficits to the NVU. T-cell infiltration was also evident in the parenchyma of FGR piglet brains. Ibuprofen treatment reduced the pro-inflammatory response in FGR piglets, reducing the number of activated microglia and enhancing astrocyte interaction with blood vessels. Ibuprofen also attenuated plasma protein leakage, regained astrocytic end-feet interaction around vessels, and decreased T-cell infiltration into the FGR brain. These findings suggest postnatal administration of ibuprofen modulates the inflammatory state, allowing for stronger interaction between vasculature and astrocytic end-feet to restore NVU integrity. Modulation of the NVU improves the FGR brain microenvironment and may be key to neuroprotection.

PMID: [34825315](#)

### **14. Assessment of embryo morphology following perinatal exposure to aspirin, ibuprofen and paracetamol using whole embryo culture system**

Sakita Mounghmaithong, Bo Wah Leung, Daljit Singh Sahota, Chi Chui Wang, Tak Yeung Leung, Liona C Poon

J Matern Fetal Neonatal Med. 2021 Nov 22;1-8. doi: 10.1080/14767058.2021.2005020. Online ahead of print.

Background: Recent evidence from a meta-analysis indicates that maternal prenatal exposure, single or repeated, to non-steroidal anti-inflammatory drugs (NSAIDs) or non-opioid painkillers, is associated with increased risk of cerebral palsy and cognitive-behavioral disorders in offspring. One potential route of action is interference with the neurulation process and hence early brain development. Objective: To examine the effect of prenatal exposure to common NSAIDs and non-opioid drugs on neurulation using an in vitro whole embryo culture system. Methods: Mouse embryos from in-bred Institute of Cancer Research albino strain mice were exteriorized on embryonic day 7.5 and cultured for 48 h in either 1 mL heat-inactivated rat serum + 0.1% dimethyl sulfoxide ("Control") or 1 mL of rat serum supplemented with six increasing concentrations of laboratory-grade aspirin, paracetamol, and ibuprofen ("Experimental"). After culture, embryo morphological and developmental parameters were documented using standardized scoring systems at each dosage concentration. The assessed concentration in rat serum culture ranged from 1.23 to 13.57 mg/mL for aspirin and 0.06-4.93 mg/mL for paracetamol and ibuprofen. The equivalent respective human dosages were 600-6600 mg and 30-2400 mg. Results: Between-group comparisons ("Control" vs "Experimental") and post-hoc pair-wise tests, adjusted for multiple comparisons, indicating no statistically significant effect on crown-rump length ( $p > .21$ ), head length ( $p > .28$ ), somite number ( $p > .25$ ), incidence of absent hindlimb buds ( $p > .18$ ), yolk sac circulation score ( $p > .07$ ) and posterior neuropore closure ( $p > .35$ ) in the aspirin, paracetamol and ibuprofen experiments. All embryos had forelimb buds, closed anterior neuropores and none had neural tube defects. Conclusion: This study has demonstrated that there are no safety concerns regarding high-dose aspirin, ibuprofen, and paracetamol on mice's embryonic development.

PMID: [34802359](#)

**15. Oligodendrocyte Development and Implication in Perinatal White Matter Injury**

Mahsa Motavaf, Xianhua Piao

Review Front Cell Neurosci. 2021 Nov 4;15:764486. doi: 10.3389/fncel.2021.764486. eCollection 2021.

Perinatal white matter injury (WMI) is the most common brain injury in premature infants and can lead to life-long neurological deficits such as cerebral palsy. Preterm birth is typically accompanied by inflammation and hypoxic-ischemic events. Such perinatal insults negatively impact maturation of oligodendrocytes (OLs) and cause myelination failure. At present, no treatment options are clinically available to prevent or cure WMI. Given that arrested OL maturation plays a central role in the etiology of perinatal WMI, an increased interest has emerged regarding the functional restoration of these cells as potential therapeutic strategy. Cell transplantation and promoting endogenous oligodendrocyte function are two potential options to address this major unmet need. In this review, we highlight the underlying pathophysiology of WMI with a specific focus on OL biology and their implication for the development of new therapeutic targets.

PMID: [34803612](#)**16. Frontal interhemispheric structural connectivity, attention, and executive function in children with perinatal stroke**

Nicole Larsen, Brandon T Craig, Alicia J Hilderley, Shane Virani, Kara Murias, Brian L Brooks, Adam Kirton, Helen L Carlson

Brain Behav. 2021 Nov 25:e2433. doi: 10.1002/brb3.2433. Online ahead of print.

Perinatal stroke affects ~1 in 1000 births and concomitant cognitive impairments are common but poorly understood. Rates of Attention Deficit/Hyperactivity Disorder (ADHD) are increased 5-10× and executive dysfunction can be disabling. We used diffusion imaging to investigate whether stroke-related differences in frontal white matter (WM) relate to cognitive impairments. Anterior forceps were isolated using tractography and sampled along the tract. Resulting metrics quantified frontal WM microstructure. Associations between WM metrics and parent ratings of ADHD symptoms (ADHD-5 rating scale) and executive functioning (Behavior Rating Inventory of Executive Function (BRIEF)) were explored. Eighty-three children were recruited (arterial ischemic stroke [AIS] n = 26; periventricular venous infarction [PVI] n = 26; controls n = 31). WM metrics were altered for stroke groups compared to controls. Along-tract analyses showed differences in WM metrics in areas approximating the lesion as well as more remote differences at midline and in the nonlesioned hemisphere. WM metrics correlated with parental ratings of ADHD and executive function such that higher diffusivity values were associated with poorer function. These findings suggest that underlying microstructure of frontal white matter quantified via tractography may provide a relevant biomarker associated with cognition and behavior in children with perinatal stroke.

PMID: [34825521](#)**17. Development of gross motor capacity and mobility performance in children with cerebral palsy: a longitudinal study**

Andrea Burgess, Sarah Reedman, Mark D Chatfield, Robert S Ware, Leanne Sakzewski, Roslyn N Boyd

Dev Med Child Neurol. 2021 Nov 20. doi: 10.1111/dmcn.15112. Online ahead of print.

**Aim:** To describe development of gross motor capacity and mobility performance in children with cerebral palsy. **Method:** This longitudinal cohort study measured gross motor capacity with the Gross Motor Function Measure and mobility performance with the Pediatric Evaluation of Disability Inventory (PEDI) between 18 months and 5 years, and the PEDI - Computer Adaptive Test (PEDI-CAT) between 8 years and 12 years. Longitudinal analyses used mixed-effects regression modelling with interaction between age and Gross Motor Function Classification System (GMFCS). Stability of GMFCS levels over time was measured using agreement. **Results:** Two hundred and twenty-two children provided 871 observations (median 4 observations, range 1-7). Children classified in GMFCS level I improved in both capacity and performance until 8 to 12 years. Children classified in GMFCS levels II and III continued to develop mobility performance after gross motor capacity had plateaued at 5 years. Children classified in GMFCS level IV plateaued at 5 years in capacity and performance. Children classified in GMFCS level V showed no changes in capacity or performance between 18 months and 8 to 12 years. Stability of GMFCS levels was 73%. **Interpretation:** Change in mobility performance over time somewhat reflected gross motor capacity trajectories. Continued improvement in mobility performance after plateau of gross motor capacity for children classified in GMFCS levels

II and III suggests importance of other personal or environmental factors.

PMID: [34800033](#)

### **18. Effects of additional inspiratory muscle training on mobility capacity and respiratory strength for school-children and adolescents with cerebral palsy: a randomized controlled trial**

Bhuvaneshwari Anand, Suruliraj Karthikbabu

Braz J Phys Ther. 2021 Nov 12;S1413-3555(21)00103-9. doi: 10.1016/j.bjpt.2021.10.006. Online ahead of print.

Background: Children and adolescents with cerebral palsy often have poor respiratory function, which is often not addressed. Objective: To examine if adding inspiratory muscle training to sensorimotor exercises would improve mobility capacity and respiratory function in children and adolescents with cerebral palsy. Methods: Forty school-children and adolescents with cerebral palsy aged 8-15 years with Gross Motor Function Classification System I-III, participated in this randomized controlled trial. The experimental group received 45 min of sensorimotor physical therapy in addition to 15 min of inspiratory muscle training for 18 sessions over six weeks. In contrast, the control group received 45 min of sensorimotor training session, three times a week over six weeks. The primary outcome measure was the six-minute walk test. The secondary outcome measures were maximal inspiratory and maximal expiratory pressure, as well as pulmonary function tests. Results: Time by group interaction showed no statistical significance between the groups in any outcome measures except for peak expiratory flow. The mean difference of 9.6 cm H<sub>2</sub>O (95% CI: 2.3, 16.8) in the MIP from baseline to 2-month follow-up supports the experimental intervention. Post-training, the between-group mean difference was 19.8 (95% CI: -18, 57.6) meter in the six-minute walk test. Conclusion: Adding inspiratory muscle training to sensorimotor physical therapy did not impact mobility capacity in children and adolescents with cerebral palsy.

PMID: [34810107](#)

### **19. Exploring demographic, medical, and developmental determinants of adaptive behaviour in children with hemiplegic cerebral palsy**

Sandra Abdel Malek, Ronit Mesterman, Lauren Switzer, Briano DiRezze, Gabrielle deVeber, Darcy Fehlings, Yona Lunskey, Michelle Phoenix, Jan Willem Gorter

Eur J Paediatr Neurol. 2021 Nov 18;36:19-25. doi: 10.1016/j.ejpn.2021.11.005. Online ahead of print.

Hemiplegic cerebral palsy (CP), the most common subtype, is characterized by high levels of mobility. Despite this, children with hemiplegic CP can face challenges functioning in and adapting to situations of everyday life. The purpose of this cross-sectional study (Hemi-NET database) was to identify factors associated with adaptive behaviour in 59 children with hemiplegic CP (ages 4-18; GMFCS I-IV). Using multivariate regression analyses, the relationship between demographic, medical, and developmental factors and adaptive behaviour (measured by the Adaptive Skills Composite score of the BASC-2) was explored. Results indicate that 34% of children had impaired adaptive skills. An autism diagnosis and lower communication functioning were significantly associated with poorer adaptive skills ( $R^2 = 0.42$ ,  $F(4, 43) = 7.87$ ,  $p < 0.001$ ), while factors such as IQ scores and GMFCS level were not. The results contribute to the growing literature that suggests that clinicians and researchers need to look beyond motor functioning when working with individuals with CP.

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### **20. Hereditary spastic paraplegia initially diagnosed as cerebral palsy**

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Introduction: Spastic diplegia presenting in infancy is common to both cerebral palsy (CP) and hereditary spastic paraplegia



(HSP). We report the clinical and genetic features of a cohort of Alberta patients with a diagnosis of HSP, who were initially diagnosed with CP. Methods: Fourteen patients with an initial diagnosis of CP were identified from an Alberta registry of HSP patients via chart review. Whole exome sequencing (WES) was performed to identify genetic causes. Results: From 90 families in the database, individuals in 29 families had a pediatric presentation of spasticity, with 20 presenting under 3 years of age. Individuals from 14 families had received an initial diagnosis of CP and correct diagnosis was made after neurogenetic assessment due to symptom progression. All had early onset (<3 years) of symptoms. WES identified pathogenic or likely pathogenic mutations in nine cases involving six genes: ATL1, PLP1, PNPLA6, SACS, SPAST, and SYNE1. In five families, WES did not reveal a genetic etiology but progression of symptoms and positive family history suggests HSP is the most likely diagnosis. Conclusion: In our cohort, 70% of HSP children presenting with spasticity under 3 years had been misdiagnosed with CP. In a young child presenting with spastic diplegia without clear history of prematurity, intrauterine growth restriction, infection or vascular insult, it is important to consider HSP. Accurate diagnosis has implications for prognosis, management, and recurrence risk.

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