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## Interventions and Management

### 1. Predictive validity of the Hand Assessment for Infants in infants at risk of unilateral cerebral palsy

Ulrike C Ryll, Lena Krumlinde-Sundholm, Cornelia H Verhage, Elisa Sicola, Giuseppina Sgandurra, Caroline Hg Bastiaenen, Ann-Christin Eliasson

Dev Med Child Neurol. 2020 Nov 29. doi: 10.1111/dmcn.14739. Online ahead of print.

**Aim:** To evaluate the sensitivity, specificity, and predictive value of the Hand Assessment for Infants (HAI) in identifying infants at risk of being diagnosed with unilateral cerebral palsy (CP), and to determine cut-off values for this purpose.  
**Method:** A convenience sample of 203 infants (106 females, 97 males) was assessed by the HAI at 3, 6, 9, and 12 months. Sensitivity, specificity, predictive values, and likelihood ratios were calculated using receiver operating characteristic curve analysis. Cut-off values were derived for different ages. The clinical outcome (unilateral CP yes/no) at 24 months or more served as an external criterion to investigate the predictive validity of HAI. Results: Half of the infants developed unilateral CP. The area under the curve ranged from 0.77 (95% CI [confidence interval] 0.63-0.91) to 0.95 (95% CI 0.90-1.00) across HAI scales and age intervals. Likewise, sensitivity ranged from 63% to 93%, specificity from 62% to 91%, and accuracy from 73% to 94%. Interpretation: HAI scores demonstrated overall accuracy that ranged from very good to excellent in predicting unilateral CP in infants at risk aged between 3.5 and 12 months. This accuracy increased with age at assessment and the earliest possible prediction was at 3.5 months of age, when appropriate HAI cut-off values for different ages were applied.

PMID: [33251586](https://pubmed.ncbi.nlm.nih.gov/33251586/)

### 2. Spatiotemporal parameters from instrumented motion analysis represent clinical measurement of upper limb function in children with cerebral palsy

Dain Shim, Ja Young Choi, Sook-Hee Yi, Eun Sook Park, Seungki Kim, Beomki Yoo, Dongho Park, Hye-Rin Park, Dong-Wook Rha

Gait Posture. 2020 Nov 12;S0966-6362(20)30632-9. doi: 10.1016/j.gaitpost.2020.11.007. Online ahead of print.

**Background:** There are various tools that measure upper limb function in children with cerebral palsy (CP) clinically, but these measurement methods are examiner-dependent and scale values are not proportional to the upper limb function which makes it difficult to quantify the function. Research question: The purpose of this study was to investigate whether the new parameters derived from 3D motion analysis reflect the upper limb function which measured by Melbourne Assessment 2 (MA2) in children with cerebral palsy (CP) compared to the clinical measurements. Methods: Forty children with CP (24 boys, 16 girls; mean [SD] age, 6 years 11 months [3 years 5 months]) were recruited. Motion capture was conducted during phases T1-T4 of Reach and Grasp Cycles. New parameters (movement time, number of movement units, index of curvature) were derived from wrist marker data. Range of motion (ROM), accuracy, dexterity, and fluency of unilateral upper limb function were assessed using MA2. Spearman rank coefficients were determined to evaluate correlations between MA2 and

the new parameters. Results and significance: Index of curvature correlated negatively with MA2 accuracy scores during T1 (rs -0.347,  $p < 0.05$ ), T2 (rs -0.471,  $p < 0.01$ ), and T3 (rs -0.660,  $p < 0.01$ ). Number of movement units correlated negatively with MA2 ROM, accuracy, and fluency scores during T1 (ROM rs -0.334; accuracy rs -0.331; fluency rs -0.375;  $p < 0.05$ ) and T3 (ROM rs -0.499; accuracy rs -0.531; fluency rs -0.515;  $p < 0.01$ ). Index of curvature and number of movement units are objective, simple parameters showing fair to good correlation with MA2 accuracy and fluency of upper limb function.

PMID: [33246774](#)

### **3. [Effectiveness of constraint-induced movement therapy in upper extremity rehabilitation in patients with cerebral palsy: A systematic review][Article in Spanish]**

M C Martínez-Costa Montero, A Sánchez Cabeza

Review Rehabilitacion (Madr). 2020 Nov 30;S0048-7120(20)30109-2. doi: 10.1016/j.rh.2020.08.002. Online ahead of print.

Background and objective: In hemiplegic cerebral palsy, learned non-use may appear. This phenomenon can be reversed by constraint-induced movement therapy in the healthy side. The aim of this article was to review the evidence of the effectiveness of this therapy on upper extremity functioning, the performance of activities of daily living and quality of life. Patients and methods: We performed a systematic review between January and April 2019 in the PubMed, COCHRANE, PEDro and TRIPDATABASE databases. We included 14 clinical studies describing their characteristics. Results: Most of the studies found significant improvements compared with control groups. Only one article investigated quality of life. Conclusions: Constraint-induced movement therapy seems to have positive effects in the motor rehabilitation of the upper extremity in patients with hemiplegic cerebral palsy. Further studies are needed to assess the individual factors of greatest influence in rehabilitation.

PMID: [33272606](#)

### **4. No support that early selective dorsal rhizotomy increase frequency of scoliosis and spinal pain - a longitudinal population-based register study from four to 25 years of age**

Annika Lundkvist Josenby, Lena Westbom

BMC Musculoskelet Disord. 2020 Nov 27;21(1):782. doi: 10.1186/s12891-020-03782-5.

Spasticity interfering with gross motor development in cerebral palsy (CP) can be reduced with selective dorsal rhizotomy (SDR). Although reported, it is unknown if SDR surgery causes later spine problems. Using CP-registry data from a geographically defined population, the objectives were to compare frequency and time to scoliosis, and spinal pain up to adult age after SDR-surgery or not in all with same medical history, functional abilities, CP-subtype and level of spasticity at 4 years of age. Variables associated with scoliosis at 20 years of age were explored. Method: In the total population with CP spastic diplegia in Skåne and Blekinge, born 1990-2006, 149 individuals had moderate to severe spasticity and no medical contraindications against SDR at 4 years of age and were included; 36 had undergone SDR at a median age of 4.0 years (range 2.5-6.6 years), and 113 had not. Frequency of scoliosis and age when scoliosis was identified, and frequency of spinal pain at 10, 15, 20 and 25 years of age were analysed using Kaplan-Meier survival curves and Fisher's exact test. Multivariable logistic regression was performed to identify variables to explain scoliosis at 20 years of age. Gross Motor Function Classification System (GMFCS) levels at 4 years of age were used for stratification. Result: Frequency of scoliosis did not significantly differ between groups having had early SDR surgery or not. In GMFCS IV, the SDR group had later onset and lower occurrence of scoliosis ( $p = 0.004$ ). Frequency of spinal pain did not differ between the groups ( $p$ -levels  $> 0.28$ ). GMFCS level was the background variable that in the logistic regression explained scoliosis at 20 years of age. Conclusion: Frequency of back pain and scoliosis in adulthood after early SDR are mainly part of the natural development with age, and not a surgery complication.

PMID: [33246436](#)

### **5. Gait Indices for Characterization of Patients with Unilateral Cerebral Palsy**

Stefanos Tsitlakidis, Martin Schwarze, Fabian Westhauser, Korbinian Heubisch, Axel Horsch, Sébastien Hagmann, Sebastian I Wolf, Marco Götze

J Clin Med. 2020 Nov 30;9(12):E3888. doi: 10.3390/jcm9123888.

As cerebral palsy (CP) is a complex disorder, classification of gait pathologies is difficult. It is assumed that unclassified patients show less functional impairment and less gait deviation. The aim of this study was to assess the different subgroups and the unclassified patients with unilateral CP using different gait indices. The Gillette Gait Index (GGI), Gait Deviation Index (GDI), Gait Profile Score (GPS) and spatiotemporal parameters derived from instrumented 3D-Gait Analysis (IGA) were assessed. Subgroups were defined using morphological and functional classification systems. Regarding the different gait indices, a ranking of the different gait patterns is evident. Significant differences were found between GMFCS level I and II, Winters et al. (Winters, Gage, Hicks; WGH) type IV and type I and the WGH-unclassified. Concerning the spatiotemporal parameters significant differences were found between GMFCS level I and II concerning velocity. The unclassified patients showed mean values for the different gait indices that were comparable to those of established subgroups. Established gait patterns cause different degrees of gait deviation and functional impairment. The unclassified patients do not differ from established gait patterns but from the unimpaired gait. Further evaluation using 3D-IGA is necessary to identify the underlying gait pathologies of the unclassified patients.

PMID: [33265919](#)

## 6. Characterizing Normal and Pathological Gait through Permutation Entropy

Massimiliano Zanin, David Gómez-Andrés, Irene Pulido-Valdeolivas, Juan Andrés Martín-Gonzalo, Javier López-López, Samuel Ignacio Pascual-Pascual, Estrella Rausell

Entropy (Basel). 2018 Jan 19;20(1):77. doi: 10.3390/e20010077.

Cerebral palsy is a physical impairment stemming from a brain lesion at perinatal time, most of the time resulting in gait abnormalities: the first cause of severe disability in childhood. Gait study, and instrumental gait analysis in particular, has been receiving increasing attention in the last few years, for being the complex result of the interactions between different brain motor areas and thus a proxy in the understanding of the underlying neural dynamics. Yet, and in spite of its importance, little is still known about how the brain adapts to cerebral palsy and to its impaired gait and, consequently, about the best strategies for mitigating the disability. In this contribution, we present the hitherto first analysis of joint kinematics data using permutation entropy, comparing cerebral palsy children with a set of matched control subjects. We find a significant increase in the permutation entropy for the former group, thus indicating a more complex and erratic neural control of joints and a non-trivial relationship between the permutation entropy and the gait speed. We further show how this information theory measure can be used to train a data mining model able to forecast the child's condition. We finally discuss the relevance of these results in clinical applications and specifically in the design of personalized medicine interventions.

PMID: [33265160](#)

## 7. Adaptive ankle exoskeleton gait training demonstrates acute neuromuscular and spatiotemporal benefits for individuals with cerebral palsy: A pilot study

Ying Fang, Greg Orekhov, Zachary F Lerner

Gait Posture. 2020 Nov 11;S0966-6362(20)30630-5. doi: 10.1016/j.gaitpost.2020.11.005. Online ahead of print.

Background: Gait abnormalities from neuromuscular conditions like cerebral palsy (CP) limit mobility and negatively affect quality of life. Increasing walking speed and stride length are essential clinical goals in the treatment of gait disorders from CP. Research question: How does over-ground gait training with an untethered ankle exoskeleton providing adaptive assistance affect mobility-related spatiotemporal outcomes and lower-extremity muscle activity in people with CP? Methods: A diverse cohort of individuals with CP (n = 6, age 9-31, Gross Motor Function Classification System Level I - III) completed four over-ground training sessions (98 ± 17 min of assisted walking) and received pre- and post-training assessments. On both assessments, participants walked over-ground with and without the exoskeleton while we recorded spatiotemporal outcomes and muscle activity. We used two-tailed paired t-tests to compare all parameters pre- and post-training, and between assisted and unassisted conditions. Results: Following training, walking speed increased 0.24 m/s (p = 0.006) and stride length increased 0.17 m (p = 0.013) during unassisted walking, while walking speed increased 0.28 m/s (p = 0.023) and stride length increased 0.15 m (p = 0.002) during exoskeleton-assisted walking. Exoskeleton training improved stride-to-stride repeatability of soleus and vastus lateralis muscle activation by up to 51 % (p ≤ 0.046), while the amount of integrated stance-phase muscle

activity was similar across visits and conditions. Relative to baseline, post-training walking with the exoskeleton resulted in a soleus activity pattern that was 39 % more similar to the typical pattern from unimpaired individuals ( $p < 0.001$ ). Significance: This study demonstrates acute spatiotemporal and neuromuscular benefits from over-ground training with adaptive ankle exoskeleton assistance, and provides rationale for completion of a longer randomized controlled training protocol.

PMID: [33248858](#)

### **8. Prospective Comparison of Subtalar Arthroereisis With Calcaneal Lengthening in the Management of Planovalgus Feet of Ambulatory Children With Spastic Cerebral Palsy?**

Amr H Ahmed, Atef A Hanna, Amr S Arafa, Mostafa H El-Sherbini, Ahmed A Omran

Foot Ankle Spec. 2020 Dec 3;1938640020974886. doi: 10.1177/1938640020974886. Online ahead of print.

**Background:** Pes planovalgus (PPV) deformity is common among cerebral palsy (CP) patients. There is no true consensus about the best way of treating this common deformity, especially when surgical interference is required. Treatment options range from orthotics to complex surgical procedures. The purpose of this prospective study was to evaluate and compare the effectiveness of 2 different procedures in the correction of symptomatic flexible PPV in ambulatory CP patients. **Methods:** A total of 57 feet in 35 patients were divided into 2 groups: group 1, subtalar arthroereisis group, using the calcaneostop technique; group 2, lateral column lengthening group, using Evans osteotomy. Patients were assessed clinically by the clinical score proposed by Yoo et al and radiologically by measuring 7 weight-bearing angles, both preoperatively and 12 months postoperatively. Patients' (or parents') satisfaction and their tolerance to braces or shoes were assessed 12 months after surgery as secondary outcome parameters. **Results:** There was a statistically significant improvement in both primary and secondary outcome parameters after both procedures in comparison to the preoperative parameters. No statistically significant differences were observed between the 2 groups regarding the outcomes of both procedures except for the greater power of arthroereisis in the correction of hindfoot valgus, which was statistically significant both clinically and radiographically. **Conclusion:** Both procedures are valid options for the surgical management of PPV in ambulatory children with spastic CP. The less-invasive nature and lower potential morbidity suggest that judicious use of arthroereisis is appropriate for some patients, especially in the context of single-event multilevel surgery. **Levels of evidence:** Level II: Prospective, comparative study.

PMID: [33269639](#)

### **9. Trends and Technologies in Rehabilitation of Foot Drop: A Systematic Review**

Fady Alnajjar, Sumayya Khalid, Riadh Zaier, Munkhjargal Gochoo

Expert Rev Med Devices. 2020 Nov 28. doi: 10.1080/17434440.2021.1857729. Online ahead of print.

**Introduction:** Foot Drop (FD) is a condition, which is very commonly found in post-stroke patients, however it can also be seen in patients with multiple sclerosis, and cerebral palsy. It is a sign of neuromuscular damage caused by the weakness of the muscles. There are various approaches of FD's rehabilitation, such as physiotherapy, surgery, and the use of technological devices. Recently, researchers have worked on developing various technologies to enhance assisting and rehabilitation of FD. **Areas covered:** This review analyzes different types of technologies available for the rehabilitation of FD. This include devices that are available commercially, as well as, the proposed studies. 101 studies published between 2015 and 2020 were identified for the review, many were excluded due to various reasons, e.g., they were not robot-based devices, did not include foot drop as one of the targeted diseases, or was insufficient information. 24 studies that met our inclusion criteria, were assessed. These studies were further classified into two different categories: robot-based ankle-foot orthosis (RAFO) and Functional Electrical Stimulation (FES) devices. **Expert opinion:** Studies included showed that both RAFO and FES showed considerable improvement in the gait cycle of the patients. Future trends are inclining towards FES and muscle synergies for further developments.

PMID: [33249938](#)

### **10. Improvements in Muscle Strength Are Associated With Improvements in Walking Capacity in Young Children With Cerebral Palsy: A Secondary Analysis**

Liesbeth F van Vulpen 1, Sonja de Groot, Eugene A A Rameckers, Jules G Becher, Annet J Dallmeijer

Pediatr Phys Ther. 2020 Dec 2. doi: 10.1097/PEP.0000000000000764. Online ahead of print.

**Purpose:** To evaluate whether changes in lower-limb muscle strength explain changes in walking capacity during 14-week periods of usual care, power training and follow-up for children with spastic cerebral palsy. **Methods:** Secondary analysis of a previously conducted double-baseline controlled trial of 22 children with spastic cerebral palsy. Generalized estimating equations were used to evaluate the relationships between within-subject changes in isometric muscle strength and walking capacity over 3 periods. **Results:** Changes in hip abductor strength were associated with changes in the Muscle Power Sprint Test, changes in gastrocnemius and hip abductor strength were associated with changes in the Shuttle Run Test, and changes in gastrocnemius strength were associated with changes in the 1-minute walk test. All associations supported better walking capacity with increased strength. **Conclusion:** Walking capacity, especially sprint capacity, can be improved by increasing strength by functional power training in this population.

PMID: [33273255](#)

### **11. Critically appraised paper: A program of functional electrical stimulation cycling, goal-directed training and adapted cycling improves gross motor function in children with cerebral palsy [commentary]**

Noula Gibson

J Physiother. 2020 Nov 24;S1836-9553(20)30123-5. doi: 10.1016/j.jphys.2020.11.002. Online ahead of print.

PMID: [33246851](#)

### **12. Wearable Adaptive Resistance Training Improves Ankle Strength, Walking Efficiency and Mobility in Cerebral Palsy: A Pilot Clinical Trial**

Benjamin C Conner, Nushka M Remec, Elizabeth K Orum, Emily M Frank, Zachary F Lerner

IEEE Open J Eng Med Biol. 2020;1:282-289. doi: 10.1109/ojemb.2020.3035316. Epub 2020 Nov 2.

**Goal:** To determine the efficacy of wearable adaptive resistance training for rapidly improving walking ability in children with cerebral palsy (CP). **Methods:** Six children with spastic CP (five males, one female; mean age 14y 11mo; three hemiplegic, three diplegic; Gross Motor Function Classification System [GMFCS] levels I and II) underwent ten, 20-minute training sessions over four weeks with a wearable adaptive resistance device. Strength, speed, walking efficiency, timed up and go (TUG), and six-minute walk test (6MWT) were used to measure training outcomes. **Results:** Participants showed increased average plantar flexor strength ( $17 \pm 8\%$ ,  $p = 0.02$ ), increased preferred walking speed on the treadmill ( $39 \pm 25\%$ ,  $p = 0.04$ ), improved metabolic cost of transport ( $33 \pm 9\%$ ,  $p = 0.03$ ), and enhanced performance on the timed up and go ( $11 \pm 9\%$ ,  $p = 0.04$ ) and six-minute walk test ( $13 \pm 9\%$ ,  $p = 0.04$ ). **Conclusions:** The observed increase in preferred walking speed, reduction in metabolic cost of transport, and improved performance on clinical tests of mobility highlights the potentially transformative nature of this novel therapy; the rate at which this intervention elicited improved function was 3 - 6 times greater than what has been reported previously.

PMID: [33251524](#)

### **13. Designing Exercise to Improve Bone Health Among Individuals With Cerebral Palsy**

Mary E Gannotti, Brianna M Liquori, Deborah E Thorpe, Robyn K Fuchs

Pediatr Phys Ther. 2020 Dec 2. doi: 10.1097/PEP.0000000000000765. Online ahead of print.

**Purpose:** Individuals with cerebral palsy (CP), ambulatory or not, have less bone strength and density than their peers. Aging individuals with CP are at a higher risk for nontraumatic fractures, progressive deformity, pain, and spinal stenosis. Critical

periods for skeletal formation are during prepuberty and adolescence. Applying mechanostat theory to exercise design for individuals with CP may be beneficial. Methods: Principles of mechanostat theory, particularly the osteogenic index, is applied to guide the design of exercise programs based on varying levels of physical capacity. Results: Recommendations are made for optimizing dosing of a variety of interventions for improving bone health among individuals with CP based on mechanostat theory with specific type, number of repetitions, and frequency. Conclusions: Researchers and clinicians are called to action to consider the role of exercise throughout the lifespan for all individuals with CP, regardless of level of severity.

PMID: [33273256](#)

#### **14. Effectiveness of Botulinum Toxin A injection in managing mobility related outcomes in adult patients with cerebral palsy - systematic review**

Nalinda D Andraweera, Prabha H Andraweera, Zohra S Lassi, Venugopal Kochiyil

Am J Phys Med Rehabil. 2020 Nov 26. doi: 10.1097/PHM.0000000000001653. Online ahead of print.

Purpose: Intramuscular Botulinum toxin A (BTX-A) is used in the management of focal spasticity in cerebral palsy (CP). We aimed to conduct a systematic review to assess current literature on the use of BTX-A in the management of mobility related outcomes among adult persons with spastic CP. Methods: All studies reporting on the use of BTX-A in the management of spastic CP among adult persons were identified by searching the following electronic databases: PubMed, CINAHL, the Cochrane Library, and EMBASE. Results: Six studies were included in the review. Most studies were conducted in mixed patient groups comprising patients with movement disorders, traumatic brain injury, cerebral palsy and other disorders requiring therapy for spasticity. BTX-A was shown to be effective in improving spasticity related outcomes among persons with CP but mixed results were shown for functional outcomes. Conclusions: More studies are required on exclusive CP cohorts using recommended and currently used scales, incorporating Quality of life and patient satisfaction scales. Results from long term follow up studies will be valuable for better evaluation of the effectiveness of BTX-A in the management of spasticity related outcomes among adult persons with CP.

PMID: [33252471](#)

#### **15. Functional outcomes of botulinum neurotoxin-A injection followed by reciprocal electrical stimulation in children with cerebral palsy: A randomized controlled trial**

Ragab K Elnaggar, Bader A Alqahtani, Mohammed F Elbanna

Restor Neurol Neurosci. 2020 Nov 23. doi: 10.3233/RNN-201088. Online ahead of print.

Background: The integration of therapeutic approaches is increasingly recommended for children with cerebral palsy, to enhance outcomes. Nevertheless, clinicians still opt for separate or combined therapies based on little credible knowledge. Objective: This study endeavored to evaluate the effect of botulinum neurotoxin-A (BoNT-A) injection and reciprocal neuromuscular electrical stimulation (rNMES) and their combination on the upper extremity function in children with spastic hemiplegia. Methods: Sixty-four children with spastic hemiplegia (aged 6- 10 years) were randomly assigned to four treatment-based groups [group I (BoNT-A), group II (rNMES), group III (combined BoNT-A and rNMES), and group IV (Control)]. All children received a physical rehabilitation program, thrice/week over three months. Unilateral upper-limb function, bimanual hand function, and real-time arm-hand function were assessed using Melbourne Assessment (MA), Assisting Hand Assessment (AHA), and Pediatric Motor Activity Log (PMAL) scales respectively pre-treatment, post-treatment, and at 6 months follow-up. Results: Post-treatment, group III achieved greater improvement in MA, AHA, and PMAL compared to other groups (all  $P < 0.05$ ), and the difference remained in favor of group III at the follow-up (all  $P < 0.05$ ). Conclusions: This study suggests that BoNT-A and rNMES combined are more effective than either of them alone to enhance upper-extremity function in children with spastic hemiplegia.

PMID: [33252102](#)

#### **16. Clinician Perspectives of Chronic Pain Management in Children and Adolescents with Cerebral Palsy and Dyskinesia**

Clare McKinnon, Jennifer White, Prue Morgan, Adrienne Harvey, Catherine Clancy, Michael Fahey, Giuliana Antolovich

Phys Occup Ther Pediatr. 2020 Nov 29;1-15. doi: 10.1080/01942638.2020.1847236. Online ahead of print.

**Aims:** To explore perspectives of clinicians from interdisciplinary teams on the barriers and facilitators to chronic pain management for children and adolescents with cerebral palsy and dyskinesia. **Methods:** Interdisciplinary focus groups (n = 2) were conducted at two Australian tertiary pediatric hospitals. Twenty-five experienced clinicians took part, including ten physiotherapists, six pediatricians, four rehabilitation physicians, four occupational therapists, and one speech and language therapist. An external moderator conducted the focus groups and data were analyzed using inductive thematic analysis. **Results:** Four key themes emerged: "balancing the intersection of pain and dyskinesia," "difficulty communicating between so many providers," "uncertainty surrounding chronic pain education," and "differing priorities." Key barriers were identified including a lack of access to some interdisciplinary team members and formalized guidance for health professionals regarding chronic pain education. **Conclusion:** Key issues were reported to impact the delivery of coordinated inter-disciplinary chronic pain management at the tertiary level for children and adolescents with cerebral palsy and dyskinesia. In the absence of strong evidence, a strategy for implementing effective chronic pain management for children and adolescents with cerebral palsy and dyskinesia and gaining clinician consensus regarding the best practice management are recommended.

PMID: [33251932](#)

### **17. Visual impairment and perceptual visual disorders in children with cerebral palsy in Nigeria**

Roseline Ekanem Duke, Justin Nwachukwu, Chima Torty, Uche Okorie, Min J Kim, Kathryn Burton, Clare Gilbert, Richard Bowman

Br J Ophthalmol. 2020 Dec 2;bjophthalmol-2020-317768. doi: 10.1136/bjophthalmol-2020-317768. Online ahead of print.

Cerebral palsy (CP) is the most common cause of childhood physical disability globally. This study describes the spectrum of ocular morbidity and visual impairment in a community-based (recruited by key informants) sample of children with CP in Cross River State, Nigeria. **Methods:** A paediatric neurologist clinically confirmed CP and assessed systemic comorbidity. Ophthalmological assessment included developmental age appropriate acuity tests, objective refraction and objective and subjective tests of perceptual visual dysfunction (PVD). **Results:** 388 children aged 4-15 years with CP were identified. Visual problems were reported by carers in only 55 (14%) cases. Binocular visual acuity impairment was seen in 20/201 by Lea symbols test (10%) and 213/388 (55%) by the mirror test. Abnormal visual fields were seen in 58/388 (14.9%); strabismus in 183 (47%) abnormal contrast sensitivity in 178 (46%) and abnormal saccades in 84 (22%), spherical refractive errors in 223 (58%), significant astigmatism in 36 (12%), accommodative dysfunction in 41 (10.6%), optic atrophy in 198 (51%). Perceptual visual disorders were present in 22 (6%) subjectively and 177 (46%) objectively. The estimated frequency of cerebral visual impairment (CVI) in children ranged from 61 (16%) to 191 (49%) if children with optic atrophy were included. **Conclusion:** Children with CP have a wide spectrum of ocular morbidity and visual impairment, underestimated by carers. Children with CP require visual acuity assessments with a range of tests which account for associated comorbidities and oculomotor dysfunction. Functional vision assessments for PVD is important. CVI is common.

PMID: [33268343](#)

### **18. Thalamic deep brain stimulation for acquired dystonia in children and young adults: a phase 1 clinical trial**

Marta San Luciano, Amy Robichaux-Viehoever, Kristen A Dodenhoff, Melissa L Gittings, Aaron C Viser, Caroline A Racine, Ian O Bledsoe, Christa Watson Pereira, Sarah S Wang, Philip A Starr, Jill L Ostrem

J Neurosurg Pediatr. 2020 Nov 27;1-10. doi: 10.3171/2020.7.PEDS20348. Online ahead of print.

**Objective:** The aim of this study was to evaluate the feasibility and preliminary efficacy and safety of combined bilateral ventralis oralis posterior/ventralis intermedius (Vop/Vim) deep brain stimulation (DBS) for the treatment of acquired dystonia in children and young adults. Pallidal DBS is efficacious for severe, medication-refractory isolated dystonia, providing 50%-60% long-term improvement. Unfortunately, pallidal stimulation response rates in acquired dystonia are modest and unpredictable, with frequent nonresponders. Acquired dystonia, most commonly caused by cerebral palsy, is more common than isolated dystonia in pediatric populations and is more recalcitrant to standard treatments. Given the limitations of pallidal

DBS in acquired dystonia, there is a need to explore alternative brain targets. Preliminary evidence has suggested that thalamic stimulation may be efficacious for acquired dystonia. Methods: Four participants, 3 with perinatal brain injuries and 1 with postencephalitic symptomatic dystonia, underwent bilateral Vop/Vim DBS and bimonthly evaluations for 12 months. The primary efficacy outcome was the change in Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) and Barry-Albright Dystonia Scale (BADs) scores between the baseline and 12-month assessments. Video documentation was used for blinded ratings. Secondary outcomes included evaluation of spasticity (Modified Ashworth Scale score), quality of life (Pediatric Quality of Life Inventory [PedsQL] and modified Unified Parkinson's Disease Rating Scale Part II [UPDRS-II] scores), and neuropsychological assessments. Adverse events were monitored for safety. Results: All participants tolerated the procedure well, and there were no safety concerns or serious adverse events. There was an average improvement of 21.5% in the BFMDRS motor subscale score, but the improvement was only 1.6% according to the BADs score. Following blinded video review, dystonia severity ratings were even more modest. Secondary outcomes, however, were more encouraging, with the BFMDRS disability subscale score improving by 15.7%, the PedsQL total score by 27%, and the modified UPDRS-II score by 19.3%. Neuropsychological assessment findings were unchanged 1 year after surgery. Conclusions: Bilateral thalamic neuromodulation by DBS for severe, medication-refractory acquired dystonia was well tolerated. Primary and secondary outcomes showed highly variable treatment effect sizes comparable to those of pallidal stimulation in this population. As previously described, improvements in quality of life and disability were not reflected in dystonia severity scales, suggesting a need for the development of scales specifically for acquired dystonia. Clinical trial registration no.: NCT03078816 (clinicaltrials.gov).

PMID: [33254134](#)

### **19. Effect of Equine-Assisted Activities on Cardiac Autonomic Function in Children with Cerebral Palsy: A Pilot Randomized-Controlled Trial**

In-Kyeong Park, Ji Young Lee, Min-Hwa Suk, Soojin Yoo, Yong-Gon Seo, Jea-Keun Oh, Jeong-Yi Kwon

J Altern Complement Med. 2020 Nov 27. doi: 10.1089/acm.2020.0346. Online ahead of print.

Objective: Children with cerebral palsy (CP) have an impaired cardiac autonomic function. Attenuated heart rate recovery (HRR), which is a valuable prognostic parameter for autonomic nervous system, is known to be associated with an increased risk of cardiovascular events and all-cause mortality. However, only few studies have observed the effects of exercise on the cardiac autonomic function in children with CP. The purpose of this pilot study was to examine the effects of equine-assisted activity (EAA) program on cardiac autonomic function in children with CP. Design: A single-blinded, parallel, two-arm pilot trial with 1:1 randomization to the EAA or control group. Setting: A tertiary university hospital and a local arena. Subjects: Twenty-six children with CP (Gross Motor Function Classification System Levels I-II). Intervention: Each lesson of the EAA program for the EAA group was conducted for 40 min twice a week, and the whole program duration was 16 weeks (a total of 32 sessions). Outcome measures: A graded exercise test was performed to measure the resting heart rate (RHR), HRR, and peak oxygen uptake (VO<sub>2</sub>peak) on both groups before and after the 16-week period. Results: The autonomic nervous function measured by the response of HRR improved at 1 min ( $p < 0.009$ ), 3 min ( $p < 0.001$ ), and 5 min ( $p < 0.004$ ) only in the EAA group. RHR significantly improved in the EAA group ( $p < 0.013$ ), whereas the VO<sub>2</sub>peak did not significantly differ between the two groups. Conclusion: The HRR and RHR of the children with CP improved after completing the 16-week EAA program. The results demonstrated that the program had a positive effect on the improvement of cardiac autonomic function in these patients. Clinical Trial Registration Number: NCT03870893.

PMID: [33252241](#)

### **20. Detecting physical abilities through smartphone sensors: an assistive technology application**

Paul Whittington, Huseyin Dogan, Keith Phalp, Nan Jiang

Disabil Rehabil Assist Technol. 2020 Dec 1;1-12. doi: 10.1080/17483107.2020.1839135. Online ahead of print.

Purpose: It is important to promote assistive technologies to improve quality of life. The proposed SmartAbility Android Application recommends assistive technologies for people with reduced physical abilities, by focussing on actions that can be performed independently. Materials and methods: The SmartAbility Application uses Android built-in sensors, e.g., accelerometer and gyroscope and application programming interfaces (APIs) to detect physical abilities, e.g., head movements and blowing and recommend suitable assistive technologies. This is supported by a MySQL database that stores assistive technologies and mappings between abilities. The underpinning research is the SmartAbility Framework that culminates the



knowledge obtained during previously feasibility trials and usability evaluations. Results: The Application was evaluated by pupils (n = 18) at special educational needs schools with physical conditions, including cerebral palsy, autism and Noonan syndrome, and assessed through the NASA Task Load Index (TLX) and System Usability Scale (SUS). Analysis using the Adjective Rating Scale highlighted that the Application achieves "Good Usability". Conclusion: The SmartAbility Application demonstrates that built-in sensors of Android devices and their APIs, can detect actions that users perform, e.g., head movements and speaking. The Application contains a database where assistive technologies are mapped to physical abilities, in order to provide suitable recommendations. It will be disseminated to assistive technology charities and manufacturers and be used by healthcare professionals as part of the rehabilitation process. Future developments of SmartAbility include the creation of a second Application designed specifically to recommend assistive technologies for the education sector, based on users' physical and cognitive abilities. IMPLICATIONS FOR REHABILITATION Assistive technology is any item, equipment or piece of software designed to increase, maintain or improve the functional capabilities of people with disabilities. SmartAbility should be introduced into rehabilitation to promote awareness of assistive technologies that are suitable for the physical abilities of the user. Our research highlighted that physical abilities can be detected using built-in sensors of Android devices, e.g. accelerometer and gyroscope. Involvement of the intended user community during evaluations is essential to ensure that a smartphone application is suitable for people with reduced physical abilities. Assistive technologies can support the rehabilitation of people with reduced physical abilities by providing increased independence and improved quality of life.

PMID: [33258392](#)

### **21. Better Together: the Australasian Academy of Cerebral Palsy and Developmental Medicine champions equity**

Kirsty Stewart, Christine Imms, Sarah McIntyre, Gaela Kilgour, Kim Clayworth

Dev Med Child Neurol. 2020 Nov 28. doi: 10.1111/dmcn.14752. Online ahead of print.

PMID: [33249564](#)

### **22. Cognitive Event-Related Potentials in Young Adults With Cerebral Palsy: A Proof-of-Concept Study**

Christine L Lackner, Jan Willem Gorter, Sidney J Segalowitz, MyStory Study Group

Clin EEG Neurosci. 2020 Dec 3;1550059420977318. doi: 10.1177/1550059420977318. Online ahead of print.

Cerebral palsy (CP) is a movement and posture disorder often accompanied by cognitive difficulties which can be assessed using event-related potentials (ERPs), an often-overlooked tool in this population. Here we describe our assessment protocol, examine its feasibility, and validate the use of single-subject ERP analyses in adolescents and young adults with CP, an analysis approach which recognizes the heterogeneity of the clinical population. This study involved a final sample of 9 adolescents/young adults with CP participating in the "MyStory" study (age range 16-29 years, Mage = 25.0 years; 6 female; Gross Motor Function Classification System level I [n = 4], II [n = 2], III [n = 1], IV [n = 1], and V [n = 1]). ERP components were elicited over medial prefrontal and central cortex (error- and correct-related negativities [ERN/CRN], error-positivity [Pe], N100, P200, N200, P300), as well as those generated over occipital cortex (P100, N170). Group and single-subject ERP statistics were computed for ERPs recorded over both areas. Using recently developed data analysis methods (independent components analysis and robust bootstrapped single-subject statistics), we measured the number of participants demonstrating significant condition differences at the timing of each ERP component of interest. We demonstrate good validity for ERPs recorded during 2 of our 3 tasks eliciting frontal activation (eg, 4 of 6 participants with usable data showed a significant single-subject medial frontal negativity condition difference in a context-switching task) and good validity for ERPs derived from a task engaging occipital regions (eg, 8 of 9 participants each showed a significant N170 face-object condition effect).

PMID: [33267615](#)

### **23. Evidence of continued reduction in the age-at-death disparity between adults with and without intellectual and/or developmental disabilities**

Scott D Landes, Katherine E McDonald, Janet M Wilmoth, Erika Carter Grosso

J Appl Res Intellect Disabil. 2020 Nov 27. doi: 10.1111/jar.12840. Online ahead of print.

**Background:** This study examines recent trends in the age-at-death disparity between adults with and without intellectual and/or developmental disabilities in the United States. **Method:** Data were from the 2005-2017 U.S. death certificates. Average age at death was compared between adults whose death certificate did or did not report an intellectual and/or developmental disability. **Results:** Age at death increased minimally for adults without, but markedly for adults with intellectual and/or developmental disabilities. As a result, the age-at-death disparity decreased: 2.2 years between adults with/without intellectual disability; 1.9 years between adults with/without Down syndrome; 2.7 years between adults with/without cerebral palsy; and 5.1 years between adults with/without rare developmental disabilities. **Conclusion:** Evidence from this study demonstrates that the age-at-death disparity between adults who did or did not have an intellectual and/or developmental disability reported on their death certificate continues to decrease, but the magnitude of the remaining disparity varied considerably by type of disability.

PMID: [33247487](#)

#### **24. A Comparison of Bispectral Index and Entropy During Sevoflurane Anesthesia Induction in Children with and without Diplegic Cerebral Palsy**

Young Sung Kim, Young Ju Won, Hyerim Jeong, Byung Gun Lim, Myoung Hoon Kong, Il Ok Lee

Entropy (Basel). 2019 May 15;21(5):498. doi: 10.3390/e21050498.

**Background:** This study compared the correlation of bispectral index (BIS) or entropy with different sevoflurane concentrations between children with and without cerebral palsy (CP) during induction. **Methods:** For eighty-two children (40 CP and 42 non-CP children), anesthesia was induced with sevoflurane. BIS and entropy (response entropy and state entropy (RE and SE)) were recorded before and after the induction of anesthesia at end-tidal sevoflurane concentrations of 1-3 vol%. The sedation status was assessed using an Observer's Assessment of Alertness/Sedation scale. The ability to predict awareness was estimated using the area under the receiver-operator characteristic curve (AUC) analysis. **Results:** RE, SE and BIS values decreased continuously over the observed concentration range of sevoflurane in both groups. The SE values while awake and the RE, SE, BIS values at 3 vol% sevoflurane were lower in children with CP than in those without CP. The AUC of the BIS was significantly better than RE or SE in children without CP. The AUC of the BIS was not significantly higher than that of the RE or SE in children with CP. **Conclusion:** BIS seems better correlated than entropy with the clinical state of loss of response in children without CP, but not in those with CP.

PMID: [33267212](#)

#### **25. Serum trace element and amino acid profile in children with cerebral palsy**

Alexey A Tinkov, Margarita G Skalnaya, Anatoly V Skalny

J Trace Elem Med Biol. 2020 Nov 12;64:126685. doi: 10.1016/j.jtemb.2020.126685. Online ahead of print.

**Background:** The existing data demonstrate that both trace elements and amino acids play a significant role in neurodevelopment and brain functioning. Certain studies have demonstrated alteration of micronutrient status in children with cerebral palsy, although multiple inconsistencies exist. **Objective:** of the present study was to assess serum trace element and mineral, as well as amino acid levels in children with cerebral palsy. **Methods:** 71 children with cerebral palsy (39 boys and 32 girls,  $5.7 \pm 2.3$  y.o.) and 84 healthy children (51 boys and 33 girls,  $5.4 \pm 2.3$  y.o.) were enrolled in the present study. Serum trace element and mineral levels were assessed using inductively-coupled plasma mass-spectrometry (ICP-MS). Amino acid profile was evaluated by means of high-pressure liquid chromatography (HPLC). **Results:** Children with cerebral palsy are characterized by significantly lower Cu and Zn levels by 6% and 8%, whereas serum I concentration exceeded the control values by 7%. A tendency to increased serum Mn and Se levels was also observed in patients with cerebral palsy. Serum citrulline, leucine, tyrosine, and valine levels were 15 %, 23 %, 15 %, and 11 % lower than those in healthy controls. Nearly twofold lower levels of serum proline were accompanied by a 44 % elevation of hydroxyproline concentrations when compared to the control values. In multiple regression model serum I, Zn, and hydroxyproline levels were found to be independently associated with the presence of cerebral palsy. Correlation analysis demonstrated a significant correlation between Cu, Mn, Se, I, and Zn levels with hydroxyproline and citrulline concentrations. **Conclusion:** The observed alterations in trace element and amino acid metabolism may contribute to neurological deterioration in cerebral palsy. However, the cross-sectional design of the study does not allow to estimate the causal trilateral relationships between cerebral palsy, altered trace

element, and amino acid metabolism.

PMID: [33249374](#)

## **26. Neurodevelopmental impairment at 2 years of age in children born before 29 weeks' gestation with bronchopulmonary dysplasia**

L Decollogne, C Epiard, M Chevallier, A Ego, L Alin, T Debillon

Arch Pediatr. 2020 Nov 27;S0929-693X(20)30239-6. doi: 10.1016/j.arcped.2020.10.012. Online ahead of print.

**Introduction:** Very preterm children are at a high risk for neurological impairment, especially those with bronchopulmonary dysplasia (BPD). The main goal of this study was to describe the neurodevelopmental impairment (NDI) at 2 years of corrected age in children born before 29 weeks' gestation between 2010 and 2015 and affected by BPD at 28 days of life. We also searched for risk factors associated with NDI, especially postnatal steroid (PNS) administration. **Material and methods:** This was a retrospective study comprising a cohort of children hospitalized at the university hospital in Grenoble, born before 29 weeks' gestation between 2010 and 2015, and included in the monitoring network "Naitre et Devenir" (RND). Infants at 2 years of corrected age were classified as having NDI if they had at least one of the following outcomes: a global developmental quotient (DQ) on the revised Brunet-Lézine scale of <85, blindness, deafness, or cerebral palsy (CP) graded as level 3 or more according to the Gross Motor Function Classification System. **Results:** A total of 129 children were included, of whom 99 were monitored at the age of 2 years: 31.3% of the population had NDI and 4% had CP. The median DQ test result was 90 (interquartile 82-97). Factors associated with NDI in univariate analysis were low gestational age, low birth weight, a cord pH<7.2, chorioamnionitis, treatment for persistent ductus arteriosus, longer oxygen therapy, and outborn status, which almost reached statistical significance. In multivariate analysis, low gestational age and outborn status remained statistically significant, while chorioamnionitis was found to have some association with NDI. While 13.1% of the followed-up population was treated with PNS, this risk factor was not associated with NDI. **Conclusion:** In a population of very preterm children, one third had NDI at 2 years of corrected age. Low gestational age, outborn status, and perinatal inflammation are associated with this unfavorable outcome. The frequency of sequelae confirms the importance of following up these children.

PMID: [33257210](#)

## **27. Commentary on 'Psychological morbidity among adults with cerebral palsy and spina bifida': how can we support adults with cerebral palsy or spina bifida to achieve better psychological outcomes?**

Mary E Gannotti

Psychol Med. 2020 Dec 2;1-2. doi: 10.1017/S0033291720004365. Online ahead of print.

PMID: [33261690](#)

## **28. Gastric antral vascular ectasia in children, rare presentation**

Matthew Pizzuto, Sarah Ellul, Mohamed Shoukry

BMJ Case Rep. 2020 Nov 30;13(11):e236896. doi: 10.1136/bcr-2020-236896.

A 14-year-old boy, a known case of perinatal hypoxic cerebral palsy, presented to paediatric emergency with acute melaena and blood staining around feeding gastrostomy site. Physical examination revealed pallor, but no signs of distress with an unremarkable abdominal examination. Routine blood tests revealed normochromic. Abdominal ultrasound scan and Meckel's scan were unremarkable. The patient underwent examination under anaesthesia of the perianal area and joint upper and lower gastrointestinal endoscopy. Streak-like gastritis with no signs of active bleeding lesions were noted and patchy areas of colitis involving the descending and sigmoid colon and the rectum. All clinical findings and evidence-based diagnosis matched gastric antral vascular ectasia. He was successfully managed conservatively with elemental hydrolysed feeding formula.

PMID: [33257371](#)

**29. A risk-stratified approach toward safely resuming OnabotulinumtoxinA injections based on dosing and ambulatory status in pediatric patients with cerebral palsy during the Coronavirus pandemic of 2019 (COVID-19)**

Matthew J McLaughlin, Mark T Fisher, Sathya Vadivelu, Justin Ramsey, Denesh Ratnasingam, Emily McGhee, Kim Hartman

J Pediatr Rehabil Med. 2020;13(3):273-279. doi: 10.3233/PRM-200756.

**Purpose:** After the onset of the Coronavirus pandemic of 2019-2020 (COVID-19), physicians who inject OnabotulinumtoxinA (BoNT-A) were left with determining risks and benefits in pediatric patients with cerebral palsy. Many of these patients have pre-existing conditions that make them more prone to COVID-19 symptoms, and this susceptibility potentially increases after BoNT-A injections. **Methods:** A retrospective chart review of 500 patients identified 256 pediatric patients with cerebral palsy who received an intramuscular BoNT-A injection to determine relative doses used for each Gross Motor Functional Classification Score (GMFCS). Data regarding age, weight, GMFCS, BoNT-A total body dosage, and inpatient hospitalizations for 6 months post-injection were collected. Differences between GMFCS levels were analyzed using one-way analysis of variance testing. Inpatient hospitalizations were recorded and assessed using relative risk to determine the population risk of hospitalization in the setting of initiating injections during the COVID-19 pandemic. **Results:** Based on GMFCS level, patients who were GMFCS I or II received fewer units of BoNT-A medication per kilogram of body weight compared to GMFCS III-V ( $p < 0.0005$ ,  $F = 25.38$ ). There was no statistically significant difference in frequency or time to hospitalization when comparing patients receiving BoNT-A compared to a control group. **Conclusions:** Resumption of BoNT-A injections during the time of COVID-19 requires a systematic approach based on risks and potential benefits. Data from this analysis does not show increased risk for patients who received injections historically; however, recommendations for resumption of injections has not previously been proposed in the setting of a pandemic. In this manuscript, a tiered approach to considerations for injections was proposed. Botulinum toxin type A injections have a history of improving spasticity in the pediatric patient with cerebral palsy. Ensuring appropriate selection of patients for injection with BoNT-A during this pandemic is increasingly important.

PMID: [33252098](#)

## Prevention and Cure

**30. Perinatal care with a view to preventing cerebral palsy**

Nadia Badawi, Sarah Mcintyre, Rod W Hunt

Review Dev Med Child Neurol. 2020 Nov 29. doi: 10.1111/dmcn.14754. Online ahead of print.

Birth prevalence of cerebral palsy (CP) is declining in high-income countries, to as low as 1.4 per 1000 live births in the most recent international reports. This represents a 35% reduction in birth prevalence over a 15-year period. This reduction is underpinned by a heightened focus of attention towards all aspects of CP, including: increased awareness, better data collection, development of national networks and registries, an explosion of research in basic science, perinatal care, neonatal neurology, public health, early detection, and targeted early intervention. Quick uptake of evidence into practice has ensued and overall improvements in clinical care occurred concurrently. It is anticipated that with continued partnerships with families, ongoing research driving further clinical improvement and vice versa, birth prevalence and severity of CP will further decline and the focus will shift to prevention in low- and middle-income countries.

PMID: [33251607](#)

**31. Potentiation of cord blood cell therapy with erythropoietin for children with CP: a 2 × 2 factorial randomized placebo-controlled trial**

Kyunghoon Min, Mi Ri Suh, Kye Hee Cho, Woogyung Park, Myung Seo Kang, Su Jin Jang, Sang Heum Kim, Seonkyeong Rhie, Jee In Choi, Hyun-Jin Kim, Kwang Yul Cha, MinYoung Kim

Stem Cell Res Ther. 2020 Nov 27;11(1):509. doi: 10.1186/s13287-020-02020-y.

**Background:** Concomitant administration of allogeneic umbilical cord blood (UCB) infusion and erythropoietin (EPO) showed therapeutic efficacy in children with cerebral palsy (CP). However, no clinical studies have investigated the effects of UCB and EPO combination therapy using a  $2 \times 2$  four-arm factorial blinded design with four arms. This randomized placebo-controlled trial aimed to identify the synergistic and individual efficacies of UCB cell and EPO for the treatment of CP. **Methods:** Children diagnosed with CP were randomly segregated into four groups: (A) UCB+EPO, (B) UCB+placebo EPO, (C) placebo UCB+EPO, and (D) placebo UCB+placebo EPO. Based on the UCB unit selection criteria of matching for  $\geq 4/6$  of human leukocyte antigen (HLA)-A, -B, and DRB1 and total nucleated cell (TNC) number of  $\geq 3 \times 10^7/\text{kg}$ , allogeneic UCB was intravenously infused and 500 IU/kg human recombinant EPO was administered six times. Functional measurements, brain imaging studies, and electroencephalography were performed from baseline until 12 months post-treatment. Furthermore, adverse events were closely monitored. **Results:** Eighty-eight of 92 children enrolled ( $3.05 \pm 1.22$  years) completed the study. Change in gross motor performance measure (GMPM) was greater in group A than in group D at 1 month ( $\Delta 2.30$  vs.  $\Delta 0.71$ ,  $P = 0.025$ ) and 12 months ( $\Delta 6.85$  vs.  $\Delta 2.34$ ,  $P = 0.018$ ) post-treatment. GMPM change ratios were calculated to adjust motor function at the baseline. Group A showed a larger improvement in the GMPM change ratio at 1 month and 12 months post-treatment than group D. At 12 months post-treatment, the GMPM change ratios were in the order of groups A, B, C, and D. These results indicate synergistic effect of UCB and EPO combination better than each single therapy. In diffusion tensor imaging, the change ratio of fractional anisotropy at spinothalamic radiation was higher in group A than group D in subgroup of age  $\geq 3$  years. Additionally, higher TNC and more HLA-matched UCB units led to better gross motor outcomes in group A. Adverse events remained unchanged upon UCB or EPO administration. **Conclusions:** These results indicate that the efficacy of allogeneic UCB cell could be potentiated by EPO for neurological recovery in children with CP without harmful effects. Trial registration: ClinicalTrials.gov, NCT01991145, registered 25 November 2013.

PMID: [33246489](https://pubmed.ncbi.nlm.nih.gov/33246489/)

### **32. Prophylactic inhibition of NF- $\kappa$ B expression in microglia leads to attenuation of hypoxic ischemic injury of the immature brain**

Nahla Zaghoul, Dalibor Kurepa, Mohammad Y Bader, Nadia Nagy, Mohamed N Ahmed

J Neuroinflammation. 2020 Dec 1;17(1):365. doi: 10.1186/s12974-020-02031-9.

**Background:** Periventricular leukomalacia (PVL), a devastating brain injury affecting premature infants, is the most common cause of cerebral palsy. PVL is caused by hypoxia ischemia (HI) and is characterized by white matter necrotic lesions, microglial activation, upregulation of NF- $\kappa$ B, and neuronal death. The microglia is the main cell involved in PVL pathogenesis. The goal of this study was to investigate the role of microglial NF- $\kappa$ B activity and its prophylactic inhibition in a neonate mouse model of HI. **Methods:** Transgenic mice with specific knockout NF- $\kappa$ B in microglia and colony stimulating factor 1 receptor Cre with floxed IKK $\beta$  (CSF-1R Cre + IKK $\beta$ flox/wt) were used. Postnatal day 5 (P5) mice underwent sham or bilateral temporary carotid artery ligation followed by hypoxia. After HI insult, inflammatory cytokines, volumetric MRI, histopathology, and immunohistochemistry for oligodendroglia and microglial activation markers were analyzed. Long-term neurobehavioral assessment, including grip strength, rotarod, and open field testing, was performed at P60. **Results:** We demonstrate that selective inhibition of NF- $\kappa$ B in microglia decreases HI-induced brain injury by decreasing microglial activation, proinflammatory cytokines, and oxidative stress. Rescue of oligodendroglia is evidenced by immunohistochemistry, decreased ventriculomegaly on MRI, and histopathology. This selective inhibition leads to attenuation of paresis, incoordination, and improved grip strength, gait, and locomotion. **Conclusion:** We conclude that NF- $\kappa$ B activation in microglia plays a major role in the pathogenesis of hypoxic ischemic injury of the immature brain, and its prophylactic inhibition offers significant neuroprotection. Using a specific inhibitor of microglial NF- $\kappa$ B may offer a new prophylactic or therapeutic alternative in preterm infants affected by HI and possibly other neurological diseases in which microglial activation plays a role.

PMID: [33261624](https://pubmed.ncbi.nlm.nih.gov/33261624/)