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Interventions and Management

1. Hand Assessment for Infants: normative reference values.

Ek L, Eliasson AC, Sicola E, Sjöstrand L, Guzzetta A, Sgandurra G, Cioni G, Krumlinde-Sundholm L.

Dev Med Child Neurol. 2019 Feb 4. doi: 10.1111/dmcn.14163. [Epub ahead of print]

AIM: To create normative reference values for unilateral and bilateral use of the hands, using the Hand Assessment for Infants (HAI), a newly developed criterion-referenced assessment measuring hand use in infants aged 3 months to 12 months at risk of cerebral palsy (CP). **METHOD:** In total, 489 HAI assessments of typically developing infants (243 females, 246 males), aged 3 months to 10 months (mean 6mo 14d [SD 2mo 5d]), were collected in Italy and Sweden. Normative growth curves based on mean and SDs were created, as well as skill acquisition curves for each test item. Correlation to age and differences between groups based on sex and nationality, as well as differences between the right and the left hand, were investigated. **RESULTS:** The growth curves showed a steady increase in mean value and a decrease in SD over age. There were no differences between groups based on sex or nationality. There was a negligible mean difference (0.1 raw score) between the right and left hands. **INTERPRETATION:** HAI normative reference values are now available, which can assist in identifying deviating hand use for each month of age, as well as a side difference between hands in infants at risk of CP.

PMID: [30719697](#)

2. Interest of children with unilateral spastic cerebral palsy in bimanual daily activities.

Oliveira RHS, Brandão MB, Mambrini JVM, Mancini MC.

Scand J Occup Ther. 2019 Feb 8:1-9. doi: 10.1080/11038128.2018.1561938. [Epub ahead of print]

BACKGROUND: Many bimanual activities are challenging for children with unilateral spastic cerebral palsy (USCP). **AIMS:** To investigate hand use by children with USCP in daily activities of their interest. **Material e methods:** Sample included twenty children with USCP, aged 8 to 14 years old. Participants identified bimanual activities of their interest and no interest. Children's performance on these activities were videotaped. Videos were coded according to the affected extremity's forms and effectiveness of use, caregiver provision and types of assistance, and child's satisfaction. The relative proportions of each parameter were compared using the signed-rank test, considering the time spent in activities of interest and no interest. **RESULTS:** We analyzed 116 activities. We found effects of interest in children's satisfaction ($p = 0.003$) and on the type of assistance ($p = 0.03$). Specifically, children demonstrated longer periods of satisfaction performing activities of their interest and caregiver physical assistance was provided for longer periods of time in activities of no interest. There were no effects on the other parameters. **CONCLUSIONS:** A model that illustrates the impact of a child's interest on the performance of daily bimanual activities is presented, grounded in our results and in the literature.

PMID: [30734615](#)

3. Transcranial Direct Current Stimulation (tDCS) in Unilateral Cerebral Palsy: A Pilot Study of Motor Effect.

Inguaggiato E, Bolognini N, Fiori S, Cioni G.

Neural Plast. 2019 Jan 14;2019:2184398. doi: 10.1155/2019/2184398. eCollection 2019.

Transcranial Direct Current Stimulation (tDCS) is an emerging tool to improve upper limb motor functions after stroke acquired in adulthood; however, there is a paucity of reports on its efficacy for upper limb motor rehabilitation in congenital or early-acquired stroke. In this pilot study we have explored, for the first time, the immediate effects, and their short-term persistence, of a single application of anodal tDCS on chronic upper limb motor disorders in children and young individuals with Unilateral Cerebral Palsy (UCP). To this aim, in a crossover sham-controlled study, eight subjects aged 10-28 years with UCP underwent two sessions of active and sham tDCS. Anodal tDCS (1.5 mA, 20 min) was delivered over the primary motor cortex (M1) of the ipsilesional hemisphere. Results showed, only following the active stimulation, an immediate improvement in unimanual gross motor dexterity of hemiplegic, but not of nonhemiplegic, hand in Box and Block test (BBT). Such improvement remained stable for at least 90 minutes. Performance of both hands in Hand Grip Strength test was not modified by anodal tDCS. Improvement in BBT was unrelated to participants' age or lesion size, as revealed by MRI data analysis. No serious adverse effects occurred after tDCS; some mild and transient side effects (e.g., headache, tingling, and itchiness) were reported in a limited number of cases. This study provides an innovative contribution to scientific literature on the efficacy and safety of anodal tDCS in UCP. This trial is registered with NCT03137940.

PMID: [30733800](#)

4. The Cerebral Palsy Profile of Health and Function: Upper-Extremity Domain's Sensitivity to Change Following Musculoskeletal Surgery.

Grampurohit N, Slavin M, Ni P, Kozin S, Jette A, Mulcahey M.

J Hand Surg Am. 2019 Feb 4. pii: S0363-5023(18)30485-4. doi: 10.1016/j.jhsa.2018.12.007. [Epub ahead of print]

PURPOSE: The Cerebral Palsy Profile of Health and Function (CP-PRO) Computerized Adaptive Tests (CAT) are quality of life measures developed specifically for use in children with cerebral palsy. This study examined the ability of the upper-extremity (UE) CP-PRO CAT to detect change in function after UE surgery compared with the Pediatric Outcomes Data Collection Instrument (PODCI), ABILHAND-Kids, and Box and Blocks test. **METHODS:** From 2009 to 2013, children with cerebral palsy who had UE musculoskeletal surgery completed the UE CP-PRO CAT, PODCI-UE, ABILHAND-Kids, and Box and Blocks tests before surgery (97 children) and at 3 postoperative intervals: 6 months (80 children), 12 months (73 children), and 24 months (52 children). Mean, SD, effect size (ES), and standardized response mean (SRM) values for each measure at each time interval and each level of the Manual Ability Classification System were calculated and compared. Finally, the minimal detectable change at the 90% confidence level was determined. **RESULTS:** Values for the ES (0.40) and SRM (0.53) for the UE CP-PRO CAT at baseline to 6 months were moderate and significantly greater than the PODCI-UE (ES, 0.18; SRM, 0.25). The ES and SRM for the PODCI-UE, ABILHAND-Kids, and Box and Blocks tests were not significantly greater than for the UE CP-PRO CAT at any period. From baseline to 6 months, the UE CP-PRO CAT detected a large and significant improvement for Manual Ability Classification System level II (SRM, 0.70; ES, 0.70). The minimal detectable change for the UE CP-PRO CAT was 5.20. **CONCLUSIONS:** The UE CP-PRO CAT is significantly better in detecting change in UE function in the first 6 months after surgery and is comparable to other measures at 12 and 24 months. **TYPE OF STUDY/LEVEL OF EVIDENCE:** Diagnostic II.

PMID: [30733101](#)

5. Psychometric Evaluation of 2 New Upper Extremity Functional Strength Tests in Children With Cerebral Palsy.

Dekkers KJFM, Smeets RJEM, Janssen-Potten YJM, Gordon AM, Speth LAWM, Rameckers EAA.

Phys Ther. 2019 Feb 4. doi: 10.1093/ptj/pzz019. [Epub ahead of print]

BACKGROUND: For children with unilateral spastic cerebral palsy (USCP), reduced muscle strength may lead to activity limitations. However, despite existence of many upper limb strength measures, none measure strength in the context of functional activities in which the strength must be maintained for several seconds. **OBJECTIVE:** The objective was to evaluate the psychometric properties of two newly developed functional hand and upper limb muscle-strength tests (Cup- and Box task) in children (7-12 years) with USCP. **DESIGN:** A longitudinal study design was used. **METHODS:** A standardized protocol with detailed descriptions of all procedures and measurements was used to determine test-retest reliability, inter-rater

reliability, and criterion validity. **RESULTS:** A total of 86 children (53 males, 33 females, mean age = 9.3 years) with USCP participated in this study, with a subset performing each measurement. Only the results of the children who are able to perform the measurement were included for the analysis. Excellent test-retest reliability (Intraclass correlation coefficients (ICC) ranging from 0.887 to 0.944; 95% confidence intervals 0.713-0.969) and inter-rater reliability (ICC ranging from 0.896-0.960; 95% confidence intervals 0.813-0.980) was observed. The Cup-Task Affected-Hand and Box-Task were moderately correlated with maximum isometric grip strength. The Cup-Task Non-Affected-Hand had a low correlation with maximum isometric grip strength. **LIMITATIONS:** Age, gender, and manual ability were not normally distributed, which could have influenced the results. **CONCLUSIONS:** For children with USCP who can perform the tasks, the Cup- and Box-Task are reliable and valid instruments for measuring functional upper limb muscle strength.

PMID: [30722023](#)

6. Developmental Trajectories for the Early Clinical Assessment of Balance by Gross Motor Function Classification System Level for Children With Cerebral Palsy.

LaForme Fiss A, McCoy SW, Bartlett D, Avery L, Hanna SE; On Track Study Team.

Phys Ther. 2019 Feb 1;99(2):217-228. doi: 10.1093/ptj/pzy132.

BACKGROUND: Children with cerebral palsy (CP) characteristically present with impairments in balance. Currently, the pattern and timing of the development of balance ability have not been described for children with CP of varying Gross Motor Function Classification System (GMFCS) levels. **OBJECTIVE:** The purpose of this study was to document longitudinal developmental trajectories in a measure of balance, the Early Clinical Assessment of Balance (ECAB) scores, along with age-specific reference percentiles and the amount of change typical over a 1-year period for children within different GMFCS levels. **DESIGN:** The design was a longitudinal cohort study. **METHODS:** Participants included 708 children with CP, aged 18 months through their 12th birthday, and their families. Children participated in 2 to 5 assessments using the GMFCS and ECAB. **RESULTS:** Longitudinal trajectories describing the average change in the ECAB score with respect to age were created by fitting separate nonlinear mixed-effect models for children in each GMFCS level. Reference percentiles were constructed using quantile regression of ECAB data from the first visit (baseline) and 12-month and 24-month visits. Using these reference points, the amount of change in percentiles was calculated for all children by subtracting the baseline percentile score from the 12-month percentile score. Children whose percentile changes are within the 80% limits can usually be described as "developing as expected" for their age and GMFCS levels. **LIMITATIONS:** Limitations of this study included use of a convenience sample, a ceiling effect of the ECAB for some children in GMFCS levels I and II, and the use of both a 12-month and 24-month study protocol that impacted the number of children available for each assessment session. **CONCLUSIONS:** When used appropriately to monitor development and change over time for children with CP, the ECAB longitudinal trajectories, reference percentiles, and the associated change scores presented here should assist therapists and families in collaborative interaction to proactively plan services and interventions relative to balance ability.

PMID: [30715490](#)

7. Maturation of feedforward toe walking motor program is impaired in children with cerebral palsy.

Lorentzen J, Willerslev-Olsen M, Hüche Larsen H, Farmer SF, Nielsen JB.

Brain. 2019 Feb 4. doi: 10.1093/brain/awz002. [Epub ahead of print]

Voluntary toe walking in adults is characterized by feedforward control of ankle muscles in order to ensure optimal stability of the ankle joint at ground impact. Toe walking is frequently observed in children with cerebral palsy, but the mechanisms involved have not been clarified. Here, we investigated maturation of voluntary toe walking in typically-developing children and typically-developed adults and compared it to involuntary toe walking in children with cerebral palsy. Twenty-eight children with cerebral palsy (age 3-14 years), 24 typically-developing children (age 2-14 years) and 15 adults (mean age 30.7 years) participated in the study. EMG activity was measured from the tibialis anterior and soleus muscles together with knee and ankle joint position during treadmill walking. In typically-developed adults, low step-to-step variability of the drop of the heel after ground impact was correlated with low tibialis anterior and high soleus EMG with no significant coupling between the antagonist muscle EMGs. Typically-developing children showed a significant age-related decline in EMG amplitude reaching an adult level at 10-12 years of age. The youngest typically-developing children showed a broad peak EMG-EMG synchronization (>100 ms) associated with large 5-15 Hz coherence between antagonist muscle activities. EMG coherence declined with age and at the age of 10-12 years no correlation was observed similar to adults. This reduction in coherence was closely related to improved step-to-step stability of the ankle joint position. Children with cerebral palsy generally showed lower EMG levels than typically-developing children and larger step-to-step variability in ankle joint position. In contrast to typically-developing children, children with cerebral palsy showed no age-related decline in tibialis anterior EMG amplitude.

Motor unit synchronization and 5-15 Hz coherence between antagonist EMGs was observed more frequently in children with cerebral palsy when compared to typically-developing children and in contrast to typically-developing participants there was no age-related decline. We conclude that typically-developing children develop mature feedforward control of ankle muscle activity as they age, such that at age 10-12 years there is little agonist-antagonist muscle co-contraction around the time of foot-ground contact during toe walking. Children with cerebral palsy, in contrast, continue to co-contract agonist and antagonist ankle muscles when toe walking. We speculate that children with cerebral palsy maintain a co-contraction activation pattern when toe walking due to weak muscles and insufficient motor and sensory signalling necessary for optimization of feedforward motor programs. These findings are important for understanding of the pathophysiology and treatment of toe walking.

PMID: [30726881](#)

8. Immediate effects of a single treadmill session with additional ankle loading on gait in children with hemiparetic cerebral palsy.

Simão CR, Regalado ICR, Spaniol AP, Fonseca DOS, Ribeiro TS, Lindquist AR.

NeuroRehabilitation. 2019 Jan 29. doi: 10.3233/NRE-182516. [Epub ahead of print]

BACKGROUND: Children with hemiparetic cerebral palsy are often characterized by reduced speed progression, shorter step length, and increased support base. These kinematic alterations result in inefficient gait. **OBJECTIVE:** To assess the immediate effects of treadmill training with additional lower limb loading on kinematic gait parameters in children with Cerebral Palsy (CP). **METHODS:** This cross-sectional, observational study, involved 20 children with hemiparetic CP that underwent single treadmill session with ankle loading. Kinematic gait data were collected by the Qualisys Motion Capture System during baseline (PRE), immediately after training (POST) and 5 minutes after post session (FOLLOW UP). **RESULTS:** The results demonstrated increase in knee ($p = 0.001$) and hip ($p = 0.005$) range of motion, maximum knee ($p < 0.001$) and hip ($p = 0.001$) flexion in swing and paretic foot height during swing ($p < 0.001$) when PRE x POST were compared. **CONCLUSION:** Treadmill gait training with additional lower limb loading was a disturbance capable of modifying the locomotor strategy of these population. The increase in hip flexion during swing phase allowed higher paretic foot clearance which may favor the improvement of gait function.

PMID: [30714979](#)

9. Locomotion and cadence detection using a single trunk-fixed accelerometer: validity for children with cerebral palsy in daily life-like conditions.

Paraschiv-Ionescu A, Newman C, Carcreff L, Gerber CN, Armand S, Aminian K.

J Neuroeng Rehabil. 2019 Feb 4;16(1):24. doi: 10.1186/s12984-019-0494-z.

BACKGROUND: Physical therapy interventions for ambulatory youth with cerebral palsy (CP) often focus on activity-based strategies to promote functional mobility and participation in physical activity. The use of activity monitors validated for this population could help to design effective personalized interventions by providing reliable outcome measures. The objective of this study was to devise a single-sensor based algorithm for locomotion and cadence detection, robust to atypical gait patterns of children with CP in the real-life like monitoring conditions. **METHODS:** Study included 15 children with CP, classified according to Gross Motor Function Classification System (GMFCS) between levels I and III, and 11 age-matched typically developing (TD). Six IMU devices were fixed on participant's trunk (chest and low back/L5), thighs, and shanks. IMUs on trunk were independently used for development of algorithm, whereas the ensemble of devices on lower limbs were used as reference system. Data was collected according to a semi-structured protocol, and included typical daily-life activities performed indoor and outdoor. The algorithm was based on detection of peaks associated to heel-strike events, identified from the norm of trunk acceleration signals, and included several processing stages such as peak enhancement and selection of the steps-related peaks using heuristic decision rules. Cadence was estimated using time- and frequency-domain approaches. Performance metrics were sensitivity, specificity, precision, error, intra-class correlation coefficient, and Bland-Altman analysis. **RESULTS:** According to GMFCS, CP children were classified as GMFCS I ($n = 7$), GMFCS II ($n = 3$) and GMFCS III ($n = 5$). Mean values of sensitivity, specificity and precision for locomotion detection ranged between 0.93-0.98, 0.92-0.97 and 0.86-0.98 for TD, CP-GMFCS I and CP-GMFCS II-III groups, respectively. Mean values of absolute error for cadence estimation (steps/min) were similar for both methods, and ranged between 0.51-0.88, 1.18-1.33 and 1.94-2.3 for TD, CP-GMFCS I and CP-GMFCS II-III groups, respectively. The standard deviation was higher in CP-GMFCS II-III group, the lower performances being explained by the high variability of atypical gait patterns. **CONCLUSIONS:** The algorithm demonstrated good performance when applied to a wide range of gait patterns, from normal to the pathological gait of highly affected children with CP using walking aids.

PMID: [30717753](#)

10. Neuromuscular electrical stimulation to improve gross motor function in children with cerebral palsy: a meta-analysis.

Salazar AP, Pagnussat AS, Pereira GA, Scopel G, Lukrafka JL.

Braz J Phys Ther. 2019 Jan 23. pii: S1413-3555(18)30674-9. doi: 10.1016/j.bjpt.2019.01.006. [Epub ahead of print]

OBJECTIVE: To systematically review the effectiveness of neuromuscular electrical stimulation (NMES) as an adjuvant therapy to improve gross motor function in children with spastic cerebral palsy. **METHODS:** MEDLINE, EMBASE, Cochrane CENTRAL, PEDro and Scopus were searched. We included randomized controlled trials examining the effects of NMES combined with other therapies on gross motor function as assessed by the Gross Motor Function Measure (GMFM) and its functional dimensions. Two reviewers independently screened, extracted data, assessed the risk of bias (PEDro) and quality of the evidence (GRADE). **RESULTS:** Six randomized controlled trials (pooled n=174) were included in the meta-analysis. NMES combined with other therapies presented medium effect size to improve gross motor function in children with cerebral palsy in comparison with conventional physical therapy or neurodevelopmental therapy. Our sensitivity analysis showed that NMES combined with other therapies was effective to improve GMFM-sitting and standing dimensions but not GMFM-walking dimension. **CONCLUSION:** Low-quality evidence suggests that NMES may be used as adjuvant therapy to improve sitting and standing dimensions of GMFM in children with spastic cerebral palsy.

PMID: [30712812](#)

11. Deep brain stimulation for dystonia-choreoathetosis in cerebral palsy: Pallidal versus thalamic stimulation.

Wolf ME, Blahak C, Saryyeva A, Schrader C, Krauss JK.

Parkinsonism Relat Disord. 2019 Jan 30. pii: S1353-8020(19)30029-X. doi: 10.1016/j.parkreldis.2019.01.029. [Epub ahead of print]

INTRODUCTION: Dystonia-choreoathetosis is common in patients with cerebral palsy, and medical treatment is mostly unsatisfactory. Deep brain stimulation (DBS) of the globus pallidus internus (GPi) has shown some effect, but there is still a need to optimize treatment strategies. We aimed to assess whether the thalamic ventral intermediate nucleus (Vim) might be an alternative DBS target in dystonia-choreoathetosis. **METHODS:** Three patients with cerebral palsy and dystonia-choreoathetosis underwent implantation of DBS electrodes concurrently in the GPi and Vim. Final selection of stimulation site and switches during follow-up with corresponding clinical outcomes were assessed. **RESULTS:** One patient with initial GPi stimulation was switched to Vim, but likewise did not improve significantly (BFM: pre-OP 142, GPi 140, Vim 134) and stimulation was discontinued. In one patient Vim was chosen as initial target for chronic DBS. Since clinical benefit was not yet satisfying, stimulation was switched to GPi resulting in further mild clinical improvement (BFM: pre-OP 99.5, Vim 82.5, GPi 82). In one patient GPi was selected and kept on follow-up due to some therapeutic effect (BFM: pre-OP 135, GPi DBS 121). **CONCLUSIONS:** The GPi still represents the most convenient DBS target in patients with dystonia-choreoathetosis. Vim DBS did not show a relevant long-term advantage in everyday life in our patients. Further alternative DBS targets need to be considered in acquired dystonia.

PMID: [30718219](#)

12. Mortality due to cardiovascular disease, respiratory disease, and cancer in adults with cerebral palsy.

Ryan JM, Peterson MD, Ryan N, Smith KJ, O'connell NE, Liverani S, Anokye N, Victor C, Allen E.

Dev Med Child Neurol. 2019 Feb 6. doi: 10.1111/dmcn.14176. [Epub ahead of print]

AIM: To compare mortality rates for cardiovascular disease, cancer, and respiratory disease between adults with cerebral palsy (CP) and the general population. **METHOD:** A cohort study was conducted using data from adults with CP in England, identified through a primary care data set (the Clinical Practice Research Datalink), with linked data on death registrations from the Office for National Statistics. Cause of death was categorized according to International Classification of Diseases codes. Standardized mortality ratios (SMRs) were calculated to compare mortality rates between adults with CP and the general population, adjusted for age, sex, and calendar year. **RESULTS:** Nine hundred and fifty-eight adults with CP were identified (52.5% males, 47.5% females; median age at start of follow-up 31y [interquartile range 22-43y]) and followed for a total of 7693 person-years. One hundred and forty-two patients (15%) died during follow-up. Adults with CP had an increased risk of death due to cardiovascular disease (SMR: 3.19, 95% confidence interval [CI] 2.20-4.62) and respiratory disease (SMR: 13.59, 95% CI 9.89-18.67), but not from malignant neoplasms (SMR: 1.42, 95% CI 0.83-2.45). **INTERPRETATION:** We found that

adults with CP in England have increased risk of death due to diseases of the circulatory and respiratory systems, supporting findings from two studies that compared cause-specific mortality rates between adults with CP in the USA and the general population. Further research is required into primary and secondary prevention of cardiovascular and respiratory disease in people with CP worldwide. **WHAT THIS PAPER ADDS:** Adults with cerebral palsy (CP) in England have 14-fold increased risk of mortality due to diseases of the respiratory system. They have a 3-fold increased risk of mortality due to diseases of the circulatory system. Adults with CP had an increased risk of death due to cerebrovascular disease and ischaemic heart disease. The elevated risk of ischaemic heart disease, however, did not reach statistical significance at the 5% per cent level.

PMID: [30727025](#)

13. Adults with cerebral palsy have higher prevalence of fracture compared to adults without cerebral palsy independent of osteoporosis and cardiometabolic diseases.

Whitney DG, Alford AI, Devlin MJ, Caird MS, Hurvitz EA, Peterson MD.

J Bone Miner Res. 2019 Feb 7. doi: 10.1002/jbmr.3694. [Epub ahead of print]

Individuals with cerebral palsy (CP) have increased risk of fracture throughout their lifespan due to an underdeveloped musculoskeletal system, excess body fat, diminished mechanical loading, and early development of noncommunicable diseases. However, the epidemiology of fracture among adults with CP is unknown. The purpose of this cross-sectional study was to determine the prevalence of fracture among a large sample of privately-insured adults with CP, as compared to adults without CP. Data were from the Optum Clinformatics® Data Mart, a de-identified nationwide claims database of beneficiaries from a single private payer. Diagnostic codes were used to identify 18-64 year old beneficiaries with and without CP, as well as any fracture, which consisted of osteoporotic pathological fracture and any type of fracture of the head/neck, thoracic, lumbar/pelvic, upper extremity, and lower extremity regions. The prevalence of any fracture was compared between adults with (n = 5,555) and without (n = 5.5 million) CP. Multivariable logistic regression was performed with all-cause fracture as the outcome and CP group as the primary exposure. Adults with CP had a higher prevalence of all-cause fracture (6.3%, 2.7%, respectively) and fracture of the head/neck, thoracic, lumbar/pelvic, upper extremity, and lower extremity regions compared to adults without CP (all, $p < 0.01$). After adjusting for sociodemographic and socioeconomic variables, adults with CP had higher odds of all-cause fracture compared to adults without CP (OR = 2.5; 95%CI = 2.2-2.7). After further adjusting for cardiometabolic diseases, adults with CP had higher odds of all-cause fracture compared to adults without CP (OR = 2.2; 95%CI = 2.0-2.5). After further adjusting for osteoporosis, adults with CP still had higher odds of all-cause fracture compared to adults without CP (OR = 2.0; 95%CI = 1.8-2.2). These findings suggest that young and middle-aged adults with CP have an elevated prevalence of all-cause fracture compared to adults without CP, which was present even after accounting for cardiometabolic diseases and osteoporosis. This article is protected by copyright. All rights reserved.

PMID: [30730595](#)

14. Sarcopenia among adults with cerebral palsy in South Korea.

Jeon I, Bang MS, Lim JY, Shin HI, Leigh JH, Kim K, Kwon BS, Jang SN, Jung SH.

PM R. 2019 Feb 7. doi: 10.1002/pmrj.12134. [Epub ahead of print]

BACKGROUND: Most adults with cerebral palsy (CP) encounter newly developing physical health problems and premature functional decline with aging. These physical and functional losses along with the characteristic symptoms of CP may heighten the risk of sarcopenia. **OBJECTIVE:** To determine the prevalence of sarcopenia among a selected group of adults with cerebral palsy and to identify the factors associated with the sarcopenia among them. **DESIGN:** Cross-sectional study **SETTING:** University hospitals and communities for persons with disabilities. **PARTICIPANTS:** A total of 80 adults with cerebral palsy (46 men and 24 women with mean age of 42.8 ± 8.86 years) were included. **METHOD:** The muscle mass, strength and physical performance were measured to diagnose sarcopenia. Participants also completed a structured questionnaire for physical, psychological or socioeconomic attributes, and health-related quality of life. **MAIN OUTCOME MEASURES:** Prevalence of sarcopenia in adults with cerebral palsy. **RESULTS:** The prevalence of sarcopenia was 47.9% and the prevalence in men was significantly higher than that in women. Sarcopenia was significantly associated with sex, the Gross Motor Function Classification System (GMFCS), the Manual Ability Classification System (MACS), body mass index (BMI), and trunk fat. Male, higher GMFCS and lower BMI were significant risk factors of sarcopenia. Sarcopenic adults with cerebral palsy showed significantly lower health-related quality of life. **CONCLUSION:** The prevalence of sarcopenia in adults with CP was higher than that of general population despite of young age of the selected group. Modifiable risk factor was a low BMI. This article is protected by copyright. All rights reserved.

PMID: [30729753](#)

15. Seizure outcome and epilepsy patterns in patients with cerebral palsy.

El Tantawi NT, Abd Elmegid DS, Atef E.

Seizure. 2019 Jan 4;65:166-171. doi: 10.1016/j.seizure.2019.01.003. [Epub ahead of print]

PURPOSE: The aim of the present study was to investigate epilepsy patterns and outcomes in patients with cerebral palsy (CP) and identify the variables that determine remission. **METHODS:** This was a retrospective cohort study. We followed 107 CP patients aged 1-16 years with newly diagnosed epilepsy. The patients were categorized according to their remission outcome, uninterrupted freedom of seizure for 2 years or longer, and 4 epilepsy patterns: A) sustained freedom from seizures before 6 months of treatment; B) delayed but sustained seizure freedom; C) relapsing-remitting course; and D) seizure freedom never attained. The variables were analysed for their prognostic relevance to the outcomes. **RESULTS:** A total of 107 patients were included; their mean age at epilepsy diagnosis was 4.2 years (SD 2.5). By the end of the 8-year follow up, 19.6% 26.1%, 31.7%, and 22.4% were in sustained remission, terminal remission, relapse, and no remission respectively. Pattern A was identified in 6.5% of the patients, pattern B in 27.1%, pattern C in 43.9%, and pattern D in 22.4%. Univariate analysis revealed that the type of CP, mobility, and number of seizure types, are among the other factors that significantly affected remission. **CONCLUSION:** A total of 45% of patients with CP and epilepsy achieved remission (with and without antiepileptics) but after a relatively long treatment duration. Remission was affected by patient- and epilepsy-related factors. More studies are required to further evaluate these factors.

PMID: [30721873](#)**16. Prevalence of cerebral palsy, intellectual disability, hearing loss, and blindness, National Health Interview Survey, 2009-2016.**

McGuire DO, Tian LH, Yeargin-Allsopp M, Dowling NF, Christensen DL.

Disabil Health J. 2019 Jan 23. pii: S1936-6574(19)30005-6. doi: 10.1016/j.dhjo.2019.01.005. [Epub ahead of print]

BACKGROUND: Developmental disabilities are present in a significant proportion of US children. Surveillance of developmental disabilities is crucial for monitoring population trends, guiding research into risk factors, and informing resource allocation. **OBJECTIVE/HYPOTHESIS:** We examined overall prevalence, prevalence by demographic characteristics, and trends over time for cerebral palsy (CP), intellectual disability (ID), moderate to severe hearing loss (MSHL), and blindness. **METHODS:** Data from the 2009-2016 National Health Interview Survey (NHIS) were analyzed for children 3-17 years of age. Question wording was consistent over time except for ID, which changed in 2011 to replace the term "mental retardation." Demographic differences and linear trends (over three time periods) were assessed by Chi-square tests and Wald-F tests. **RESULTS:** Prevalence estimates per 1000 children ages 3-17 years for CP, ID, MSHL, and blindness were 3.2 (95% CI: 2.7, 3.7), 11.1 (95% CI: 10.2, 12.1), 6.4 (95% CI: 5.6, 7.2), and 1.6 (95% CI: 1.3, 2.0), respectively. Disability prevalence was higher for children with low birthweight and from families of lower parental education, income \leq 200% of federal poverty level, and public insurance. Older children had higher ID prevalence; boys had significantly higher CP and ID prevalences. Only ID demonstrated a significantly increased trend over time ($p = 0.0002$). **CONCLUSIONS:** We provide nationally representative prevalence estimates for four developmental disabilities; recent estimates are comparable to those from records-based studies. Prevalences were stable except for ID, which increased after 2010, coincident with the questionnaire change. A substantial number of US children continue to have these disabilities and service needs.

PMID: [30713095](#)**17. Long-term neuropsychiatric morbidity in children exposed prenatally to preeclampsia.**

Nahum Sacks K, Friger M, Shoham-Vardi I, Sergienko R, Spiegel E, Landau D, Sheiner E.

Early Hum Dev. 2019 Jan 31;130:96-100. doi: 10.1016/j.earlhumdev.2019.01.016. [Epub ahead of print]

INTRODUCTION: There are contradicting findings in the current literature regarding the association between in-utero exposure to preeclampsia and the long-term neuropsychiatric health of the offspring. The objective of this study is to assess whether prenatal exposure to preeclampsia increases the risk of long-term neuropsychiatric morbidity. **METHODS:** A retrospective population-based cohort study compared neuropsychiatric morbidity between singletons exposed and unexposed to preeclampsia. The study included all the singletons that were born between 1991 and 2014 in a single regional tertiary medical center. A generalized estimating equation (GEE) model was used to control for confounders and maternal clusters. **RESULTS:** Of the 253,808 singletons that met the inclusion criteria; 3.0% were born to mothers diagnosed with mild

preeclampsia (n = 7660), 0.9% with severe preeclampsia (n = 2366) and 0.03% with eclampsia (n = 81). A significant linear association was noted between the severity of the preeclampsia (no preeclampsia, mild, severe preeclampsia and eclampsia) and the incidence of neuropsychiatric morbidity of the offspring (1.0%, vs. 1.2% vs. 1.9% vs. 1.2% respectively, p = 0.003). In a GEE model which was used to control for maternal clusters, gestational diabetes, maternal age, gestational age and time-to-event preeclampsia was found to be an independent risk factor for neuropsychiatric morbidity in the offspring (adjusted OR = 1.36; 95% CI 1.14-1.63). **CONCLUSION:** Offspring exposed prenatally to preeclampsia have a significantly higher risk of developing a neuropsychiatric morbidity during childhood.

PMID: [30711915](#)

18. Mental health disorders, participation, and bullying in children with cerebral palsy.

Whitney DG, Peterson MD, Warschausky SA.

Dev Med Child Neurol. 2019 Feb 1. doi: 10.1111/dmcn.14175. [Epub ahead of print]

AIM: To examine how social factors might mitigate the elevated risk of mental health disorders in children with cerebral palsy (CP). **METHOD:** This cross-sectional study included 6- to 17-year-olds with (n=111; 40.4% 6-11y, 59.6% 12-17y) and without (n=29 909; 50.2% 6-11y, 49.8% 12-17y) CP from the 2016 National Survey of Children's Health. Mental health disorders included depression, anxiety, behavior/conduct problems, and attention-deficit/hyperactivity disorder. Social factors included participation in activities, bully victimization, and difficulty with friendships. **RESULTS:** After adjusting for sociodemographic factors and the presence of chronic pain, children with CP had higher odds of anxiety (odds ratio [OR] 4.4; 95% confidence interval [CI] 1.9-8.5), behavior/conduct problems (OR 3.9; 95% CI 1.4-11.3), and multimorbidity (OR 2.8; 95% CI 1.1-7.0), but not depression (OR 1.4; 95% CI 0.6-3.8) or attention-deficit/hyperactivity disorder (OR 1.7; 95% CI 0.6-4.6), compared to controls. With adjustment for participation in activities, the odds of anxiety, behavior/conduct problems, and multimorbidity remained increased in children with CP. With adjustment for difficulty with friendships, the odds of anxiety, behavior/conduct problems, and multimorbidity were no longer increased in children with CP. With adjustment for bully victimization, the odds of behavior/conduct problems and multimorbidity were attenuated in children with CP; however, the odds of anxiety remained increased. **INTERPRETATION:** The elevated prevalence of certain mental health disorders in children with CP is partly associated with modifiable social factors.

PMID: [30710352](#)

19. Experiences of children and parents in MiYoga, an embodied mindfulness yoga program for cerebral palsy: A mixed method study.

Mak CK, Whittingham K, Boyd RN.

Complement Ther Clin Pract. 2019 Feb;34:208-216. doi: 10.1016/j.ctcp.2018.12.006. Epub 2018 Dec 19.

BACKGROUND AND PURPOSE: A mindfulness yoga program (MiYoga) was developed and trialled with children with cerebral palsy and their parents. This mixed-method study explores the experiences of children and parents who participated in MiYoga, to assess its acceptability, feasibility and implementation. **MATERIALS AND METHODS:** Of the forty-two child-parent dyads who participated in the MiYoga randomised control trial, 19 children and 22 parents were interviewed individually in a semi-structured way about their experiences of MiYoga. Participants rated their mood on a 5-point scale before and after each session and completed short questionnaires at the end of each session. **RESULTS:** Children and parents reported improved mood after each MiYoga session. Parents reported being more aware of their thoughts and feelings and possibly became more aware of their day-to-day mindlessness. **CONCLUSION:** MiYoga significantly improved children and parents' mood. Parents reported gains in awareness as well as challenges of adhering to the home practice.

PMID: [30712729](#)

20. Application of a wearable switch to perform a mouse left click for a child with mix type of cerebral palsy: a single case study.

Yamamoto A, Kihara K, Yagi M, Matsumoto Y, Tsuneishi S, Otaka H, Yonezawa M, Takada S.

Disabil Rehabil Assist Technol. 2019 Feb 7:1-6. doi: 10.1080/17483107.2018.1520309. [Epub ahead of print]

PURPOSE: Children with cerebral palsy may face difficulties using handheld pointing devices, due to involuntary muscle movements. This study aimed at describing the idea of the new wearable sensor switch and assessing its feasibility as an access solution in a case of mixed-type cerebral palsy. **METHODS:** The study participant was a 17-year-old male with mixed-type cerebral palsy characterized by chorea-athetotic movements and bilateral spasticity with gross motor function classification system level V. He exhibited sudden and irregular involuntary upper limb movements when sitting. Because spastic finger movements limited his ability to use a handheld mouse, he used a trackball near his neck as a pointing device (previous input method). The wearable switch system using a stretchable strain sensor was introduced; the sensor was attached to a groove worn on the dorsal regions of the right hand crossing the proximal interphalangeal and metacarpophalangeal joints of the middle finger (new input method). The switch turned on when the subject flexed his middle finger. **RESULTS:** The user successfully turned the switch on and typed almost the same numbers of characters per trial compared with the previous input method. The speed of his head movements during typing reduced ($p < .01$), and his sitting posture was nearly upright during computer operation ($p < .01$). No involuntary movement, requiring physical assistance, was observed when using the wearable switch. **CONCLUSION:** The new switch system can be a new option for people with difficulty using standard handheld input devices due to paralysis and involuntary muscle movements. Implications for rehabilitation Cerebral palsy is a major cause of motor dysfunction and spasticity and dyskinesia in the fingers and upper limbs may prevent children with cerebral palsy from using handheld input devices. Wearable devices may be useful for children with cerebral palsy who have limited access to handheld pointing devices. We developed a new wearable switch to control devices using a flexible stretchable sensor. The wearable switch contributed to the improvement of sitting posture and reduction of neck burden during the typing task at the speed equivalent to that using the previous method in a child with mixed type of cerebral palsy exhibiting choreoathetotic movements and bilateral spasticity.

PMID: [30729835](#)

21. Voluntary Elbow Extension-Flexion Using Single Joint Hybrid Assistive Limb (HAL) for Patients of Spastic Cerebral Palsy: Two Cases Report.

Shimizu Y, Kadone H, Kubota S, Ueno T, Sankai Y, Hada Y, Yamazaki M.

Front Neurol. 2019 Jan 22;10:2. doi: 10.3389/fneur.2019.00002. eCollection 2019.

Cerebral palsy (CP) patients with spastic diplegia struggle to perform activities of daily life (ADL) using their upper arms. The single-joint-type Hybrid Assistive limb (HAL) for upper limbs is a new portable robot that can provide elbow motion support in accordance with bioelectric activation of patient's biceps and triceps brachii muscles. The purpose of this study is to assess the feasibility and efficacy of the use of HAL for CP patients. Two patients were enrolled in this study. (Case 1: a 19-years-old male, at the Gross Motor Function Classification System (GMFCS) level IV, Case 2: a 17-years-old male at GMFCS level III). Both these patients experienced difficulty in voluntary elbow extension in ADLs. The HAL intervention (eight sessions; voluntary extension-flexion training of the elbow with HAL and clinical evaluation) was conducted for both sides in Case 1 and for the right side in Case 2. Clinical assessments were conducted as follows: Surface electromyography was used to evaluate the muscle activities of the biceps, triceps brachii, trapezius, and pectoralis major during elbow extension-flexion. The voluntary extension-flexion angles of the elbow, the coactivation index of the biceps and triceps brachii muscles, synergy analysis, and the Action Research Arm Test (ARAT) scores were assessed before and after the HAL sessions; the FIM score was evaluated before and after the entire intervention. In Case 1, the voluntary extension angle tended to increase after the HAL sessions. In both cases, the ARAT scores improved after the sessions. The FIM scores improved after HAL intervention. The voluntary extension-flexion of the elbow using the HAL may be a feasible option for rehabilitation of CP patients.

PMID: [30723447](#)

22. "Now I am a techie too" - parental perceptions of using mobile technology for communication by children with complex communication needs in the Global South.

Hettiarachchi S, Kitnasamy G, Gopi D.

Disabil Rehabil Assist Technol. 2019 Feb 8:1-12. doi: 10.1080/17483107.2018.1554713. [Epub ahead of print]

PURPOSE: Parental perceptions are key to the uptake of augmentative and alternative communication (AAC) devices for their children with complex communication needs. This study aimed to explore the perceptions of parents in a resource poor Global South country on the use of mobile technology as AAC devices. **MATERIALS AND METHODS:** Sixteen participants (11 female; 5 male) were included in the study. Focus group discussions, face-to-face interviews and telephone interviews were conducted with the aid of an interview guide. The interview data were analysed using the key principles of Framework analysis and through the lens of critical disability studies. **RESULTS:** Six broad themes emerged. Most participants indicated a penchant for mobile technology, though its current use with their children was mainly as a teaching tool rather than a

communication device. Concerns were raised about the cost of mobile technology, which if used within communication, was only as a temporary stop-gap measure with limited knowledge. The power of mainstream technology to challenge prevalent notions of disability was also highlighted by the participants. **CONCLUSIONS:** There is an openness to using mainstream mobile technology by parents with their children with complex communication needs. This use is currently reserved mainly for educational purposes while its power to challenge disability-related stereotypes is acknowledged. More parent training is required to encourage the use of mobile technology as AAC devices for communication. **Implications for rehabilitation:** Current parent perspectives on mobile technology as AAC devices must be explored, given its potential impact on the uptake of these devices to support communication in their children with complex communication needs. Mainstream mobile technology could challenge perceptions of disability and therefore, be more acceptable to parents for their children with complex communication needs. Parental training is required to increase knowledge on the use of mobile technology as AAC devices for communication to enable informed choice-making.

PMID: [30735067](#)

Prevention and Cure

23. Sex-Specific Genetic Susceptibility To Adverse Neurodevelopmental Outcome in Offspring of Pregnancies at Risk of Early Preterm Delivery.

Varner MW, Costantine MM, Jablonski KA, Rouse DJ, Mercer BM, Leveno KJ, Reddy UM, Buhimschi C, Wapner RJ, Sorokin Y, Thorp JM, Ramin SM, Malone FD, Carpenter M, O'sullivan MJ, Peaceman AM, Dudley DJ, Caritis SN; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network.

Am J Perinatol. 2019 Feb 7. doi: 10.1055/s-0039-1678535. [Epub ahead of print]

OBJECTIVE: To evaluate sex-specific genetic susceptibility to adverse neurodevelopmental outcome (ANO, defined as cerebral palsy [CP], mental, or psychomotor delay) at risk for early preterm birth (EPTB, < 32 weeks). **STUDY DESIGN:** Secondary case-control analysis of a trial of magnesium sulfate (MgSO₄) before anticipated EPTB for CP prevention. Cases are infants who died by the age of 1 year or developed ANO. Controls, matched by maternal race and infant sex, were neurodevelopmentally normal survivors. Neonatal DNA was evaluated for 80 polymorphisms in inflammation, coagulation, vasoregulation, excitotoxicity, and oxidative stress pathways using Taqman assays. The primary outcome for this analysis was sex-specific ANO susceptibility. Conditional logistic regression estimated each polymorphism's odds ratio (OR) by sex stratum, adjusting for gestational age, maternal education, and MgSO₄-corticosteroid exposures. Holm-Bonferroni corrections, adjusting for multiple comparisons ($p < 7.3 \times 10^{-4}$), accounted for linkage disequilibrium between markers. **RESULTS:** Analysis included 211 cases (134 males; 77 females) and 213 controls (130 males; 83 females). An interleukin-6 (IL6) polymorphism (rs2069840) was associated with ANO in females (OR: 2.6, 95% confidence interval [CI]: 1.5-4.7; $p = 0.001$), but not in males (OR: 0.8, 95% CI: 0.5-1.2; $p = 0.33$). The sex-specific effect difference was significant ($p = 7.0 \times 10^{-4}$) and was unaffected by MgSO₄ exposure. No other gene-sex associations were significant. **CONCLUSION:** An IL6 gene locus may confer susceptibility to ANO in females, but not males, after EPTB.

PMID: [30731481](#)

24. Metabolomic Profiling of Cerebral Palsy Brain Tissue Reveals Novel Central Biomarkers and Biochemical Pathways Associated with the Disease: A Pilot Study.

Alpay Savasan Z, Yilmaz A, Ugur Z, Aydas B, Bahado-Singh RO, Graham SF.

Metabolites. 2019 Feb 2;9(2). pii: E27. doi: 10.3390/metabo9020027.

Cerebral palsy (CP) is one of the most common causes of motor disability in childhood, with complex and heterogeneous etiopathophysiology and clinical presentation. Understanding the metabolic processes associated with the disease may aid in the discovery of preventive measures and therapy. Tissue samples (caudate nucleus) were obtained from post-mortem CP cases ($n = 9$) and age- and gender-matched control subjects ($n = 11$). We employed a targeted metabolomics approach using both ¹H NMR and direct injection liquid chromatography-tandem mass spectrometry (DI/LC-MS/MS). We accurately identified and quantified 55 metabolites using ¹H NMR and 186 using DI/LC-MS/MS. Among the 222 detected metabolites, 27 showed significant concentration changes between CP cases and controls. Glycerophospholipids and urea were the most commonly selected metabolites used to develop predictive models capable of discriminating between CP and controls. Metabolomics enrichment analysis identified folate, propanoate, and androgen/estrogen metabolism as the top three significantly perturbed pathways. We report for the first time the metabolomic profiling of post-mortem brain tissue from patients who died from cerebral palsy. These findings could help to further investigate the complex etiopathophysiology of CP while identifying

predictive, central biomarkers of CP.

PMID: [30717353](#)

25. Involvement of the synapse-specific zinc transporter ZnT3 in cadmium-induced hippocampal neurotoxicity.

Ben Mimouna S, Le Charpentier T, Lebon S, Van Steenwinckel J, Messaoudi I, Gressens P.

J Cell Physiol. 2019 Feb 4. doi: 10.1002/jcp.28245. [Epub ahead of print]

The present study examined the involvement of zinc (Zn)-transporters (ZnT3) in cadmium (Cd)-induced alterations of Zn homeostasis in rat hippocampal neurons. We treated primary rat hippocampal neurons for 24 or 48 hr with various concentrations of CdCl₂ (0, 0.5, 5, 10, 25, or 50 μM) and/or ZnCl₂ (0, 10, 30, 50, 70, or 90 μM), using normal neuronal medium as control. By The CellTiter 96® Aqueous One Solution Cell Proliferation Assay (MTS; Promega, Madison, WI) assay and immunohistochemistry for cell death markers, 10 and 25 μM of Cd were found to be noncytotoxic doses, and both 30 and 90 μM of Zn as the best concentrations for cell proliferation. We tested these selected doses. Cd, at concentrations of 10 or 25 μM (and depending on the absence or presence of Zn), decreased the percentage of surviving cells. Cd-induced neuronal death was either apoptotic or necrotic depending on dose, as indicated by 7-AAD and/or annexin V labeling. At the molecular level, Cd exposure induced a decrease in hippocampal brain-derived neurotrophic factor-tropomyosin receptor kinase B (BDNF-TrkB) and Erk1/2 signaling, a significant downregulation of the expression of learning- and memory-related receptors and synaptic proteins such as the NMDAR NR2A subunit and PSD-95, as well as the expression of the synapse-specific vesicular Zn transporter ZnT3 in cultured hippocampal neurons. Zn supplementation, especially at the 30 μM concentration, led to partial or total protection against Cd neurotoxicity both with respect to the number of apoptotic cells and the expression of several genes. Interestingly, after knockdown of ZnT3 by small interfering RNA transfection, we did not find the restoration of the expression of this gene following Zn supplementation at 30 μM concentration. These data indicate the involvement of ZnT3 in the mechanism of Cd-induced hippocampal neurotoxicity.

PMID: [30714133](#)

26. Enduring Neuroprotective Effect of Subacute Neural Stem Cell Transplantation After Penetrating TBI.

Kassi AAY, Mahavadi AK, Clavijo A, Caliz D, Lee SW, Ahmed AI, Yokobori S, Hu Z, Spurlock MS, Wasserman JM, Rivera KN, Nodal S, Powell HR, Di L, Torres R, Leung LY, Rubiano AM, Bullock RM, Gajavelli S.

Front Neurol. 2019 Jan 17;9:1097. doi: 10.3389/fneur.2018.01097. eCollection 2018.

Traumatic brain injury (TBI) is the largest cause of death and disability of persons under 45 years old, worldwide. Independent of the distribution, outcomes such as disability are associated with huge societal costs. The heterogeneity of TBI and its complicated biological response have helped clarify the limitations of current pharmacological approaches to TBI management. Five decades of effort have made some strides in reducing TBI mortality but little progress has been made to mitigate TBI-induced disability. Lessons learned from the failure of numerous randomized clinical trials and the inability to scale up results from single center clinical trials with neuroprotective agents led to the formation of organizations such as the Neurological Emergencies Treatment Trials (NETT) Network, and international collaborative comparative effectiveness research (CER) to re-orient TBI clinical research. With initiatives such as TRACK-TBI, generating rich and comprehensive human datasets with demographic, clinical, genomic, proteomic, imaging, and detailed outcome data across multiple time points has become the focus of the field in the United States (US). In addition, government institutions such as the US Department of Defense are investing in groups such as Operation Brain Trauma Therapy (OBTT), a multicenter, pre-clinical drug-screening consortium to address the barriers in translation. The consensus from such efforts including "The Lancet Neurology Commission" and current literature is that unmitigated cell death processes, incomplete debris clearance, aberrant neurotoxic immune, and glia cell response induce progressive tissue loss and spatiotemporal magnification of primary TBI. Our analysis suggests that the focus of neuroprotection research needs to shift from protecting dying and injured neurons at acute time points to modulating the aberrant glial response in sub-acute and chronic time points. One unexpected agent with neuroprotective properties that shows promise is transplantation of neural stem cells. In this review we present (i) a short survey of TBI epidemiology and summary of current care, (ii) findings of past neuroprotective clinical trials and possible reasons for failure based upon insights from human and preclinical TBI pathophysiology studies, including our group's inflammation-centered approach, (iii) the unmet need of TBI and unproven treatments and lastly, (iv) present evidence to support the rationale for sub-acute neural stem cell therapy to mediate enduring neuroprotection.

PMID: [30719019](#)

27. Exogenous Neural Precursor Cell Transplantation Results in Structural and Functional Recovery in a Hypoxic-Ischemic Hemiplegic Mouse Model.

Rumajogee P, Altamentova S, Li L, Li J, Wang J, Kuurstra A, Khazaei M, Beldick S, Menon RS, van der Kooy D, Fehlings MG.

eNeuro. 2018 Dec 4;5(5). pii: ENEURO.0369-18.2018. doi: 10.1523/ENEURO.0369-18.2018. eCollection 2018 Sep-Oct.

Cerebral palsy (CP) is a common pediatric neurodevelopmental disorder, frequently resulting in motor and developmental deficits and often accompanied by cognitive impairments. A regular pathobiological hallmark of CP is oligodendrocyte maturation impairment resulting in white matter (WM) injury and reduced axonal myelination. Regeneration therapies based on cell replacement are currently limited, but neural precursor cells (NPCs), as cellular support for myelination, represent a promising regeneration strategy to treat CP, although the transplantation parameters (e.g., timing, dosage, mechanism) remain to be determined. We optimized a hemiplegic mouse model of neonatal hypoxia-ischemia that mirrors the pathobiological hallmarks of CP and transplanted NPCs into the corpus callosum (CC), a major white matter structure impacted in CP patients. The NPCs survived, engrafted, and differentiated morphologically in male and female mice. Histology and MRI showed repair of lesioned structures. Furthermore, electrophysiology revealed functional myelination of the CC (e.g., restoration of conduction velocity), while cylinder and CatWalk tests demonstrated motor recovery of the affected forelimb. Endogenous oligodendrocytes, recruited in the CC following transplantation of exogenous NPCs, are the principal actors in this recovery process. The lack of differentiation of the transplanted NPCs is consistent with enhanced recovery due to an indirect mechanism, such as a trophic and/or "bio-bridge" support mediated by endogenous oligodendrocytes. Our work establishes that transplantation of NPCs represents a viable therapeutic strategy for CP treatment, and that the enhanced recovery is mediated by endogenous oligodendrocytes. This will further our understanding and contribute to the improvement of cellular therapeutic strategies.

PMID: [30713997](https://pubmed.ncbi.nlm.nih.gov/30713997/)