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## Interventions and Management

### 1. Shoulder arthroplasty in patients with cerebral palsy: a matched cohort study to patients with osteoarthritis.

Marigi EM, Statz JM, Sperling JW, Sanchez-Sotelo J, Cofield RH, Morrey ME.

J Shoulder Elbow Surg. 2019 Sep 25. pii: S1058-2746(19)30513-0. doi: 10.1016/j.jse.2019.07.018. [Epub ahead of print]

**BACKGROUND:** Patients with cerebral palsy (CP) often experience shoulder impairment via spasticity, muscle contractures, and joint instability. Currently, few studies investigate shoulder arthroplasty (SA) in patients with CP. This study reviewed the outcomes of both anatomic total shoulder arthroplasty (TSA) and reverse total shoulder arthroplasty (RSA) in patients with CP. **METHODS:** Over a 30-year-period, 5 patients undergoing SA (2 TSA, 3 RSA) with a diagnosis of CP were identified. The cohort included 4 male patients with a mean age of 50.4 years (range, 44-58 years). CP patients were matched 1:2 based on age, sex, body mass index, and year of surgery with a group of patients undergoing SA for osteoarthritis (OA). **RESULTS:** Survival from implant revision for both TSA and RSA in CP was 100% at both 2 and 5 years postoperatively. Clinical complications were only observed in 2 patients after TSA, with 1 patient requiring revision at 14 years postoperatively. Collectively, there was no difference in the rate of complications and implant survival between patients with CP vs. OA. Prior to the surgical procedure, all CP patients had severe or moderate pain, with no moderate or severe pain postoperatively. Notable postoperative increases from preoperative baselines were noted in forward elevation (57°-106°), abduction (48°-84°), and external rotation (30°-64°). RSA had significantly improved postoperative abduction compared to TSA (97° vs. 64°,  $P < .01$ ). **CONCLUSIONS:** SA is a safe, durable procedure in patients with CP to clinically improve pain, function, and satisfaction. RSA was associated with better function and fewer complications than TSA.

PMID: [31563508](#)

### 2. Functional Outcome of Adulthood Selective Dorsal Rhizotomy for Spastic Diplegia.

Park TS, Uhm SY, Walter DM, Meyer NL, Dobbs MB.

Cureus. 2019 Jul 21;11(7):e5184. doi: 10.7759/cureus.5184.

**Objective** The medical evidence supporting the efficacy of selective dorsal rhizotomy (SDR) on children with spastic diplegia is strong. However, the outcome of SDR on adults with spastic diplegia remains undetermined. The aim is to study the effectiveness and morbidities of SDR performed on adults for the treatment of spastic diplegia. **Methods** Patients who received SDR in adulthood for the treatment of spastic diplegia were surveyed. The survey questionnaire addressed the living situation, education level, employment, health outcomes, postoperative changes of symptoms, changes in ambulatory function, adverse effects of SDR and orthopedic surgery after SDR. **Results** The study included 64 adults, who received SDR for spastic diplegia. The age at the time of surgery was between 18 and 50 years. The age at the time of the survey was between 20 and 52 years. The follow-up period ranged from one to 28 years. The study participants reported post-SDR improvements of the quality of walking in 91%, standing in 81%, sitting in 57%, balance while walking 75%, ability to

exercise in 88%, endurance in 77%, and recreational sports in 43%. Muscle and joint pain present before surgery improved in 64% after surgery. Concerning the level of ambulatory function, all patients who walked independently in all environments maintained the same level of ambulatory function. Eighteen percent of the patients who walked independently in some environments improved to the independent walking in all environments. All patients who walked with an assistive device before SDR maintained the assistive walking after SDR. Concerning adverse effects of SDR, 50% (32 of 64 patients) developed numbness in the various parts of the legs. Two patients reported a complete loss of sensation in parts of the legs, and one patient reported numbness and constant pain in the bilateral lower extremities. Ten patients (16%) reported recurrent spasticity after SDR, and three patients (5%) reported ankle clonus, which is an objective sign of spasticity. Tendon lengthening surgery after SDR was needed in 27% and hip and knee surgery in 2% and 6%, respectively. Conclusions The great majority of our 64 patients, who received adulthood SDR for spastic diplegia, improved the quality of ambulation and abated signs of early aging. Numbness and diminished sensation in the lower extremity was the most common adverse effect of the adulthood SDR.

PMID: [31565593](#)

### **3. CORR Insights®: Guided Growth Improves Coxa Valga and Hip Subluxation in Children with Cerebral Palsy.** Cosgrove A.

Clin Orthop Relat Res. 2019 Sep 16. doi: 10.1097/CORR.0000000000000967. [Epub ahead of print]

PMID: [31567709](#)

### **4. Comment on: "Botulinum Toxin in the Management of Children with Cerebral Palsy".**

Langdon K, Copeland L, Edwards P, Rodwell K, McLennan K, Carroll T, Bandaranayake S, Scheinberg A, Waugh MC, Burnett H, Wimalasundera N, Hennel S, Lim E, O'Flaherty S.

Paediatr Drugs. 2019 Oct 4. doi: 10.1007/s40272-019-00358-2. [Epub ahead of print]

PMID: [31583614](#)

### **5. Authors' Reply to K. Langdon and Colleagues' Comment on: "Botulinum Toxin in the Management of Children with Cerebral Palsy".**

Multani I, Manji J, Hastings-Ison T, Khot A3, Graham K.

Paediatr Drugs. 2019 Oct 4. doi: 10.1007/s40272-019-00359-1. [Epub ahead of print]

PMID: [31583615](#)

### **6. Examining the role of precision medicine with oral baclofen in pediatric patients with cerebral palsy.**

McLaughlin MJ, Abdel-Rahman S, Leeder JS.

Curr Phys Med Rehabil Rep. 2019 Mar;7(1):40-45. Epub 2019 Jan 23.

**PURPOSE OF REVIEW:** a)Despite its widespread use, oral baclofen requires a critical review of the pharmacology to determine potential precision medicine applications to improve medication administration. Discussing the dose→exposure→response relationship of oral baclofen allows a conceptual framework in which designing clinical trials would become more successful. This paper seeks to examine some of the areas where variability in exposures can exist lead to undesired clinical responses. **RECENT FINDINGS:** b)Several factors are at play to implement precision medicine with oral baclofen in the pediatric patient with cerebral palsy. Variations in intestinal absorption, oral baclofen clearance, pharmacogenomic variants, and distribution of this medication into the cerebrospinal fluid cause differences in the amount of baclofen available at the GABA-B receptor site to cause a clinical response. **SUMMARY:** c)Oral baclofen has significant variability in disposition and clinical response. Research to determine the causes for this variability and controlling for these factors would allow improvement in clinical outcomes.

PMID: [31579558](#)

### **7. Lower extremity strength profile in ambulatory adults with cerebral palsy and spastic diplegia; norm values and reliability for hand-held dynamometry.**

Eken MM, Lamberts RP, Koschnick S, Du Toit J, Veerbeek BE, Langerak NG.

PM R. 2019 Oct 4. doi: 10.1002/pmrj.12257. [Epub ahead of print]

**OBJECTIVES:** To present strength levels of lower extremity muscle groups and test-retest reliability of hand-held dynamometry (HHD) measurements in ambulatory adults with CP and typically developed (TD) adults. **DESIGN:** Case-control study. **SETTING:** Human motion laboratory. **PARTICIPANTS:** Fifty-four adults with CP (28 males; GMFCS level I/II/III: n = 25/20/9; mean age (SD) = 38 (7) year) and 62 TD adults (31 males; mean age (SD) = 37 (5) year). **INTERVENTIONS:** Not applicable. **MAIN OUTCOME MEASURE(S):** Maximum strength levels were obtained during voluntary isometric contraction of eight lower extremity muscle groups in adults with CP and spastic diplegia and TD adults using HHD. Three trials were performed per muscle group per leg. Test-retest reliability was investigated by calculating intraclass correlation coefficient (ICC), coefficient of variation (CV) and typical error of measurement (TEM). **RESULTS:** Force and torque levels were significantly lower in all eight lower extremity muscle groups. Excellent ICC levels were observed in TD, GMFCS I and II (>0.90), and moderate to excellent (0.82-0.97) in GMFCS III. CV and TEM were higher in adults with CP compared to TD adults, especially in GMFCS III. **LIMITATIONS:** No subtypes other than adults with CP and spastic diplegia were included. **CONCLUSION:** Lower extremity strength profiles demonstrate substantial muscle weakness in ambulatory adults with CP compared to TD adults, which highlights the importance to address muscle weakness in this population group. These strength profiles may serve as norm values for clinicians and researchers. In addition, HHD showed to be reliable to assess lower extremity strength in adults with CP.

PMID: [31585499](#)

### **8. Comparison of Gait Ability of a Child with Cerebral Palsy According to the Difference of Dorsiflexion Angle of Hinged Ankle-Foot Orthosis: A Case Report.**

Son I, Lee D, Hong S, Lee K, Lee G.

Am J Case Rep. 2019 Oct 3;20:1454-1459. doi: 10.12659/AJCR.916814.

**BACKGROUND** The purpose of this study was to compare gait abilities in a child with spastic diplegia according to different dorsiflexion angles on hinged ankle-foot orthosis (hinged AFO). **CASE REPORT** This study is a case report of a child who was diagnosed with spastic diplegia and ambulated independently with the use of a hinged AFO. For gait analysis, the GAITRite® was used under 3 different conditions including barefoot, wearing regular of hinged AFO, and wearing a dorsiflexion 10° hinged AFO. The gait velocity and cadence were collected as temporal parameters, while step length, stride length, and single and double leg support time were collected as temporal spatial parameters. As a result, when a regular hinged AFO was worn on the barefoot, the gait velocity and cadence per minute were increased, whereas the step length and stride length, the single and double leg support time decreased. The gait velocity, cadence, step length, and stride length were significantly increased when dorsiflexion 10° hinged AFO was applied compared to barefoot. The gait velocity, cadence, step length, and stride length increased with dorsiflexion 10° hinged AFO compared to regular hinged AFO. **CONCLUSIONS** The results of this study demonstrated that wearing a dorsiflexion 10° hinged AFO would have a positive effect on improving gait ability of a child with cerebral palsy rather than wearing a bare foot and a general hinged AFO.

PMID: [31578314](#)

### **9. Effect of robotic-assisted gait training in a large population of children with motor impairment due to cerebral palsy or acquired brain injury.**

Beretta E, Storm FA, Strazzer S, Frascarelli F, Petrarca M, Colazza A, Cordone G, Biffi E, Morganti R, Maghini C, Piccinini L, Reni G, Castelli E.

Arch Phys Med Rehabil. 2019 Sep 25. pii: S0003-9993(19)31092-5. doi: 10.1016/j.apmr.2019.08.479. [Epub ahead of print]

**OBJECTIVE:** To evaluate retrospectively the effect of robotic rehabilitation in a large group of children with motor impairment; an additional goal was to identify the effects in children with cerebral palsy and acquired brain injury and with different levels of motor impairment according to the Gross Motor Function Classification System. Finally, we examined the effect of time elapsed from injury on children's functions. **DESIGN:** A cohort, pretest-posttest retrospective study was conducted. **SETTING:** Hospitalized care. **PARTICIPANTS:** 182 children, 110 with acquired brain injury (ABI) and 72 with

cerebral palsy (CP) and with Gross Motor Function Classification System (GMFCS) levels I-IV were evaluated retrospectively. INTERVENTIONS: Patients underwent a combined treatment of robotic-assisted gait training and physical therapy. MAIN OUTCOME MEASURE(S): All the patients were evaluated before and after the training using the 6-minute walk test and the Gross Motor Function Measure. A linear mixed model with three fixed factors and one random factor was used to evaluate improvements. RESULTS: The 6-minute walk test showed improvement in the whole group and in both ABI and CP. The Gross Motor Function Measure showed improvement in the whole group and in the patients with ABI but not in children with CP. The GMFCS analysis showed that all outcomes improved significantly in all classes within the ABI subgroup, whereas improvements were significant only for GMFCS III in children with CP. CONCLUSIONS: Children with motor impairment can benefit from a combination of robotic rehabilitation and physical therapy. Our data suggest positive results for the whole group and substantial differences between ABI and CP subgroups, with better results for children with ABI, that seem to be consistently related to time elapsed from injury.

PMID: [31562873](#)

### **10. Short- and Mid-Term Improvement of Postural Balance after a Neurorehabilitation Program via Hippotherapy in Patients with Sensorimotor Impairment after Cerebral Palsy: A Preliminary Kinetic Approach.**

Viruega H, Gaillard I, Carr J, Greenwood B, Gaviria M.

Brain Sci. 2019 Sep 29;9(10). pii: E261. doi: 10.3390/brainsci9100261.

There is still a lack of studies focused on trunk neurorehabilitation. Accordingly, it is unclear which therapeutic modalities are the most effective in improving static/dynamic balance after brain damage. We designed a pilot study on hippotherapy to assess its short- and mid-term effect on dynamic postural balance in patients with moderate-to-severe sensorimotor impairment secondary to cerebral palsy. Five patients aged  $15.4 \pm 6.1$  years old were recruited. All of them had moderate-to-severe alterations of the muscle tone with associated postural balance impairment. Standing and walking were also impaired. Ten minutes horse riding simulator followed by twenty minutes hippotherapy session were conducted during five session days separated by one week each. We analyzed the displacement of the Center of Pressure (COP) on the sitting surface of the simulator's saddle by means of a customized pressure pad. We measured the general behavior of the COP displacement as well as the postural adjustments when pace changed from walk to trot to walk during the sessions and among sessions. Statistical analysis revealed an improved postural control both by the end of the session and from session 1 to session 5. These results suggest that hippotherapy might support regularization of postural control in a long-term neurorehabilitation context.

PMID: [31569505](#)

### **11. Autonomy in participation in cerebral palsy from childhood to adulthood.**

Schmidt AK, van Gorp M, van Wely L, Ketelaar M, Hilberink SR, Roebroek ME; Perrin-Decade Pip Study Groups.

Dev Med Child Neurol. 2019 Oct 2. doi: 10.1111/dmcn.14366. [Epub ahead of print]

AIM: To determine the long-term development of autonomy in participation of individuals with cerebral palsy (CP) without intellectual disability. METHOD: Individuals with CP ( $n=189$ , 117 males, 72 females; mean age [SD] 21y 11mo [4y 11mo], range 12-34y); were assessed cross-sectionally (46%) or up to four times (54%), between the ages of 12 and 34 years. Autonomy in participation was classified using phase 3 of the Rotterdam Transition Profile. A logistic generalized estimating equation regression model was used to analyse autonomy in six domains (independent variables: age, Gross Motor Function Classification System [GMFCS] level, and interaction between age and GMFCS level). Proportions of autonomy were compared to references using binomial tests ( $p<0.05$ ). RESULTS: In most domains, over 90% of participants ( $n=189$ , 400 observations, 80% in GMFCS levels I and II) reached autonomy in participation in their late twenties, except for intimate/sexual relationships. Those in GMFCS levels III to V compared to those in GMFCS levels I and II had less favourable development of autonomy in the transportation, intimate relationships, employment, and housing domains, and more favourable development in the finances domain. Compared to references, fewer individuals with CP were autonomous in participation. INTERPRETATION: This knowledge of autonomy may guide the expectations of young people with CP and their caregivers. Furthermore, rehabilitation professionals should address autonomy development in intimate relationships, employment, and housing, especially in individuals with lower gross motor function. WHAT THIS PAPER ADDS: Individuals with cerebral palsy without intellectual disability achieved autonomy in most participation domains. Regarding intimate relationships, they continued to have less experience compared to age-matched references. Development of autonomy was less favourable for individuals in Gross Motor Function Classification System levels III to V.

PMID: [31578717](#)

## 12. Investigation of the relationship between quality of life, activity-participation and environmental factors in adolescents with cerebral palsy.

Burak M, Kavlak E.

NeuroRehabilitation. 2019 Sep 18. doi: 10.3233/NRE-191288. [Epub ahead of print]

**BACKGROUND AND OBJECTIVE:** The aim of this study is to examine the relationship between quality of life, activity-participation and environmental factors in adolescents with cerebral palsy. **METHODS:** Seventy-five (75) adolescents (M:45, F:30) aged between 14-18 years (mean: 15.52±1.60 yrs) were included in the study. Participants were divided into three groups: Level I, Level II and Level III according to the Gross Motor Function Classification System. Gross Motor Function Classification System, Gross Motor Function Measure, Functional Independence Scale, Manual Ability Classification System, Pediatric Quality of Life Inventory and International Classification of Functioning, Disability and Health Child-Youth version Short Form (ICF-CY) (14-18 yrs) were used for assessments. **RESULTS:** It is found that there is a moderate and high level of correlation between quality of life and activity participation and body functions, a moderate and high level of correlation between quality of life and activity participation and body functions with gross motor function levels, and a moderate and low level correlation between environmental factors and gross motor function levels ( $p < 0.05$ ). **CONCLUSIONS:** The fact that the ICF-CY short form used for cerebral palsied children is compatible with other assessment scales suggests that the use of ICF-CY short forms may be useful in assessing the health status of individuals.

PMID: [31561397](#)

## 13. A novel mouse model of contralateral C7 transfer via the pretracheal route: A feasibility study.

Ye X, Shen YD, Feng JT, Wang F, Gao ZR, Lei GW, Yu AP, Wang CP, Liang CM, Xu WD.

J Neurosci Methods. 2019 Sep 29;328:108445. doi: 10.1016/j.jneumeth.2019.108445. [Epub ahead of print]

**BACKGROUND:** Contralateral seventh cervical nerve transfer (contralateral C7 transfer) is a novel treatment for patients with spastic paralysis, including stroke and traumatic brain injury. However, little is known on changes in plasticity that occur in the intact hemisphere after C7 transfer. An appropriate surgical model is required. **NEW METHOD:** We described in detail the anatomy of the C7 in a mouse model. We designed a pretracheal route by excising the contralateral C6 lamina ventralis, and the largest nerve defect necessary for direct neurorrhaphy was compared with defect lengths in a prespinal route. To test feasibility, we performed in-vivo surgery and assessed nerve regeneration by immunofluorescence, histology, electrophysiology, and behavioral examinations. **RESULTS:** Two types of branching were found in the anterior and posterior divisions of C7, both of which were significantly larger than the sural nerve. The length of the nerve defect was drastically reduced after contralateral C6 lamina ventralis excision. Direct tension-free neurorrhaphy was achieved in 66.7% of mice. The expression of neurofilament in the distal segment of the regenerated C7 increased. Histological examination revealed remyelination. Behavioral tests and electrophysiology tests showed functional recovery in a traumatic brain injury mouse. **COMPARISON WITH EXISTING METHODS:** This is the first direct tension-free neurorrhaphy mouse model of contralateral C7 transfer which shortened the time of nerve regeneration; previous models have used nerve grafting. **CONCLUSIONS:** This paper describes a simple, reproducible, and effective mouse model of contralateral C7 transfer for studying brain plasticity and exploring potential new therapies after unilateral cerebral injury.

PMID: [31577920](#)

## 14. Novel synaptic plasticity enhancer drug to augment functional recovery with rehabilitation.

Takahashi T.

Curr Opin Neurol. 2019 Sep 23. doi: 10.1097/WCO.0000000000000748. [Epub ahead of print]

**PURPOSE OF REVIEW:** Stroke is a devastating illness which severely attenuates quality of life because of paralysis. Despite recent advances in therapies during acute phase such as thrombolytic therapy, clinical option to intervene the process of rehabilitation is limited. No pharmacological intervention that could enhance the effect of rehabilitation has not been established. Recent articles, which are summarized in the review article, reported novel small compound which accelerates training-dependent motor function recovery after brain damage. **RECENT FINDINGS:** A novel small compound, edonergic maleate, binds to collapsin response mediator protein 2 (CRMP2) and enhance synaptic plasticity leading to the acceleration of rehabilitative training-dependent functional recovery after brain damage in rodent and nonhuman primate. The clinical trial to test this effect in human is now ongoing. Future preclinical and clinical studies will delineate the potentials of this compound.

SUMMARY: A novel CRMP2-binding small compound, edonerpic maleate, accelerates motor function recovery after brain damage in rodent and nonhuman primate.

PMID: [31567431](#)

### 15. Combined prenatal and postnatal prediction of early neonatal compromise risk.

Eden RD, Evans MI, Britt DW, Evans SM, Gallagher P, Schiffrin BS.

J Matern Fetal Neonatal Med. 2019 Oct 3;1-181. doi: 10.1080/14767058.2019.1676714. [Epub ahead of print]

Objective: Electronic fetal monitoring/ cardiotocography (EFM) is nearly ubiquitous, but nearly everyone acknowledges there is room for improvement. We have contextualized monitoring by breaking it down into quantifiable components and adding to that, other factors that have not been formally used: ie the assessment of uterine contractions, and the presence of maternal, fetal, and obstetrical risk factors. We have created an algorithm, the Fetal Reserve Index (FRI) that significantly improves the detection of at-risk cases. We hypothesized that extending our approach of monitoring to include the immediate newborn period could help us better understand the physiology and pathophysiology of the decrease in fetal reserve during labor and the transition from fetal to neonatal homeostasis, thereby further honing the prediction of outcomes. Such improved and earlier understanding could then potentiate earlier, and more targeted use of neuroprotective attempts during labor treating decreased fetal reserve and improving the fetus' transition from fetal to neonatal life minimizing risk of neurologic injury. Study design: We have analyzed a 45-year-old research database of closely monitored labors, deliveries, and an additional hour of continuous neonatal surveillance. We applied the FRI prenatally and created a new metric, the INCHON index that combines the last FRI with umbilical cord blood and 4-minute umbilical artery blood parameters to predict later neonatal acid/base balance. Using the last FRI scores, we created 3 neonatal groups. Umbilical cord and catheterized umbilical artery bloods at 4, 8, 16, 32, and 64 minutes were measured for base excess, pH, and PO<sub>2</sub>. Continuous neonatal heart rate was scored for rate, variability, and reactivity. Results: Neonates commonly do not make a smooth transition from fetal to postnatal physiology. Even in low risk babies, 85% exhibited worsening pH and base excess during the first 4 minutes; 34% of neonates reached levels considered at high risk for metabolic acidosis ( $\leq -12$  mmol/L) and neurologic injury. Neonatal heart rate commonly exhibited sustained, significant tachycardia with loss of reactivity and variability. One quarter of all cases would be considered Category III if part of the fetal tracing. Our developed metrics (FRI and INCHON) clearly discriminated and predicted low, medium, and high-risk neonatal physiology. Conclusions: The immediate neonatal period often imposes generally unrecognized risks for the newborn. INCHON improves identification of decreased fetal reserve and babies at risk, thereby permitting earlier intervention during labor (intrauterine resuscitation) or potentially postnatally (brain cooling) to prevent neurologic injury. We believe that perinatal management would be improved by routine, continuous neonatal monitoring - at least until heart rate reactivity is restored. FRI and INCHON can help identify problems much earlier and more accurately than currently and keep fetuses and babies in better metabolic shape.

PMID: [31581872](#)

### 16. In clinical practice, cerebral MRI in newborns is highly predictive of neurodevelopmental outcome after therapeutic hypothermia.

Tharmapooopathy P, Chisholm P, Barlas A, Varsami M, Gupta N, Ekitzidou G, Ponnusamy V, Kappelou O, Evanson J, Rosser G, Shah DK.

Eur J Paediatr Neurol. 2019 Sep 11. pii: S1090-3798(19)30135-7. doi: 10.1016/j.ejpn.2019.09.005. [Epub ahead of print]

OBJECTIVE: In the trials, a substantial proportion of newborns who underwent therapeutic hypothermia (TH) had an adverse outcome after hypoxic-ischaemic encephalopathy (HIE). Cooled babies were noted to have fewer cerebral lesions on MRI but when present lesions were predictive of adverse outcome. We investigate the predictive value of cerebral MRI in babies who undergo cooling in the clinical setting outside of the clinical trials in a prospective UK cohort. RESULTS: Of 75 babies recruited from four centres, neurodevelopment was available for 69 (92%) with 29% (20/69) being abnormal. The unfavourable MRI group (n = 22) had significantly lower motor (p < 0.001), language (p < 0.001) and cognition (p < 0.001) scores on Bayley -III assessment, compared to the favourable MRI group (n = 47). On multiple regression there was a significant relationship between basal ganglia and thalami abnormality and motor (p = 0.002), cognition (p = 0.011) and language (p = 0.013) outcomes. Half of the babies who had an MRI predictive of adverse outcome (11/22) had highest grade cerebral palsy. Cerebral MRI had 95% sensitivity, 94% specificity, 91% PPV and 98% NPV in predicting neurodevelopment. CONCLUSIONS: In this clinical cohort, fewer children had adverse neurodevelopment after TH compared to the TH trials. However, half the children who had an MRI predictive of adverse ND outcome had the most severe form of cerebral palsy. Cerebral MRI is a valuable tool for prognostication in clinical practice and is a valid surrogate outcome for research.

PMID: [31563495](#)

### 17. Positive allosteric modulation of the $\alpha 7$ nicotinic acetylcholine receptor as a treatment for cognitive deficits after traumatic brain injury.

Titus DJ, Johnstone T, Johnson NH, London SH, Chapalamadugu M, Hogenkamp D, Gee KW, Atkins CM.

PLoS One. 2019 Oct 3;14(10):e0223180. doi: 10.1371/journal.pone.0223180. eCollection 2019.

Cognitive impairments are a common consequence of traumatic brain injury (TBI). The hippocampus is a subcortical structure that plays a key role in the formation of declarative memories and is highly vulnerable to TBI. The  $\alpha 7$  nicotinic acetylcholine receptor (nAChR) is highly expressed in the hippocampus and reduced expression and function of this receptor are linked with cognitive impairments in Alzheimer's disease and schizophrenia. Positive allosteric modulation of  $\alpha 7$  nAChRs with AVL-3288 enhances receptor currents and improves cognitive functioning in naïve animals and healthy human subjects. Therefore, we hypothesized that targeting the  $\alpha 7$  nAChR with the positive allosteric modulator AVL-3288 would enhance cognitive functioning in the chronic recovery period of TBI. To test this hypothesis, adult male Sprague Dawley rats received moderate parasagittal fluid-percussion brain injury or sham surgery. At 3 months after recovery, animals were treated with vehicle or AVL-3288 at 30 min prior to cue and contextual fear conditioning and the water maze task. Treatment of TBI animals with AVL-3288 rescued learning and memory deficits in water maze retention and working memory. AVL-3288 treatment also improved cue and contextual fear memory when tested at 24 hr and 1 month after training, when TBI animals were treated acutely just during fear conditioning at 3 months post-TBI. Hippocampal atrophy but not cortical atrophy was reduced with AVL-3288 treatment in the chronic recovery phase of TBI. AVL-3288 application to acute hippocampal slices from animals at 3 months after TBI rescued basal synaptic transmission deficits and long-term potentiation (LTP) in area CA1. Our results demonstrate that AVL-3288 improves hippocampal synaptic plasticity, and learning and memory performance after TBI in the chronic recovery period. Enhancing cholinergic transmission through positive allosteric modulation of the  $\alpha 7$  nAChR may be a novel therapeutic to improve cognition after TBI.

PMID: [31581202](#)

### 18. A Physical Therapy Intervention to Advance Cognitive and Motor Skills: A Single Subject Study of a Young Child With Cerebral Palsy.

Dusing SC, Harbourne RT, Lobo MA, Westcott-McCoy S, Bovaird JA, Kane AE, Syed G, Marcinowski EC, Koziol NA, Brown SE.

Pediatr Phys Ther. 2019 Oct;31(4):347-352. doi: 10.1097/PEP.0000000000000635.

BACKGROUND: Physical therapy interventions for children with severe motor impairments do not address the relationship between motor and cognitive development. PURPOSE: Evaluate the potential of a physical therapy intervention focusing on enhancing cognitive and motor outcomes in a child with severe motor impairments. DESIGN: AB phase design without reversal. METHODS: One child participated in 8 assessments from 4 to 29 months of age. The START-Play intervention was provided for 3 months following 4 baseline assessments over 12 months. Total Gross Motor Function Measure (GMFM), Sitting, Reaching, and Problem Solving assessments were completed. Visual inspection, 2 standard deviation (SD) Band Method, and percent of nonoverlapping data methods evaluated change. RESULTS: This child had improved GMFM total and sitting scores, increased frequency of toys contacts, and increased rate of problem-solving behaviors following intervention. CONCLUSION: START-Play shows promise for children with severe motor impairments. Additional research is needed to evaluate efficacy.

PMID: [31568380](#)

### 19. Commentary on "A Physical Therapy Intervention to Advance Cognitive and Motor Skills: A Single Subject Study of a Young Child With Cerebral Palsy".

McNamara L1, Velde AT, Novak I.

Pediatr Phys Ther. 2019 Oct;31(4):353. doi: 10.1097/PEP.0000000000000643.

PMID: [31568381](#)

**20. Mental health problems in cerebral palsy: comprehensive management for children and their families.**

Gillberg C.

Dev Med Child Neurol. 2019 Sep 30. doi: 10.1111/dmcn.14359. [Epub ahead of print]

PMID: [31571200](#)**21. Promoting School Engagement in Children with Cerebral Palsy: A Narrative Based Program.**

Pereira A, Rosário P, Lopes S, Moreira T, Magalhães P, Núñez JC, Vallejo G, Sampaio A.

Int J Environ Res Public Health. 2019 Sep 27;16(19). pii: E3634. doi: 10.3390/ijerph16193634.

This study assessed the efficacy of an educational program focused on the promotion of school engagement in children with Cerebral Palsy. A 9 weeks, narrative-based intervention program, with a pre-post neuropsychological and self-report evaluation, was developed with a dual focus: a self-regulation theoretical model and executive function stimulation. Fifteen children with Cerebral Palsy participated in the study. Results showed a significant main effect of time ( $F(2,82) = 6.04$ ,  $p = 0.0066$ , partial  $\eta^2 = 0.30$ ;  $F(2,82) = 9.91$ ,  $p = 0.0006$ , partial  $\eta^2 = 0.41$ ;  $F(2,82) = 26.90$ ,  $p < 0.0001$ , partial  $\eta^2 = 0.66$ ) in the three dimensions of school engagement. Findings indicate that the program to train self-regulated competences and executive function skills was efficacious in promoting school engagement in children with Cerebral Palsy. Educational implications were discussed.

PMID: [31569711](#)**22. Classification of Articulator Movements and Movement Direction from Sensorimotor Cortex Activity.**

Salari E, Freudenburg ZV, Branco MP, Aarnoutse EJ, Vansteensel MJ, Ramsey NF.

Sci Rep. 2019 Oct 2;9(1):14165. doi: 10.1038/s41598-019-50834-5.

For people suffering from severe paralysis, communication can be difficult or nearly impossible. Technology systems called brain-computer interfaces (BCIs) are being developed to assist these people with communication by using their brain activity to control a computer without any muscle activity. To benefit the development of BCIs that employ neural activity related to speech, we investigated if neural activity patterns related to different articulator movements can be distinguished from each other. We recorded with electrocorticography (ECoG), the neural activity related to different articulator movements in 4 epilepsy patients and classified which articulator participants moved based on the sensorimotor cortex activity patterns. The same was done for different movement directions of a single articulator, the tongue. In both experiments highly accurate classification was obtained, on average 92% for different articulators and 85% for different tongue directions. Furthermore, the data show that only a small part of the sensorimotor cortex is needed for classification (ca. 1 cm<sup>2</sup>). We show that recordings from small parts of the sensorimotor cortex contain information about different articulator movements which might be used for BCI control. Our results are of interest for BCI systems that aim to decode neural activity related to (actual or attempted) movements from a contained cortical area.

PMID: [31578420](#)**23. Development of Wheeled Mobility indicators to advance the quality of spinal cord injury rehabilitation: SCI-High Project.**

Bayley MT, Kirby RL, Farahani F, Titus L, Smith C, Routhier F, Gagnon DH, Stapleford P, Alavinia SM, Craven BC.

J Spinal Cord Med. 2019 Oct;42(sup1):130-140. doi: 10.1080/10790268.2019.1647934.

Background: Wheeled mobility is critical for individuals with Spinal Cord Injury or Disease (SCI/D) related paralysis. The World Health Organization (WHO) developed guidelines highlighting eight steps in wheelchair service delivery: (1) referral and appointment; (2) assessment; (3) prescription; (4) funding and ordering; (5) product preparation; (6) fitting; (7) user training; and, (8) follow-up maintenance/repairs. This article describes the processes used to develop structure, process and outcome indicators that reflect the WHO guidelines within the Domain of Wheeled Mobility rehabilitation for Canadians. Methods: Wheeled mobility experts within the SCI-High Project Team used the WHO guideline to inform the Construct

refinement and development of a Driver diagram. Following seven meetings, the Driver diagram and review of outcome measures and literature synthesis regarding wheelchair service delivery informed indicator selection and group consensus. Results: The structure indicator examines the proportion of SCI/D service providers within a rehabilitation program who have specialized wheelchair training to ensure prescription, preparation, fitting, and maintenance quality. The process indicator evaluates the average number of hours of wheelchair service delivery provided per patient during rehabilitation. The intermediary outcome indicator (rehabilitation discharge), is a target capacity score on the Wheelchair Skills Test Questionnaire (WST-Q). The final outcome indicators (at 18 months post rehabilitation admission) are the Life Space Assessment (LSA) and the Wheelchair Use Confidence Scale (WheelCon) short form mean scores. Conclusion: Routine implementation of the selected Wheeled Mobility structure, process and outcome indicators should measurably advance care within the Wheeled Mobility Domain for Canadians living with SCI/D by 2020.

PMID: [31573457](#)

#### **24. CP-North: living life in the Nordic countries? A retrospective register research protocol on individuals with cerebral palsy and their parents living in Sweden, Norway, Denmark, Finland and Iceland.**

Alriksson-Schmidt AI, Ahonen M, Andersen GL, Eggertsdóttir G, Haula T, Jahnsen R, Jarl J, Jeglinsky-Kankainen I, Jonsdóttir G, Seid AK, Ásgeirsdóttir TL, Møller-Madsen B, Nordbye-Nielsen K, Saha S, Steskal D, Sääksvuori L, Hägglund G.

BMJ Open. 2019 Oct 1;9(10):e024438. doi: 10.1136/bmjopen-2018-024438.

**INTRODUCTION:** Cerebral palsy (CP) is one of the most common neurodevelopmental disabilities. Yet, most individuals with CP are adults. How individuals with CP fare in terms of health, quality of life (QoL), education, employment and income is largely unknown. Further, little is known about the effects of having a child with CP on the parents. The Nordic countries are known for their strong welfare systems, yet it is unknown to what extent the added burden related to disability is actually compensated for. We will explore how living with CP affects health, QoL, healthcare utilisation, education, labour market outcomes, socioeconomic status and mortality throughout the lifespan of individuals with CP and their parents. We will also investigate if these effects differ between subgroups, within and across the Nordic countries. **METHODS AND ANALYSES:** CP-North is a multidisciplinary 4-year (1 August 2017 to 31 July 2021) register research project. The research consortium comprises researchers and users from Sweden, Norway, Denmark, Iceland and Finland. Data from CP registries and follow-up programmes, or cohorts of individuals with CP, will be merged with general national registries. All individual studies are structured under three themes: medical outcomes, social and public health outcomes, and health economics. Both case-control and cohort designs will be included depending on the particular research question. Data will be analysed in the individual countries and later merged across nations. **ETHICS AND DISSEMINATION:** The ethics approval processes in each individual country are followed. Findings will be published (open access) in international peer-reviewed journals in related fields. Updates on CP-North will be published online at <http://rdi.arcada.fi/cpnorth/en/>.

PMID: [31575533](#)

#### **25. Blinding and bias in randomized controlled trials: when to measure the effectiveness of blinding.**

Copeland L, Edwards P, Sakzewski L, Thorley M, Kentish M, Ware RS, Boyd RN.

Dev Med Child Neurol. 2019 Sep 30. doi: 10.1111/dmcn.14369. [Epub ahead of print]

PMID: [31571206](#)

## Prevention and Cure

#### **26. Trophic factors are essential for the survival of grafted oligodendrocyte progenitors and for neuroprotection after perinatal excitotoxicity.**

Hirose-Ikeda M, Chu B, Zhao P, Akil O, Escalante E, Vergnes L, Cepeda C, Espinosa-Jeffrey A.

Neural Regen Res. 2020 Mar;15(3):557-568. doi: 10.4103/1673-5374.266066.

The consequences of neonatal white matter injury are devastating and represent a major societal problem as currently there is

no cure. Prematurity, low weight birth and maternal pre-natal infection are the most frequent causes of acquired myelin deficiency in the human neonate leading to cerebral palsy and cognitive impairment. In the developing brain, oligodendrocyte (OL) maturation occurs perinatally, and immature OLs are particularly vulnerable. Cell replacement therapy is often considered a viable option to replace progenitors that die due to glutamate excitotoxicity. We previously reported directed specification and mobilization of endogenous committed and uncommitted neural progenitors by the combination of transferrin and insulin growth factor 1 (TSC1). Here, considering cell replacement and integration as therapeutic goals, we examined if OL progenitors (OLPs) grafted into the brain parenchyma of mice that were subjected to an excitotoxic insult could rescue white matter injury. For that purpose, we used a well-established model of glutamate excitotoxic injury. Four-day-old mice received a single intraparenchymal injection of the glutamate receptor agonist N-methyl-D-aspartate alone or in conjunction with TSC1 in the presence or absence of OLPs grafted into the brain parenchyma. Energetics and expression of stress proteins and OL developmental specific markers were examined. A comparison of the proteomic profile per treatment was also ascertained. We found that OLPs did not survive in the excitotoxic environment when grafted alone. In contrast, when combined with TSC1, survival and integration of grafted OLPs was observed. Further, energy metabolism in OLPs was significantly increased by N-methyl-D-aspartate and modulated by TSC1. The proteomic profile after the various treatments showed elevated ubiquitination and stress/heat shock protein 90 in response to N-methyl-D-aspartate. These changes were reversed in the presence of TSC1 and ubiquitination was decreased. The results obtained in this pre-clinical study indicate that the use of a combinatorial intervention including both trophic support and healthy OLPs constitutes a promising approach for long-term survival and successful graft integration. We established optimal conditioning of the host brain environment to promote long-term survival and integration of grafted OLPs into an inflamed neonate host brain. Experimental procedures were performed under the United States Public Health Service Guide for the Care and Use of Laboratory Animals and were approved by the Institutional Animal Care Committee at (UCLA) (ARC #1992-034-61) on July 1, 2010.

PMID: [31571668](#)