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## Interventions and Management

### 1. Less-Affected Hand Function in Children With Hemiparetic Unilateral Cerebral Palsy: A Comparison Study With Typically Developing Peers.

Rich TL, Menk JS, Rudser KD, Feyma T, Gillick BT.

Neurorehabil Neural Repair. 2017 Nov 1:1545968317739997. doi: 10.1177/1545968317739997. [Epub ahead of print]

**BACKGROUND:** Neurorehabilitation interventions in children with unilateral cerebral palsy (UCP) target motor abilities in daily life yet deficits in hand skills persist. Limitations in the less-affected hand may affect overall bimanual hand skills. **OBJECTIVE:** To compare hand function, by timed motor performance on the Jebsen-Taylor Test of Hand Function (JTTHF) and grip strength of children with UCP to children with typical development (CTD), aged 8 to 18 years old. Exploratory analyses compared hand function measures with regard to neurophysiological outcomes measured by transcranial magnetic stimulation and between group comparisons of hemispheric motor threshold. **METHODS:** Baseline hand skills were evaluated in 47 children (21 UCP; 26 CTD). Single-pulse transcranial magnetic stimulation testing assessed corticospinal tract and motor threshold. **RESULTS:** The mean difference of the less-affected hand of children with UCP to the dominant hand of CTD on the JTTHF was 21.4 seconds (95% CI = 9.32-33.46,  $P = .001$ ). The mean difference in grip strength was -30.8 N (95% CI = -61.9 to 0.31,  $P = .052$ ). Resting motor thresholds between groups were not significant, but age was significantly associated with resting motor threshold ( $P < .001$ ;  $P = .001$ ). Children with UCP ipsilateral pattern of motor representation demonstrated greater mean differences between hands than children with contralateral pattern of motor representation ( $P < .001$ ). All results were adjusted for age and sex. **CONCLUSIONS:** The less-affected hand in children with UCP underperformed the dominant hand of CTD. Limitations were greater in children with UCP ipsilateral motor pattern. Rehabilitation in the less-affected hand may be warranted. Bilateral hand function in future studies may help identify the optimal rehabilitation and neuromodulatory intervention.

[PMID: 29130382](#)

### 2. Effect of Botulinum Toxin A on Muscle Healing and its Implications in Aesthetic and Reconstructive Surgery.

Silberstein E, Maor E, Sukmanov O, Bogdanov Berezovsky A, Shoham Y, Krieger Y.

Aesthet Surg J. 2017 Nov 14. doi: 10.1093/asj/sjx207. [Epub ahead of print]

**BACKGROUND:** Muscle activity contributes to the enhancement of facial aging deformity, blepharospasm, cerebral palsy spasticity, trismus, torticollis, and other conditions. Myotomy of the involved muscles in order to reduce the deformity has variable success rates due to muscle healing and regeneration of activity. **OBJECTIVES:** The goal of this study was to investigate whether blocking striated muscle activity with Botulinum toxin (BtxA) during the healing time after myotomy alters the healing process and reduces long-term muscle activity. **METHODS:** Eighteen Sprague Dawley rats were divided into 3 groups: group A ( $n = 7$ ) underwent myotomy of their Latissimus Dorsi muscle; group B ( $n = 7$ ) underwent myotomy and injection of BtxA into their severed muscle; group C ( $n = 4$ ) injection of BtxA only. Muscle strength was tested periodically using a grip test. **RESULTS:** Starting at week 16 and until the termination of study at week 22, group B (Myotomy + BtxA)

showed significant reduction in muscle power compared to the two control groups. **CONCLUSIONS:** Addition of BtxA injection into a muscle immediately after myotomy may interfere with muscle healing and contribute to a more successful long-term result.

[PMID: 29145580](#)

### **3. Intrathecal baclofen in dyskinetic cerebral palsy: effects on function and activity.**

Eek MN, Olsson K, Lindh K, Askljung B, Pålman M, Corneliusson O, Himmelmann K.

Dev Med Child Neurol. 2017 Nov 17. doi: 10.1111/dmcn.13625. [Epub ahead of print]

**AIM:** To investigate the effect of intrathecal baclofen (ITB) on function and activity in dyskinetic cerebral palsy (CP). **METHOD:** A retrospective cohort study of records from 25 children (15 males, 10 females; mean age 10y 11mo, SD 4y 9mo). Five were classified in Gross Motor Function Classification level IV and 20 in level V. Parents were interviewed about activities in daily life, sitting, communication, pain, sleep, and gross and fine motor function. Differences before and 1 year after ITB were graded as positive, no change, or negative. Assessments of dystonia (using the Barry-Albright Dystonia Scale) and muscle tone (Ashworth Scale) were made. Joint range of motion (ROM) was measured. **RESULTS:** Both dystonia and increased muscle tone, present in all participants before ITB, decreased after ( $p < 0.001$ ). Passive ROM was restricted, with no difference after. Parents reported improvements in activities in daily life ( $p < 0.001$ ), sitting ( $p < 0.001$ ), communication ( $p < 0.001$ ), and fine motor function ( $p = 0.013$ ), but no change in gross motor function. Before ITB, pain and disturbed sleep were reported. There was a reduction in pain ( $p = 0.002$ ) and sleep improved ( $p = 0.004$ ) after ITB. **INTERPRETATION:** After ITB in individuals with dyskinetic CP, improvements were found in sitting, communication, and fine motor skills. There was a reduction in dystonia and muscle tone, and pain and sleep improved. **WHAT THIS PAPER ADDS:** Intrathecal baclofen can affect specific aspects of functioning in dyskinetic cerebral palsy. Sitting, communication, and fine motor function improved. Dystonia and spasticity were reduced. Pain was reduced and sleep improved.

[PMID: 29148568](#)

### **4. Artificial Walking Technologies to Improve Gait in Cerebral Palsy: Multichannel Neuromuscular Stimulation.**

Rose J, Cahill-Rowley K, Butler EE.

Artif Organs. 2017 Nov;41(11):E233-E239. doi: 10.1111/aor.13058.

Cerebral palsy (CP) is the most common childhood motor disability and often results in debilitating walking abnormalities, such as flexed-knee and stiff-knee gait. Current medical and surgical treatments are only partially effective in improving gait abnormalities and may cause significant muscle weakness. However, emerging artificial walking technologies, such as step-initiated, multichannel neuromuscular electrical stimulation (NMES), can substantially improve gait patterns and promote muscle strength in children with spastic CP. NMES may also be applied to specific lumbar-sacral sensory roots to reduce spasticity. Development of tablet computer-based multichannel NMES can leverage lightweight, wearable wireless stimulators, advanced control design, and surface electrodes to activate lower-limb muscles. Musculoskeletal models have been used to characterize muscle contributions to unimpaired gait and identify high muscle demands, which can help guide multichannel NMES-assisted gait protocols. In addition, patient-specific NMES-assisted gait protocols based on 3D gait analysis can facilitate the appropriate activation of lower-limb muscles to achieve a more functional gait: stance-phase hip and knee extension and swing-phase sequence of hip and knee flexion followed by rapid knee extension. NMES-assisted gait treatment can be conducted as either clinic-based or home-based programs. Rigorous testing of multichannel NMES-assisted gait training protocols will determine optimal treatment dosage for future clinical trials. Evidence-based outcome evaluation using 3D kinematics or temporal-spatial gait parameters will help determine immediate neuroprosthetic effects and longer term neurotherapeutic effects of step-initiated, multichannel NMES-assisted gait in children with spastic CP. Multichannel NMES is a promising assistive technology to help children with spastic CP achieve a more upright, functional gait.

[PMID: 29148138](#)

## 5. Relationship between radiographic patella-alta pathology and walking dysfunction in children with bilateral spastic Cerebral Palsy.

Hösl M, Böhm H, Seltmann M, Dussa CU, Döderlein L.

Gait Posture. 2017 Nov 10;60:28-34. doi: 10.1016/j.gaitpost.2017.11.006. [Epub ahead of print]

**BACKGROUND:** Patella-alta is very common in patients with Cerebral Palsy (CP). While several diagnostic x-ray indices have been developed for patella-alta in general, the specific relationship with walking dysfunction in CP is only partly understood. **METHODS:** 33 participants with bilateral spastic CP between 4 and 20 years (GMFCS I-II without previous surgery) that underwent 3D gait analysis as well as a radiographic exam within 0.8 (SD 1.2) months were retrospectively included. The Caton-Deschamps, the Insall-Salvati and the Koshino-Index, as well as the moment-arms of the quadriceps, the patellar-tendon length and patellar tilt angle were analyzed from x-rays. During gait, tempo-spatial parameters, the knee flexion kinematics, the knee moments and the moment impulse were calculated and correlated to x-ray parameters. **RESULTS:** Smaller quadriceps moment-arms were related to slower walking speed ( $r=0.48$ ,  $P=0.005$ ) and less knee extension during stance ( $r=0.68$   $P<0.001$ ). Smaller quadriceps moment arms and longer patellar-tendons were also significantly related to a larger knee flexion moment impulse in the second half of the stance phase ( $r=-0.36$ ,  $P=0.045$  and  $r=0.39$ ,  $P=0.028$ ) and hence to more abnormal knee loads. Yet, none of the traditional indices was related to any parameter of gait. **INTERPRETATION:** Traditional radiographic indices for patella-alta possess little to no informative value for walking dysfunction in individuals with CP suspected to have knee pathology. Smaller moment-arms are a key feature of patellofemoral pathology in CP reducing the knee extensor mechanism, an aspect which is not sufficiently picked up by traditional indices.

[PMID: 29149666](#)

## 6. The relationship between the physical cost index and knee extensor strength in children with hemiplegic cerebral palsy.

Takaki K, Kusumoto Y.

J Phys Ther Sci. 2017 Oct;29(10):1784-1787. doi: 10.1589/jpts.29.1784. Epub 2017 Oct 21.

[Purpose] Lower extremity strength is a contributing factor to energy efficiency of gait. However, this contribution has not previously been evaluated in children with hemiplegic cerebral palsy (CP). The aim of this study was to evaluate the association between energy consumption, measured by the physical cost index (PCI), and strength of lower extremity, measured by the maximum knee extensor strength (MKES), in children with hemiplegic CP. [Subjects and Methods] Subjects were 10 children (4 males and 6 females; age, 7-17 years) with hemiplegic CP, but no history of orthopedic intervention or botulinum toxin treatment over the 1 year prior to the assessment. The PCI was measured during a 6-min walk test, and MKES using hand-held dynamometry, with the highest of two measures used for analysis. [Results] A negative correlation was identified between the PCI and MKES (R-value, -0.81 (affected) and -0.83 (unaffected) lower limb). [Conclusion] Higher lower extremity strength was associated with lower fatigability during a 6-min walk test in children with hemiplegic CP, providing evidence for the inclusion of strengthening exercises for both the affected and unaffected extremities in the rehabilitation of these children.

[PMID: 29133972](#)

## 7. Ultrasonographic evaluation of changes in the muscle architecture of the gastrocnemius with botulinum toxin treatment for lower extremity spasticity in children with cerebral palsy.

Kawano A, Yanagizono T, Kadouchi I, Umezaki T, Chosa E.

J Orthop Sci. 2017 Nov 13. pii: S0949-2658(17)30293-2. doi: 10.1016/j.jos.2017.10.012. [Epub ahead of print]

**BACKGROUND:** Botulinum toxin A treatment involves injecting botulinum toxin A to relax muscle spasticity. Using ultrasonography, this study examined changes in the muscle architecture before and after treatment to evaluate the influence of botulinum toxin A injection on muscles. **METHODS:** The participants included 18 children (mean age, 6.2 years) with cerebral palsy who were treated with botulinum toxin A for lower extremity spasticity and 27 healthy children (mean age, 6.4 years) as a control group. In all cases, botulinum toxin A was injected into the gastrocnemius muscle. The muscle length, muscle width, and pennation angle (which indicates the degree of muscle fiber tone), were measured using B-mode ultrasonography before and 12 weeks after injection. **RESULTS:** The muscle length and muscle width were shorter in the cerebral palsy group than in the control group. The pennation angle in the cerebral palsy group significantly decreased after injection from  $28.2 \pm 3.6^\circ$  to  $25.8 \pm 2.5^\circ$  in the resting position of the ankle and from  $18.6 \pm 2.8^\circ$  to  $15.9 \pm 1.7^\circ$  in the maximum dorsiflexion position of the ankle. In the control group, the pennation angle was  $25.9 \pm 3.2^\circ$  in the resting position of the ankle and  $15.1 \pm 2.5^\circ$  in the maximum dorsiflexion position of the ankle. The rate of increase of fascicle length during passive movement from the resting

position of the ankle to the maximum dorsiflexion position was 143.9% in the cerebral palsy group, which was significantly less than the value of 157.7% in the control group. After botulinum toxin A treatment, the rate of increase of fascicle length in the cerebral palsy group increased to 155.1%. **CONCLUSIONS:** The decrease in the pennation angle after botulinum toxin A treatment is considered to be the result of a reduction of spasticity and subsequent structural changes in flaccid muscle fibers.

[PMID: 29146092](#)

## 8. Management of hypertonia in cerebral palsy.

Nahm NJ, Graham HK, Gormley ME Jr, Georgiadis AG.

Curr Opin Pediatr. 2017 Nov 11. doi: 10.1097/MOP.0000000000000567. [Epub ahead of print]

**PURPOSE OF REVIEW:** The review provides an update on the treatment of hypertonia in cerebral palsy, including physical management, pharmacotherapy, neurosurgical, and orthopedic procedures. **RECENT FINDINGS:** Serial casting potentiates the effect of Botulinum neurotoxin A injections for spasticity. Deep brain stimulation, intraventricular baclofen, and ventral and dorsal rhizotomy are emerging tools for the treatment of dystonia and/or mixed tone. The long-term results of selective dorsal rhizotomy and the timing of orthopedic surgery represent recent advances in the surgical management of hypertonia. **SUMMARY:** Management of hypertonia in cerebral palsy targets the functional goals of the patient and caregiver. Treatment options are conceptualized as surgical or nonsurgical, focal or generalized, and reversible or irreversible. The role of pharmacologic therapies is to improve function and mitigate adverse effects. Further investigation, including clinical trials, is required to determine the role of deep brain stimulation, intraventricular baclofen, orthopedic procedures for dystonia, and rhizotomy.

[PMID: 29135566](#)

## 9. [Evaluation of dysphagia. Results after one year of incorporating videofluoroscopy into its study introduction].

[Article in Spanish]

García Romero R, Ros Arnal I, Romea Montañés MJ, López Calahorra JA, Gutiérrez Alonso C, Izquierdo Hernández B, Martín de Vicente C.

An Pediatr (Barc). 2017 Nov 9. pii: S1695-4033(17)30304-1. doi: 10.1016/j.anpedi.2017.07.009. [Epub ahead of print]

**INTRODUCTION:** Dysphagia is very common in children with neurological disabilities. These patients usually suffer from respiratory and nutritional problems. The videofluoroscopic swallowing study (VFSS) is the most recommended test to evaluate dysphagia, as it shows the real situation during swallowing. **OBJECTIVES:** To analyse the results obtained in our centre after one year of the implementation of VFSS, the clinical improvement after confirmation, and the prescription of an individualised treatment for the patients affected. **MATERIAL AND METHODS:** VFSS performed in the previous were collected. The following variables were analysed: age, pathology, degree of neurological damage, oral and pharyngeal and/or oesophageal dysphagia and its severity, aspirations, prescribed treatment, and nutritional and respiratory improvement after diagnosis. A statistical analysis was performed using SPSS v21. **RESULTS:** A total of 61 VFSS were performed. Dysphagia was detected in more than 70%, being moderate-severe in 58%. Aspirations and/or penetrations were recorded in 59%, of which 50% were silent. Adapted diet was prescribed to 56%, and gastrostomy was performed on 13 (21%) patients. A statistical association was found between neurological disease and severity of dysphagia. The degree of motor impairment is related to the presence of aspirations. After VFSS evaluation and treatment adjustment, nutritional improvement was found in Z-score of weight (+0.3SD) and BMI (+0.4SD). There was respiratory improvement in 71% of patients with dysphagia being controlled in the Chest Diseases Department. **CONCLUSIONS:** After implementation of VFSS, a high percentage of patients were diagnosed and benefited from a correct diagnosis and treatment. VFSS is a fundamental diagnostic test that should be included in paediatric centres as a diagnostic method for children with suspected dysphagia.

[PMID: 29129487](#)

### **10. Psychometric properties of parent and child reported sleep assessment tools in children with cerebral palsy: a systematic review.**

Bautista M, Whittingham K, Edwards P, Boyd RN.

Dev Med Child Neurol. 2017 Nov 16. doi: 10.1111/dmcn.13609. [Epub ahead of print]

AIM: To determine whether any parent and child report sleep measure tools have been validated in children aged 0-18 years with cerebral palsy (CP). METHOD: A systematic search of five databases was performed up to June 2017. Studies were included if a sleep measure tool was used to evaluate sleep in children 0-18 years with CP based on international classifications of sleep. Sleep measures were assessed for psychometric data in children with CP. RESULTS: Only one paper which used the Schlaffragebogen für Kinder mit Neurologischen und Anderen Komplexen Erkrankungen (SNAKE) questionnaire met the study criteria. The four other measures frequently used in children with CP had no psychometric data available for their use in children with CP. The SNAKE questionnaire has been validated only in children with CP in Gross Motor Function Classification System level V. The Sleep Disturbance Scale for Children and the Pediatric Sleep Questionnaire had the strongest psychometric properties in typically developing children, but has not yet been validated in children with CP. INTERPRETATION: Current sleep measures being administered in typically developing children are also often used in children with CP, but have not been well validated in this group of children.

[PMID: 29143316](#)

### **11. Parenting stress and life satisfaction in mothers of children with cerebral palsy: The mediating effect of social support.**

Wang Y, Huang Z, Kong F.

J Health Psychol. 2017 Nov 1:1359105317739100. doi: 10.1177/1359105317739100. [Epub ahead of print]

In this study, we investigated the mediating effect of social support on the relationship between parenting stress and life satisfaction in Chinese mothers of children with cerebral palsy (N = 369). The results showed that family support and friend support, but not significant-other support, had mediating effects on the relationship between parenting stress and life satisfaction. Moreover, the mediating effect of friend support was equal to family support. These results suggest that the focus should be on reducing parenting stress and increasing support from family and friends to help improve life satisfaction in mothers of children with cerebral palsy.

[PMID: 29129110](#)

### **12. Do fidgety general movements predict cerebral palsy and cognitive outcome in clinical follow-up of very preterm infants?**

Olsen J, Marschik P, Spittle A.

Acta Paediatr. 2017 Nov 13. doi: 10.1111/apa.14126. [Epub ahead of print]

[No abstract available]

[PMID: 29131395](#)

### **13. DMCN 2017 highlights: advances in cerebral palsy, encephalitis, paediatric stroke, and more.**

Dan B.

Dev Med Child Neurol. 2017 Dec;59(12):1209. doi: 10.1111/dmcn.13587.

[No abstract available]

[PMID: 29134644](#)

## Prevention and Cure

### 14. Feasibility of Using the General Movements Assessment of Infants in the United States.

Ricci E, Einspieler C, Craig AK.

Phys Occup Ther Pediatr. 2017 Nov 16:1-11. doi: 10.1080/01942638.2017.1395380. [Epub ahead of print]

**AIMS:** To pilot the practicality of administering the Prechtl General Movements Assessment of infants (GMA) in the Neonatal Intensive Care Unit (NICU) setting and at home to infants at risk for developing cerebral palsy (CP). Additional aims included assessing inter-rater reliability and comparing GMA predictions to AIMS motor assessment at 12 months. **METHODS:** 12 "at risk" infants were recruited by convenience sample. Video recordings were obtained in the NICU and provided by parents after discharge. These recordings were analyzed by two trained examiners to assess infants in the writhing and fidgety movement periods (birth to 16 weeks). Infants were assessed at 12 months corrected age using the Alberta Infant Motor Scale (AIMS) with scores lower than 5th centile considered a motor delay. **RESULTS:** 33 of 42 videos (79%) were of sufficient quality to permit interpretation and there was 97% inter-examiner subcategory agreement and 100% overall developmental trajectory (abnormal/normal) agreement. The GMA demonstrated a sensitivity of 60% and a specificity of 100% in predicting AIMS score (age appropriate or delayed). **CONCLUSIONS:** Clinical feasibility of GMA obtained in the NICU was demonstrated however feasibility of parents providing video samples after discharge was not demonstrated, indicating a need for a parent-friendly method.

[PMID: 29144840](#)

### 15. Use of paracetamol, ibuprofen or aspirin in pregnancy and risk of cerebral palsy in the child.

Petersen TG, Liew Z, Andersen AN, Andersen GL, Andersen PK, Martinussen T, Olsen J, Rebordosa C, Toll anes MC, Uldall P, Wilcox AJ, Strandberg-Larsen K.

Int J Epidemiol. 2017 Nov 14. doi: 10.1093/ije/dyx235. [Epub ahead of print]

**BACKGROUND:** It has been debated whether mild analgesics, mainly paracetamol, adversely affect aspects of neurodevelopment. We examined whether mother's use of paracetamol, aspirin or ibuprofen in pregnancy is associated with increased risk of cerebral palsy (CP) in the child. **METHOD:** We included 185 617 mother-child pairs from the Danish National Birth Cohort and the Norwegian Mother and Child Cohort Study. We created harmonized definitions of analgesic use in pregnancy, as well as indications for analgesic use and other potential confounders. Children with CP were identified in nationwide registers. We estimated the average causal effect of analgesics on risk of CP using marginal structural models with stabilized inverse probability weights. **RESULTS:** Paracetamol use was reported in 49% of all pregnancies, aspirin in 3% and ibuprofen in 4%. Prenatal exposure to paracetamol ever in pregnancy was associated with increased risk of overall CP [adjusted odds ratio (aOR) 1.3, 95% confidence interval (CI): 1.0-1.7] and unilateral spastic CP (aOR 1.5, 95% CI: 1.0-2.2). The association appeared to be driven by an increased risk of unilateral spastic CP in children exposed in second trimester (aOR 1.6, 95% CI: 1.0-2.5). Children ever prenatally exposed to aspirin in pregnancy had an elevated risk of bilateral spastic CP (aOR 2.4, 95% CI: 1.1-5.3) compared with unexposed. **CONCLUSION:** We observed an increased risk of spastic CP in children prenatally exposed to paracetamol and aspirin. Although we controlled for several important indications for analgesic use, we cannot exclude the possibility of confounding by underlying diseases.

[PMID: 29149272](#)

### 16. Reengineering Electronic Fetal Monitoring Interpretation: Using the Fetal Reserve Index to Anticipate the Need for Emergent Operative Delivery.

Eden RD, Evans MI, Evans SM, Schiffrin BS.

Reprod Sci. 2017 Jan 1:1933719117737849. doi: 10.1177/1933719117737849. [Epub ahead of print]

**OBJECTIVE:** The near-ubiquitous use of electronic fetal monitoring has failed to lower the rates of both cerebral palsy and emergency operative deliveries (EODs). Its performance metrics have low sensitivity, specificity, and predictive values for both. There are many EODs, but the vast majority have normal outcomes. The EODs, however, cause serious disruption in the delivery suite routine with increased complications, anxiety, and concern for all. **METHODS:** We developed the fetal reserve index (FRI) as multicomponent algorithm including 4 FHR components (analyzed individually), uterine activity, and maternal, obstetrical, and fetal risk factors to assess risk of cerebral palsy and EOD. Scores were categorized into green, yellow, and red zones. Here, we studied 300 patients by the FRI, all of whom had normal neonatal outcomes. We attempted to distinguish the clinical course of those cases which required an EOD versus controls which did not. **RESULTS:** 51 cases with EOD had FRIs much lower than 249 non-EOD cases. The red zone was reached more frequently ( $P < .001$ ) and lasted longer (1.06 vs 0.05

hours;  $P < .001$ ). Reaching the red zone had a sensitivity of 92% for EOD, with a positive predictive value of 64% and a false positive rate of 10.4%. **CONCLUSIONS:** Our data suggest the FRI can significantly lower the incidence of EODs by identifying the opportunity for intrauterine resuscitation. Our approach can reduce the disruptive effects of EODs and their concomitant increased risks of complications. The FRI may provide a metric that can refine labor management to reduce CP and EODs.

[PMID: 29137550](#)

### **17. Sonic Hedgehog Agonist Protects Against Complex Neonatal Cerebellar Injury.**

Nguyen V, Sabeur K, Maltepe E, Ameri K, Bayraktar O, Rowitch DH.

Cerebellum. 2017 Nov 13. doi: 10.1007/s12311-017-0895-0. [Epub ahead of print]

The cerebellum undergoes rapid growth during the third trimester and is vulnerable to injury and deficient growth in infants born prematurely. Factors associated with preterm cerebellar hypoplasia include chronic lung disease and postnatal glucocorticoid administration. We modeled chronic hypoxemia and glucocorticoid administration in neonatal mice to study whole cerebellar and cell type-specific effects of dual exposure. Chronic neonatal hypoxia resulted in permanent cerebellar hypoplasia. This was compounded by administration of prednisolone as shown by greater volume loss and Purkinje cell death. In the setting of hypoxia and prednisolone, administration of a small molecule Smoothed-Hedgehog agonist (SAG) preserved cerebellar volume and protected against Purkinje cell death. Such protective effects were observed even when SAG was given as a one-time dose after dual insult. To model complex injury and determine cell type-specific roles for the hypoxia inducible factor (HIF) pathway, we performed conditional knockout of von Hippel Lindau (VHL) to hyperactivate HIF1 $\alpha$  in cerebellar granule neuron precursors (CGNP) or Purkinje cells. Surprisingly, HIF activation in either cell type resulted in no cerebellar deficit. However, in mice administered prednisolone, HIF overactivation in CGNPs resulted in significant cerebellar hypoplasia, whereas HIF overactivation in Purkinje cells caused cell death. Together, these findings indicate that HIF primes both cell types for injury via glucocorticoids, and that hypoxia/HIF + postnatal glucocorticoid administration act on distinct cellular pathways to cause cerebellar injury. They further suggest that SAG is neuroprotective in the setting of complex neonatal cerebellar injury.

[PMID: 29134361](#)

### **18. A proteomic investigation into mechanisms underpinning corticosteroid effects on neural stem cells.**

Al-Mayyahi RS, Sterio LD, Connolly JB, Adams CF, Al-Tumah WA, Sen J, Emes RD, Hart SR, Chari DM.

Mol Cell Neurosci. 2017 Nov 8. pii: S1044-7431(17)30043-X. doi: 10.1016/j.mcn.2017.11.006. [Epub ahead of print]

Corticosteroids (CSs) are widely used clinically, for example in pediatric respiratory distress syndrome, and immunosuppression to prevent rejection of stem cell transplant populations in neural cell therapy. However, such treatment can be associated with adverse effects such as impaired neurogenesis and myelination, and increased risk of cerebral palsy. There is increasing evidence that CSs can adversely influence key biological properties of neural stem cells (NSCs) but the molecular mechanisms underpinning such effects are largely unknown. This is an important issue to address given the key roles NSCs play during brain development and as transplant cells for regenerative neurology. Here, we describe the use of label-free quantitative proteomics in conjunction with histological analyses to study CS effects on NSCs at the cellular and molecular levels, following treatment with methylprednisolone (MPRED). Immunocytochemical staining showed that both parent NSCs and newly generated daughter cells expressed the glucocorticoid receptor, with nuclear localisation of the receptor induced by MPRED treatment. MPRED markedly decreased NSC proliferation and neuronal differentiation while accelerating the maturation of oligodendrocytes, without concomitant effects on cell viability and apoptosis. Parallel proteomic analysis revealed that MPRED induced downregulation of growth associated protein 43 and matrix metalloproteinase 16 with upregulation of the cytochrome P450 family 51 subfamily A member 1. Our findings support the hypothesis that some neurological deficits associated with CS use may be mediated via effects on NSCs, and highlight putative target mechanisms underpinning such effects.

[PMID: 29128319](#)

**19. Protocol for hospital based-surveillance of cerebral palsy (CP) in Hanoi using the Paediatric Active Enhanced Disease Surveillance mechanism (PAEDS-Vietnam): a study towards developing hospital-based disease surveillance in Vietnam.**

Khandaker G, Van Bang N, Dũng TQ, Giang NTH, Chau CM, Van Anh NT, Van Thuong N, Badawi N, Elliott EJ.

BMJ Open. 2017 Nov 9;7(11):e017742. doi: 10.1136/bmjopen-2017-017742.

**INTRODUCTION:** The epidemiology, pathogenesis, management and outcomes of cerebral palsy (CP) in low-income and middle-income countries including Vietnam are unknown because of the lack of mechanisms for standardised collection of data. In this paper, we outline the protocol for developing a hospital-based surveillance system modelled on the Paediatric Active Enhanced Disease Surveillance (PAEDS) system in Australia. Using PAEDS-Vietnam we will define the aetiology, motor function and its severity, associated impairments, and nutritional and rehabilitation status of children with CP in Hanoi, Vietnam. These essential baseline data will inform future health service planning, health professional education and training, and family support. **METHODS AND ANALYSIS:** This is a hospital-based prospective surveillance of children with CP presenting to the rehabilitation, neurology and general paediatric services at the National Children's Hospital and St Paul Hospital in Hanoi. We will use active, prospective daily case-finding for all children with CP aged <18 years who are hospitalised or present to outpatient departments. Following parental consent, data will be collected using a modified version of the Australian Cerebral Palsy Register questionnaire. The data collection form has been developed in consultation with local and international experts and translated into Vietnamese. Information collected will include demographics, maternal health and birth history, type and severity of CP, known risk factors for CP, and nutrition, immunisation, education and rehabilitation status.

[PMID: 29127227](#)