

Monday 2 July 2018

Cerebral Palsy Alliance is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at research.cerebralpalsy.org.au

Professor Nadia Badawi AM

Macquarie Group Foundation Chair of Cerebral Palsy

[Subscribe to CP Research News](#)

Please note: This research bulletin represents only the search results for cerebral palsy and related neurological research as provided by the PubCrawler service. The articles listed below do not represent the views of Cerebral Palsy Alliance.

Interventions and Management

1. Hyper-excitability of brainstem pathways in cerebral palsy.

Smith AT, Gorassini MA.

J Neurophysiol. 2018 Jun 27. doi: 10.1152/jn.00185.2018. [Epub ahead of print]

Individuals with cerebral palsy (CP) experience impairments in the control of head and neck movements, suggesting dysfunction in brainstem circuitry. To examine if brainstem circuitry is altered in CP we compared reflexes evoked in the sternocleidomastoid (SCM) muscle by trigeminal nerve stimulation in adults with CP and age/sex-matched controls. Increasing the intensity of trigeminal nerve stimulation produced progressive increases in the long-latency suppression of ongoing SCM EMG in controls. In contrast, participants with CP showed progressively increased facilitation around the same reflex window, suggesting heightened excitability of brainstem pathways. We also examined if there was altered activation of cortico-brainstem pathways in response to pre-natal injury of the brain. Motor-evoked potentials (MEPs) in the SCM that were conditioned by a prior trigeminal afferent stimulation were more facilitated in CP compared to controls, especially in ipsilateral MEPs that are likely mediated by cortico-reticulospinal pathways. In some participants with CP, but not in controls, a combined trigeminal nerve and cortical stimulation near threshold intensities produced large, long-lasting responses in both the SCM and biceps brachii muscles. We propose that the enhanced excitatory responses evoked from trigeminal and cortical inputs in CP are produced by heightened excitability of brainstem circuits, resulting in the augmented activation of reticulospinal pathways. Enhanced activation of reticulospinal pathways in response to early injury of the corticospinal tract may provide a compensated activation of the spinal cord, or alternatively, contribute to impairments in the precise control of head and neck functions.

PMID: [29947590](#)

2. Haptic Exploratory Procedures of Children and Youth with and without Cerebral Palsy.

Taylor S, Girdler S, McCutcheon S, McLean B, Parsons R, Falkmer T, Jacoby P, Carey L, Elliott C.

Phys Occup Ther Pediatr. 2018 Jun 26:1-15. doi: 10.1080/01942638.2018.1477228. [Epub ahead of print]

AIMS: Compare haptic exploratory procedures (EPs) and exploratory movements (EMs) of children. This study also tested the interrater reliability of a novel digital recording method. METHODS: Participants were 31 children with typical development (TD) (aged 6 years 1 month to 15 years 9 months; 14 male) and 23 children with spastic unilateral cerebral palsy (CP) (aged 6 years to 15 years 5 months; 13 males; right hemiplegia, n = 12). RESULTS: There were no statistically significant differences between groups for expected EP ($p = .15$), additional EPs ($p = .78$), or EMs ($p = .69$) but there was for mean duration of exploration ($p < .001$) and accuracy ($p < .001$). This suggests that although children with CP performed similar haptic EPs for each object as children with TD, they took more time and were less accurate in their identification. There was substantial agreement between the two raters' observations of expected EP, $\kappa = .64$, $p < .0005$. CONCLUSION: Children with CP performed similar haptic EPs as their TD peers. However, despite similarities, the results indicate that for children with CP manual ability was not the primary determinant of accuracy or speed of identification. This study provides evidence for a reliable method of recording haptic EPs.

PMID: [29944033](#)

3. Three Methods of Pelvic Fixation for Scoliosis in Children with Cerebral Palsy: Differences at 5-Year Follow-Up.

Abousamra O, Sullivan BT, Samdani AF, Yaszay B, Cahill PJ, Newton PO, Sponseller PD. Spine (Phila Pa 1976). 2018 Jun 22. doi: 10.1097/BRS.0000000000002761. [Epub ahead of print]

OBJECTIVE: To assess correction of pelvic obliquity in children with cerebral palsy (CP) scoliosis postoperatively and 5 years after posterior spinal fusion with pelvic fixation using unit rods, sacral-alar-iliac (SAI) screws, or iliac screws. **SUMMARY OF BACKGROUND DATA:** There are multiple options for pelvic fixation in children with scoliosis secondary to CP. The long-term differences in outcomes between these fixation methods are still unclear. **METHODS:** A multicenter review identified records of 70 children with CP who underwent posterior spinal fusion for scoliosis using unit rods (n=9), SAI screws (n=19), or iliac screws (n=42). Patients younger than 18 years with 5-year follow-up were included. Pelvic obliquity and major coronal curve measurements were compared using preoperative, (first erect) postoperative, and 5-year follow-up radiographs. Implant-related complications were noted. Alpha=0.05. **RESULTS:** For all groups, there was a significant difference between preoperative and postoperative pelvic obliquity that was maintained at 5 years. At 5-year follow-up, pelvic obliquity was significantly higher in the IS group (12°) compared with the unit rod group (4°, p=0.001) and SAI screw group (6°) (p=0.006). Implant-related complications were as follows: unit rod group, 1 patient (reoperation); SAI screw group, none; iliac screw group, 6 patients, including 3 cases of loss of connection between the rod and the iliac screw, 2 prominent screws, and 1 loose screw. **CONCLUSION:** Correction of pelvic obliquity for children with CP-related scoliosis was achieved postoperatively using unit rods, SAI screws, and iliac screws. Implant-related complications and reoperations were most common in the iliac screw group. At 5-year follow-up, the iliac screw group had loss of major curve correction and less correction of pelvic obliquity than the unit rod and SAI screw groups.

PMID: [29939974](#)

4. Releasing the tether: Weight normalization following corrective spinal fusion in cerebral palsy.

DeFrancesco CJ, Miller DJ, Cahill PJ, Spiegel DA, Flynn JM, Baldwin KD. J Orthop Surg (Hong Kong). 2018 May-Aug;26(2):2309499018782556. doi: 10.1177/2309499018782556.

PURPOSE: Feeding difficulties are common among patients with cerebral palsy (CP) and neuromuscular (NM) scoliosis. We theorize that posterior spinal fusion (PSF) reduces intra-abdominal pressure, resulting in improved feeding and subsequent weight gain. We hypothesized that, among nonambulatory patients with CP and NM scoliosis, we would observe significant gain in weight following PSF. **METHODS:** Fifty subjects with nonambulatory CP who underwent PSF for NM scoliosis were included. Age and weight were recorded for the preoperative year; on the day of surgery; and at 6-month, 1-year, and 2-year follow-up. Weights were converted to weight percentiles using CP-specific growth charts. The weight percentile distributions were compared between time points using descriptive statistics as well as regression analysis. **RESULTS:** The average change in weight from the day of surgery to 2-year follow-up was +3.4 percentiles. Patients who started out under the 50th percentile gained an average of 17.3 percentiles in the first year after PSF (p = 0.009). Regression analysis showed that patients with baseline weight <50th percentile tended to gain in weight percentile over the first postoperative year ($\beta = 1.990$, p = 0.001). No trend was present among this group prior to surgery (p = 0.692) or during the second postoperative year (p = 0.945). No trends were noted prior to or after surgery for patients with baseline weights \geq 50th percentile. No significant association was observed between curve severity (measured by preoperative Cobb angle) and weight change. **CONCLUSIONS:** This series is the first to document significant weight gain after PSF for NM scoliosis, supporting the theory that spinal correction improves digestive function.

PMID: [29938586](#)

5. O 037 - Estimating musculotendon forces in children with cerebral palsy: The importance of the use of electromyography in neuromusculoskeletal modelling.

Veerkamp K, Schallig W, Harlaar J, Pizzolato C, Carty CP, Lloyd DG, van der Krogt MM. Gait Posture. 2018 Jun 19. pii: S0966-6362(18)30782-3. doi: 10.1016/j.gaitpost.2018.06.055. [Epub ahead of print] No abstract available.

PMID: [29954656](#)

6. Vibration therapy in patients with cerebral palsy: a systematic review.

Ritzmann R, Stark C, Krause A. Neuropsychiatr Dis Treat. 2018 Jun 18;14:1607-1625. doi: 10.2147/NDT.S152543. eCollection 2018. Review.

The neurological disorder cerebral palsy (CP) is caused by unprogressive lesions of the immature brain and affects movement, posture, and the musculoskeletal system. Vibration therapy (VT) is increasingly used to reduce the signs and symptoms associated with this developmental disability. The purpose of this narrative review was systematically to appraise published research regarding acute and long-term effects of VT on functional, neuromuscular, and structural parameters. Systematic

searches of three electronic databases identified 28 studies that fulfilled the inclusion criteria. Studies were analyzed to determine participant characteristics, VT-treatment protocols, effect on gross motor function (GMF), strength, gait, posture, mobility, spasticity, reflex excitability, muscle tone, mass, and bone strength within this population, and outcome measures used to evaluate effects. The results revealed that one acute session of VT reduces reflex excitability, spasticity, and coordination deficits. Subsequently, VT has a positive effect on the ability to move, manifested for GMF, strength, gait, and mobility in patients with CP. Effects persist up to 30 minutes after VT. Long-term effects of VT manifest as reduced muscle tone and spasticity occurring concomitantly with improved movement ability in regard to GMF, strength, gait, and mobility, as well as increased muscle mass and bone-mineral density. Posture control remained unaffected by VT. In conclusion, the acute and chronic application of VT as a nonpharmacological approach has the potential to ameliorate CP symptoms, achieving functional and structural adaptations associated with significant improvements in daily living. Even though further studies including adult populations validating the neuromuscular mechanisms underlying the aforementioned adaptations should be fostered, growing scientific evidence supports the effectiveness of VT in regard to supplementing conventional treatments (physiotherapy and drugs). Therefore, VT could reduce CP-associated physical disability and sensorimotor handicaps. Goals for patients and their caregivers referring to greater independence and improved safety may be achieved more easily and time efficiently.

PMID: [29950843](#)

7. An innovative solution to reduce muscle deformation during ultrasonography data collection.

Cenni F, Schless SH, Monari D, Bar-On L, Aertbeliën E, Bruyninckx H, Hanssen B, Desloovere K.
J Biomech. 2018 Jun 18. pii: S0021-9290(18)30429-9. doi: 10.1016/j.jbiomech.2018.06.002. [Epub ahead of print]

BACKGROUND: 3D freehand ultrasound enables the creation of volumetric data. The acquisition of morphological features, such as muscle volume, is influenced by the variations in force applied to the skin with the ultrasound probe. To minimise the deformations, a concave-shaped plastic mount combined with a custom-shaped gel pad was developed for the ultrasound head, named Portico. This study analyses to what extent the Portico reduces muscle deformation and corresponding errors in estimating muscle volume. **METHOD:** Twenty medial gastrocnemius (MG) muscles were assessed (10 from typically developing children; 10 from children with spastic cerebral palsy). Two repetitions were acquired in each of the following approaches: (1) with the lower leg submerged in a water tank as a non-deformed reference; (2) probe-on-skin (PoS) as the conventional approach and (3) the newly introduced Portico. PoS and Portico data were registered with respect to the ones corresponding in a water tank. An in-house software package (Py3DFreeHandUS) was used to process the data and MG volume was estimated using MeVisLab. The minimal detectable change (MDC) was calculated. **RESULTS:** With respect to the PoS approach, the Portico reduced muscle deformation by 46%. For both the typically developing and spastic cerebral palsy cohorts, lower MDCs were found when using the Portico. **DISCUSSION:** Despite the improvements, the Portico did not yield statistically more reliable MG volume estimations than the traditional PoS approach. Further improvement can be attained by optimising the fit between the gel pad and the curvature of the limb, using a larger choice of Portico geometries.

PMID: [29935732](#)

8. Muscle Shortening and Spastic Cocontraction in Gastrocnemius Medialis and Peroneus Longus in Very Young Hemiparetic Children.

Vinti M, Bayle N, Merlo A, Authier G, Pesenti S, Jouve JL, Chabrol B, Gracies JM, Boulay C.
Biomed Res Int. 2018 May 21;2018:2328601. doi: 10.1155/2018/2328601. eCollection 2018.

OBJECTIVES: Muscle shortening and spastic cocontraction in ankle plantar flexors may alter gait since early childhood in cerebral palsy (CP). We evaluated gastrosoleus complex (GSC) length, and gastrocnemius medialis (GM) and peroneus longus (PL) activity during swing phase, in very young hemiparetic children with equinovalgus. **METHODS:** This was an observational, retrospective, and monocentric outpatient study in a pediatric hospital. Ten very young hemiparetic children (age 3 ± 1 yrs) were enrolled. These CP children were assessed for muscle extensibility (Tardieu scale XV1) in GSC (angle of arrest during slow-speed passive ankle dorsiflexion with the knee extended) and monitored for GM and PL electromyography (EMG) during the swing phase of gait. The swing phase was divided into three periods (T1, T2, and T3), in which we measured a cocontraction index (CCI), ratio of the Root Mean Square EMG (RMS-EMG) from each muscle during that period to the peak 500 ms RMS-EMG obtained from voluntary plantar flexion during standing on tiptoes (from several 5-second series, the highest RMS value was computed over 500 ms around the peak). **RESULTS:** On the paretic side: (i) the mean XV1-GSC was 100° (8°) (median (SD)) versus 106° (3°) on the nonparetic side ($p = 0.032$, Mann-Whitney); (ii) XV1-GSC diminished with age between ages of 2 and 5 (Spearman, $\rho = 0.019$); (iii) CCI_{GM} and CCI_{PL} during swing phase were higher than on the nonparetic side (CCI_{GM}, 0.32 (0.20) versus 0.15 (0.09), $p < 0.01$; CCI_{PL}, 0.52 (0.30) versus 0.24 (0.17), $p < 0.01$), with an early difference significant for PL from T1 ($p = 0.03$). **CONCLUSIONS:** In very young hemiparetic children, the paretic GSC may rapidly shorten in the first years of life. GM and PL cocontraction during swing phase are excessive, which contributes to dynamic equinovalgus. Muscle extensibility (XV1) may have to be monitored and preserved in the first years of life in children with CP. Additional measurements of cocontraction may further help target treatments with botulinum toxin, especially in peroneus longus.

PMID: [29951529](#)

9. O 026 - Negative impact of muscle weakness and spasticity on gait in children with unilateral cerebral palsy.

Papageorgiou E, Simon-Martinez C, Van Campenhout A, Desloovere K.

Gait Posture. 2018 Jun 21. pii: S0966-6362(18)30771-9. doi: 10.1016/j.gaitpost.2018.06.044. [Epub ahead of print] No abstract available.

PMID: [29954655](#)**10. How does patellar tendon advancement alter the knee extensor mechanism in children treated for crouch gait?**

Bittmann MF, Lenhart RL, Schwartz MH, Novacheck TF, Hetzel S, Thelen DG.

Gait Posture. 2018 Jun 5;64:248-254. doi: 10.1016/j.gaitpost.2018.06.005. [Epub ahead of print]

BACKGROUND: The patellar tendon advancement (PTA) procedure, often coupled with a distal femoral extension osteotomy (DFEO), is increasingly used to treat persistent crouch gait. In this study, we investigated relationships between patella position, knee flexion, and the patellar tendon moment arm in children treated with the DFEO and PTA procedures.

METHODS: We retrospectively analyzed pre- and post-operative radiographs and gait metrics from 63 knees that underwent DFEO and PTA procedures at Gillette Children's Specialty Healthcare. A computational musculoskeletal model of the knee was used to simulate the PTA procedure and predict the effects on the patellar tendon moment arm. **RESULTS:** Approximately 80% of the knees exhibited patella alta prior to surgery. Post-operatively, 86% of the knees exhibited patella baja. The surgically altered patella position produced a 13% increase in the patellar tendon moment arm in extended knee postures, which agreed well with model predictions. However, the computational model also suggests that baja may compromise patellar tendon moment arms in flexed knee postures. Crouch gait was significantly reduced postoperatively, with a $27 \pm 18^\circ$ reduction in average knee flexion in stance. There was considerable inter-subject variability in outcomes with nine knees not exhibiting a meaningful enhancement of knee extension ($<15^\circ$ change). The subjects who improved were significantly younger and exhibited greater enhancement of the patellar tendon moment arm after surgery. **CONCLUSIONS:** This study shows that the PTA procedure enhances the lever arm of the knee extensor mechanism, and this factor may be important in resolving crouch gait.

PMID: [29958159](#)**11. Bilateral Bicondylar Osteochondritis Dissecans in a Child with Spastic Diplegia and Crouch Gait: A Case Report.**

Nhan DT, Garcia MR, Lee RJ.

JBJS Case Connect. 2018 Apr-Jun;8(2):e41. doi: 10.2106/JBJS.CC.17.00271.

CASE: The cause of osteochondritis dissecans is unknown. Various hypotheses suggest mechanical, ischemic, and hereditary causes. We describe a 13-year-old girl with spastic diplegia, a form of cerebral palsy, who had an associated crouch gait and presented with bilateral osteochondral defects of the medial and lateral femoral condyles. **CONCLUSION:** This case highlights the potential role of repetitive microtrauma, likely due to the poor biomechanical forces in a crouch gait, and provides support for a mechanical cause of osteochondritis dissecans.

PMID: [29952775](#)**12. O 019 - Do Botulinum Toxin-A and lower leg casting alter calf muscle and tendon lengths in children with spastic cerebral palsy?**

Peeters N, Hanssen B, Cenni F, Schless SH, De Beukelaer N, Degelaen M, den Broeck CV, Van Campenhout A, Desloovere K, Bar-On L.

Gait Posture. 2018 Jun 19. pii: S0966-6362(18)30764-1. doi: 10.1016/j.gaitpost.2018.06.037. [Epub ahead of print]

INTRODUCTION: Ankle joint hyper-resistance in children with spastic cerebral palsy (SCP) is commonly treated with Botulinum Toxin-A (BoNT-A) injections in the medial gastrocnemius (MG) combined with lower-leg casting. The overall aim of this combined treatment is to reduce spasticity and increase range of motion (1). Since hyper-resistance assessment mainly focuses on the joint level, whereas the treatment is directed at the muscle, it is worthwhile investigating the individual effects of BoNT-A and casting on MG and tendon lengths, to provide insight into the working mechanisms and to help improving treatment efficacy. **RESEARCH QUESTION:** What are the effects of BoNT-A injections and lower-leg casting on the MG and tendon lengths, at resting position and maximum dorsiflexion, in children with SCP? **METHODS:** Children with SCP were assigned by minimization to receive either two weeks of lower-leg casts ($n = 12$, mean age 8.27 years; GMFCS-level I-III) or MG BoNT-A injections ($n = 11$, mean age: 6.75 years; GMFCS-level I-III). Data was acquired by 3D-freehand-ultrasound (2) at baseline and two weeks post-intervention with the knee in flexion ($30.9^\circ \pm 3.7^\circ$) and the ankle in resting position and maximum dorsiflexion (maxDF). The same assessor extracted muscle and tendon lengths from the 3D reconstructions twice, and the standard error of measurement (SEM) was quantified. Muscle tendon unit (MTU) length was calculated as the summation of muscle (ML) and tendon length (TL). The change in ML and TL between rest and maxDF was used to calculate

extensibility. Within-group treatment effect was evaluated with Wilcoxon signed rank tests and treatment differences, with Mann-Whitney U tests. Post-treatment changes were considered significant when $>SEM$ and $p < 0.05$. RESULTS: At baseline, groups did not differ for age, joint angles and lengths. Post-casting, resting angle, maxDF, MTU and TL at maxDF significantly increased. While two weeks post-BoNT-A-injection only MTU length and ML at rest significantly increased. There was no treatment effect on the extensibility. The change in maxDF, and ML at rest were significantly larger post-casting compared to post-BoNT-A. Similarly, the post-treatment change in MTU length at maxDF was significantly larger after casting compared to BoNT-A. DISCUSSION: The results suggest that two weeks casting resulted in increased maxDF and MTU-length by increased TL (or compliance). This confirms previous research on the effects of ankle foot orthoses on MG morphology (3). BoNT-A on the other hand, affected the muscle's resting length, however without gain in extensibility or MTU-length. This emphasizes the requirement to combine both treatments, but also cautions the use of stretching casts for having adverse effects on the tendon. The treatment-effects on the MTU on the long-term and their carry over effect to gait is material for further investigation.

PMID: [29937118](#)

13. Impaired anticipatory vision and visuomotor coordination affects action planning and execution in children with hemiplegic cerebral palsy.

Surkar SM, Hoffman RM, Davies B, Harbourne R, Kurz MJ.

Res Dev Disabil. 2018 Jun 22;80:64-73. doi: 10.1016/j.ridd.2018.06.009. [Epub ahead of print]

BACKGROUND: Action-planning and execution deficits in children with hemiplegic cerebral palsy (HCP) are potentially due to deficits in the integration of sensory information, such as vision, with motor output. AIMS: To determine differences in anticipatory visual patterns in children with HCP compared to typically developing (TD) children, and to assess visuomotor coordination in children with HCP. METHODS AND PROCEDURES: We included 13 children with HCP (Age = $6.8 + 2.9$ yrs) and 15 TD children (Age = $5.8 + 1.1$ yrs). The experimental task used in this study is a valid action-planning task, which consisted of initially reaching and grasping an object placed at a fixed position, followed by placing the object in a random target position. Visual patterns were recorded using a head-mounted eye-tracker system and arm movements were recorded using motion capture (120 Hz). OUTCOMES AND RESULTS: Children with HCP had delayed anticipatory gaze time and longer latency than TD children during the planning and execution phases. Children with HCP also had a higher frequency of gaze shifts, longer reaction times (RT) and movement times (MT) than TD children. CONCLUSIONS AND IMPLICATIONS: Children with HCP may have deficits in anticipatory vision, which potentially affected planning and executing a goal-directed action. Therapeutic interventions focusing on improving visuomotor coordination may improve the motor performance in children with HCP.

PMID: [29940386](#)

14. Prophylactic antibiotics in soft-tissue procedures in children with cerebral palsy.

Perotti LR, Abousamra O, Rogers KJ, Miller F, Sees JP.

J Child Orthop. 2018 Jun 1;12(3):279-281. doi: 10.1302/1863-2548.12.279.

PURPOSE: Data on the benefits of perioperative prophylactic antibiotics in the paediatric population are lacking. In this study, we aimed to assess the rate of infection after isolated soft-tissue procedures in patients with cerebral palsy with and without preoperative prophylactic antibiotics between 2009 and 2015. METHODS: We reviewed the records of all children with cerebral palsy who underwent isolated soft-tissue procedures (on the upper and lower limb) at our hospital between 2009 and 2015. Children with at least 30-day postoperative follow-up were included. Children who had groin incisions were excluded. RESULTS: Two groups were identified: the antibiotic group (77 children with 203 incisions and 343 procedures) had one surgical site infection; the no-antibiotic group (48 children with 102 incisions and 177 procedures) had no surgical site infections. CONCLUSION: These results suggest that the use of preoperative antibiotics does not change the rate of postoperative surgical site infections.

PMID: [29951128](#)

15. Comparative study of home and community participation among children with and without cerebral palsy.

Milićević M, Nedović G.

Res Dev Disabil. 2018 Jun 26;80:74-83. doi: 10.1016/j.ridd.2018.06.010. [Epub ahead of print]

BACKGROUND: Children with cerebral palsy (CP) are at increased risk of reduced participation. Parental evaluation of child's participation is often the decision-making factor in the process of special education and/or rehabilitation. AIMS: Examine and compare home and community participation of children with CP and typical development (TD) and the associations between their parents' desire for change and participation dimensions in both settings. METHODS AND PROCEDURES: This cross-sectional study included a convenience sample of 110 children with CP (55% males; mean age 12.7 years) and 134 children with TD (49% males; mean age 12.1 years). The Participation and Environment Measure for Children and Youth (PEM-CY) was used. OUTCOMES AND RESULTS: Home and community participation and

environmental supportiveness of children with CP were lower compared to children with TD ($p < .001$, family income controlled). The effect sizes indicated that there may be no clinically important difference in participation frequency. Parents of children with CP desired change if participation was less diverse at home, less frequent in the community, or if involvement was lower in both settings (environmental supportiveness and income controlled). **CONCLUSIONS AND IMPLICATIONS:** At home, parents expressed a desire for change more intensely through the range of activities, while parents of children with TD emphasized participation frequency. In the community, parents of children with CP equally perceived participation diversity and focused more on frequency and involvement.

PMID: [29957491](#)

16. Community-based parent-delivered early detection and intervention programme for infants at high risk of cerebral palsy in a low-resource country (Learning through Everyday Activities with Parents (LEAP-CP): protocol for a randomised controlled trial.

Benfer KA, Novak I, Morgan C, Whittingham K, Khan NZ, Ware RS, Bell KL, Bandaranayake S, Salt A, Ghosh AK, Bhattacharya A, Samanta S, Moula G, Bose D, Tripathi S, Boyd RN.
BMJ Open. 2018 Jun 22;8(6):e021186. doi: 10.1136/bmjopen-2017-021186.

INTRODUCTION: Cerebral palsy (CP) is the most common childhood physical disability, with 80% estimated to be in low-middle-income countries. This study aims to (1) determine the accuracy of General Movements (GMs)/Hammersmith Infant Neurological Examination (HINE) for detecting CP at 18 months corrected age (CA); (2) determine the effectiveness of a community-based parent-delivered early intervention for infants at high risk of CP in West Bengal, India (Learning through Everyday Activities with Parents for infants with CP; LEAP-CP). **METHODS:** This study comprises two substudies: (1) a study of the predictive validity of the GMs and HINE for detecting CP; (2) randomised, double-blinded controlled trial of a novel intervention delivered through peer trainers (Community Disability Workers, CDW) compared with health advice (15 fortnightly visits). 142 infants at high risk of CP ('absent fidgety' GMs; 'high risk score' on HINE) aged 12-40 weeks CA will be recruited to the intervention substudy, with infants randomised based on a computer-generated sequence. Researchers will be masked to group allocation, and caregivers and CDWs naïve to intervention status. Visits will include therapeutic modules (goal-directed active motor/cognitive strategies and LEAP-CP games) and parent education. Health advice is based on the Integrated Management of Childhood Illness, WHO. Infants will be evaluated at baseline, post intervention and 18 months CA. The primary hypothesis is that infants receiving LEAP-CP will have greater scaled scores on the Pediatric Evaluation of Disability Inventory-Computer Adaptive Test (mobility domain) at 18 months compared with health advice. Secondary outcomes include infant functional motor, cognitive, visual and communication development; infant growth; maternal mental health. **ETHICS AND DISSEMINATION:** This study is approved through appropriate Australian and Indian ethics committees (see in text) with families providing written informed consent. Findings from this trial will be disseminated through peer-reviewed journal publications and conference presentations.

PMID: [29934387](#)

Prevention and Cure

17. Parental socioeconomic status and risk of cerebral palsy in the child: evidence from two Nordic population-based cohorts.

Forthun I, Strandberg-Larsen K, Wilcox AJ, Moster D, Petersen TG, Vik T, Lie RT, Uldall P, Tollånes MC.
Int J Epidemiol. 2018 Jun 26. doi: 10.1093/ije/dyy139. [Epub ahead of print]

BACKGROUND: We investigated whether the risk of cerebral palsy (CP) in the child varies by parents' socioeconomic status, in Denmark and Norway. **METHODS:** We included almost 1.3 million children born in Denmark during 1981-2007 and 2.4 million children born in Norway during 1967-2007, registered in the Medical Birth registries. Data on births were linked to Statistics Denmark and Norway to retrieve information on parents' education and relationship status and, in Denmark, also income. CP diagnoses were obtained from linkage with national registries. We used multivariate log-binomial regression models to estimate relative risk (RR) of CP according to parental socioeconomic status. **RESULTS:** There was a strong trend of decreasing risk of CP with additional education of both the mother and the father. These trends were nearly identical for the two parents, with a one-third reduction in risk for those with the highest education compared with parents with the lowest education. When both parents had high education, risk of CP was further reduced (RR 0.58, 0.53-0.63). Women with partners had a reduction in risk (RR 0.79, 0.74-0.85) compared with single mothers overall. Risk patterns were stable over time, across countries and within spastic bilateral and unilateral CP. Household income was not associated with risk of CP.

CONCLUSIONS: Risk of CP in two Scandinavian countries was lower among educated parents and mothers with a partner, but unrelated to income. Factors underlying this stable association with education are unknown, but could include differences in potentially modifiable lifestyle factors and health behaviours.

PMID: [29947785](#)

18. Association of NOS1 gene polymorphisms with cerebral palsy in a Han Chinese population: a case-control study.

Yu T, Xia L, Bi D, Wang Y, Shang Q, Zhu D, Song J, Wang Y, Wang X, Zhu C, Xing Q.
 BMC Med Genomics. 2018 Jun 25;11(1):56. doi: 10.1186/s12920-018-0374-6.

BACKGROUND: Cerebral palsy (CP) is the leading cause of motor disability in children; however, its pathogenesis is unknown in most cases. Growing evidence suggests that Nitric oxide synthase 1 (NOS1) is involved in neural development and neurologic diseases. The purpose of this study was to determine whether genetic variants of NOS1 contribute to CP susceptibility in a Han Chinese population. **METHODS:** A case-control study involving 652 CP patients and 636 healthy controls was conducted. Six SNPs in the NOS1 gene (rs3782219, rs6490121, rs2293054, rs10774909, rs3741475, and rs2682826) were selected, and the MassARRAY typing technique was applied for genotyping. Data analysis was conducted using SHEsis online software, and multiple test corrections were performed using SNPSpD online software. **RESULTS:** There were no significant differences in genotype and allele frequencies between patients and controls for the SNPs except rs6490121, which deviated from Hardy-Weinberg equilibrium and was excluded from further analyses. Subgroup analysis revealed differences in genotype frequencies between the CP with neonatal encephalopathy group (CP + NE) and control group for rs10774909, rs3741475, and rs2682826 (after SNPSpD correction, $p = 0.004$, 0.012 , and 0.002 , respectively). The T allele of NOS1 SNP rs3782219 was negatively associated with spastic quadriplegia (OR = 0.742, 95% CI = 0.600-0.918, after SNPSpD correction, $p = 0.023$). There were no differences in allele or genotype frequencies between CP subgroups and controls for the other genetic polymorphisms. **CONCLUSIONS:** NOS1 is associated with CP + NE and spastic quadriplegia, suggesting that NOS1 is likely involved in the pathogenesis of CP and that it is a potential therapeutic target for treatment of cerebral injury.

PMID: [29940959](#)

19. Early human brain development: Starring the subplate.

Hadders-Algra M.

Neurosci Biobehav Rev. 2018 Jun 20;92:276-290. doi: 10.1016/j.neubiorev.2018.06.017. [Epub ahead of print] Review.

This review summarizes early human brain development on the basis of neuroanatomical data and functional connectomics. It indicates that the most significant changes in the brain occur during the second half of gestation and the first three months post-term, in particular in the cortical subplate and cerebellum. As the transient subplate pairs a high rate of intricate developmental changes and interactions with clear functional activity, two phases of development are distinguished: a) the transient cortical subplate phase, ending at 3 months post-term when the permanent circuitries in the primary motor, somatosensory and visual cortices have replaced the subplate; and subsequently, b) the phase in which the permanent circuitries dominate. In the association areas the subplate dissolves in the remainder of the first postnatal year. During both phases developmental changes are paralleled by continuous reconfigurations in network activity. The reviewed literature also suggests that disruption of subplate development may play a pivotal role in developmental disorders, such as cerebral palsy, autism spectrum disorders, attention deficit hyperactivity disorder and schizophrenia.

PMID: [29935204](#)