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Interventions and Management

1. REACH: study protocol of a randomised trial of rehabilitation very early in congenital hemiplegia.

Boyd RN, Ziviani J, Sakzewski L, Novak I, Badawi N, Pannek K, Elliott C, Greaves S, Guzzetta A, Whittingham K, Valentine J, Morgan C, Wallen M, Eliasson AC, Findlay L, Ware R, Fiori S, Rose S.

BMJ Open. 2017 Sep 18;7(9):e017204. doi: 10.1136/bmjopen-2017-017204.

OBJECTIVES: Congenital hemiplegia is the most common form of cerebral palsy (CP). Children with unilateral CP show signs of upper limb asymmetry by 8 months corrected age (ca) but are frequently not referred to therapy until after 12 months ca. This study compares the efficacy of infant-friendly modified constraint-induced movement therapy (Baby mCIMT) to infant friendly bimanual therapy (Baby BIM) on upper limb, cognitive and neuroplasticity outcomes in a multisite randomised comparison trial. **METHODS AND ANALYSIS:** 150 infants (75 in each group), aged between 3 and 6 months ca, with asymmetric brain injury and clinical signs of upper extremity asymmetry will be recruited. Children will be randomised centrally to receive equal doses of either Baby mCIMT or Baby BIM. Baby mCIMT comprises restraint of the unimpaired hand using a simple restraint (eg, glove, sock), combined with intensive parent implemented practice focusing on active use of the impaired hand in a play-based context. In contrast, Baby BIM promotes active play requiring both hands in a play-based context. Both interventions will be delivered by parents at home with monthly home visits and interim telecommunication support by study therapists. Assessments will be conducted at study entry; at 6, 12 months ca immediately postintervention (primary outcome) and 24 months ca (retention). The primary outcome will be the Mini-Assisting Hand Assessment. Secondary outcomes include the Bayley Scale for Infant and Toddler Development (cognitive and motor domains) and the Hand Assessment of Infants. A subset of children will undertake MRI scans at 24 months ca to evaluate brain lesion severity and brain (re)organisation after intervention. **ETHICS AND DISSEMINATION:** Full ethical approvals for this study have been obtained from the relevant sites. The findings will be disseminated in peer-reviewed publications. **TRIAL REGISTRATION NUMBER:** Australian and New Zealand Clinical Trials Registry: ACTRN12615000180516, Pre results.

[PMID: 28928195](#)

2. Use of virtual reality intervention to improve reaction time in children with cerebral palsy: A randomized controlled trial.

Pourazar M, Mirakhori F, Hemayattalab R, Bagherzadeh F.

Dev Neurorehabil. 2017 Sep 21:1-6. doi: 10.1080/17518423.2017.1368730. [Epub ahead of print]

PURPOSE: The purpose of this study was to investigate the training effects of Virtual Reality (VR) intervention program on reaction time in children with cerebral palsy. **METHODS:** Thirty boys ranging from 7 to 12 years (mean = 11.20; SD = .76) were selected by available sampling method and randomly divided into the experimental and control groups. Simple Reaction Time (SRT) and Discriminative Reaction Time (DRT) were measured at baseline and 1 day after completion of VR

intervention. Multivariate analysis of variance (MANOVA) and paired sample t-test were performed to analyze the results. RESULTS: MANOVA test revealed significant effects for group in posttest phase, with lower reaction time in both measures for the experimental group. Based on paired sample t-test results, both RT measures significantly improved in experimental group following the VR intervention program. CONCLUSIONS: This paper proposes VR as a promising tool into the rehabilitation process for improving reaction time in children with cerebral palsy.

[PMID: 28933977](#)

3. Evaluation of the Reliability of the Challenge when used to Measure Advanced Motor Skills of Children with Cerebral Palsy.

Wright FV, Lam CY, Mistry B, Walker J.

Phys Occup Ther Pediatr. 2017 Sep 18:1-13. doi: 10.1080/01942638.2017.1368765. [Epub ahead of print]

AIMS: The Challenge was designed as an extension to the GMFM-66 to assess advanced motor skills of children with cerebral palsy (CP) who walk/run independently. This study evaluated the Challenge's inter-rater and test-retest reliability. METHODS: Thirty children with CP (GMFCS level I [n = 24] and II [n = 6]) completed the Challenge, with re-testing one to two weeks later. Seven physiotherapist assessors passed the Challenge criterion test pre-administration. A single assessor administered and scored test and retest sessions (test-retest reliability). A second assessor independently scored one of these sessions (inter-rater reliability). RESULTS: Inter-rater reliability was excellent (ICC = 0.97, 95%CI 0.94-0.99, CoV < 10%), with no bias (Bland-Altman plot). Test-retest ICC was excellent (ICC = 0.94, 95% CI 0.88-0.97. CoV < 10%, and Minimum Detectable Change (MDC90) was 4.47 points. Many participants indicated practising at home pre-retest session. CONCLUSIONS: There was strong rating consistency between assessors. While test-retest ICC estimates were also high, Challenge scores were higher at retest. The MDC90 was still in a range (>4.5 points) that seems clinically viable for change detection. Test-retest reliability could be reassessed with children instructed not to practice between assessments to determine the extent to which between-session practice influenced scores.

[PMID: 28922044](#)

4. Garment Therapy does not Improve Function in Children with Cerebral Palsy: A Systematic Review.

Wells H, Marquez J, Wakely L.

Phys Occup Ther Pediatr. 2017 Sep 18:1-22. doi: 10.1080/01942638.2017.1365323. [Epub ahead of print]

AIMS: To conduct a systematic review asking, does garment therapy improve motor function in children with cerebral palsy? METHODS: A systematic review with meta-analysis was conducted to review the literature. Inclusion criteria involved the wearing of therapy suits/garments in children with cerebral palsy. The primary outcome of interest was movement related function and secondary outcomes included impairment, participation, parental satisfaction and adverse outcomes of garment wear. RESULTS: 14 studies with 234 participants were included, of which 5 studies were included for meta-analysis. Garment therapy showed a nonsignificant effect on post-intervention function as measured by the Gross Motor Function Measure when compared to controls (MD = -1.9; 95% CI = -6.84, 3.05). Nonsignificant improvements in function were seen long-term (MD = -3.13; 95% CI = -7.57, 1.31). Garment therapy showed a significant improvement in proximal kinematics (MD = -5.02; 95% CI = -7.28, -2.76), however significant improvements were not demonstrated in distal kinematics (MD = -0.79; 95% CI = -3.08, 1.49). CONCLUSIONS: This review suggests garment therapy does not improve function in children with cerebral palsy. While garment therapy was shown to improve proximal stability, this benefit must be considered functionally and consider difficulties associated with garment use.

[PMID: 28922041](#)

5. Comparison of efficacy between dorsal root entry zone lesioning and selective dorsal rhizotomy for spasticity of cerebral origin.

Sitthinamsuwan B, Phonwijit L, Khampalikit I, Nitising A, Nunta-Aree S, Suksompong S.

Acta Neurochir (Wien). 2017 Sep 17. doi: 10.1007/s00701-017-3322-x. [Epub ahead of print]

BACKGROUND: Severe spasticity adversely affects patient functional status and caregiving. No previous study has compared efficacy between dorsal root entry zone lesioning (DREZL) and selective dorsal rhizotomy (SDR) for reduction of spasticity. This study aimed to investigate the efficacy of DREZL and SDR for attenuating spasticity, and to compare efficacy between these two methods. **METHODS:** All patients who underwent DREZL, SDR, or both for treatment of intractable spasticity caused by cerebral pathology at Siriraj Hospital during 2009 to 2016 were recruited. Severity of spasticity was assessed using Modified Ashworth Scale (MAS) and Adductor Tone Rating Scale (ATRS). Ambulatory status was also evaluated. **RESULTS:** Fifteen patients (13 males) with a mean age of 30.3 ± 17.5 years were included. Eight, six, and one patient underwent DREZL, SDR, and combined cervical DREZL and lumbosacral SDR, respectively. Eight of ten patients with preoperative bed-bound status had postoperative improvement in ambulatory status. Spasticity was significantly reduced in the DREZL group ($p < 0.001$), the SDR group ($p < 0.001$), and in overall analysis ($p < 0.001$). SDR was effective in both pediatric and adult spasticity patients. A significantly greater reduction in spasticity as assessed by MAS score ($p < 0.001$) and ATRS score ($p = 0.015$) was found in the DREZL group. Transient lower limb weakness was found in a patient who underwent SDR. **CONCLUSIONS:** DREZL is more effective for reducing spasticity, but is more destructive than SDR. DREZL should be preferred for bed-ridden patients, and SDR for ambulatory patients. Both operations are helpful for improving ambulatory status. Gait improvement was observed only in patients who underwent SDR. Adult patients with spasticity of cerebral origin benefit from SDR.

[PMID: 28920167](#)

6. What is the price for the Duchenne gait pattern in patients with cerebral palsy?

Salami F, Niklasch M, Krautwurst BK, Dreher T, Wolf SI.

Gait Posture. 2017 Sep 7;58:453-456. doi: 10.1016/j.gaitpost.2017.09.006. [Epub ahead of print]

Duchenne gait is characterized by trunk lean towards the affected stance limb with the pelvis stable or elevated on the swinging limb side during single limb stance phase. We assessed the relationship between hip abduction moments and trunk kinetics in patients with cerebral palsy showing excessive lateral trunk motion. Data of 18 subjects with bilateral spastic cerebral palsy (CP) and 20 aged matched typically developing subjects (TD) were collected retrospectively. Criteria for patient selection were barefoot walking without aid presenting with excessive lateral trunk motion. Subjects had been monitored by conventional 3D gait analysis of the lower extremity including four markers for monitoring trunk motion. Post-hoc, a generic musculoskeletal full body model (OpenSim 3.3) assuming a rigid trunk articulated to the pelvis by a single ball joint was applied for analyzing joint kinematics and kinetics of the lower limb joints including this spine joint. Joint angle ranges of motion, maximum joint moments and powers in the frontal plane as well as mechanical work were calculated and averaged within groups showing prominent differences between groups in all parameters. To the best of our knowledge, this is the first work explicitly looking into the kinetics of Duchenne gait in patients with CP, clinically known as compensation for unloading hip abductor muscles. The results show that excessive lateral trunk motion may indeed be an extremely effective compensation mechanism to unload the hip abductors in single limb stance but for the price of a drastic increase in demand on trunk muscle effort and work.

[PMID: 28918356](#)

7. Long-term follow-up after tibialis anterior tendon shortening in combination with Achilles tendon lengthening in spastic equinus in cerebral palsy.

Kläusler M, Speth BM, Brunner R, Tirosh O, Camathias C, Rutz E.

Gait Posture. 2017 Aug 30;58:457-462. doi: 10.1016/j.gaitpost.2017.08.028. [Epub ahead of print]

Using Tibialis Anterior Shortening (TATS) in combination with Achilles Tendon Lengthening (TAL) to treat spastic equinus in children with cerebral palsy (CP) was described in 2011. Short-term results have indicated a good outcome, especially an improvement of the drop foot in swing phase and the correction of equinus in stance phase. The aim of this study was to analyse the results of the long-term follow-up and to determine the relapse rate of TATS and TAL. The kinematics of the

sagittal, frontal and transversal planes were measured by using instrumented 3D gait analysis at three defined time points and then described using the Gait Profile Score (GPS) and Movement Analysis Profile (MAP). The data was exported into Gaitabase and then the preoperative (T0), short-term (T1) and long-term (T2) follow-up data was statistically compared. 23 patients (mean age at index-surgery=14.9years) were included, there was a mean follow-up time of 5.8 years. 3 children (13%) have shown a relapse. The data of 12 children with spastic hemiplegia (12 legs), as well as 8 children with spastic diplegia (10 legs) has been analysed. There has been a significant ($p<0.05$) improvement in GPS and MAP for ankle dorsiflexion (describes equinus and drop foot) of the operated legs versus not operated legs. TATS in combination with TAL shows a satisfactory long-term result after 5.8 years in the correction of fixed equinus and drop foot in children with CP. Postoperatively all subjects were able to walk without an AFO.

[PMID: 28918357](#)

8. What areas of functioning are influenced by aquatic physiotherapy? Experiences of parents of children with cerebral palsy.

Güeita-Rodríguez J, García-Muro F, Rodríguez-Fernández ÁL, Lambeck J, Fernández-de-Las-Peñas C, Palacios-Ceña D.

Dev Neurorehabil. 2017 Sep 21:1-9. doi: 10.1080/17518423.2017.1368728. [Epub ahead of print]

OBJECTIVES: To explore the experiences regarding aquatic physiotherapy among parents of children with cerebral palsy and to identify a list of relevant intervention categories for aquatic physiotherapy treatments. **METHODS:** We conducted semi-structured interviews and focus groups using the components of the International Classification of Functioning, Disability and Health (ICF) as a frame of reference to explore and code experiences regarding aquatic physiotherapy. A non-probabilistic purposive sampling strategy was used. Content analysis methods and ICF linking processes were used to analyze data. **RESULTS:** From the parents' perspective ($n = 34$), both the Body Functions and Activities and Participation components were mainly influenced by aquatic physiotherapy. Also, parents described Environmental Factors acting as barriers affecting progress during therapy. **CONCLUSIONS:** Parents identified a wide range of categories influenced by aquatic physiotherapy. Social and contextual aspects were highlighted, as well as a series of changes related to the illness as a result of treatment.

[PMID: 28933572](#)

9. Vision Assessments and Interventions for Infants 0-2 Years at High Risk for Cerebral Palsy: A Systematic Review.

Chorna OD, Guzzetta A, Maitre NL.

Pediatr Neurol. 2017 Jul 20. pii: S0887-8994(17)30544-1. doi: 10.1016/j.pediatrneurol.2017.07.011. [Epub ahead of print]

We performed a systematic review and evaluated the level of evidence of vision interventions and assessments for infants at high risk for or with a diagnosis of cerebral palsy from 0 to 2 years of age. Articles were evaluated based on the level of methodologic quality, evidence, and clinical utilization. Thirty publications of vision assessments and five of vision interventions met criteria for inclusion. Assessments included standard care neuroimaging, electrophysiology, and neuro-ophthalmologic examination techniques that are utilized clinically with any preverbal or nonverbal pediatric patient. The overall level of evidence of interventions was strong for neuroprotective interventions such as caffeine and hypothermia but weak for surgery, visual training, or developmental programs. There are few evidence-based interventions and assessments that address cerebral/cortical visual impairment-related needs of infants and toddlers at high risk for or with cerebral palsy. Recommendation guidelines include the use of three types of standard care methodologies and two types of protective interventions.

[PMID: 28918222](#)

10. Reliability and validity of the Korean-language version of the Communication Function Classification System in children with cerebral palsy.

Choi JY, Hwang EH, Rha D, Park ES.

Child Care Health Dev. 2017 Sep 20. doi: 10.1111/cch.12507. [Epub ahead of print]

PURPOSE: The Communication Function Classification System (CFCS) and Viking Speech Scale (VSS) are useful systems for describing the broad communication function and speech intelligibility, respectively, of children with cerebral palsy (CP). The aims of this study were to determine the reliability and validity of the Korean version of the CFCS and also to investigate the association between the CFCS and the VSS and other functional classifications for children with CP. **MATERIALS AND METHODS:** Participants were 50 children with CP (33 males, 17 females; mean age 7.2 years, range 4-16 years) recruited from a rehabilitation hospital. We analysed the interrater and intrarater reliabilities of the Korean version of the CFCS and VSS between parents, a physiatrist, and a speech-language pathologist (SLP). The social function domain of the Paediatric Evaluation of Disability Inventory was assessed to examine the concurrent validity of the CFCS and VSS. **RESULTS:** The intrarater reliabilities of the CFCS and VSS were excellent in a physiatrist ($\kappa = 0.92$, $\kappa = 0.94$, respectively) and an SLP ($\kappa = 0.98$, $\kappa = 0.98$) and very good in parents ($\kappa = 0.87$, $\kappa = 0.89$). The interrater reliability of the CFCS and VSS was very good between the physiatrist and SLP ($\kappa = 0.87$, $\kappa = 0.89$) and good between parents and the SLP ($\kappa = 0.63$, $\kappa = 0.78$) and between parents and the physiatrist ($\kappa = 0.61$, $\kappa = 0.76$). The CFCS and VSS were strongly related with the social function domain of Paediatric Evaluation of Disability Inventory. In addition, we found very strong associations between the VSS and CFCS. **CONCLUSIONS:** The Korean version of the CFCS is a valid and reliable tool to classify communication ability and is strongly associated with the VSS, a reliable tool to classify speech intelligibility.

[PMID: 28929518](#)

11. 'It's important that we learn too': Empowering parents to facilitate participation in physical activity for children and youth with disabilities.

Willis CE, Reid S, Elliott C, Nyquist A, Jahnsen R, Rosenberg M, Girdler S.

Scand J Occup Ther. 2017 Sep 20:1-14. doi: 10.1080/11038128.2017.1378367. [Epub ahead of print]

AIM: The actions and behaviors of parents have been identified as key factors that influence a child's participation in physical activity. However, there is limited knowledge of how parents can be supported to embody facilitative roles. This study aimed to explore how an ecological intervention encourages parents of children with disabilities to develop as facilitators, to enable ongoing physical activity participation in a child's local environment. **METHODS:** A qualitative design using grounded theory was employed. Forty four parents (26 mothers, 18 fathers) of 31 children with a range of disabilities (mean age 12y 6m (SD 2y 2m); 18 males) partaking in the Local Environment Model intervention at Beitostolen Healthsports Centre in Norway participated in the study. Data were derived from the triangulation of semi-structured interviews and participant observation. Data analysis was an iterative approach of constant comparison, where data collection, memo writing, open, axial and selective coding analysis, were undertaken simultaneously. Findings were consolidated into a model describing the central phenomenon and its relationship to other categories. **RESULTS:** Thematic concepts uncovered in this study describe a social process of parent learning and empowerment, comprising three primary components; (i) active ingredients of the intervention that enabled learning and empowerment to transpire, (ii) parent learning and empowerment as a process, and (iii) related outcomes. **CONCLUSION:** A family-centered approach, encompassing family-to-family support, may enhance physical activity

[PMID: 28927322](#)

12. Psychometric evaluation of the Scandinavian version of the caregiver priorities and child health index of life with disabilities.

Pettersson K, Bjerke KM, Jahnsen R, Öhrvik J, Rodby-Bousquet E.

Disabil Rehabil. 2017 Sep 19:1-7. doi: 10.1080/09638288.2017.1378930. [Epub ahead of print]

PURPOSE: To examine test-retest reliability and construct validity of the Scandinavian version of the caregiver priorities and child health index of life with disabilities (CPCHILD) questionnaire for children with cerebral palsy (CP). **METHODS:** Families were recruited in Sweden and Norway and stratified according to the gross motor function classification system levels I-V for children born 2000-2011, mean age 7.9 (SD 3.2). Construct validity based on the first questionnaire (n = 106) was

evaluated for known groups, using linear regression analysis. Intraclass correlation coefficient was used to estimate test-retest reliability ($n = 64$), and Cronbach's alpha was calculated as an indicator of internal consistency. RESULTS: The questionnaire showed construct validity and the ability to discriminate between levels of gross motor function for the total score and all domain scores ($p < 0.05$). Test-retest reliability was high with intraclass correlation coefficient of 0.92 for the total score and of 0.72-0.92 for the domain scores. Cronbach's alpha was 0.96 for the total score and 0.83-0.96 for the domain scores. CONCLUSIONS: The Scandinavian version of the CPCHILD for children with CP seems to be a valid and reliable proxy measure for health related quality of life. Implications for rehabilitation Valid and reliable outcome measures are needed to evaluate whether follow-up programs enhance health related quality of life in different countries. The Scandinavian version of the caregiver priorities and child health index of life with disabilities (CPCHILD) was evaluated for known-groups validity and test-retest reliability. The Scandinavian version of the CPCHILD is a sound and valid measurement for evaluation and comparison of health related quality of life of children with cerebral palsy in different countries.

[PMID: 28927310](#)

13. Role of Anesthesiologist in the Management of a Child with Cerebral Palsy.

Shaikh SI, Hegade G.

Anesth Essays Res. 2017 Jul-Sep;11(3):544-549. doi: 10.4103/0259-1162.194569.

Cerebral palsy (CP) refers to a spectrum of nonprogressive neurological disorders with disturbances in posture and movement, resulting from perinatal intrauterine insult to developing infant brain. Many conditions associated with CP require surgery. Such cases pose important gastrointestinal, respiratory, and other perioperative considerations. Anesthetic management in these cases is delicate. Intraoperative complications including hypovolemia, hypothermia, muscle spasms, seizures, and delayed recovery might complicate the anesthetic management. A thorough preanesthetic evaluation allows for a better intra- and post-operative care. Postoperative analgesia is important, particularly in orthopedic surgeries one for pain relief. This review highlights the clinical manifestations in CP and anesthetic considerations in such child presenting for various surgeries.

[PMID: 28928544](#)

14. Serious incident investigations for cerebral palsy are "poor quality," says watchdog.

Iacobucci G.

BMJ. 2017 Sep 21;358:j4368. doi: 10.1136/bmj.j4368.

[No abstract available]

[PMID: 28935821](#)

Prevention and Cure

15. Expression of Concern to: Therapeutic potential of human embryonic stem cell transplantation in patients with cerebral palsy.

Shroff G, Gupta A, Barthakur JK.

J Transl Med. 2017 Sep 18;15(1):193. doi: 10.1186/s12967-017-1292-7.

The Editor-in-Chief of the Journal of Translational Medicine is issuing an editorial expression of concern to alert readers that concerns have been raised regarding the ethics of this study [1] and the potential association of the risk of teratoma formation with the transplantation of embryonic stem cells. Appropriate editorial action will be taken once this has been fully investigated. The authors disagree with this notice.

Expression of concern for

Therapeutic potential of human embryonic stem cell transplantation in patients with cerebral palsy. [J Transl Med. 2014]

[PMID: 28923074](#)

16. Umbilical cord blood cells for treatment of cerebral palsy; timing and treatment options.

McDonald CA, Fahey MC, Jenkin G, Miller SL.

Pediatr Res. 2017 Sep 22. doi: 10.1038/pr.2017.236. [Epub ahead of print]

Cerebral palsy is the most common cause of physical disability in children, and there is no cure. Umbilical cord blood (UCB) cell therapy for the treatment of children with cerebral palsy is currently being assessed in clinical trials. While there is much interest in the use of UCB stem cells for neuroprotection and neuroregeneration, the mechanisms of action are not fully understood. Further, UCB contains many stem and progenitor cells of interest, and we will point out that individual cell types within UCB may elicit specific effects. UCB is a clinically proven source of hematopoietic stem cells (HSCs). It also contains mesenchymal stromal cells (MSCs), endothelial progenitor cells (EPCs) and immunosuppressive cells such as regulatory T cells (Tregs) and monocyte-derived suppressor cells. Each of these cell types may be individual candidates for the prevention of brain injury following hypoxic and inflammatory events in the perinatal period. We will discuss specific properties of cell types in UCB, with respect to their therapeutic potential and the importance of optimal timing of administration. We propose that tailored cell therapy and targeted timing of administration will optimise results for future clinical trials in the neuroprotective treatment of perinatal brain injury. Pediatric Research accepted article preview online, 22 September 2017. doi:10.1038/pr.2017.236.

[PMID: 28937975](#)

17. Maternal obesity is associated with chorioamnionitis and earlier indicated preterm delivery among expectantly managed women with preterm premature rupture of membranes.

Hadley EE, Discacciati A, Costantine MM, Munn MB, Pacheco LD, Saade GR, Chiossi G.

J Matern Fetal Neonatal Med. 2017 Sep 22:1-8. doi: 10.1080/14767058.2017.1378329. [Epub ahead of print]

OBJECTIVE: To determine the association between maternal obesity and delivery due to chorioamnionitis prior to labor onset, among expectantly managed women with preterm premature rupture of membranes (pPROM). **METHODS:** This was a secondary analysis of a multicenter randomized trial of magnesium sulfate versus placebo to prevent cerebral palsy or death among offspring of women with anticipated delivery at 24-31-week gestation. After univariable analysis, Cox proportional hazard evaluated the association between maternal obesity and chorioamnionitis, while Laplace regression investigated how obesity affects the gestational age at delivery of the first 20% of women developing the outcome of interest. **RESULTS:** A total of 164 of the 1942 women with pPROM developed chorioamnionitis prior to labor onset. Obese women had a 60% increased hazard of developing such complication (adjusted HR 1.6, 95%CI 1.1-2.1, p = .008), prompting delivery 1.5 weeks earlier, as the 20th survival percentile was 27.2-week gestation (95%CI 26-28.6) among obese as opposed to 28.8 weeks (95%CI 27.4-30.1) (p = .002) among nonobese women. **CONCLUSIONS:** Maternal obesity is a risk factor for chorioamnionitis prior to labor onset. Future studies will determine if obesity is important enough to change the management of latency after pPROM according to maternal BMI.

[PMID: 28936902](#)

18. The extent of intrauterine growth restriction determines the severity of cerebral injury and neurobehavioural deficits in rodents.

Ruff CA, Faulkner SD, Rumajogee P, Beldick S, Foltz W, Corrigan J, Basilious A, Jiang S, Thiyagalingam S, Yager JY, Fehlings MG.

PLoS One. 2017 Sep 21;12(9):e0184653. doi: 10.1371/journal.pone.0184653. eCollection 2017.

BACKGROUND: Cerebral Palsy (CP) is the most common physical pediatric neurodevelopmental disorder and spastic diplegic injury is its most frequent subtype. CP results in substantial neuromotor and cognitive impairments that have significant socioeconomic impact. Despite this, its underlying pathophysiological mechanisms and etiology remain incompletely understood. Furthermore, there is a need for clinically relevant injury models, which a) reflect the heterogeneity of the condition and b) can be used to evaluate new translational therapies. To address these key knowledge gaps, we characterized a chronic placental insufficiency (PI) model, using bilateral uterine artery ligation (BUAL) of dams. This injury model results in intrauterine growth restriction (IUGR) in pups, and animals recapitulate the human phenotype both in terms of neurobehavioural and anatomical deficits. **METHODS:** Effects of BUAL were studied using luxol fast blue (LFB)/hematoxylin & eosin (H&E) staining, immunohistochemistry, quantitative Magnetic Resonance Imaging (MRI), and Catwalk neurobehavioural tests. **RESULTS:** Neuroanatomical analysis revealed regional ventricular enlargement and corpus callosum thinning in IUGR animals, which was correlated with the extent of growth restriction. Olig2 staining revealed reductions in oligodendrocyte density in white and grey matter structures, including the corpus callosum, optic chiasm, and nucleus accumbens. The caudate nucleus, along with other brain structures such as the optic chiasm, internal capsule, septofimbrial and lateral septal nuclei, exhibited reduced size in animals with IUGR. The size of the pretectal nucleus was reduced only in moderately injured animals. MAG/NF200 staining demonstrated reduced myelination and axonal counts in the corpus callosum of IUGR animals. NeuN staining revealed changes in neuronal density in the hippocampus and in the thickness of hippocampal CA2 and CA3 regions. Diffusion weighted imaging (DWI) revealed regional white and grey matter changes at 3 weeks of age. Furthermore, neurobehavioural testing demonstrated neuromotor impairments in animals with IUGR in paw intensities, swing speed, relative print positions, and phase dispersions. **CONCLUSIONS:** We have characterized a rodent model of IUGR and have demonstrated that the neuroanatomical and neurobehavioural deficits mirror the severity of the IUGR injury. This model has the potential to be applied to examine the pathobiology of and potential therapeutic strategies for IUGR-related brain injury. Thus, this work has potential translational relevance for the study of CP.

[PMID: 28934247](#)

19. Hypertonia-linked protein Trak1 functions with mitofusins to promote mitochondrial tethering and fusion.

Lee CA, Chin LS, Li L.

Protein Cell. 2017 Sep 18. doi: 10.1007/s13238-017-0469-4. [Epub ahead of print]

Hypertonia is a neurological dysfunction associated with a number of central nervous system disorders, including cerebral palsy, Parkinson's disease, dystonia, and epilepsy. Genetic studies have identified a homozygous truncation mutation in Trak1 that causes hypertonia in mice. Moreover, elevated Trak1 protein expression is associated with several types of cancers and variants in Trak1 are linked to childhood absence epilepsy in humans. Despite the importance of Trak1 in health and disease, the mechanisms of Trak1 action remain unclear and the pathogenic effects of Trak1 mutation are unknown. Here we report that Trak1 has a crucial function in regulation of mitochondrial fusion. Depletion of Trak1 inhibits mitochondrial fusion, resulting in mitochondrial fragmentation, whereas overexpression of Trak1 elongates and enlarges mitochondria. Our analyses revealed that Trak1 interacts and colocalizes with mitofusins on the outer mitochondrial membrane and functions with mitofusins to promote mitochondrial tethering and fusion. Furthermore, Trak1 is required for stress-induced mitochondrial hyperfusion and pro-survival response. We found that hypertonia-associated mutation impairs Trak1 mitochondrial localization and its ability to facilitate mitochondrial tethering and fusion. Our findings uncover a novel function of Trak1 as a regulator of mitochondrial fusion and provide evidence linking dysregulated mitochondrial dynamics to hypertonia pathogenesis.

[PMID: 28924745](#)

20. Magnesium Sulfate Prevents Neurochemical and Long-Term Behavioral Consequences of Neonatal Excitotoxic Lesions: Comparison Between Male and Female Mice.

Daher I, Le Dieu-Lugon B, Dourmap N, Lecuyer M, Ramet L, Gomila C, Ausseil J, Marret S, Leroux P, Roy V, El Mestikawy S, Daumas S, Gonzalez B, Leroux-Nicollet I, Cleren C.

J Neuropathol Exp Neurol. 2017 Oct 1;76(10):883-897. doi: 10.1093/jnen/nlx073.

Magnesium sulfate (MgSO₄) administration to mothers at risk of preterm delivery is proposed as a neuroprotective strategy against neurological alterations such as cerebral palsy in newborns. However, long-term beneficial or adverse effects of MgSO₄ and sex-specific sensitivity remain to be investigated. We conducted behavioral and neurochemical studies of MgSO₄ effects in males and females, from the perinatal period to adolescence in a mouse model of cerebral neonatal lesion. The lesion was produced in 5-day-old (P5) pups by ibotenate intracortical injection. MgSO₄ (600 mg/kg, i.p.) prior to ibotenate prevented lesion-induced sensorimotor alterations in both sexes at P6 and P7. The lesion increased glutamate level at P10 in the prefrontal cortex, which was prevented by MgSO₄ in males. In neonatally lesioned adolescent mice, males exhibited more sequelae than females in motor and cognitive functions. In the perirhinal cortex of adolescent mice, the neonatal lesion induced an increase in vesicular glutamate transporter 1 density in males only, which was negatively correlated with cognitive scores. Long-term sequelae were prevented by neonatal MgSO₄ administration. MgSO₄ never induced short- or long-term deleterious effect on its own. These results also strongly suggest that sex-specific neuroprotection should be foreseen in preterm infants.

[PMID: 28922852](#)

21. Stem cells and cell-based therapies for cerebral palsy: A call for rigor.

Jantzie LL, Scafidi J, Robinson S.

Pediatr Res. 2017 Sep 18. doi: 10.1038/pr.2017.233. [Epub ahead of print]

Cell-based therapies hold significant promise for infants at risk for cerebral palsy (CP) from perinatal brain injury (PBI). PBI leading to CP results from multi-faceted damage to neural cells. Complex developing neural networks are injured by neural cell damage plus unique perturbations in cell signaling. Given that cell-based therapies can simultaneously repair multiple injured neural components during critical neurodevelopmental windows, these interventions potentially offer efficacy for patients with CP. Currently, use of cell-based interventions in infants at risk for CP is limited by critical gaps in knowledge. In this review, we will highlight key questions facing the field, including: Who are optimal candidates for treatment? What are goals of therapeutic interventions? What are best strategies for agent delivery, including timing, dosage, location and type? And, how are short- and long-term efficacy reliably tracked? Challenges unique to treating PBI with cell-based therapies, and lessons learned from cell-based therapies in closely related neurological disorders in the mature central nervous system (CNS), will be reviewed. Our goal is to update pediatric specialists who may be counseling families about the current state of the field. Finally, we will evaluate how rigor can be increased in the field to ensure the safety and best interests of this vulnerable patient population. *Pediatric Research* accepted article preview online, 18 September 2017. doi:10.1038/pr.2017.233.

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22. Cerebral palsy; clinical safety of clomiphene citrate; BJOG's impact.

Chien P.

BJOG. 2017 Oct;124(11):1635. doi: 10.1111/1471-0528.14347.

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