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## Interventions and Management

### 1. Early prediction of unilateral cerebral palsy in infants with asymmetric perinatal brain injury - Model development and internal validation.

Ryll UC, Wagenaar N, Verhage CH, Blennow M, de Vries LS, Eliasson AC.

Eur J Paediatr Neurol. 2019 Apr 27. pii: S1090-3798(18)30428-8. doi: 10.1016/j.ejpn.2019.04.004. [Epub ahead of print]

**BACKGROUND:** Early diagnosis of unilateral cerebral palsy is important after asymmetric perinatal brain injury (APBI). Our objective is to estimate the risk of unilateral cerebral palsy (UCP) in infants with APBI during the first months of life using neuroimaging and clinical assessment. **PATIENTS AND METHODS:** Prognostic multivariable prediction modeling study including 52 infants (27 males), median gestational age 39.3 weeks with APBI from Sweden (n = 33) and the Netherlands (n = 19). **INCLUSION CRITERIA:** (1) neonatal MRI within one month after term equivalent age (TEA), (2) Hand Assessment for Infants (HAI) between 3.5 and 4.5 months of (corrected) age. UCP was diagnosed  $\geq 24$  months of age. Firth regression with cross-validation was used to construct and internally validate the model to estimate the risk for UCP based on the predictors corticospinal tract (CST) and basal ganglia/thalamus (BGT) involvement, contralesional HAI Each hand sum score (EaHS), gestational age and sex. **RESULTS:** UCP was diagnosed in 18 infants (35%). Infants who developed UCP more often had involvement of the CST and BGT on neonatal MRI and had lower contralesional HAI EaHS compared to those who did not develop UCP. The final model showed excellent accuracy for UCP prediction between 3.5 and 4.5 months (area under the curve, AUC = 0.980; 95% CI 0.95-1.00). **CONCLUSIONS:** Combining neonatal MRI, the HAI, gestational age and sex accurately identify the prognostic risk of UCP at 3.5-4.5 months in infants with APBI.

PMID: [31078397](#)

### 2. Accuracy Constraints Improve Symmetric Bimanual Coordination for Children with and without Unilateral Cerebral Palsy.

Hung YC, Zeng W.

Dev Neurorehabil. 2019 May 15:1-9. doi: 10.1080/17518423.2019.1616845. [Epub ahead of print]

**PURPOSE:** To evaluate the influence of accuracy constraints on functional symmetric bimanual coordination for children with Unilateral Spastic Cerebral Palsy (USCP). **METHODS:** Ten children with USCP (average age: 9.6; MACS levels: I-II), ten typically developing children, and ten adults lifted a tray with a water bottle on top. Two accuracy constraints of handle size and cap condition were manipulated. **RESULTS:** Children with USCP exhibited greater bilateral asymmetry in hand vertical position, timing, upper arm, and elbow control than other groups. Smaller handle decreased bilateral timing differences at lift onset and offset, and decreased bilateral elbow asymmetry at reach and lift offset. Without a cap (accuracy constraint), they showed greater trunk involvement, and less bilateral vertical position and lift offset timing differences (all p < .05). **CONCLUSIONS:** Children with USCP showed impaired symmetric bimanual coordination. Higher accuracy

constraints improved some bimanual spatial and temporal control. Therefore, task accuracy constraints should be manipulated carefully for training.

PMID: [31088323](#)

### **3. Computed Tomography of Femoral Anteversion in Children With Cerebral Palsy.**

Roberts BW.

Radiol Technol. 2019 May;90(5):489CT-503CT.

Cerebral palsy (CP) is a common childhood disability that affects musculoskeletal development. In particular, CP might contribute to increased femoral anteversion and associated difficulties in ambulation, increasing the risk of hip dysplasia and dislocation. Computed tomography provides useful information about the effects of CP on the anatomy and functionality of the femur and hip joint. Radiologic technologists should work collaboratively with other health care professionals to empower patients with CP and their caregivers to improve quality of life.

PMID: [31088959](#)

### **4. Clinical and Gait Parameters Related to Pelvic Retraction in Patients with Spastic Hemiplegia.**

Park KB, Park H, Park BK, Abdel-Baki SW, Kim HW.

J Clin Med. 2019 May 14;8(5). pii: E679. doi: 10.3390/jcm8050679.

Pelvic retraction during walking is a common finding seen in patients with spastic hemiplegia. However, potential factors related to this condition have not been comprehensively examined in a systemic manner in previous studies. The purpose of this study was to elucidate any clinical and gait parameters related to pelvic retraction in patients with hemiplegic cerebral palsy. A total of 212 independent ambulatory patients were enrolled in the study. Group I consisted of 113 patients who had persistent pelvic retraction, and Group II of 99 with a normal range of pelvic rotation throughout the gait cycle as evidenced by kinematic analysis. A multivariate logistic regression analysis using a clustering technique was performed, with use of eight gait factors and five clinical factors. Decreased ankle dorsiflexion, increased hip internal rotation, increased anterior pelvic tilt, the Winters classification type II, and asymmetrical posturing of the upper extremity during gait were found to be related to pelvic retraction. This is the only study including a broader array of assessment domains of both clinical and gait parameters with a considerably large and homogenous population with hemiplegia. Further studies will be needed to see whether the rectification of those parameters may improve abnormal gait and pelvic retraction in hemiplegia.

PMID: [31091787](#)

### **5. Cultural adaptation and reliability analysis of the early clinical assessment of balance.**

Gontijo APB, Starling JMP, Oliveira GD, Meier D, Mancini MC.

Rev Paul Pediatr. 2019 May 9. pii: S0103-05822019005008101. doi: 10.1590/1984-0462/;2019;37;3;00001. [Epub ahead of print] [Article in English, Portuguese]

**OBJECTIVE:** To translate the Early Clinical Assessment of Balance (ECAB), an assessment scale developed specifically for children and adolescents with cerebral palsy into Brazilian Portuguese, evaluate semantic, idiomatic, experiential and conceptual equivalences, and to examine the face validity and the reliability within and between examiners of the Brazilian version. **METHODS:** The following steps were done: translation by two independent translators; synthesis of translations; back translation into English; analysis of back-translations by a multidisciplinary committee and the author of the test to develop the final version of the test; test application training; administration of the translated version of ECAB (videotaped) in 60 children and adolescents with cerebral palsy; intra and inter-examiner reliability assessment. Reliability was assessed by intraclass correlation coefficient (CCI). **RESULTS:** The discrepancies found were related mainly to semantic equivalence and, therefore, there was no need to make cultural adaptations in any of the 13 items on the scale. The rate of agreement was greater than 90% and the reliability of the ECAB-Portuguese total score was excellent both for the intra-rater test (CCI=1.00) and for the inter-rater test (CCI=0.998). Likewise, the reliability evaluation of each of the scale items was also excellent. **CONCLUSIONS:** The translated version of the ECAB into Portuguese provides a tool for the evaluation of the specific balance for children and adolescents with cerebral palsy with different levels of functioning.

PMID: [31090845](#)

## 6. Combining balance-training interventions with other active interventions may enhance effects on postural control in children and adolescents with cerebral palsy: a systematic review and meta-analysis.

Araújo PA, Starling JMP, Oliveira VC, Gontijo APB, Mancini MC.

Braz J Phys Ther. 2019 May 3. pii: S1413-3555(18)30795-0. doi: 10.1016/j.bjpt.2019.04.005. [Epub ahead of print]

**BACKGROUND:** Improvement of postural control in children and adolescents with cerebral palsy is a primary goal in child rehabilitation. **OBJECTIVE:** A systematic review investigated whether combining balance-training interventions with other active interventions enhances the effects of the active intervention alone on postural control of children and adolescents with cerebral palsy. **METHODS:** Searches were performed in MEDLINE, PEDro, CINAHL, Cochrane and EMBASE databases without date or language restrictions. Randomized controlled trials investigating the combination of balance-training interventions with other active interventions on the postural control of children and adolescents with cerebral palsy were included. Two independent reviewers screened studies, extracted data, and assessed methodological quality of included studies. Meta-analysis was conducted, and quality of the evidence followed the GRADE methodology. Pooled data was presented using standardized mean difference and 95% confidence interval. **RESULTS:** Seven studies involving 194 participants were included in this review. A large additional effect on postural control was found when balance-training interventions were combined with Neurodevelopmental Treatment at short-term (1.3, 0.5-2.0,  $p=0.001$ ). The quality of the evidence was very low due to publication bias, imprecision and inconsistency. **CONCLUSION:** Combining balance-training interventions with other active interventions may enhance effects on postural control of this population at short-term. As the estimated effect had only very low quality of evidence to support it, larger studies with low risk of bias are needed.

PMID: [31076254](#)

## 7. LEARN2MOVE 0-2 years, a randomized early intervention trial for infants at very high risk of cerebral palsy: neuromotor, cognitive, and behavioral outcome.

Hielkema T, Hamer EG, Boxum AG, La Bastide-Van Gemert S, Dirks T, Reinders-Messelink HA, Maathuis CGB, Verheijden J, H B Geertzen J, Hadders-Algra M; L2M 0-2 Study Group.

Disabil Rehabil. 2019 May 13:1-10. doi: 10.1080/09638288.2019.1610508. [Epub ahead of print]

**PURPOSE:** Evidence for efficacy of early intervention in infants at high risk of cerebral palsy (CP) is limited. We compared outcome of infants at very high risk of CP after receiving the family centered program COPing with and Caring for infants with special needs (COPCA) or typical infant physiotherapy. **MATERIALS AND METHODS:** Forty-three infants were randomly assigned before the corrected age of 9 months to 1 year of COPCA ( $n=23$ ) or typical infant physiotherapy ( $n=20$ ). Neuromotor development, cognition, and behavior was assessed until 21 months corrected age. Video-recorded physiotherapy sessions were quantitatively analyzed for further process analyses. Outcome was evaluated with nonparametric tests and linear mixed effect models. **RESULTS:** During and after the interventions, infant outcome in both intervention groups was similar [primary outcome Infant Motor Profile: COPCA 82 (69-94), typical infant physiotherapy 81 (69-89); Hodges Lehman estimate of the difference 0 (confidence interval -5;4)]. Outcome was not associated with contents of intervention. **CONCLUSIONS:** One year of COPCA and 1 year of typical infant physiotherapy in infants at high risk of CP resulted in similar neurodevelopmental outcomes. It is conceivable that combinations of active ingredients from different approaches are needed for effective early intervention. **IMPLICATIONS FOR REHABILITATION** For infants at very high risk of cerebral palsy, 1 year of intervention with the family-centred programme Coping with and Caring for infants with special needs resulted in similar infant outcome as 1 year of typical infant physiotherapy. Infant's neuromotor, cognitive, and behavioural outcome was not associated with specific interventional elements, implying that the various elements may have a similar effect on developmental outcome. We suggest that a specific mix of ingredients of different approaches may work best, resulting in comprehensive care including both infant and family needs.

PMID: [31079510](#)

## 8. The role of social media in selective dorsal rhizotomy for children: information sharing and social support.

Canty MJ, Breitbart S, Siegel L, Fehlings D, Milo-Manson G, Alotaibi NM, Ibrahim GM.

Childs Nerv Syst. 2019 May 11. doi: 10.1007/s00381-019-04197-x. [Epub ahead of print]

**PURPOSE:** Selective dorsal rhizotomy (SDR) is a surgical treatment for spasticity, primarily in cerebral palsy (CP). There is a growing trend for patients to seek medical information from their peers on social media platforms. This study qualitatively and

quantitatively assessed the use of social media as an information-sharing and support-seeking tool by patients and caregivers. **METHODS:** A search was performed on Facebook, Twitter, and YouTube. Public information was quantitatively assessed by category, users, year of creation, and country of origin. Representative samples of comments and posts were then qualitatively assessed by thematic analysis. **RESULTS:** One hundred eighty-five Facebook groups and pages, 97 YouTube videos, and 14 Twitter accounts were identified, based in 13 countries. SDR and CP groups had a mean membership of 3063 and 2339, respectively; SDR and CP pages had a mean number of "likes" of 1650 and 10,711, respectively. Total YouTube video views were 593,135 (mean 6115). Total Twitter followers were 62,609 (mean 2160). Qualitative analysis identified seven categories of comments: emotional support and forming connections (22.34%), sharing information and advice (15.96%), appreciation and successes (31.91%), challenges and difficulties (8.51%), advertising/offering services (4.79%), inequities and access (4.79%), and social media as a second opinion (11.7%). **CONCLUSIONS:** This study outlines the use of social media platforms in the distribution of information regarding SDR. We highlight the importance placed by patients and caregivers on the advice of their peers. The current report should inform healthcare providers' interactions with patients with respect to information seeking and provision of support.

PMID: [31079181](#)

### **9. Sedation and analgesia in children with cerebral palsy: a narrative review.**

Rabach I, Peri F, Minute M, Aru E, Lucafò M, Di Mascio A, Cozzi G, Barbi E.

World J Pediatr. 2019 May 16. doi: 10.1007/s12519-019-00264-0. [Epub ahead of print]

**BACKGROUND:** Patients with cognitive impairment due to cerebral palsy experience pain more often than healthy peers and frequently require diagnostic and therapeutic painful procedures. Analgesia and procedural sedation outside the operating room are often required, but they may not adequately be provided because of the inability to accurately recognize and classify the state of pain and for the perceived higher risk of complications. **DATA SOURCES:** We reviewed the available literature to highlight the specific risk factors and area of criticism, that should be further improved. We searched the Cochrane Library, Medline, Pubmed from 1987 to September 2018 using key words such as 'cerebral palsy and children and pain' or 'sedation and cerebral palsy and children'. **RESULTS:** While different pain scales are useful in recognizing pain expressions, anxiety scales are not available. Moreover, studies on non-pharmacological techniques do not always have comparable results. Several risk factors, from anatomic abnormalities to liver and kidney functioning, should be kept in mind before proceeding with sedation. **CONCLUSIONS:** Large trials are needed to assess the impact of non-pharmacological techniques and to evaluate which pain control strategy (pharmacological and non-pharmacological) should be used in different settings.

PMID: [31098933](#)

### **10. Noninvasive Brain Stimulation for Rehabilitation of Paediatric Motor Disorders Following Brain Injury: Systematic Review of Randomized Controlled Trials.**

Elbanna ST, Elshennawy S, Ayad MN.

Arch Phys Med Rehabil. 2019 May 9. pii: S0003-9993(19)30302-8. doi: 10.1016/j.apmr.2019.04.009. [Epub ahead of print]

**OBJECTIVE:** To assess the evidence of the effectiveness of noninvasive brain stimulation (NIBS) for rehabilitation of paediatric motor disorders after brain injury. **DATA SOURCES:** Ovid, Cochrane, Science Direct, Web of Science, EBSCOhost, PubMed, and Google Scholar databases were searched up to August 2017 by two independent reviewers. **STUDY SELECTION:** Randomized control trials (RCTs) published in English were included if; Population: Paediatric patients with motor disorders following brain injury. **INTERVENTION:** NIBS, including transcranial direct current stimulation (tDCS) or repetitive transcranial magnetic stimulation (rTMS). **OUTCOMES:** Measures related to motor disorders (upper limb functional abilities, gait, balance, and spasticity). Fourteen RCTs were included (10 studies used tDCS, while 4 studies used rTMS). **DATA EXTRACTION:** Predefined data were tabulated by one reviewer and verified by another reviewer. Methodological quality was assessed using the PEDro scale; also levels of evidence adapted from Sackett were used. **DATA SYNTHESIS:** A grouped meta-analysis was performed on balance, gait parameters, and upper limb function. Data were pooled using a random-effects model to assess the immediate effect and one-month follow-up of NIBS. According to the PEDro scale, 3 studies were excellent, 8 studies were good and 3 studies were fair. The level of evidence of all of the included studies was 1b, except for three studies with grade 2a. There were significant improvements in all upper limb functions [standardized mean differences (SMDs) ranging from 0.94 to 1.83 (P values= 0.0001)], balance [SMDs ranging between -0.48 to 0.83 (P values< 0.05) and some gait variables. **CONCLUSION:** Paediatric patients with brain injury can be safely stimulated by NIBS, and there is evidence for the efficacy of rTMS in improving upper limb function, and tDCS in improving balance and majority of gait variables with persisted effects for 1-month. The efficacy of spasticity is uncertain.

PMID: [31078616](#)

**11. MEG recordings of patients with cerebral palsy before and after the application of pico-Tesla weak magnetic fields.**

Anninos P, Kotini A, Adamopoulos A, Tsagas N.

J Integr Neurosci. 2019 Mar 30;18(1):17-21. doi: 10.31083/j.jin.2019.01.104.

MEG data for five cerebral palsy patients were taken using a whole-head 122-channel MEG system. An experiment was designed to identify the possible effect of external pico-Tesla weak magnetic fields. The subjects were five male volunteers 17-46 years of age. External stimulation, field amplitude 1-7.5 pico-Tesla, was applied to each subject at their alpha-rhythm frequency. Fast Fourier transforms were applied to the data of all MEG channels and the rhythms of the patients were evaluated before and after pico-Tesla transcranial magnetic stimulation. The appliance of pico-Tesla weak magnetic fields showed the brains of the cerebral palsy patients had an enhance of the frequencies of (2-7 Hz) for each patient. This was followed by an improvement and normalization of their MEG. The results had a statistical significance in four out of five subjects (80%) and suggested the stimulation provided a positive contribution to the management of the symptoms of cerebral palsy patients.

PMID: [31091844](#)**12. One third of school-aged children with cerebral palsy have neuropsychiatric impairments in a population-based study.**

Pählman M1,2, Gillberg C1, Himmelmann K2,3.

Acta Paediatr. 2019 May 11. doi: 10.1111/apa.14844. [Epub ahead of print]

AIM: To describe motor function and associated impairments, particularly autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), in school-aged children with cerebral palsy (CP). METHODS: Population-based study of all children with CP born 1999-2006 from the county of Västra Götaland, Sweden; 264 children (141 males, 123 females). Information was obtained from the CP Register of western Sweden (data collected at 4-8 years of age) and all medical records at 10-17 years of age. RESULTS: CP was spastic in 76%, dyskinetic in 17% and ataxic in 7% of all children. Sixty-three percent were independent walkers. Associated impairments were present in 75%. Vision was impaired in 19%, hearing in 8% and speech in 54%. Intellectual disability (ID) was present in 53% and epilepsy in 41%. ID had increased from 42% to 53% since preschool-age. Neuropsychiatric impairments were present in 32% of the children; ASD in 18% and ADHD in 21%. All impairments, except for ASD and ADHD, increased with more severe motor impairment. CONCLUSION: Three in four school-aged children with CP have associated impairments, underscoring the need to broadly assess every child. The high rate of ASD and ADHD points to the importance of in-depth studies of such impairments in CP. This article is protected by copyright. All rights reserved.

PMID: [31077607](#)**13. "With CO-OP I'm the boss" - experiences of the cognitive orientation to daily occupational performance approach as reported by young adults with cerebral palsy or spina bifida.**

Öhrvall AM, Bergqvist L, Hofgren C, Peny-Dahlstrand M.

Disabil Rehabil. 2019 May 12:1-8. doi: 10.1080/09638288.2019.1607911. [Epub ahead of print]

PURPOSE: Restrictions to activity and participation in persons with cerebral palsy or spina bifida are often due to both motor and executive dysfunction. Hence methods focusing solely on motor issues are not enough to enhance participation. The Cognitive Orientation to daily Occupational Performance Approach™ is a performance-based approach offering clients opportunities to create their own strategies to learn skills. The aim of the present study was to explore and describe experiences of the Cognitive Orientation to daily Occupational Performance Approach as reported by young adults with cerebral palsy or spina bifida. METHODS: Qualitative content analysis was used. Semi-structured individual interviews were conducted with the 10 participants aged 16-28, post-intervention and at 6-months follow-up. RESULTS: The participants described how the Cognitive Orientation to daily Occupational Performance Approach enhanced their self-efficacy. Four categories describing the participants' experiences emerged: "CO-OP is a different way of learning", "CO-OP sometimes puts a strain on me", "CO-OP supports my way of thinking and doing" and "CO-OP boosts me". CONCLUSION: The young adults expressed that the Cognitive Orientation to daily Occupational Performance intervention, although sometimes challenging, was worth the effort because it provided them with an opportunity to master everyday-life problems by using meta-cognitive thinking, which enhanced their self-efficacy. Implications for rehabilitation The Cognitive Orientation to daily Occupational Performance Approach™ - was perceived to provide opportunities to master everyday-life problems by using meta-cognitive thinking. The

Cognitive Orientation to daily Occupational Performance Approach boosted the persons feeling of self-efficacy. The Cognitive Orientation to daily Occupational Performance Approach is person-centred and supports the person's own way of learning.

PMID: [31081393](#)

#### **14. Using participatory action research to examine barriers and facilitators to physical activity among rural adolescents with cerebral palsy.**

Walker A, Colquitt G, Elliott S, Emter M, Li L.

Disabil Rehabil. 2019 May 15:1-12. doi: 10.1080/09638288.2019.1611952. [Epub ahead of print]

**PURPOSE:** The purpose of this study was to use a qualitative, community-based participatory action research method - Photovoice - to identify perceived facilitators and barriers to physical activity among adolescents with cerebral palsy (CP) in a rural community. **MATERIALS AND METHODS:** Fifteen participants including adolescents with CP (n = 7) and parents (n = 8) were included in this study. The researchers followed the nine-step methodology recommended for Photovoice. During the training session, participants completed versions of the Barriers to Physical Activity Questionnaire for People with Mobility Impairments. This questionnaire was used to generate descriptive information about participant barriers and facilitators. Participants were given 14 days to take photographs after which researchers used in-depth and focus group interviews structured by the SHOWeD method. Content analysis of transcripts was used to identify common themes. **RESULTS AND CONCLUSIONS:** Photographs and accompanying text were presented to local stakeholders and an action plan to increase physical activity for adolescents with CP was created. Perceived barriers included lack of inclusiveness, family isolation, and limited accessibility of equipment and resources. Facilitators included support services for families and adaptive sport leagues. Photovoice serves as a powerful tool to initiate change to promote physical activity among rural adolescents with CP. Implications for rehabilitation Adolescents with cerebral palsy living in rural areas face unique barriers to physical activity. Accessibility of equipment and the structural environment can serve as barriers to participation. Lack of accessibility can lead to feelings of isolation. Families need support services outside of rehabilitation settings to support physical activity for their children and overcome potential barriers.

PMID: [31088164](#)

#### **15. Home participation of children with and without cerebral palsy in Serbia: an exploratory study.**

Milićević M.

Disabil Rehabil. 2019 May 17:1-11. doi: 10.1080/09638288.2019.1610506. [Epub ahead of print]

**PURPOSE:** This cross-sectional study explored home participation of children with and without cerebral palsy aged 7-18 years and the effect of the environment on this participation. **METHOD:** A convenience sample of 110 children with cerebral palsy (55% males; mean age 12.7 years) and 134 children without cerebral palsy (49% males; mean age 12.0 years) was included. Parents completed the Participation and Environment Measure for Children and Youth. Mann-Whitney U-test,  $\chi^2$  tests and radar plots were used to analyze item-level differences between two groups. Participation of children with cerebral palsy was analyzed subsequently in relation to their functional limitations using the Spearman's rank correlation. **RESULTS:** Children with cerebral palsy participated in home activities less than children without cerebral palsy did, as perceived by their parents. The least differences were observed in activities that typically did not require much physical engagement. Number of activities done at home and the involvement level mostly correlated with fine manual and intellectual functioning. Barriers included physical layout, factors related to the activity (physical and cognitive demands), and limited resources (services, information, money). **CONCLUSIONS:** It is important to understand the uniqueness of each home environment in order to enhance participation of children with cerebral palsy in home setting. **IMPLICATIONS FOR REHABILITATION** The child's relationships with family members, social demands of activities and attitudes and actions of others, as supportive factors, should be considered by professionals to facilitate home participation. There is the need to develop strategies to facilitate children's independence in order to optimize participation outcomes in home-based activities. Differences identified in this study may assist professionals in the design of a context that improves home participation of children with cerebral palsy.

PMID: [31099275](#)

#### **16. Maternal Noninfectious Fever Enhances Cell Proliferation and Microglial Activation in the Neonatal Rat Dentate Gyrus.**

Pancaró C, Boulanger-Bertolus J, Segal S, Watson CJ, St Charles I, Mashour GA, Marchand JE.

Anesth Analg. 2019 Jun;128(6):1190-1198. doi: 10.1213/ANE.0000000000004051.

**BACKGROUND:** Fever and increased maternal interleukin-6 (IL-6) plasma levels in labor are associated with an increased risk of adverse events in offspring, including neonatal seizures, cerebral palsy, and low intelligence scores at school age. However, the neural changes in the neonate that might mediate the adverse effects of maternal noninfectious fever are not fully characterized. This study was designed to test the hypothesis that induced maternal noninfectious fever alters neonatal neural progenitor cell proliferation and enhances microglial activation in the rat dentate gyrus of the hippocampus. **METHODS:** Systemic vehicle or IL-6 was given 3 times to near-term pregnant rats ( $n = 7/\text{group}$ ) every 90 minutes, and maternal core temperature was recorded. Neonatal brains were processed and analyzed for dentate gyrus cell proliferation (using Ki-67,  $n = 10/\text{group}$ , and glial fibrillary acidic protein,  $n = 6/\text{group}$ ) and resident microglia activation (using ionized calcium-binding adaptor protein-1 [Iba-1],  $n = 6/\text{group}$ ). In separate studies, the authors assessed microglia proliferation using Ki-67/Iba-1 costaining ( $n = 5/\text{group}$ ). **RESULTS:** Compared to controls, exposure to IL-6 resulted in significant maternal temperature increase [mean temperature difference  $0.558^{\circ}\text{C}$  (95% CI, 0.417-0.698;  $P < .0001$ )]. Following maternal IL-6, Ki-67 cell proliferation in the dentate gyrus was 55 % higher in neonates whose mother received IL-6 ( $38.8 \pm 9.2$ ) compared with those that received vehicle ( $25.1 \pm 7.8$ ); mean difference 13.7 (95% CI, 5.68-21.71); ( $P = .0021$ ). Glial fibrillary acidic protein cell proliferation was 40% higher in the neonatal dentate gyrus whose mother received IL-6 when compared to controls ( $713 \pm 85.52$  vs  $500 \pm 115$ ); mean difference 212 (95% CI, 82.2-343.4); ( $P = .004$ ). Resident microglial activation was 90% higher in the dentate gyrus of neonates whose mother received IL-6 when compared to controls ( $71.8 \pm 9.3$  vs  $37.8 \pm 5.95$ ); mean Iba-1 in stained cells was significantly different between IL-6 and vehicle groups 34 (95% CI, 23.94-44.05); ( $P < .0001$ ). Proliferating microglia, determined by the colocalization of Ki-67 and Iba-1, were not different in the vehicle ( $8.8 \% \pm 3.19 \%$ ) and the IL-6 ( $5.6 \% \pm 2.3 \%$ ) groups (mean difference 3.2% (95% CI, -0.8-7.25) ( $P = .1063$ ). **CONCLUSIONS:** IL-6 is sufficient to induce maternal systemic temperature increases in near-term pregnant rats as well as neuronal, glial, and neuroinflammatory changes in the dentate gyrus of the neonatal hippocampus. These alterations might disrupt fetal neurodevelopment during a vulnerable period.

PMID: [31094787](#)

### 17. Mortality in children with cerebral palsy in rural Bangladesh: a population-based surveillance study.

Jahan I, Karim T, Das MC, Muhit M, McIntyre S, Smithers-Sheedy H, Badawi N, Khandaker G.

Dev Med Child Neurol. 2019 May 12. doi: 10.1111/dmcn.14256. [Epub ahead of print]

**AIM:** To determine the mortality rate, immediate cause of death (CoD), and predictors of death in children with cerebral palsy (CP) in rural Bangladesh. **METHOD:** We carried out a prospective population-based surveillance study of children with CP aged 0 to 18 years registered with the Bangladesh Cerebral Palsy Register (BCPR) between January 2015 and December 2016, with subsequent follow-up until December 2017. Verbal autopsy was applied to assign immediate CoD. Crude mortality rates, hazard ratios of death, and survival probabilities were estimated. **RESULTS:** Twenty-nine of the 678 children in the BCPR died during the study period, resulting in a crude mortality rate of 19.5 per 1000 person-years of observation (total follow-up duration 1486.8 person-years; mean 2y [standard deviation 6mo]). The leading immediate CoD was meningitis ( $n=9$ ) and pneumonia ( $n=8$ ). Survival probability and hazard ratio of death was significantly associated with age, Gross Motor Functional Classification System level, and associated impairments. Severe underweight and/or severe stunting was significantly overrepresented among deceased children than others in the cohort ( $p<0.05$ ) when compared with the World Health Organization reference population. **INTERPRETATION:** The majority of deaths were due to potentially preventable causes. The life expectancy of these children could have been extended by ensuring primary healthcare and nutritional supplementation. **WHAT THIS PAPER ADDS:** Mortality rate in children with cerebral palsy (CP) in rural Bangladesh is 19.5 per 1000 person-years. The majority of children with CP died from potentially preventable and treatable conditions. Motor severity, associated impairments, and malnutrition make children with CP vulnerable to premature death in rural Bangladesh.

PMID: [31081134](#)

## Prevention and Cure

### 18. The role of magnesium sulfate (MgSO<sub>4</sub>) in fetal neuroprotection.

Adrianes Bachnas M, Ilham Aldika Akbar M, Gumilar Dachlan E, Dekker G.

J Matern Fetal Neonatal Med. 2019 May 15:1-361. doi: 10.1080/14767058.2019.1619688. [Epub ahead of print]

Prevention of neurologic disability associated with preterm birth is one of the major challenges in current perinatal medicine. Magnesium sulfate (MgSO<sub>4</sub>), the focus of this review has been proposed as major step forward for that matter. MgSO<sub>4</sub> is easily accessible, cheap and has been proposed as a mandatory part of the management of inevitable preterm birth. The results of the various RCT's on the use of MgSO<sub>4</sub> for neuroprotection has been the subject of many systematic reviews, other studies focused on dosing schedules, side effects and only a few focused on exploring magnesium's mechanism of action. Meanwhile, many guidelines worldwide have plugged MgSO<sub>4</sub> as an essential ingredient of daily best practice when managing inevitable preterm birth because it has been shown to reduce the risk of severe neurologic deficit, in particular, cerebral palsy in appropriately selected patients. The more premature, the greater benefit associated with the use of antenatal MgSO<sub>4</sub>. The dose of 4 g given intravenously 15 minutes continued by 1 g/h until maximum 24 hours and minimum for 4 hours is the standard regimen proposed in most guidelines. It should be noted however that a recent study found that a total dose of 64 g was associated with the maximum protective effect. Only the protocol used by the largest RCT, the BEAM trial, with a loading dose of 6 g initially followed by a 2-g/h maintenance dose, if continued for 24 hours would give a total dose over 50 g. Other studies report on an increased risk of neonatal death with these high doses. Several studies expressed concerns about the risk of serious side effects for both mother and neonate. The results from the systematic review showed that the most commonly used dosage, 4 g bolus continued by 1 g/h maintenance, did not increase neonatal mortality and other suspected neonatal complication such as neonatal asphyxia, spontaneous intestinal perforation, necrotizing enterocolitis, and feeding intolerance. Giving a single bolus injection of 4 g MgSO<sub>4</sub> for stimulating BDNF production in highly "suspicious" preterm labor, and 4 g again when preterm birth become inevitable may be best from a safety perspective and also appears to have a stronger rationale.

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### **19. Stem cell therapy for preventing neonatal diseases in the 21st century: Current understanding and challenges.**

Nitkin CR, Rajasingh J, Pisano C, Besner GE, Th  baud B, Sampath V.

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Diseases of the preterm newborn such as bronchopulmonary dysplasia, necrotizing enterocolitis, cerebral palsy, and hypoxic-ischemic encephalopathy continue to be major causes of infant mortality and long-term morbidity. Effective therapies for the prevention or treatment for these conditions are still lacking as recent clinical trials have shown modest or no benefit. Stem cell therapy is rapidly emerging as a novel therapeutic tool for several neonatal diseases with encouraging pre-clinical results that hold promise for clinical translation. However, there are a number of unanswered questions and facets to the development of stem cell therapy as a clinical intervention. There is much work to be done to fully elucidate the mechanisms by which stem cell therapy is effective (e.g., anti-inflammatory versus pro-angiogenic), identifying important paracrine mediators, and determining the timing and type of therapy (e.g., cellular versus secretomes), as well as patient characteristics that are ideal. Importantly, the interaction between stem cell therapy and current, standard-of-care interventions is nearly completely unknown. In this review, we will focus predominantly on the use of mesenchymal stromal cells for neonatal diseases, highlighting the promises and challenges in clinical translation towards preventing neonatal diseases in the 21st century.

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