Cerebral palsy research news

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Interventions and Management

1. Comparing the effects of modified constraint-induced movement therapy and bimanual training in children with hemiplegic cerebral palsy mainstreamed in regular school: A randomized controlled study
Hasan Bingöl, Mintaze Kerem Günel

Arch Pediatr. 2022 Jan 14;S0929-693X(21)00244-X. doi: 10.1016/j.arcped.2021.11.017. Online ahead of print.

Purpose: The aim of this study was to compare the effects of modified constraint-induced movement therapy (mCIMT) and bimanual training (BIT) based on the International Classification of Functioning, Disability, and Health, Children and Youth (ICF-CY) conceptual framework. Research method: A total of 32 children (mean age 10.43 years [SD 2.9 years]; 15 girls, 17 boys) whose functional motor and communication levels, according to the Manual Ability Classification System, Gross Motor Function Classification System, and Communication Function Classification System, changed between level I and III were randomly distributed to one of the mCIMT or BIT groups with equivalent dosing frequencies and intensities (10 weeks, 3 days/week, 2.5 h/day). Upper extremity body function outcomes (handheld dynamometer), activity outcomes (Quality of Upper Extremity Skills Test, The Children's Hand-use Experience Questionnaire, ABILHAND-Kids, Pediatric Upper Extremity Motor Activity Log), and participation outcomes (Child and Adolescent Scale of Participation) were assessed before and after treatment, and at 16 weeks postintervention. The clinical trial number of the study is NCT04577391. Results: mCIMT resulted in more significant improvements in all outcomes than BIT at the immediate postintervention period (T2), which were maintained in the mCIMT group throughout the 16-week postintervention period ($p<0.001$; dmCIMT > dBIT). Conclusion: The potential advantage of mCIMT versus BIT is the larger short-term effect sizes (ESs) and the more sustainable improvements.

PMID: 35039189

2. Development of a standards-based phenotype model for gross motor function to support learning health systems in pediatric rehabilitation
Nikolas Koscielniak, Gretchen Piatt, Charles Friedman, Alexandra Vinson, Rachel Richesson, Carole Tucker

Learn Health Syst. 2021 May 5;6(1):e10266. doi: 10.1002/lrh2.10266. eCollection 2022 Jan.

Introduction: Research and continuous quality improvement in pediatric rehabilitation settings require standardized data and a systematic approach to use these data. Methods: We systematically examined pediatric data concepts from a pediatric learning network to determine capacity for capturing gross motor function (GMF) for children with Cerebral Palsy (CP) as a

demonstration for enabling infrastructure for research and quality improvement activities of an LHS. We used an iterative approach to construct phenotype models of GMF from standardized data element concepts based on case definitions from the Gross Motor Function Classification System (GMFCS). Data concepts were selected using a theory and expert-informed process and resulted in the construction of four phenotype models of GMF: an overall model and three classes corresponding to deviations in GMF for CP populations. Results: Sixty five data element concepts were identified for the overall GMF phenotype model. The 65 data elements correspond to 20 variables and logic statements that instantiate membership into one of three clinically meaningful classes of GMF. Data element concepts and variables are organized into five domains relevant to modeling GMF: Neurologic Function, Mobility Performance, Activity Performance, Motor Performance, and Device Use. Conclusion: Our experience provides an approach for organizations to leverage existing data for care improvement and research in other conditions. This is the first consensus-based and theory-driven specification of data elements and logic to support identification and labeling of GMF in patients for measuring improvements in care or the impact of new treatments. More research is needed to validate this phenotype model and the extent that these data differentiate between classes of GMF to support various LHS activities.

PMID: 35036550

3. Epidural Analgesia Versus Lumbar Plexus Blockade After Hip Reconstruction Surgery in Children With Cerebral Palsy and Intrathecal Baclofen Pumps: A Comparison of Safety and Efficacy
Aneesh V Samineni, Susan E Eklund, Patricia E Miller, Kristin Buxton, Brian D Snyder, Travis H Matheney, Colyn J Watkins, Scellig S D Stone, Walid Alrayashi, Roland Brusseau, Benjamin J Shore

J Pediatr Orthop. 2022 Jan 20. doi: 10.1097/BPO.0000000000002056. Online ahead of print.

Background: Epidural analgesia is commonly used for pain control after reconstructive hip surgery, but its use is controversial in the presence of an intrathecal baclofen pump (ITB). The purpose of this retrospective study was to investigate the rate of serious anesthetic and postoperative complications as well as the efficacy of epidural analgesia compared with lumbar plexus blocks (LPBs) for pain management after neuromuscular hip reconstruction in children with cerebral palsy (CP) and ITB. Methods: Pediatric patients with CP and ITB undergoing hip reconstructive surgery from 2010 to 2019 were retrospectively identified. Patients receiving epidural analgesia were compared with those receiving LPB. Morphine milligram equivalents per kilogram were used as a surrogate measure for pain-related outcomes, as pain scores were reported with wide ranges (eg, 0 to 5/10), making it unfeasible to compare them across the cohort. Postoperative complications were graded using the modified Clavien-Dindo classification. Results: Forty-four patients (26/44, 59% male) underwent surgery at an average age of 10.3 years (SD=3.4 y, range: 4 to 17 y). The majority utilized LPB (28/44, 64%) while the remaining utilized epidural (16/44, 36%). There were no differences in rates of serious complications, including no cases of ITB malfunction, damage, or infection. During the immediate postoperative course, patients who received LPB had higher morphine milligram equivalents per kilogram requirements than patients who received epidural analgesia. Conclusions: In patients with CP undergoing hip reconstruction surgery with an ITB in situ, epidural anesthesia was associated with improved analgesia compared with LPB analgesia, with a similar risk for adverse outcomes. Epidural catheters placed using image-guided insertion techniques can avoid damage to the ITB catheter while providing effective postoperative pain control without increasing rates of complications in this complex patient population.

PMID: 35051954

4. A new framework for analysis of three-dimensional shape and architecture of human skeletal muscles from in vivo imaging data
Bart Bolsterlee

J Appl Physiol (1985). 2022 Jan 20. doi: 10.1152/japplphysiol.00638.2021. Online ahead of print.

A new framework is presented for comprehensive analysis of the three-dimensional shape and architecture of human skeletal muscles from magnetic resonance and diffusion tensor imaging data. The framework comprises three key features: (1) identification of points on the surface of and inside a muscle that have a correspondence to points on and inside another muscle, (2) reconstruction of average muscle shape and average muscle fibre orientations, and (3) utilization of data on between-muscle variation to visualize and make statistical inferences about changes or differences in muscle shape and architecture. The general use of the framework is demonstrated by its application to three case studies. Analysis of data obtained before and after eight weeks of strength training revealed there was little regional variation in hypertrophy of the vastus medialis and vastus lateralis,

and no systematic change in pennation angle. Analysis of passive muscle lengthening revealed heterogeneous changes in shape of the medial gastrocnemius, and confirmed the ability of the methods to detect subtle changes in muscle fibre orientation. Analysis of the medial gastrocnemius of children with unilateral cerebral palsy showed that muscles in the more-affected limb were shorter, thinner and less wide than muscles in the less-affected limb, and had slightly more pennate muscle fibres in the central and proximal part of the muscle. Amongst other applications, the framework can be used to explore the mechanics of muscle contraction, investigate adaptations of muscle architecture, build anatomically realistic computational models of skeletal muscles, and compare muscle shape and architecture between species.

PMID: 35050794

5. The effect of prolonged walking on muscle fatigue and neuromuscular control in children with cerebral palsy
Sanne Ettema, Laura M Oudenhoven, Karin Roeleveld, Annemieke I Buizer, Marjolein M van der Krogt

Gait Posture. 2022 Jan 7;93:7-13. doi: 10.1016/j.gaitpost.2022.01.004. Online ahead of print.

Background: Muscle fatigue of the lower limbs is considered a main contributor to the perceived fatigue in children with cerebral palsy (CP) and is expected to occur during prolonged walking. In adults without disabilities, muscle fatigue has been proposed to be associated with adaptations in complexity of neuromuscular control. Research question: What are the effects of prolonged walking on signs of muscle fatigue and complexity of neuromuscular control in children with CP? Methods: Ten children with CP and fifteen typically developing (TD) children performed a standardised protocol on an instrumented treadmill consisting of three stages: six-minutes walking at preferred speed (6 MW), moderate-intensity walking (MIW, with two minutes at heart rate > 70% of predicted maximal heart rate) and four-minutes walking at preferred speed (post-MIW). Electromyography (EMG) data were analysed for eight muscles of one leg during three time periods: 6 MW-start, 6 MW-end and post-MIW. Signs of muscle fatigue were quantified as changes in EMG median frequency and EMG root mean square (RMS). Complexity of neuromuscular control was quantified by total variance accounted for by one synergy (tVAF1). Muscle coactivation was assessed for antagonistic muscle pairs. Results: EMG median frequency was decreased at 6 MW-end and post -MIW compared to 6 MW-start in children with CP ($p < 0.05$), but not in TD children. In both groups, EMG-RMS ($p < 0.01$) and muscle coactivation ($p < 0.01$) were decreased at 6 MW-end and post-MIW compared to 6 MW-start. tVAF1 decreased slightly at 6 MW-end and post-MIW compared to 6 MW-start in both groups ($p < 0.05$). Changes were most pronounced from 6 MW-start to 6 MW-end. Significance: Children with CP presented signs of muscle fatigue after prolonged walking, while no effects were found for TD. Both groups showed minimal changes in tVAF1, suggesting signs of muscle fatigue are not associated with changes in complexity of neuromuscular control.

PMID: 35042058

6. Physical activity intention and attendance behaviour in Finnish youth with cerebral palsy - results from a physical activity intervention: an application of the theory of planned behaviour
Alfredo Ruiz, Kwok Ng, Pauli Rintala, Kaisa Kaseva, Taija Finni

Review J Exerc Rehabil. 2021 Dec 27;17(6):370-378. doi: 10.12965/jer.2142588.294. eCollection 2021 Dec.

Physical activity is associated with better health in individuals with cerebral palsy (CP). Numerous physical activity interventions have been designed to promote physical activity among youth with CP. No previous studies have explored the factors contributing to the intention to participate and predicting attendance behaviour for these interventions. Using theory of planned behaviour (TPB), this study explored the prediction of physical activity intention and attendance behaviour in a physical activity intervention aiming to promote physical activity in a sample of young individuals with CP. Males with CP aged 9-21 years were asked to complete measures of attitude, subjective norms, perceived behavioural control and, intentions towards a physical activity intervention. Participants had no cognitive impairments to understand and follow instructions, were categorised into Gross Motor Function Classification System I-III, did not receive any specific lower limbs' medical treatment, or did not participate in a strength training program for lower limbs within 6 months before the study. Subjective norms were found to be the only significant predictor of intention, accounting for 83% of variance in intention. Intention and perceived behaviour control were found to be a nonsignificant predictor of attendance behaviour in youth with CP. The results show that TPB is a relevant tool in the prediction of intention towards a physical activity intervention in Finnish youth with CP.

PMID: 35036385

7. The effects of sling exercise program on balance and body activities in children with spastic cerebral palsy
Eun-Ju Song, Eun-Jung Lee, Hae-Yeon Kwon

J Exerc Rehabil. 2021 Dec 27;17(6):410-417. doi: 10.12965/jer.2142608.304. eCollection 2021 Dec.

The purpose of this study was to investigate the static and dynamic balance and body activities after administering a trunk stability exercise program using a sling for children with spastic cerebral palsy of Gross Motor Function Classification System (GMFCS) levels III-IV. This study was conducted based on a quasi-experimental study design. Six of the study participants were assigned to the control group and six were assigned to the experimental group using simple random sampling. Both groups underwent a double-blind clinical trial study in which exercise therapy was performed for 40 min twice a week for 8 weeks. The experimental group underwent the sling exercise program and the control group underwent neuro-developmental treatment. The results showed that static and dynamic balance were significantly different before and after intervention in both the experimental and control groups ($P<0.05$), and there was also a statistically significant difference between the two groups ($P<0.05$). Gross motor function and activities of daily life showed significant improvement before and after intervention in the experimental group ($P<0.05$), but there was no statistically significant difference in the control group ($P<0.05$). There was a statistically significant difference between the two groups ($P<0.05$). Therefore, the sling exercise program can be used as an effective treatment for improving balance and physical activity in children with cerebral palsy of GMFCS levels III-IV who have difficulty walking. In addition, such exercise will have a positive impact on the independence of such children and help them to participate in social activities.

PMID: 35036390

8. Effects of modified pilates on trunk, postural control, gait and balance in children with cerebral palsy: a single-blinded randomized controlled study
Hatice Adıguzel, Bulent Elbasan

Acta Neurol Belg. 2022 Jan 18. doi: 10.1007/s13760-021-01845-5. Online ahead of print.

Objective: This study aimed to determine the effects of modified pilates exercises (MPE) and neurodevelopmental therapy (NDT) on trunk, postural control, gait, and balance in children with cerebral palsy (CP). Methods: 18 children with CP between gross motor function classification system (GMFCS) I and III were randomized into two groups as study (Group A, MPE) and control (Group B, NDT). Physiotherapy (PT) took place 2 days a week for 8 weeks. Trunk control measurement scale (TCMS), seated postural control measurement (SPCM), pediatric reach test (PRT), pediatric berg balance measurement (PBBM), 6 minute walking test (6MWT), observational gait scale (OGS), core stability performance measurements, and muscle strength tests were performed. Results: Mean age of group A ($n = 9$) was 9 ± 1.58 years, and group B ($n = 9$) was 10 ± 2.73 years. Significant differences were found in the SPCM posture ($p = 0.000$), TCMS ($p = 0.004$), OGS right ($p = 0.019$) and left ($p = 0.001$) scores, abdominal fatigue test (AFT) ($p = 0.014$), modified side bridge (MSBT) test (right $p = 0.04$, left $p = 0.031$), pressure biofeedback unit test (PBU) ($p = 0.024$), and sit-ups test (SUT) ($p = 0.011$) in favor of group A. According to the initial measurements of the percentage changes of the tests, significantly difference was found in PBBMR ($p = 0.001$), PBBML ($p = 0.000$), SPCM posture (0.001), TCMS (0.000), MBSTET (0.000), MSBT left ($p = 0.034$), AFT ($p = 0.002$), PBU ($p = 0.015$), SUT ($p = 0.000$), MPUT ($p = 0.018$), and OGS right ($p = 0.029$) in favor of group A. Conclusion: The results revealed that MPEs in children with CP positively affects trunk, postural control, gait, and balance compared to NDT. It is concluded that MPE can be used as an alternative treatment approach in children with CP.

PMID: 35040072

9. Measuring Effects on Pain and Quality of Life after Abobotulinum Toxin A Injections in Children with Cerebral Palsy
Christian Wong, Ian Westphall, Josephine Sandahl Michelsen

Toxins (Basel). 2022 Jan 5;14(1):43. doi: 10.3390/toxins14010043.

Sixty-seven percent of children with cerebral palsy (CCP) experience pain. Pain is closely interrelated to diminished quality of

life. Despite this, pain is an overlooked and undertreated clinical problem. The objective of this study was to examine the analgesic effect of a single lower extremity intramuscular injection of Abobotulinum toxin A/Dysport in CCP. Twenty-five CCP with at least moderate pain (r-FLACC ≥ 4) during passive range of motion were included. Localized pain and pain in everyday living were measured by r-FLACC and the Paediatric Pain Profile (PPP), respectively. Functional improvements were evaluated by the goal attainment scale (SMART GAS). Quality of life was evaluated by either the CPCHILD or the CP-QOL. The subjects were evaluated at baseline before injection, then after 4, 12, and 28 weeks. Twenty-two subjects had a significant mean and maximum localized pain reduction ($p < 0.001$) at four weeks post-treatment in 96% (21/22). The reduction was maintained at 12 (19/19) and 28 weeks (12/15). Daily pain evaluated by the PPP was significantly reduced and functional SMART GAS goals were significantly achieved from 4 to 28 weeks. Quality of life improved significantly at four weeks (CPCHILD). Significant functional gains and localized and daily pain reduction were seen from 4 to 28 weeks.

PMID: 35051020

10. Cognitive Orientation to Daily Occupational Performance (CO-OP) in Children with Cerebral Palsy: A Systematic Review with Meta-analysis : L'approcheCO-OP auprès des enfants atteints de paralysie cérébrale: revue systématique et méta-analyse
Meysam Roostaei, Hamid Dalvand, Mehdi Rassafiani, Greg Kelly, Bahman Razi

Can J Occup Ther. 2022 Jan 19;84174211066651. doi: 10.1177/00084174211066651. Online ahead of print.

Cognitive orientation to daily occupational performance (CO-OP) is a client-centered treatment approach that was developed in the 1990s by occupational therapists. Purpose: Exploring current evidence about the effectiveness of CO-OP on children with cerebral palsy (CP). Method: Major electronic databases were searched. A narrative synthesis of current literature and meta-analyses on randomized control trials (RCTs) were conducted on changes in occupational performance. Findings: Seven studies with 103 participants were included. Four studies were RCTs with moderate levels of evidence, and three studies had single-subject designs. Although beneficial effects of CO-OP on goal achievement and transferring learned skills were reported, meta-analyses showed that CO-OP had no significant effect on the performance (WMD = 1.52, 95% CI = -1.58 to 4.63, P = .33) and satisfaction domains (WMD = 1.71, 95% CI = -1.14 to 4.57, P = .24) of Canadian Occupational Performance Measure scores compared to alternative interventions. Implications: CO-OP improves occupational performance but not more than alternative interventions. Results are inconclusive due to small sample sizes and heterogeneity of alternative interventions and participants. Therefore, research with a larger number of participants with sound RCT methods is needed.

PMID: 35044278

11. Cerebral Palsy in Child Neurology and Neurodevelopmental Disabilities Training: An Unmet Need
Jenny L Wilson, Young-Min Kim, Jennifer A O'Malley, Rose Gelineau-Morel, Laura Gilbert, Jennifer M Bain, Bhooma R Aravamuthan

J Child Neurol. 2022 Jan 17;8830738211072711. doi: 10.1177/08830738211072711. Online ahead of print.

Background: Cerebral palsy (CP) is the most common cause of childhood motor disability. However, there is limited guidance on training of child neurologists and neurodevelopmental disability specialists in the care of individuals with cerebral palsy. We sought to determine training program directors' impressions of the importance and adequacy of training in the diagnosis and management of cerebral palsy. Methods: In this cross-sectional study, all 82 child neurology and neurodevelopmental disability program directors were asked to complete a survey querying program characteristics, aspects of training in cerebral palsy, importance of cerebral palsy training, and perceived competence at graduation in cerebral palsy care. Results: There were 35 responses (43% response rate). Nearly all program directors (91%) reported "learning to diagnose cerebral palsy" as very important, and most (71%) felt that "learning to manage cerebral palsy" was very important. Although most program directors reported trainees to be very or extremely competent in cerebral palsy diagnosis (77%), only 43% of program directors felt that trainees were very or extremely competent in cerebral palsy management. Time spent with cerebral palsy faculty was associated with higher reported competence in cerebral palsy diagnosis (P = .03) and management (P < .01). The presence of a cerebral palsy clinic was associated with higher reported competence in cerebral palsy management (P = .03). Conclusions: Child neurology and neurodevelopmental disability program directors reported that training in cerebral palsy is important for residents; however, a significant proportion felt that residents were not very well prepared to manage cerebral palsy. The development of cerebral palsy curricula and exposure to cerebral palsy clinics may improve training, translating to better care

of individuals with cerebral palsy.

PMID: 35037781

12. Mortality, In-Hospital Morbidity, Care Practices, and 2-Year Outcomes for Extremely Preterm Infants in the US, 2013-2018

Edward F Bell, Susan R Hintz, Nellie I Hansen, Carla M Bann, Myra H Wyckoff, Sara B DeMauro, Michele C Walsh, Betty R Vohr, Barbara J Stoll, Waldemar A Carlo, Krisa P Van Meurs, Matthew A Rysavy, Ravi M Patel, Stephanie L Merhar, Pablo J Sánchez, Abbot R Laptook, Anna Maria Hibbs, C Michael Cotten, Carl T D'Angio, Sarah Winter, Janell Fuller, Abhik Das, Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

JAMA. 2022 Jan 18;327(3):248-263. doi: 10.1001/jama.2021.23580.

Importance: Despite improvement during recent decades, extremely preterm infants continue to contribute disproportionately to neonatal mortality and childhood morbidity. Objective: To review survival, in-hospital morbidities, care practices, and neurodevelopmental and functional outcomes at 22-26 months' corrected age for extremely preterm infants. Design, setting, and participants: Prospective registry for extremely preterm infants born at 19 US academic centers that are part of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. The study included 10 877 infants born at 22-28 weeks' gestational age between January 1, 2013, and December 31, 2018, including 2566 infants born before 27 weeks between January 1, 2013, and December 31, 2016, who completed follow-up assessments at 22-26 months' corrected age. The last assessment was completed on August 13, 2019. Outcomes were compared with a similar cohort of infants born in 2008-2012 adjusting for gestational age. Exposures: Extremely preterm birth. Main outcomes and measures: Survival and 12 in-hospital morbidities were assessed, including necrotizing enterocolitis, infection, intracranial hemorrhage, retinopathy of prematurity, and bronchopulmonary dysplasia. Infants were assessed at 22-26 months' corrected age for 12 health and functional outcomes, including neurodevelopment, cerebral palsy, vision, hearing, rehospitalizations, and need for assistive devices. Results: The 10 877 infants were 49.0% female and 51.0% male; 78.3% (8495/10848) survived to discharge, an increase from 76.0% in 2008-2012 (adjusted difference, 2.0%; 95% CI, 1.0%-2.9%). Survival to discharge was 10.9% (60/549) for live-born infants at 22 weeks and 94.0% (2267/2412) at 28 weeks. Survival among actively treated infants was 30.0% (60/200) at 22 weeks and 55.8% (535/958) at 23 weeks. All in-hospital morbidities were more likely among infants born at earlier gestational ages. Overall, 8.9% (890/9956) of infants had necrotizing enterocolitis, 2.4% (238/9957) had early-onset infection, 19.9% (1911/9610) had late-onset infection, 14.3% (1386/9705) had severe intracranial hemorrhage, 12.8% (1099/8585) had severe retinopathy of prematurity, and 8.0% (666/8305) had severe bronchopulmonary dysplasia. Among 2930 surviving infants with gestational ages of 22-26 weeks eligible for follow-up, 2566 (87.6%) were examined. By 2-year follow-up, 8.4% (214/2555) of children had moderate to severe cerebral palsy, 1.5% (38/2555) had bilateral blindness, 2.5% (64/2527) required hearing aids or cochlear implants, 49.9% (1277/2561) had been rehospitalized, and 15.4% (393/2560) required mobility aids or other supportive devices. Among 2458 fully evaluated infants, 48.7% (1198/2458) had no or mild neurodevelopmental impairment at follow-up, 29.3% (709/2419) had moderate neurodevelopmental impairment, and 21.2% (512/2419) had severe neurodevelopmental impairment. Conclusions and relevance: Among extremely preterm infants born in 2013-2018 and treated at 19 US academic medical centers, 78.3% survived to discharge, a significantly higher rate than for infants born in 2008-2012. Among infants born at less than 27 weeks' gestational age, rehospitalization and neurodevelopmental impairment were common at 2 years of age.

PMID: 35040888

13. Outcome Analysis of Severe Hyperbilirubinemia in Neonates Undergoing Exchange Transfusion

Ruili Zhang, Wenqing Kang, Xiaoli Zhang, Lina Shi, Rui Li, Yanmei Zhao, Jing Zhang, Xiao Yuan, Shasha Liu, Wenhua Li, Falin Xu, Xiuyong Cheng, Changlian Zhu

Neuropediatrics. 2022 Jan 17. doi: 10.1055/s-0041-1742156. Online ahead of print.

Objective: Severe neonatal hyperbilirubinemia can cause neurological disability or mortality if not effectively managed. Exchange transfusion (ET) is an efficient treatment to prevent bilirubin neurotoxicity. The purpose of this study was to evaluate outcomes in severe neonatal hyperbilirubinemia with ET and to identify the potential risk factors for poor outcomes. Methods: Newborns of ≥28 weeks of gestational age with severe hyperbilirubinemia who underwent ET from January 2015 to August 2019 were included. Demographic data were recorded and analyzed according to follow-up outcomes at 12 months of corrected

age. Poor outcomes were defined as death due to bilirubin encephalopathy or survival with at least one of the following complications: cerebral palsy, psychomotor retardation (psychomotor developmental index < 70), mental retardation (mental developmental index < 70), or hearing impairment. Results: A total of 524 infants were eligible for recruitment to the study, and 62 infants were lost to follow-up. The outcome data from 462 infants were used for grouping analysis, of which 398 cases (86.1%) had normal outcomes and 64 cases (13.9%) suffered poor outcomes. Bivariate logistic regression analysis showed that peak total serum bilirubin (TSB) (odds ratio [OR] = 1.011, 95% confidence interval [CI] = 1.008-1.015, p = 0.000) and sepsis (OR = 4.352, 95% CI = 2.013-9.409, p < 0.001) were associated with poor outcomes of hyperbilirubinemia. Receiver operator characteristic curve analysis showed that peak TSB ≥452.9 μmol/L could predict poor outcomes of severe hyperbilirubinemia. Conclusion: Peak TSB and sepsis were associated with poor outcomes in infants with severe hyperbilirubinemia, and peak TSB ≥452.9 μmol/L could predict poor outcomes.

PMID: 35038754

14. Recent Investigations on Neurotransmitters' Role in Acute White Matter Injury of Perinatal Glia and Pharmacotherapies-Glia Dynamics in Stem Cell Therapy
Narasimha M Beeraka, P R Hemanth Vikram, M V Greeshma, Chinnappa A Uthaiah, Tahani Huria, Junqi Liu, Pramod Kumar, Vladimir N Nikolenko, Kirill V Bulygin, Mikhail Y Sinelnikov, Olga Sukocheva, Ruitai Fan

Review Mol Neurobiol. 2022 Jan 18. doi: 10.1007/s12035-021-02700-7. Online ahead of print.

Periventricular leukomalacia (PVL) and cerebral palsy are two neurological disease conditions developed from the premyelinated white matter ischemic injury (WMI). The significant pathophysiology of these diseases is accompanied by the cognitive deficits due to the loss of function of glial cells and axons. White matter makes up 50% of the brain volume consisting of myelinated and non-myelinated axons, glia, blood vessels, optic nerves, and corpus callosum. Studies over the years have delineated the susceptibility of white matter towards ischemic injury especially during pregnancy (prenatal, perinatal) or immediately after child birth (postnatal). Impairment in membrane depolarization of neurons and glial cells by ischemia-invoked excitotoxicity is mediated through the overactivation of NMDA receptors or non-NMDA receptors by excessive glutamate influx, calcium, or ROS overload and has been some of the well-studied molecular mechanisms conducive to the injury of white matter. Expression of glutamate receptors (GluR) and transporters (GLT1, EACC1, and GST) has significant influence in glial and axonal-mediated injury of premyelinated white matter during PVL and cerebral palsy. Predominantly, the central premyelinated axons express extensive levels of functional NMDA GluR receptors to confer ischemic injury to premyelinated white matter which in turn invoke defects in neural plasticity. Several underlying molecular mechanisms are yet to be unraveled to delineate the complete pathophysiology of these prenatal neurological diseases for developing the novel therapeutic modalities to mitigate pathophysiology and premature mortality of newborn babies. In this review, we have substantially discussed the above multiple pathophysiological aspects of white matter injury along with glial dynamics, and the pharmacotherapies including recent insights into the application of MSCs as therapeutic modality in treating white matter injury.

PMID: 35041139

15. C-section of Preclinical Animal Model of Chorioamnionitis Triggered by Group B Streptococcus (GBS)
Taghreed A Ayash, Seline Y Vancolen, Marie-Julie Allard, Guillaume Sébire

J Vis Exp. 2021 Dec 29;(178). doi: 10.3791/63221.

Group B Streptococcus (GBS) is one of the most common bacteria isolated during human pregnancy. It is a leading cause of placental infection/inflammation, termed chorioamnionitis. Chorioamnionitis exposes the developing fetus to a high risk of organ injuries, perinatal morbidity, and mortality, as well as life-long neurobehavioral impairments and other non-neurological developmental issues. The two most frequent subtypes of GBS isolates from maternal and fetal tissues are serotypes Ia (13%-23%) and III (25%-53%). Our lab has developed and characterized a rat model of GBS-induced chorioamnionitis to study subsequent impacts on the central nervous system of the developing fetus and to understand underlying mechanistic aspects. This article presents the design as well as uses of the preclinical rat model, which closely reproduces the hallmark of GBS-induced chorioamnionitis in humans. This article aims to help scientists reproduce the experimental design as well as to provide support through examples of troubleshooting. The present model may also contribute to potential discoveries through uncovering causes, mechanisms, and novel therapeutic avenues, which remain unsettled in many developmental impairments arising from chorioamnionitis. Furthermore, the use of this model may be extended to the studies of perinatal non-neurological

common and severe morbidities affecting, for instance, the retina, bowel, lung, and kidney. The main interest of this research is in the field of GBS-induced fetal neurodevelopmental impairments such as cerebral palsy (CP), attention deficit hyperactivity disorder (ADHD), and autism spectrum disorder (ASD). The rationale supporting this model is presented in this article, followed by procedures and results.

PMID: 35037652