# Cerebral palsy research news

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## Interventions and Management

**1. Correction: Efficacy of integrating a semi-immersive virtual device in the HABIT-ILE intervention for children with unilateral cerebral palsy: a non-inferiority randomized controlled trial**

G Saussez, R Bailly, R Araneda, J Paradis, D Ebner-Karestinos, A Klöcker, E S Sogbossi, I Riquelme, S Brochard, Y Bleyenheuft

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No abstract available

Erratum for
Efficacy of integrating a semi-immersive virtual device in the HABIT-ILE intervention for children with unilateral cerebral palsy: a non-inferiority randomized controlled trial.
Saussez G, Bailly R, Araneda R, Paradis J, Ebner-Karestinos D, Klöcker A, Sogbossi ES, Riquelme I, Brochard S, Bleyenheuft Y.
J Neuroeng Rehabil. 2023 Jul 29;20(1):98. doi: 10.1186/s12984-023-01218-4.

PMID: 38326808

**2. Effect of the Dynamic Orthotic Garment on Postural Control, and Endurance in Children with Spastic Diplegic Cerebral Palsy: A Randomized Controlled Trial**

Hatem A Emara, Ahmed H Al-Johany, Osama A Khaled, Abdullah M Al-Shenqiti, Abdul Rahman H Ali, Marwan M Aljohani, Eman Sobh

J Multidiscip Healthc. 2024 Jan 30:17:419-428. doi: 10.2147/JMDH.S438474. eCollection 2024.

Purpose: To investigate the effect of dynamic orthotic garments (Thera togs) on foot pressure distribution, postural control, and endurance in children with spastic diplegic CP. Patients and methods: This is a single-blind randomized controlled clinical trial involving 34 (8-10 years) with spastic diplegic CP. The control group received conventional physical therapy (CPT), whereas the study group received CPT in addition to wearing TheraTogs. We recorded foot pressure distribution, trunk control measurement scale, trunk position sense, Pediatric Berg Balance Scale (PBS), and six-minute walking distance (6MWD). Results: Both groups showed improvement. The study group had significant improvement in foot pressure distribution (p-value 0.003, 0.001, <0.001 for forefoot, midfoot, and rearfoot mean pressures respectively, and 0.005, <0.001, and 0.005 for forefoot, midfoot, and rearfoot peak pressures respectively), Pediatric balance scale, The trunk control measurement scale, and Trunk position sense (p-value < 0.001) and six-minute walking distance (p-value 0.029). Our data suggest that adding TheraTogs to conventional physiotherapy improves foot pressure, postural control, and endurance in children with spastic diplegic cerebral palsy. Conclusion: Both TheraTogs and conventional physical therapy corrected foot pressure distribution, trunk control, improved balance, and increased 6MWD in children with spastic diplegic CP but the improvement was more significant in TheraTogs group. Clinical trial registration: NCT05271149.

PMID: 38314010

**3. Correlations between Trunk Control and Balance in Children with Bilateral Spastic Cerebral Palsy**

Sapna Tiwari, Pratiksha Tilak Rao, Suruliraj Karthikbabu

Percept Mot Skills. 2024 Feb 5:315125231226297. doi: 10.1177/00315125231226297. Online ahead of print.

Impairments of postural responses are a salient feature of children with cerebral palsy (CP). While the systems approach describes balance in seven components, the relationship between trunk control and balance in children with CP has not been previously examined with all seven of these components. In this study, we aimed to identify correlations between trunk control and all seven systems approach balance components in children with bilateral spastic CP. Our participants were 30 children (M age = 11.83, SD = 2.32 years) with CP having a Gross Motor Function Classification System level ranging from I to III. We assessed trunk control with the Trunk Control Measurement Scale, including static and dynamic balance (selective voluntary control and reaching). Balance in standing was assessed using Kids-Mini-BESTest involving four domains: anticipatory, reactive, sensory orientation and stability in gait. We used Spearman's rank correlations to correlate trunk control and balance, and we obtained a moderate correlation between the trunk control measurement scale and the Kids-Mini-BESTest in children with both bilateral spastic CP ($rs = .618$, $p < .001$) and spastic diplegic CP ($rs = .52$, $p = .02$). Analysis of the correlations between separate domains of the Kids-Mini-BESTest and the trunk control measurement scale subscales revealed moderate correlations between the static sitting balance subscale and all four domains of the Kids-Mini-BESTest. The dynamic selective motor control subscale of the trunk control measurement scale moderately correlated with the anticipatory domain of the Kids-Mini-BESTest. The dynamic reaching subscale also correlated moderately with anticipatory and stability in gait domains. This correlation was statistically significant in the 13 to 17-year-old age group and was strong among females, whereas the correlation was moderate in males. Trunk control was moderately associated with balance considering all the systems theory components of balance in children with bilateral spastic cerebral palsy.

PMID: 38315610

**4. What Do We Really Know About the Natural History of Spastic Hip Dysplasia and Pain in Total-involvement Cerebral Palsy? A Systematic Review**

Alexa J Karkenny, Catherine Mackey, Melinda S Sharkey

J Pediatr Orthop. 2024 Feb 7. doi: 10.1097/BPO.0000000000002639. Online ahead of print.

Background: Hip surveillance protocols and surgery for spastic hip dysplasia have become standard of care for children with cerebral palsy (CP) out of concern for long-term sequelae, including pain. It is unclear if available data support that spastic hip dysplasia/dislocation independently correlates with pain in total-involvement CP. A better understanding of this correlation may help guide decision-making for these medically complex patients. Methods: We undertook a systematic literature review to assess published data on the association of spastic hip dysplasia and pain in total-involvement CP using PubMed (which includes the MedLine databases) and EMBASE databases. A total of 114 English-language articles were identified. Fifteen articles met the inclusion criteria and were evaluated using the PRISMA guidelines for systematic reviews. Results: Of 15 articles that specifically assessed the association of spastic hip dysplasia and pain, 5 articles provided strong evidence per our criteria regarding the correlation of pain and spastic hip dysplasia. All 5 articles described the severity of CP in their studied population, radiographically defined hip displacement, included a control group, and described how pain was assessed. Nevertheless, there was no standard classification of dysplasia between studies and the ages of patients and methods of pain determination varied. Four of the articles provided level III evidence and one provided level II evidence. Of these 5 articles with the strongest available evidence, data from 2 did not support a correlation between hip dysplasia and hip pain, 2 supported a correlation, and 1 was equivocal. Conclusions: Even the best available evidence on spastic hip dysplasia and pain reveals no consensus or conclusion on whether spastic hip dysplasia and dislocation in total-involvement CP is independently correlated with pain. Level of evidence: Level III-Prognostic study.

PMID: 38323400

**5. Selective dorsal rhizotomy and its effect on muscle force during walking: A comprehensive study**

Emiliano Pablo Ravera, Adam Rozumalski

J Biomech. 2024 Feb 1:164:111968. doi: 10.1016/j.jbiomech.2024.111968. Online ahead of print.

Selective dorsal rhizotomy (SDR) is commonly used to permanently reduce spasticity in children with cerebral palsy (CP). However, studies have yielded varying results regarding muscle strength and activity after SDR. Some studies indicate weakness or no changes, while a recent study using NMSK simulations demonstrates improvements in muscle forces during walking. These findings suggest that SDR may alleviate spasticity, reducing dynamic muscle constraints and enhancing muscle force without altering muscle activity during walking in children with CP. In this study, we combined NMSK simulations with

physical examinations to assess children with CP who underwent SDR, comparing them to well-matched peers who did not undergo the procedure. Each group (SDR and No-SDR) included 81 children, with pre- and post-SDR assessments. Both groups were well-matched in terms of demographics, clinical characteristics, and gait parameters. The results of the physical examination indicate that SDR significantly reduces spasticity without impacting muscle strength. Furthermore, our findings show no significant differences in gait deviation index improvements and walking speed between the two groups. Additionally, there were no statistically significant changes in muscle activity during walking before and after SDR for both groups. NMSK results demonstrate a significant increase in muscle force in the semimembranosus and calf muscles during walking, compared to children with CP who received other clinical treatments. Our findings confirm that although SDR does not significantly impact muscle strength compared to other treatments, it creates a more favorable dynamic environment for suboptimal muscle force production, which is essential for walking.

PMID: 38325195

**6. Understanding immunity and exercise in the context of cerebral palsy**

Tammy Strickland

Dev Med Child Neurol. 2024 Feb 8. doi: 10.1111/dmcn.15880. Online ahead of print.

No abstract available

PMID: 38332490

**7. Reliability, Knowledge Translation, and Implementability of the Spanish Version of the Hammersmith Infant Neurological Examination**

Álvaro Hidalgo-Robles, Javier Merino-Andrés, Ángel Luis Rodríguez-Fernández, Mónica Gutiérrez-Ortega, Irene León-Estrada, Maribel Ródenas-Martínez

Healthcare (Basel). 2024 Feb 1;12(3):380. doi: 10.3390/healthcare12030380.

Purpose. This study aimed to: (a) translate and cross-culturally adapt the Hammersmith Infant Neurological Examination (HINE) into Spanish; (b) evaluate its intra- and inter-examiner reliability; (c) support a knowledge translation and tool implementation program in early intervention; and (d) evaluate its reliability and implementation for professionals one year after receiving training. Materials and methods. The translation followed the World Health Organization's recommendations. Reliability was assessed in 25 infants aged between 3 and 15 months with identifiable risks of cerebral palsy (CP). The implementation was also evaluated by analyzing the reliability of professionals without previous experience of the tool by using a pre-survey and a follow-up survey one year after training. The survey covered aspects related to the use of early detection tools of CP and the use of HINE, including attitudes, opinions, and perceptions. Results. An excellent intra- and inter-examiner agreement was obtained for the total score of the HINE intra-class correlation coefficient (ICC = 0.98 in both indices). One year after training, the professionals also showed excellent reliability values (ICC = 0.99), as well as an increase in sensitization and skills in evidence-based practices for the early detection of "high risk" of CP. Conclusions. The Spanish version of HINE is a reliable measure for the neurological evaluation of "high risk" of CP and can be administered after standardized training and without costs to acquire the evaluation. This allows its accessible and widespread implementation in the clinical context.

PMID: 38338265

**8. Longitudinal assessment of brain lesions in children with cerebral palsy and association with motor functioning**

Olga Laporta-Hoyos, Simona Fiori, Kerstin Pannek, Alex M Pagnozzi, Robert S Ware, Roslyn N Boyd

Eur J Paediatr Neurol. 2024 Jan 28:49:27-34. doi: 10.1016/j.ejpn.2023.11.011. Online ahead of print.

Background: The semi-quantitative scale of structural brain Magnetic Resonance Imaging (sqMRI) is a valid and reliable measure of brain lesion extent in children with cerebral palsy (CP) >3-years. This system scores lesion burden for each major brain region. The sum of the scores gives a global score ranging from 0 to 48. Purpose: To investigate how sqMRI scores changed from infancy to school-age, and whether these were associated with lesion load, age at first assessment, and gross motor function and its changes. Materials and methods: Twenty-eight children with CP underwent MRI and motor (Gross Motor Function Measure-66; GMFM-66) assessments when <40-months and again when 8-12-years. We investigated whether (i) toddler/preschool-age sqMRI scores (Time 1) reflected school-age sqMRI scores (Time 2); (ii) temporal changes in sqMRI scores (Time 1-Time 2 difference) were related to the child's age at Time 1 and lesion extent; (iii) early or later sqMRI scores were associated with motor functioning; (iv) sqMRI scores' longitudinal changes were associated with motor changes. Results: Except for the corticosubcortical (grey-matter only) layers, sqMRI scores were significantly higher ('higher lesion load') at

Time 1 than at Time 2. Age at Time 1 was not associated with temporal changes in global sqMRI scores. Higher lesion load at Time 2, but not at Time 1, was associated with smaller temporal changes in the global sqMRI score. The sqMRI scores were associated with concurrent, but not future or past motor GMFM-66 scores. Longitudinal changes in sqMRI scores were not associated with longitudinal changes in motor GMFM-66 scores. Conclusion: sqMRI scores of brain lesion extent at school-age are lower and a better indication of later-life motor functioning than very early life sqMRI scores. It may be best to interpret MRI white matter lesions with caution in very early life due to possible changes in lesion appearance and the unpredictable role of functional plasticity.

PMID: 38330549

**9. Effect of action observation training on the oral phase of swallowing in children with cerebral palsy: a pilot randomized controlled trial**

Maryam Mokhlesin, Fariba Yadegari, Mehdi Noroozi, Aida Ravarian, Zahra Sadat Ghoreishi

Logoped Phoniatr Vocol. 2024 Feb 6:1-9. doi: 10.1080/14015439.2023.2300081. Online ahead of print.

Swallowing disorder is prevalent in children with cerebral palsy (CP), and previous studies have shown that motor-based programs benefit children with CP by facilitating motor learning. We hypothesized that action observation training (AOT) could enhance motor learning and improve the oral phase of swallowing in children. In this two-group parallel double-blind randomized controlled trial, the intervention group received AOT and sensorimotor therapy, while the control group received a sham and sensorimotor therapy. The function of the oral phase of swallowing, as the primary outcome, was measured pre-intervention, post-intervention, and at one month of follow-up. Secondary outcomes included reported symptoms of feeding problems and the impact of the child's swallowing disorder on the main caregiver, which were measured pre-intervention and post-intervention. The result of the Mann-Whitney U test showed a significant difference between the two groups in the function of the oral phase of swallowing after the intervention. Additionally, the intervention had a large effect size. However, no significant difference was found in the parent-reported scores of the feeding/swallowing impact survey and symptoms of feeding problems between the two groups. In conclusion, this pilot study provides preliminary evidence of the clinical efficacy of AOT as a safe neurorehabilitation method to improve the oral phase of swallowing in children with CP. However more studies are needed in the future.

PMID: 38319122

**10. The Effect of Robotic Rehabilitation on Hand Functions and Quality of Life in Children with Cerebral Palsy: A Prospective Randomized Controlled Study**

Sevda Adar, Duygu Keskin, Ümit Dündar, Hasan Toktaş, Hilal Yeşil, Selma Eroğlu, Nuran Eyvaz, Ersin Beştaş, Ali Demircan

Am J Phys Med Rehabil. 2024 Jan 31. doi: 10.1097/PHM.0000000000002430. Online ahead of print.

Objective: This study aimed to examine the impact of robotic hand rehabilitation on hand function and quality of life in children with cerebral palsy. Design: Children with cerebral palsy aged 7-16 years were divided into robotic rehabilitation (n = 9) or conventional rehabilitation (n = 10) groups for hand rehabilitation of 30 sessions. The primary outcomes were the Fugl-Meyer Assessment for Upper Extremity, and Box and Block Test. The secondary outcomes were the Manual Ability Classification System, Modified Ashworth Scale, hand grasp and finger strengths, ABILHAND-Kids, Functional Independence Measure for Children, and PedsQL Quality of Life Inventory-CP Module. Results: In the robotic rehabilitation group, a significant improvement was found in all parameters after treatment ($p < 0.05$), except for the Functional Independence Measure ($p = 0.081$). In the conventional rehabilitation group, there was significant improvement after treatment in the Modified Ashworth Scale, Fugl-Meyer Assessment for Upper Extremity, hand grasp strength, Box and Block Test, ABILHAND-Kids, and PedsQL Quality of Life Inventory-CP Module ($p < 0.05$). Before and after treatment, all outcome parameters in the groups were similar ($p > 0.05$). Conclusions: Robotic hand rehabilitation is effective in improving motor function, manual dexterity, spasticity and quality of life in children with cerebral palsy. However, it was not demonstrated to be superior to conventional rehabilitation.

PMID: 38320248

**11. Psychometric Evaluation of the Persian Version of the Functional Mobility Scale: Assessing Validity and Reliability**

Razieh Sadeghian Afarani, Saeid Fatorehchy, Mehdi Rassafiani, Mohsen Vahedi, Hamidreza Azadi, Nazila Akbarfahimi

Phys Occup Ther Pediatr. 2024 Feb 5:1-12. doi: 10.1080/01942638.2024.2314489. Online ahead of print.

Aim: This study aimed to assess the content, concurrent validity, test-retest, and intra-rater reliability of the Persian version of the Functional Mobility Scale (FMS) for evaluating functional mobility in children and adolescents with cerebral palsy (CP).

Methods: Following international standards for measurement translation, we developed a Persian version of the FMS. A total of 160 participants took part in this study. Concurrent validity was assessed using Spearman's coefficient to correlate with the Gross Motor Function Classification System (GMFCS). Test-retest (n = 30) and intra-rater (n = 30) reliability of the FMS were also examined by Cohen's weighted kappa coefficient. Results: Concurrent validity ranged from -0.912 to -0.941 for children and -0.912 to -0.936 for adolescents. Test-retest ranged from 0.902 to 1. Intra-rater ranged from 0.933 to 0.987. Conclusion: The Persian version of the FMS demonstrates very strong validity and almost perfect reliability for assessing and classifying functional mobility in children and adolescents with CP. These findings suggest that this tool could be a useful addition to clinical practice and research for the Persian-speaking population.

PMID: 38317376

**12. Higher risk of cerebral palsy, seizures/epilepsy, visual- and hearing impairments, cancer, injury and child abuse in children with congenital anomalies: Data from the EUROlinkCAT study**

Stine Kjaer Urhoj, Joan Morris, Maria Loane, Elisa Ballardini, Laia Barrachina-Bonet, Clara Cavero-Carbonell, Alessio Coi, Mika Gissler, Joanne Given, Anna Heino, Sue Jordan, Amanda Neville, Michele Santoro, Joachim Tan, David Tucker, Diana Wellesley, Ester Garne, Mads Damkjaer

Acta Paediatr. 2024 Feb 7. doi: 10.1111/apa.17136. Online ahead of print.

Aim: The aim is to examine the risk of cerebral palsy, seizures/epilepsy, visual- and hearing impairments, cancer, injury/poisoning and child abuse in children with and without a congenital anomaly up to age 5 and 10 years. Methods: This is a population-based data linkage cohort study linking information from the European Surveillance of Congenital Anomalies network (EUROCAT) and birth registries to hospital discharge databases. We included 91 504 live born children with major congenital anomalies born from 1995 to 2014 from nine EUROCAT registries in five countries and 1 960 727 live born children without congenital anomalies (reference children). Prevalence and relative risk (RR) were estimated for each of the co-morbidities using Kaplan-Meier survival estimates. Results: Children with congenital anomalies had higher risks of the co-morbidities than reference children. The prevalences in the reference children were generally very low. The RR was 13.8 (95% CI 12.5-15.1) for cerebral palsy, 2.5 (95% CI 2.4-2.6) for seizures/epilepsy, 40.8 (95% CI 33.2-50.2) for visual impairments, 10.0 (95% CI 9.2-10.9) for hearing loss, 3.6 (95% CI 3.2-4.2) for cancer, 1.5 (95% CI 1.4-1.5) for injuries/poisoning and 2.4 (95% CI 1.7-3.4) for child abuse. Conclusion: Children with congenital anomalies were more likely to be diagnosed with the specified co-morbidities compared to reference children.

PMID: 38324400

**13. Characteristics of Visual Function in Children With Cerebral Palsy and Intellectual Disabilities in Urban Beijing**

Jun Tao, Rui Hao, Yatu Guo, Wei Zhang

Transl Vis Sci Technol. 2024 Feb 1;13(2):7. doi: 10.1167/tvst.13.2.7.

Objective: To investigate ocular development and the characteristics of visual function among children with cerebral palsy (CP) and intellectual disabilities in Beijing's Chaoyang District schools. Methods: A total of 160 children (320 eyes) with CP and intellectual disabilities, including 86 males and 74 females aged between 6 and 18 years old (median, 13.5 years), were included in this study. A total of 214 healthy children aged 6 to 18 years (median, 10 years) were recruited as a control group for visual function, including 116 males and 98 females. Subjective far vision, objective vision (electrophysiological sweep visual evoked potential), corrected vision, near stereopsis, ametropia, the anterior segment, and the fundus were examined. Results: A total of 232 eyes (76.32%) were ametropic among 304 eyes that could cooperate; 200 eyes (65.79%) were astigmatic, 16 eyes (5.26%) were hyperopic, and 120 eyes (39.47%) were myopic. A total of 64 children had strabismus (40%), and 24 had nystagmus (15%). The near stereopsis test showed that 72 children (64.29%) demonstrated 100″ and less. A total of 214 healthy children aged 6 to 18 years were recruited as a control group for visual function. There was a significant difference in visual functions between children with intellectual disabilities and those without ($Z = -10.370$; $P < 0.001$). Conclusions: The prevalence of abnormal visual function in children with CP and intellectual disability was significantly higher than that in healthy children. Among them, myopia is the main refractive error, and the correction rate was low. Translational relevance: The electrical signals generated by stimulating the retina with black and white stripes are transmitted to the brain. Scanning electrophysiological devices can capture the activity of the cerebral cortex and convert it into an electroencephalogram. Scanning electrophysiological electrooculography is used to examine the objective vision of children with cerebral palsy.

PMID: 38334704

**14. Supplementary Respiratory Therapy Improves Pulmonary Function in Pediatric Patients with Cerebral Palsy: A Systematic Review and Meta-Analysis**

Erika Kolumbán, Márton Szabados, Márk Hernádfői, Uyen Nguyen Do To, Rita Nagy, Ádám Zolcsák, Katalin Eszter Müller,

Zoltán Sipos, Dániel Sándor Veres, Anett Szőllősi, Péter Hegyi, Miklós Garami, Ibolya Túri

Review J Clin Med. 2024 Feb 2;13(3):888. doi: 10.3390/jcm13030888.

Background: Despite medical advances, individuals with cerebral palsy (CP) face significant respiratory challenges, leading to heightened hospitalization rates and early mortality among this population. We hypothesize that integrating supplementary respiratory therapy into standard rehabilitation will result in significant improvements in pulmonary function, enhanced respiratory muscle strength, and an overall increase in the quality of life among pediatric patients with CP. Methods: A systematic search of literature across five databases was conducted, and random-effects meta-analyses were performed to assess the impact of supplementary respiratory therapy on (a) pulmonary function: forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), FVC/FEV1 ratio, peak expiratory flow (PEF), and (b) respiratory muscle strength: maximal inspiratory and expiratory pressure (MIP, MEP), and (c) quality of life. Certainty of evidence was determined by the GRADE assessment. Results: Analysis of data from 11 eligible randomized controlled trials revealed clinically meaningful changes in pulmonary function. We found a relevant mean difference (MD) in absolute PEF of 0.50 L/s (95% confidence interval (CI): 0.19; 0.82 p = 0.0107). The certainty of the evidence ranged from moderate to high. Conclusions: This study presents current evidence on the impact of various supplementary respiratory therapies for CP patients classified under gross motor function classification level I-IV, demonstrating clinically meaningful improvements in pulmonary function and respiratory muscle strength. These improvements suggest the potential for an enhanced quality of life. Our findings hold the promise of serving as a foundational reference for potential revisions to conventional rehabilitation care, incorporating supplementary respiratory therapy.

PMID: 38337582

**15. The Neurorehabilitation of Neurological Movement Disorders Requires Rigorous and Sustained Research**

Akiyoshi Matsugi, Naoki Yoshida, Hideki Nakano, Yohei Okada

Editorial J Clin Med. 2024 Feb 1;13(3):852. doi: 10.3390/jcm13030852.

Movement disorders that stem from neurological conditions such as stroke, cerebral palsy, multiple sclerosis (MS), Parkinson's disease (PD), and spinocerebellar degeneration (SCD) can significantly impair a person's activities of daily living (ADL) [...].

PMID: 38337549

**16. The Knowledge Translation of Early Cerebral Palsy (KiTE CP) Study: Implementing Screening among a High-risk Prospective Cohort of Australian infants**

Amanda Kl Kwong, Abbey Eeles, Peter J Anderson, Nadia Badawi, Roslyn N Boyd, Kate L Cameron, Jeanie Cheong, Paul Colditz, Pieter Koorts, Cathryn Crowle, Russell C Dale, Lex W Doyle, Michael Fahey, Joanne George, Rod W Hunt, Lynda McNamara, Catherine Morgan, Iona Novak, Joy E Olsen, Nadia Reid, Ingrid Rieger, Koa Whittingham, Alicia J Spittle

J Pediatr. 2024 Feb 7:113949. doi: 10.1016/j.jpeds.2024.113949. Online ahead of print.

Objective: To describe the implementation of the international guidelines for the early diagnosis of cerebral palsy (CP) and engagement in the screening process in an Australian cohort of infants with neonatal risk factors for CP. Study design: Prospective cohort study of infants with neonatal risk factors recruited at <6 months CA from 11 sites in the states of Victoria, New South Wales, and Queensland, Australia. First, we implemented a multi-modal knowledge translation strategy including barrier identification, technology integration and special interest groups. Screening was implemented as follows: infants with clinical indications for neuroimaging underwent magnetic resonance imaging and/or cranial ultrasound. The General Movements Assessment (GMA) was recorded clinically or using an app (Baby Moves). Infants with absent or abnormal fidgety movements on GMA videos were offered further assessment using the Hammersmith Infant Neurological Examination (HINE). Infants with atypical findings on 2/3 assessments met criteria for high risk of CP. Results: Of the 597 infants (56% male) recruited, 95% (n=565) received neuroimaging, 90% (n=537) had scorable GMA videos (2% unscorable/8% no video), and 25% (n=149) HINE. Overall, 19% of the cohort (n=114/597) met criteria for high risk of CP, 57% (340/597) had at least two normal assessments (of neuroimaging, GMA or HINE), and 24% (n=143/597) had insufficient assessments. Conclusions: Early CP screening was implemented across participating sites using a multi-modal knowledge translation strategy. Although the COVID-19 pandemic affected recruitment rates, there was high engagement in the screening process. Reasons for engagement in early screening from parents and clinicians warrant further contextualization and investigation.

PMID: 38336205

**17. Increasing Prevalence of Cerebral Palsy Among Two-year Old Children Born at <27 Weeks of Gestation: A Cohort Study**

Sara B DeMauro, Scott A McDonald, Roy J Heyne, Betty R Vohr, Andrea F Duncan, Jamie E Newman, Abhik Das, Susan R Hintz; NICHD Neonatal Research Network

J Pediatr. 2024 Feb 7:113944. doi: 10.1016/j.jpeds.2024.113944. Online ahead of print.

Objective: To evaluate changes in prevalence and severity of cerebral palsy (CP) among surviving children born at <27 weeks of gestation over time and to determine associations between CP and other developmental domains, functional impairment, medical morbidities, and resource utilization among two-year old children who were born extremely preterm. Study design: Retrospective cohort study using prospective registry data, conducted at 25 centers of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Participants were children born at <27 weeks of gestation and followed at 18 through 26 months corrected age (CA) from 2008 through 2019. Outcomes of interest were changes in prevalence of any CP and severity of CP over time, and associations between CP and other neurodevelopmental outcomes, functional impairment, and medical comorbidities. Adjusted logistic, linear, multinomial logistic, and robust Poisson regression evaluated the relationships between child characteristics, CP severity, and outcomes. Results: Among 6,927 surviving children with complete follow-up data, 3,717 (53.7%) had normal neurologic examinations, 1,303 (18.8%) had CP, and the remainder had abnormal neurologic examinations not classified as CP. Adjusted rates of any CP increased each year of the study period (aOR 1.11 per year, 95% CI 1.08-1.14). Cognitive development was significantly associated with severity of CP. Children with CP were more likely to have multiple medical comorbidities, neurosensory problems, and poor growth at follow-up. Conclusions: The rate of CP among surviving children who were born extremely preterm increased from 2008 through 2019. At 18 to 26 months CA, neurodevelopmental and medical comorbidities are strongly associated with all severity levels of CP.

PMID: 38336201

**18. Maternal obesity and cerebral palsy: What does an association signify?**

Russell S Kirby

Paediatr Perinat Epidemiol. 2024 Feb 9. doi: 10.1111/ppe.13054. Online ahead of print.

No abstract available

PMID: 38334035

**19. Pharmacologic Management of Sialorrhea in Neonatal and Pediatric Patients**

Caitlyn V Bradford, Avery M Parman, Peter N Johnson, Jamie L Miller

J Pediatr Pharmacol Ther. 2024;29(1):6-21. doi: 10.5863/1551-6776-29.1.6. Epub 2024 Feb 7.

Sialorrhea, defined as an excess flow of saliva or excessive secretions, is common in patients with cerebral palsy and other neurologic disorders and is associated with clinical complications such as increased risk of local skin reactions, infections, aspiration, pneumonia, and dehydration. Upon failure of non-pharmacologic measures, clinicians have several noninvasive pharmacologic options available to manage sialorrhea. This review of the literature provides detailed descriptions of medications used, efficacy, safety, and practical considerations for use of non-injectable pharmacologic agents. The literature search included published -human studies in the English language in PubMed and Google Scholar from 1997 to 2022. Relevant citations within articles were also screened. A total of 15 studies representing 719 pediatric patients were included. Glycopyrrolate, atropine, scopolamine, and trihexyphenidyl all have a potential role for sialorrhea management in children; however, glycopyrrolate remains the most studied option with 374 (n = 52.0%) of the 719 patients included in the systematic review receiving this medication. Overall, glycopyrrolate showed similar efficacy but higher tolerability than its comparators in 2 comparative studies and is often considered the first-line agent. Patient-specific (age, route of administration) and medication -specific (dosage formulation, medication strength) considerations must be weighed when initiating a new therapy or switching to another medication upon treatment failure. Owing to the high propensity of adverse events with all agents, clinicians should consider initiating doses at the lower end of the dosage range, as previous studies have noted a dose-dependent relationship.

PMID: 38332959

**20. Motor, cognitive and behavioural outcomes after neonatal hypoxic-ischaemic encephalopathy**

María Montesclaros Hortigüela, Miriam Martínez-Biarge, David Conejo, Cristina Vega-Del-Val, Juan Arnaez; Grupo ARAHIP

An Pediatr (Engl Ed). 2024 Feb 7:S2341-2879(24)00011-5. doi: 10.1016/j.anpede.2024.01.009. Online ahead of print.

Introduction: The current neurodevelopmental status of patients with neonatal hypoxic-ischaemic encephalopathy (HIE) in Spain is unknown. Recent European studies highlight a shift of severe pathology towards mild motor disorders and emotional problems. The aim of this study was to analyse neurodevelopmental outcomes in a cohort of neonates with HIE at age 3 years. Patients and method: Multicentre observational study of neonates born at 35 or more weeks of gestation with moderate to severe HIE in 2011-2013 in 12 hospitals in a large Spanish region (91 217 m2), with the recruitment extended through 2017 in the coordinating hospital. We analysed the findings of neonatal neuroimaging and neurodevelopmental test scores at 3 years (Bayley-III, Peabody Picture Vocabulary Test and Child Behavior Checklist). The sample included 79 controls with no history of perinatal asphyxia. Results: Sixty-three patients were recruited, of whom 5 (7.9%) were excluded due to other pathology and 14 (24%) died. Of the 44 survivors, 42 (95.5%) were evaluated. Of these 42, 10 (24%) had adverse outcomes (visual or hearing impairment, epilepsy, cerebral palsy or developmental delay). Other detected problems were minor neurological signs in 6 of the 42 (14%) and a higher incidence of emotional problems compared to controls: introversion (10.5% vs. 1.3%), anxiety (34.2% vs. 11.7%) and depression (28.9% vs. 7.8%) ($P < .05$). The severity of the lesions on neuroimaging was significantly higher in patients with motor impairment ($P = .004$) or who died or had an adverse outcome ($P = .027$). Conclusion: In addition to classical sequelae, the followup of patients with neonatal HIE should include the diagnosis and treatment of minor motor disorders and social and emotional problems.

PMID: 38331678

**21. Differential effects of growth restriction and immaturity on predicted psychomotor development at 4 years of age in preterms**

Arne Jensen, Niels Rochow, Manfred Voigt, Gerhard Neuhäuser

AJOG Glob Rep. 2024 Jan 9;4(1):100305. doi: 10.1016/j.xagr.2023.100305. eCollection 2024 Feb.

Background: Fetal growth restriction and immaturity are associated with poor neurocognitive development and child psychopathology affecting educational success at school and beyond. However, the differential effects of either obstetrical risk factor on predicted psychomotor development have not yet been deciphered. Objective: This study aimed to separately study the impact of growth restriction and that of immaturity on predicted psychomotor development at the preschool age of 4.3 (standard deviation, 0.8) years using birthweight percentiles in a prospective cohort of preterm infants born at ≤37+6/7 weeks of gestation. Differences between small for gestational age newborns with intrauterine growth restriction and those without were described. We examined predicted total psychomotor development score, predicted developmental disability index, calculated morphometric vitality index, and predicted intelligence quotient, Porteus Maze test score, and neurologic examination optimality score in 854 preterm infants from a large prospective screening cohort (cranial ultrasound screening, n=5,301). Study design: This was a prospective cranial ultrasound screening study with a single-center cohort observational design (data collection done from 1984-1988, analysis done in 2022). The study included 5,301 live-born infants, of whom 854 (16.1%) were preterm infants (≤37+6/7 weeks' gestation), and was conducted on the day of discharge of the mother at 5 to 8 days postpartum from a level 3 perinatal center. Predicted psychomotor development, as assessed by the predicted total psychomotor development score, predicted developmental disability index, calculated morphometric vitality index, predicted intelligence quotient, Porteus Maze test score, and neurologic examination optimality score were calculated. We related psychomotor development indices and measures to gestational age in 3 groups of birthweight percentiles (ie, 10%, 50%, and 90% for small, appropriate, and large for gestational age newborns, respectively) using linear regression analysis, analysis of variance, multivariate analysis of variance, and t test procedures. Results: The key result of our study is the observation that in preterm infants born at ≤37+6/7 weeks of gestation, growth restriction as compared with immaturity is the prime risk factor for impairment of overall predicted psychomotor development, intelligence quotient, Porteus Maze test results, and neurologic examination optimality score at the preschool age of 4.3 (standard deviation, 0.8) years ($P<.001$). This is particularly true for intrauterine growth restriction. These detrimental effects of growth restriction become more prominent with decreasing gestational age ($P<.001$). As expected, growth restriction in preterm infants born at ≤37+6/7 weeks of gestation was associated with a number of obstetrical risk factors, including hypertension in pregnancy ($P<.001$), multiple pregnancy ($P<.001$), pathologic cardiotocography ($P=.001$), and low pH ($P=.007$), increased pCO2 ($P=.009$), and poor pO2 ($P<.001$) in umbilical arterial blood. Of note, there were no differences in cerebral hemorrhage or white matter damage among small, appropriate, and large for gestational age birthweight percentile groups, suggesting an independent mechanism of brain injury caused by preterm growth restriction resulting in poor psychomotor development. Conclusion: Compared with immaturity, growth restriction in preterm infants has more intense detrimental effects on psychomotor development, necessitating improved risk stratification. This finding has implications for clinical management, parental consultation, and early intervention strategies to improve school performance, educational success, and mental health in children. The mechanisms of brain injury specific to growth restriction in preterm infants require further elucidation.

PMID: 38327671

**22. Investigating the Impact on Long-Term Outcomes and the Necessity of Hereditary Thrombophilia Screening in Presumed or Perinatal Arterial Ischemic Stroke**

Ömer Bektaş, Özben Akıncı Göktaş, Begüm Atasay, Serap Teber

Clin Appl Thromb Hemost. 2024 Jan-Dec:30:10760296241231944. doi: 10.1177/10760296241231944.

This study aimed to investigate the influence of prothrombotic risk factors on long-term outcomes of patients with perinatal arterial ischemic stroke. The study was conducted through an analysis of monitoring results that were regularly maintained for approximately 20 years at a tertiary stroke-monitoring center. The study assessed prothrombotic risk factors, radiological area of involvement, clinical presentation, treatments, clinical outcomes, and long-term outcomes of the 48 patients included in the study, with a mean monitoring time of 77.6 ± 45.7 months (range: 6-204). Our results showed that the presence of prothrombotic risk factors did not affect long-term outcomes. However, patients with middle cerebral artery infarction had the highest risk of developing cerebral palsy, whereas those with presumed stroke had the highest risk of developing epilepsy. This study suggests that prothrombotic risk factors should not be evaluated during the acute stage unless there is a strong suspicion of the patient's history, and prevention or early diagnosis of presumed stroke patients will positively impact their long-term prognosis.

PMID: 38327150

**23. Individuals with cerebral palsy and their families need an evidence-based quality seal for interventions**

John Coughlan, Nonyelum Nweke, Matthieu G Chatelin, Dorothy Kisarale, Nathalie L Maitre

Dev Med Child Neurol. 2024 Feb 7. doi: 10.1111/dmcn.15862. Online ahead of print.

No abstract available

PMID: 38326963

**24. A comparative analysis of oropharyngeal functions in preterm and term children with cerebral palsy**

Seda Nur Kemer, Selen Serel-Arslan

Early Hum Dev. 2024 Feb 2:190:105964. doi: 10.1016/j.earlhumdev.2024.105964. Online ahead of print.

This study aims to compare term and preterm children with Cerebral Palsy (CP) in terms of their oropharyngeal functions. A total of 50 children with CP participated in the study, and were divided into two groups according to their birth history including preterm group (gestational age below 37 weeks; 60 % female; mean age = 6.86 ± 4.35 years) and term group (gestational age between 37 and 41 weeks; 60 % female; mean age = 6.48 ± 4.86 years). Chewing and swallowing functions were evaluated in terms of oropharyngeal functions. Chewing evaluation was performed by using the Karaduman Chewing Performance Scale (KCPS) and the Turkish version of the Mastication Observation and Evaluation Instrument (T-MOE). The pediatric version of the Eating Assessment Tool (PEDI-EAT-10) was used to evaluate swallowing performance of children. In addition, the Behavioral Pediatric Feeding Assessment Scale (BPFAS) was used to assess feeding behaviors of children. There were significant differences between groups in terms of KCPS ($p = 0.03$), T-MOE ($p = 0.01$), and PEDI-EAT-10 scores ($p = 0.04$). There was a significant difference between groups in terms of the parental frequency score from the BPFAS ($p = 0.04$). Oropharyngeal functions of preterm children with CP were more adversely affected than term children with CP. Clinicians working with children with CP should be aware of the risks of preterm birth on oropharyngeal functions, and take precautions for oropharyngeal dysfunction in the early period in preterm children with CP.

PMID: 38325005

**25. Neurodevelopmental outcome of neonatal seizures: A longitudinal study**

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Eur J Paediatr Neurol. 2024 Jan 28:49:17-26. doi: 10.1016/j.ejpn.2024.01.007. Online ahead of print.

Introduction: Neonatal seizures (NS) are the most common neurological emergency in the neonatal period. The International League Against Epilepsy (ILAE) proposed a new classification of NS based on semiology and highlighted the correlation between semiology and aetiology. However, neurodevelopmental outcomes have not been comprehensively evaluated based on this new classification. Aims: To evaluate neurodevelopmental outcomes and potential risk factors for severe outcomes in NS. Methods: Patients with video electroencephalogram confirmed NS were evaluated. Seizure aetiology, cerebral magnetic resonance imaging (MRI) data, background electroencephalograms data, general movements, and neurodevelopmental outcomes were analysed. Severe outcomes were one of the following: death, cerebral palsy, Griffiths developmental quotient <70, epilepsy, deafness, or blindness. Results: A total of 74 neonates were evaluated: 62 (83.8 %) with acute provoked NS (primarily hypoxic-ischaemic encephalopathy), and 12 (16.2 %) with neonatal-onset epilepsies (self-limited neonatal epilepsy,

developmental and epileptic encephalopathy, cerebral malformations). Of these, 32 (43.2 %) had electrographic seizures, while 42 (56.7 %) had electroclinical seizures - 38 (90.5 %) were motor (42.1 % clonic) and 4 (9.5 %) were non-motor phenomena. Severe outcomes occurred in 33 of the 74 (44.6 %) participants. In multivariate analysis, neonatal-onset epilepsies (odds ratio [OR]: 1.3; 95 % confidence interval [CI]: 1.1-1.6), status epilepticus (OR: 5.4; 95 % CI: 1.5-19.9), and abnormal general movements (OR: 3.4; 95 % CI: 1.9-7.6) were associated with severe outcomes. Conclusions: At present, hypoxic-ischaemic encephalopathy remains the most frequent aetiology of NS. The prognosis of neonatal-onset epilepsies was worse than that of acute provoked NS, and status epilepticus was the most predictive factor for adverse outcomes.

PMID: 38324990

**26. Comparison and discussion of behavior and pathology of four kinds of cerebral palsy disease models**

Jinyan Xu, Siyang Yan, Chen Xia, Jianyi Xue, Wentao Yu, Yuanjie Yan, Zhenjin Yin

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Explore the differences in behavioral and pathological manifestations of rat models of cerebral palsy made by different methods and discuss what types of studies these models are suitable for. Behavioral evaluation and pathological section observation were used to observe and evaluate the model. Conclusion: except for the absence of data of bilateral common carotid artery ligation rats, the other three methods could all achieve a successful cerebral palsy disease model for both behavioral and pathological. For researchers, the selection of intraperitoneal infection model in pregnant rats or unilateral ischemia and hypoxia model in infant rats is sufficient to meet the experimental needs, whereas the selection of the combined method for modeling does not show enough advantages, which not only causes the waste of financial and human resources but also increases the possibility of experimental error made by intervention factors.

PMID: 38323913

**27. Randomized controlled trial comparing the impacts of Saccharomyces boulardii and Lactobacillus rhamnosus OF44 on intestinal flora in cerebral palsy rats: insights into inflammation biomarkers and depression-like behaviors**

Chunuo Chu, Shang Huang, Xin Wang, Guoqiang Zhao, Wenqi Hao, Yiyi Zhong, Zhihui Ma, Congfu Huang, Yuanping Peng, Fengxiang Wei

Transl Pediatr. 2024 Jan 29;13(1):72-90. doi: 10.21037/tp-23-566. Epub 2024 Jan 24.

Background: Cerebral palsy (CP) is a unique neurological disorder which adversely affects motion. Cytokines and gut microbial composition contribute to CP and other diseases, such as reproductive tract inflammation and bone loss. Importantly, Saccharomyces boulardii (S. boulardii) reduces the degree of inflammation and improves overall health status. As our previous study showed that Lactobacillus rhamnosus (L. rhamnosus) OF44, a selected strain of gut bacteria originally used to treat reproductive tract inflammation and bone loss, has effects similar to that of S. boulardii, we decided to use L. rhamnosus OF44 on CP rats. Validation of the effects of L. rhamnosus OF44 on CP adds to its confirmed effects in treating osteoporosis and reproductive tract microbiota disorders, increasing its potential as a probiotic. The purpose of this was to ascertain whether L. rhamnosus OF44 can alleviate the symptoms of CP. Methods: CP rat models were created through left carotid artery ligation. Following this, 100-day old CP rats were exposed to L. rhamnosus OF44, S. boulardii, or normal saline gastric gavage daily for 28 days. Grouping of the rats is determined randomly. Before and after the gavage, behavioral experiments were conducted and the inflammation levels assessed via measurements of interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor alpha (TNF-α) inflammatory markers. The efficacy of the outcome is measured by performing statistical analysis like the t-test on the data to see its significance. Additionally, variations inside gut microbiome were evaluated via 16S ribosomal RNA sequencing. Results: Before intervention, CP rats failed to exhibit depression-like behavior (P=0.6). L. rhamnosus OF44 treatment significantly reduced the level of IL-6 (P=4.8e-05), S. boulardii treatment significantly reduced the level of TNF-α (P=0.04). In addition, both treatments altered the composition and complexity of the gut microbiome. Conclusions: Our results indicated that L. rhamnosus OF44 has potential in alleviating inflammation and altering the gut microbial composition in CP, and that it has the potential to clinically treat CP. There are some limitations of this study. For example, dietary differences and their effects on gastrointestinal dysfunction are not considered in this study, and only two behavioral experiments were used.

PMID: 38323178

**28. Use of primary health care services among children and adolescents with cerebral palsy**

Stine Johansen, Guro L Andersen, Stian Lydersen, Runa Kalleson, Sandra Julsen Hollung

Dev Med Child Neurol. 2024 Feb 6. doi: 10.1111/dmcn.15879. Online ahead of print.

Aim: To investigate the use of general practitioners and urgent care centres (UCC) among children and adolescents with

cerebral palsy (CP) compared to a control group, and per gross motor function level. Method: Data on children with CP born 1996 to 2014 were collected from the Norwegian Quality and Surveillance Registry for Cerebral Palsy. A control group was extracted from Statistics Norway. The date and diagnosis codes for general practitioner and UCC contacts from 2006 to 2015 were collected from the Norwegian Control and Payment of Health Reimbursement Database. Incidence rate ratios (IRR) for the number of contacts per person-year with 95% confidence intervals (CI) were calculated using Poisson regression. Risk differences with 95% CI were used to compare cumulative diagnosis incidences between children with CP and the control group. Results: The study included 2510 children (1457 males; 58.1%) with CP and 12 041 (7003 males; 58.2%) without CP (mean age in both groups 7 years 2 months, SD 4 years 8 months, range 0-19 years), with 336 250 contacts. Children with CP had more general practitioner (IRR 1.47; 95% CI 1.29-1.67) and UCC (IRR 1.30; 95% CI 1.13-1.50) contacts than children without CP, for all ages. IRRs remained unchanged when comparing children with CP in Gross Motor Function Classification System (GMFCS) levels I and II to children without CP. Among children with CP, contact increased as GMFCS levels increased, and they were in contact most often for respiratory and general and unspecified diagnoses. The risk for epilepsy was highest for those in contact with general practitioners. Interpretation: Children with CP, including those with less severe motor impairments, contacted general practitioners and UCCs more than children without CP. However, contact increased as gross motor impairment increased. They had contact for many diagnoses, mostly respiratory.

PMID: 38321621

**29. Health literacy in adolescents and young adults with cerebral palsy: a mixed methods systematic review**

Jacqueline Y Ding, Stacey L Cleary, Prue E Morgan

Review Disabil Rehabil. 2024 Feb 5:1-13. doi: 10.1080/09638288.2024.2311879. Online ahead of print.

Purpose: To identify evidence of health literacy in young people with cerebral palsy (13-38 years), describe current strategies they use to access and build their health knowledge, and explore associations between health literacy and quality of life (QoL). Methods: Four electronic databases were systematically searched (2001 to June 2023) to identify studies describing components of health literacy in this population. Two reviewers screened for eligibility, then extracted data and assessed methodological quality of included studies. Data were synthesised using a convergent integrated analysis framework and summarised with a narrative synthesis. Results: Eleven studies were included (N = 363). Evidence of health literacy was demonstrated through a range of strategies young people employed to identify their specific information needs, develop health literacy skills, and learn experientially. The preferred method for building health knowledge was obtaining information from trusted sources. Information gaps were identified in topics such as ageing with cerebral palsy, sexuality and navigating intimate relationships. There were minimal data on health literacy and QoL. Conclusions: Young people with cerebral palsy want tailored and credible health information to increase participation in making informed health-related decisions. Building capacity and development of self-efficacy may assist with the identification of emerging health literacy needs.

PMID: 38314775

**30. Whole-Blood Gene Expression Profile After Hypoxic-Ischemic Encephalopathy**

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Randomized Controlled Trial JAMA Netw Open. 2024 Feb 5;7(2):e2354433. doi: 10.1001/jamanetworkopen.2023.54433.

Importance: Induced hypothermia, the standard treatment for hypoxic-ischemic encephalopathy (HIE) in high-income countries (HICs), is less effective in the low-income populations in South Asia, who have the highest disease burden. Objective: To investigate the differences in blood genome expression profiles of neonates with HIE from an HIC vs neonates with HIE from South Asia. Design, setting, and participants: This case-control study analyzed data from (1) a prospective observational study involving neonates with moderate or severe HIE who underwent whole-body hypothermia between January 2017 and June 2019 and age-matched term healthy controls in Italy and (2) a randomized clinical trial involving neonates with moderate or severe HIE in India, Sri Lanka, and Bangladesh recruited between August 2015 and February 2019. Data were analyzed between October 2020 and August 2023. Exposure: Whole-blood RNA that underwent next-generation sequencing. Main outcome and measures: The primary outcomes were whole-blood genome expression profile at birth associated with adverse outcome (death or disability at 18 months) after HIE in the HIC and South Asia cohorts and changes in whole-genome expression profile during the first 72 hours after birth in neonates with HIE and healthy controls from the HIC cohort. Blood samples for RNA extraction were collected before whole-body hypothermia at 4 time points (6, 24, 48, and 72 hours after birth) for the HIC cohort. Only 1 blood sample was drawn within 6 hours after birth for the South Asia cohort. Results: The HIC cohort was composed of 35 neonates (21 females [60.0%]) with a median (IQR) birth weight of 3.3 (3.0-3.6) kg and gestational age of 40.0 (39.0-40.6) weeks. The South Asia cohort consisted of 99 neonates (57 males [57.6%]) with a median (IQR) birth weight of 2.9 (2.7-3.3) kg and gestational age of 39.0 (38.0-40.0) weeks. Healthy controls included 14 neonates (9 females [64.3%]) with a median (IQR) birth weight of 3.4 (3.2-3.7) kg and gestational age of 39.2 (38.9-40.4) weeks. A total of

1793 significant genes in the HIC cohort and 99 significant genes in the South Asia cohort were associated with adverse outcome (false discovery rate <0.05). Only 11 of these genes were in common, and all had opposite direction in fold change. The most significant pathways associated with adverse outcome were downregulation of eukaryotic translation initiation factor 2 signaling in the HIC cohort (z score = -4.56; P < .001) and aldosterone signaling in epithelial cells in the South Asia cohort (z score = null; P < .001). The genome expression profile of neonates with HIE (n = 35) at birth, 24 hours, 48 hours, and 72 hours remained significantly different from that of age-matched healthy controls in the HIC cohort (n = 14). Conclusions and relevance: This case-control study found that disease mechanisms underlying HIE were primarily associated with acute hypoxia in the HIC cohort and nonacute hypoxia in the South Asia cohort. This finding might explain the lack of hypothermic neuroprotection.

PMID: 38306098