Cerebral palsy research news

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Interventions and Management

1. Effectiveness of Constraint-Induced Movement Therapy for Children With Hemiparesis Associated With Cerebral Palsy: A Systematic Review

Adam Regalado, Bonnie Decker, Breanna M Flaherty, Lindsee Zimmer, India Brown

Am J Occup Ther. 2023 May 1;77(3):7703205160. doi: 10.5014/ajot.2023.050152.
Importance: This systemic review synthesizes the existing literature to determine whether constraint-induced movement therapy (CIMT) is more effective than other approaches in improving upper extremity function in children diagnosed with hemiparesis associated with cerebral palsy (CP). Objective: To advance the knowledge of the effectiveness of CIMT for occupational therapy practitioners by critiquing research conducted over the past 20 yr. Data sources: Databases used in the search were CINAHL, Health Source: Nursing/Academic Edition, PsycINFO, PubMed, Research Gate, and Google Scholar. Studies published from 2001 to 2021 were reviewed. Study selection and data collection: Articles were included if (1) the primary diagnosis was hemiparesis associated with CP; (2) participants were younger than age 21 yr; (3) constraint-induced therapy, CIMT, or other modified forms of CIMT were offered as an intervention; and (4) there was at least one group in the study. Findings: Forty studies were included in the analysis. The results demonstrate that CIMT produces improved affected upper extremity function when compared with general rehabilitation. However, there were no differences in outcomes when bimanual approaches were compared with CIMT. Conclusions and relevance: The data support that CIMT is a beneficial and effective treatment when used to improve the upper extremity function of children with hemiparesis associated with CP. However, more Level 1b studies are needed to compare CIMT with bimanual therapy to determine which one is most effective and under which conditions. What This Article Adds: This systematic review demonstrates that CIMT is an effective intervention when compared with other therapeutic approaches. This intervention can be used by occupational therapy practitioners who work with children diagnosed with hemiparesis associated with CP.

PMID: 37358836

2. Combining Unimanual and Bimanual Therapies for Children with Hemiparesis: Is There an Optimal Delivery Schedule?

Ka Lai K Au, Julie L Knitter, Susan Morrow-McGinty, Talita C Campos, Jason B Carmel, Kathleen M Friel

Behav Sci (Basel). 2023 Jun 9;13(6):490. doi: 10.3390/bs13060490.

Constraint-induced movement therapy (CIMT) and bimanual therapy (BT) are among the most effective hand therapies for children with unilateral cerebral palsy (uCP). Since they train different aspects of hand use, they likely have synergistic effects. The aim of this study was to examine the efficacy of different combinations of mCIMT and BT in an intensive occupational therapy program for children with uCP. Children (n = 35) participated in intensive modified CIMT (mCIMT) and BT, 6 weeks, 5 days/week, 6 h/day. During the first 2 weeks, children wore a mitt over the less-affected hand and engaged in functional and play activities with the affected hand. Starting in week 3, bimanual play and functional activities were added progressively, 1 hour/week. This intervention was compared to two different schedules of block interventions: (1) 3 weeks of mCIMT followed by 3 weeks of BT, and (2) 3 weeks of BT followed by 3 weeks of mCIMT. Hand function was tested before, after, and two months after therapy with the Assisting Hand Assessment (AHA), Pediatric Evaluation of Disability

Inventory (PEDI), and Canadian Occupational Performance Measure (COPM). All three groups of children improved in functional independence (PEDI; $p < 0.031$), goal performance (COPM Performance; $p < 0.0001$) and satisfaction (COPM Satisfaction; $p < 0.0001$), which persisted two months post-intervention. All groups showed similar amounts of improvement, indicating that the delivery schedule for mCIMT and BT does not significantly impact the outcomes.

PMID: 37366742

3. Identifying Postural Instability in Children with Cerebral Palsy Using a Predictive Model: A Longitudinal Multicenter Study

Carlo Marioi Bertoncelli, Domenico Bertoncelli, Sikha S Bagui, Subhash C Bagui, Stefania Costantin, Federico Solla

Diagnostics (Basel). 2023 Jun 20;13(12):2126. doi: 10.3390/diagnostics13122126.

Insufficient postural control and trunk instability are serious concerns in children with cerebral palsy (CP). We implemented a predictive model to identify factors associated with postural impairments such as spastic or hypotonic truncal tone (TT) in children with CP. We conducted a longitudinal, double-blinded, multicenter, descriptive study of 102 teenagers with CP with cognitive impairment and severe motor disorders with and without truncal tone impairments treated in two specialized hospitals (60 inpatients and 42 outpatients; 60 males, mean age 16.5 ± 1.2 years, range 12 to 18 yrs). Clinical and functional data were collected between 2006 and 2021. TT-PredictMed, a multiple logistic regression prediction model, was developed to identify factors associated with hypotonic or spastic TT following the guidelines of "Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis". Predictors of hypotonic TT were hip dysplasia ($p = 0.01$), type of etiology (postnatal > perinatal > prenatal causes; $p = 0.05$), male gender, and poor manual ($p = 0.01$) and gross motor function ($p = 0.05$). Predictors of spastic TT were neuromuscular scoliosis ($p = 0.03$), type of etiology (prenatal > perinatal > postnatal causes; $p < 0.001$), spasticity (quadri/triplegia > diplegia > hemiplegia; $p = 0.05$), presence of dystonia ($p = 0.001$), and epilepsy (refractory > controlled, $p = 0.009$). The predictive model's average accuracy, sensitivity, and specificity reached 82%. The model's accuracy aligns with recent studies on applying machine learning models in the clinical field.

PMID: 37371021

4. Globus pallidus internus activity increases during voluntary movement in children with dystonia

Estefania Hernandez-Martin, Maral Kasiri, Sumiko Abe, Jennifer MacLean, Joffre Olaya, Mark Liker, Jason Chu, Terence D Sanger

iScience. 2023 Jun 7;26(7):107066. doi: 10.1016/j.isci.2023.107066. eCollection 2023 Jul 21.

The rate model of basal ganglia function predicts that muscle activity in dystonia is due to disinhibition of thalamus resulting from decreased inhibitory input from pallidum. We seek to test this hypothesis in children with dyskinetic cerebral palsy undergoing evaluation for deep brain stimulation (DBS) to analyze movement-related activity in different brain regions. The results revealed prominent beta-band frequency peaks in the globus pallidus interna (GPi), ventral oralis anterior/posterior (VoaVop) subnuclei of the thalamus, and subthalamic nucleus (STN) during movement but not at rest. Connectivity analysis indicated stronger coupling between STN-VoaVop and STN-GPi compared to GPi-STN. These findings contradict the hypothesis of decreased thalamic inhibition in dystonia, suggesting that abnormal patterns of inhibition and disinhibition, rather than reduced GPi activity, contribute to the disorder. Additionally, the study implies that correcting abnormalities in GPi function may explain the effectiveness of DBS targeting the STN and GPi in treating dystonia.

PMID: 37389183

5. Sensory integration versus Masgutova neuro-sensorimotor reflex integration program on controlling primitive reflexes and gross motor abilities in children with diplegic cerebral palsy

Mustafa A Mohamed, Manal Salah El-Dein, Sahar M Nour El-Deen, Mahmoud S El Fakharany

Physiother Res Int. 2023 Jun 29;e2030. doi: 10.1002/pri.2030. Online ahead of print.

Background and objective: An abnormality in muscular tone, lack of postural control, and a lack of coordination are all linked to the retention of primitive and immature postural reflexes. The Purpose of this study aimed of detecting which therapeutic approach is more effective in integrating retained primitive reflexes, either Masgutova neuro-sensorimotor reflex integration or Sensory integration (SI) program. Methods: Forty children with spastic diplegic cerebral palsy (CP) (11 girls and 29 boys), involved in the current study and their ages ranged from 3 to 6 years old. They were divided at random into two groups (A and B), patients in the study group (A) (n = 20) were treated by Masgutova neuro-sensorimotor reflex integration program (MNRI) while those of study group (B) (n = 20), were subjected to Sensory integration program (SIP), A standardized physical treatment regimen was provided to both groups (Stretching exercise, Strengthening exercise, and facilitation of developing motor milestones) All children were evaluated by using GMFM-88 and (PDMS-2) reflexes subtest before and after treatment

that lasted for three successive months at a frequency of three sessions per week. Results: There was a statistically substantial increase in GMFM scores and control of primitive reflexes post treatment in each group compared to those of the pretreatment mean values ($p > 0.05$). There was also a statistically non-significance difference between group A and group B regarding post treatment results ($p > 0.05$). Implications on physiotherapy practice: SI and MNRI programs can equally be used in the treatment of children with spastic CP who suffer from retained primitive reflexes and delayed gross motor function.

PMID: 37381746

6. Editorial: Statistical model-based computational biomechanics: applications in joints and internal organs

Bhushan Borotikar, Tinashe E M Mutsvangwa, Shireen Y Elhabian, Emmanuel A Audenaert

Editorial Front Bioeng Biotechnol. 2023 Jun 13;11:1232464. doi: 10.3389/fbioe.2023.1232464. eCollection 2023.

No abstract available

PMID: 37383523

7. Neonatal treatment with resveratrol decreases postural and strength impairments and improves mitochondrial function in the somatosensory cortex rats submitted to cerebral palsy

Vanessa da Silva Souza, Raul Manhães-de-Castro, Sabrina da Conceição Pereira, Caio Matheus Santos da Silva Calado, Beatriz Souza de Silveira, Eulália Rebeca da Silva Araújo, Severina Cassia de Andrade Silva, Osmar Henrique Dos Santos Junior, Claudia Jacques Lagranha, Luan Kelwyny Thaywã Marques da Silva, Ana Elisa Toscano

Neurochem Int. 2023 Jun 27;105568. doi: 10.1016/j.neuint.2023.105568. Online ahead of print.

Cerebral palsy is a neurodevelopmental disease characterized by postural, motor, and cognitive disorders, being one of the main causes of physical and intellectual disability in childhood. To minimize functional impairments, the use of resveratrol as a therapeutic strategy is highlighted due to its neuroprotective and antioxidant effects in different regions of the brain. Thus, this study aimed to investigate the effects of neonatal treatment with resveratrol on postural development, motor function, oxidative balance, and mitochondrial biogenesis in the brain of rats submitted to a cerebral palsy model. Neonatal treatment with resveratrol attenuated deficits in somatic growth, postural development, and muscle strength in rats submitted to cerebral palsy. Related to oxidative balance, resveratrol in cerebral palsy decreased the levels of MDA and carbonyls. Related to mitochondrial biogenesis, was observed in animals with cerebral palsy treated with resveratrol, an increase in mRNA levels of TFAM, in association with the increase of citrate synthase activity. The data demonstrated a promising effect of neonatal resveratrol treatment, improving postural and muscle deficits induced by cerebral palsy. These findings were associated with improvements in oxidative balance and mitochondrial biogenesis in the brain of rats submitted to cerebral palsy.

PMID: 37385449

8. A procedure and model for the identification of uni- and biarticular structures passive contribution to inter-segmental dynamics

Axel Koussou, Raphaël Dumas, Eric Desailly

Sci Rep. 2023 Jun 29;13(1):10535. doi: 10.1038/s41598-023-37357-w.

Inter-segmental moments come from muscles contractions, but also from passive moments, resulting from the resistance of the periarticular structures. To quantify the passive contribution of uni- and biarticular structures during gait, we propose an innovative procedure and model. 12 typically developed (TD) children and 17 with cerebral palsy (CP) participated in a passive testing protocol. The relaxed lower limb joints were manipulated through full ranges of motion while kinematics and applied forces were simultaneously measured. The relationships between uni-/biarticular passive moments/forces and joint angles/musculo-tendon lengths were modelled by a set of exponential functions. Then, subject specific gait joint angles/musculo-tendon lengths were input into the determined passive models to estimate joint moments and power attributable to passive structures. We found that passive mechanisms contribute substantially in both populations, mainly during push-off and swing phases for hip and knee and push-off for the ankle, with a distinction between uni- and biarticular structures. CP children showed comparable passive mechanisms but larger variability than the TD ones and higher contributions. The proposed procedure and model enable a comprehensive assessment of the passive mechanisms for a subject-specific treatment of the stiffness implying gait disorders by targeting when and how passive forces are impacting gait.

PMID: 37386101

9. Feasibility of a Home-Based Mirror Therapy Program in Children with Unilateral Spastic Cerebral Palsy

Anna Ortega-Martínez, Rocío Palomo-Carrión, Carlos Varela-Ferro, Maria Caritat Bagur-Calafat

Healthcare (Basel). 2023 Jun 19;11(12):1797. doi: 10.3390/healthcare11121797.

Children with Unilateral Spastic Cerebral Palsy (US CP) have motor and somatosensory impairments that affect one side of their body, impacting upper limb functioning. These impairments contribute negatively to children's bimanual performance and quality of life. Intensive home-based therapies have been developed and have demonstrated their feasibility for children with US CP and their parents, especially when therapies are designed with the proper coaching of families. Mirror Therapy (MT) is being studied to become an approachable intensive and home-based therapy suitable for children with US CP. The aim of this study is to analyze the feasibility of a five-week home-based program of MT for children with US CP that includes coaching by the therapist. Six children aged 8-12 years old performed the therapy for five days per week, 30 min per day. A minimum of 80% of compliance was required. The feasibility included compliance evaluations, total dosage, perceived difficulty of the exercises, and losses of follow-ups. All children completed the therapy and were included in the analysis. The total accomplishment was 86.47 ± 7.67. The perceived difficulty of the exercises ranged from 2.37 to 4.51 out of 10. In conclusion, a home-based program of Mirror Therapy is a safe, cost-efficient, and feasible therapy for children with US CP when the therapist is involved as a coach during the entire program.

PMID: 37372915

10. Evaluation of Knee Position Sense in Children with Motor Disabilities and Children with Typical Development: A Cross-Sectional Study

Åsa Bartonek, Marie Eriksson, Annika Ericson, Mikael Reimeringer, Cecilia Lidbeck

Children (Basel). 2023 Jun 13;10(6):1056. doi: 10.3390/children10061056.

In children with motor disabilities, knee position during walking is often of concern in rehabilitation. This study aimed to investigate knee joint position sense. Thirty-seven children with Cerebral Palsy (CP), 21 with Myelomeningocele (MMC), 19 with Arthrogryposis (AMC), and 42 TD children participated in the study. Knee joint position sense, i.e., the difference between the criterion angle and the reproduced angle (JPS-error), was assessed in sitting while 3D motion capture was recorded at flexed knee 70 (Knee70), 45 (Knee45), and 20 (Knee20) degrees, and after three seconds at maintained criterion angle (CAM) and maintained reproduced angle (RAM). No differences were found between the groups in JPS-error, CAM, and RAM. At Knee70, CAM differed between the right and left legs in the TD group ($p = 0.014$) and RAM in the MMC group ($p = 0.021$). In the CP group, CAM was greater than RAM at Knee70 in the left leg ($p = 0.002$), at Knee45 in both legs ($p = 0.004$, $p = 0.025$), and at Knee20 in the right leg ($p = 0.038$). Difficulties in maintaining the knee position at CAM in the CP group sheds light on the need for complementary judgments of limb proprioception in space to explore the potential influence on knee position during walking.

PMID: 37371287

11. Intensive Therapy of the Lower Limbs and the Trunk in Children with Bilateral Spastic Cerebral Palsy: Comparing a Qualitative Functional and a Functional Approach

Vanessa van Tittelboom, Lieve Heyrman, Josse De Cat, Patrick Algoet, Nicky Peeters, Ipek Alemdaroğlu-Gürbüz, Frank Plasschaert, Katrin Van Herpe, Guy Molenaers, Nele De Bruyn, Ellen Deschepper, Kaat Desloovere, Patrick Calders, Hilde Feys, Christine Van den Broeck

J Clin Med. 2023 Jun 15;12(12):4078. doi: 10.3390/jcm12124078.

Few studies have examined the effect of intensive therapy on gross motor function and trunk control in children with cerebral palsy (CP). This study evaluated the effects of an intensive burst of therapy on the lower limbs and trunk by comparing qualitative functional and functional approaches. This study was designed as a quasi-randomized, controlled, and evaluator-blinded trial. Thirty-six children with bilateral spastic CP (mean age = 8 y 9 mo; Gross Motor Function Classification II and III) were randomized into functional (n = 12) and qualitative functional (n = 24) groups. The main outcome measures were the Gross Motor Function Measure (GMFM), the Quality Function Measure (QFM), and the Trunk Control Measurement Scale (TCMS). The results revealed significant time-by-approach interaction effects for all QFM attributes and the GMFM's standing dimension and total score. Post hoc tests showed immediate post-intervention gains with the qualitative functional approach for all QFM attributes, the GMFM's standing and walking/running/jumping dimension and total score, and the total TCMS score. The qualitative functional approach shows promising results with improvements in movement quality and gross motor function.

PMID: 37373771

12. Retracted: Systematic Evaluation of the Effect of Rehabilitation of Lower Limb Function in Children with Cerebral Palsy Based on Virtual Reality Technology

Journal Of Healthcare Engineering

Retraction of Publication J Healthc Eng. 2023 Jun 21;2023:9832521. doi: 10.1155/2023/9832521. eCollection 2023.

[This retracts the article DOI: 10.1155/2021/6625604.].

PMID: 37388131

13. Reliability of the Gait Outcomes Assessment List questionnaire

Jean L Stout, Marissa Thill, Meghan E Munger, Kathryn Walt, Elizabeth R Boyer

Dev Med Child Neurol. 2023 Jun 30. doi: 10.1111/dmcn.15677. Online ahead of print.

Aim: To report the test-retest reliability of the parent version of the Gait Outcomes Assessment List (GOAL) questionnaire for item, domain, total score, and goal importance in children with cerebral palsy (CP) functioning in Gross Motor Function Classification System (GMFCS) levels I to III. Method: The GOAL questionnaire was completed twice, 3 to 31 days apart, in a prospective cohort study of 112 caregivers of children aged 4 to 17 years with CP (40% unilateral; GMFCS level I = 53; II = 35; III = 24; 76 males). All had an outpatient visit over a 1-year period. The standard error of measurement (SEM), minimum detectable change, and agreement were calculated for all responses, including goal importance. Results: The SEM for the total score was 3.1 points for the cohort (GMFCS level I = 2.3, GMFCS level II = 3.8, GMFCS level III = 3.6). The standardized domain and item scores were less reliable than the total score and varied according to GMFCS level. The gait function and mobility domain exhibited the best reliability for the cohort (SEM = 4.4), whereas the use of braces and mobility aids domain exhibited the lowest (SEM = 11.9). Goal importance was reliable (cohort average agreement 73%). Interpretation: The parent version of GOAL has acceptable levels of test-retest reliability for most domains and items. Caution is advised when interpreting the least reliable scores. Essential information necessary for accurate interpretation is provided.

PMID: 37392015

14. Lifelong Fitness in Ambulatory Children and Adolescents with Cerebral Palsy II: Influencing the Trajectory

Susan V Duff, Justine D Kimbel, Marybeth Grant-Beuttler, Theresa Sukal-Moulton, Noelle G Moreau, Kathleen M Friel

Behav Sci (Basel). 2023 Jun 15;13(6):504. doi: 10.3390/bs13060504.

Physical activity of at least moderate intensity in all children contributes to higher levels of physical and psychological health. While essential, children with cerebral palsy (CP) often lack the physical capacity, resources, and knowledge to engage in physical activity at a sufficient intensity to optimize health and well-being. Low levels of physical activity place them at risk for declining fitness and health, contributing to a sedentary lifestyle. From this perspective, we describe a framework to foster a lifelong trajectory of fitness in ambulatory children with CP (GMFCS I-III) as they progress into adolescence and adulthood, implemented in conjunction with a training program to augment bone and muscle health. First, we recommend that altering the fitness trajectory of children with CP will require the use of methods to drive behavioral change prior to adolescence. Second, to promote behavior change, we suggest embedding lifestyle intervention into fitness programming while including meaningful activities and peer socialization to foster self-directed habit formation. If the inclusion of lifestyle intervention to drive behavior change is embedded into fitness programs and found to be effective, it may guide the delivery of targeted programming and community implementation. Participation in comprehensive programming could alter the long-term trajectory of musculoskeletal health while fostering strong self-efficacy in persons with CP.

PMID: 37366756

15. F-words and early intervention ingredients for non-ambulant children with cerebral palsy: A scoping review

Ana Carolina De Campos, Álvaro Hidalgo-Robles, Egmar Longo, Claire Shrader, Ginny Paleg

Review Dev Med Child Neurol. 2023 Jun 28. doi: 10.1111/dmcn.15682. Online ahead of print.

Aim: To explore the ingredients of early interventions provided to young children with cerebral palsy (CP) who are classified in Gross Motor Function Classification System (GMFCS) levels IV and V, and to identify the 'F-words' addressed by the interventions. Method: Searches were completed in four electronic databases. Inclusion criteria were the original experimental studies that fitted the following PCC components: population, young children (aged 0-5 years, at least 30% of the sample) with CP and significant motor impairment (GMFCS levels IV or V, at least 30% of the sample); concept, non-surgical and non-

pharmacological early intervention services measuring outcomes from any of the International Classification of Functioning, Disability and Health domains; and context, studies published from 2001 to 2021, from all settings and not limited to any specific geographical location. Results: Eighty-seven papers were included for review, with qualitative (n = 3), mixed-methods (n = 4), quantitative descriptive (n = 22), quantitative non-randomized (n = 39), and quantitative randomized (n = 19) designs. Fitness (n = 59), family (n = 46), and functioning (n = 33) ingredients were addressed by most experimental studies, whereas studies on fun (n = 6), friends (n = 5), and future (n = 14) were scarce. Several other factors (n = 55) related to the environment, for example, service provision, professional training, therapy dose, and environmental modifications, were also relevant. Interpretation: Many studies positively supported formal parent training and use of assistive technology to promote several F-words. A menu of intervention ingredients was provided, with suggestions for future research, to incorporate them into a real context within the family and clinical practice.

PMID: 37381598

16. Use and Effectiveness of Electrosuit in Neurological Disorders: A Systematic Review with Clinical Implications

David Perpetuini, Emanuele Francesco Russo, Daniela Cardone, Roberta Palmieri, Andrea De Giacomo, Raffaello Pellegrino, Arcangelo Merla, Rocco Salvatore Calabrò, Serena Filoni

Review Bioengineering (Basel). 2023 Jun 2;10(6):680. doi: 10.3390/bioengineering10060680.

Electrical stimulation through surface electrodes is a non-invasive therapeutic technique used to improve voluntary motor control and reduce pain and spasticity in patients with central nervous system injuries. The Exopulse Mollii Suit (EMS) is a non-invasive full-body suit with integrated electrodes designed for self-administered electrical stimulation to reduce spasticity and promote flexibility. The EMS has been evaluated in several clinical trials with positive findings, indicating its potential in rehabilitation. This review investigates the effectiveness of the EMS for rehabilitation and its acceptability by patients. The literature was collected through several databases following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. Positive effects of the garment on improving motor functions and reducing spasticity have been shown to be related to the duration of the administration period and to the dosage of the treatment, which, in turn, depend on the individual's condition and the treatment goals. Moreover, patients reported wellbeing during stimulation and a muscle-relaxing effect on the affected limb. Although additional research is required to determine the efficacy of this device, the reviewed literature highlights the EMS potential to improve the motor capabilities of neurological patients in clinical practice.

PMID: 37370612

17. Prevalence of cerebral palsy and factors associated with cerebral palsy subtype: A population-based study in Belgium

Evy Dhondt, Bernard Dan, Frank Plasschaert, Marc Degelaen, Charlotte Dielman, Delphine Dispa, Iulia Ebetiuc, Danielle Hasaerts, Sandra Kenis, Costanza Lombardo, Karine Pelc, Vanessa Wermenbol, Els Ortibus; Belgian Cerebral Palsy Register

Eur J Paediatr Neurol. 2023 Jun 14;46:8-23. doi: 10.1016/j.ejpn.2023.06.003. Online ahead of print.

Aim: To report on the prevalence, neuroimaging patterns, and function of children with cerebral palsy (CP) in Belgium for birth years 2007-2012, and identify distinctive risk indicators and differences in outcome between CP subtypes. Methods: Antenatal and perinatal/neonatal factors, motor and speech function, associated impairments, and neuroimaging patterns were extracted from the Belgian Cerebral Palsy Register. Prevalence was estimated per 1000 (overall, ante/perinatal, spastic, dyskinetic CP) or 10,000 (post-neonatal, ataxic CP) live births. Multinomial logistic regression analyses were performed to ascertain the effects of antenatal/perinatal/neonatal factors and neuroimaging patterns on the likelihood of dyskinetic or ataxic CP relative to spastic CP, and test the likelihood of the occurrence of impaired motor and speech function and associated impairments in dyskinetic or ataxic CP relative to spastic CP. Results: In total, 1127 children with CP were identified in Belgium. The birth prevalence of overall CP was 1.48 per 1000 live births. The likelihood of dyskinetic CP increases if the child was born to a mother aged ≥35 years, mechanically ventilated, and had predominant grey matter injury, while an increased likelihood of ataxic CP is associated with ≥2 previous deliveries. Children with dyskinetic and ataxic CP are more likely to function with impairments in motor, speech, and intellectual abilities. Conclusion: Distinctive risk indicators and differences in outcome between CP subtypes were identified. These factors can be incorporated into clinical practice to facilitate early, accurate, and reliable classification of CP subtype, and may lead to individually tailored neonatal care and other (early) intervention options.

PMID: 37364404

18. Strengthening Equitable Access to Care and Support for Children with Cerebral Palsy and Their Caregivers

Aysha Jawed, Michelle Mowry

Children (Basel). 2023 Jun 1;10(6):994. doi: 10.3390/children10060994.

Cerebral palsy is one of the most prevalent groups of motor disorders affecting children and adults across the world. As increasingly more children with cerebral palsy are living longer into adulthood, it is ever more crucial to ensure access to timely and needed early intervention from the onset of diagnosis, on a continuum, to optimize medical, developmental, socio-emotional, and academic outcomes for these children over time. The American Academy of Pediatrics (AAP), in collaboration with the American Academy of Cerebral Palsy and Developmental Medicine (AACPDM), substantially revised the clinical practice guidelines for cerebral palsy in 2022, after their prior publication of the guidelines in 2006. The revised guidelines account for a range of considerations that are in line with the biopsychosocial, risk and resilience, and family-centered care models as well as promote a more strengths-based approach to care. Furthermore, there is increased emphasis in the guidelines on promoting equitable access to care as part of contributing towards health equity for all children with cerebral palsy. In addition, the 2022 guidelines clearly present recommendations for earlier diagnosis of cerebral palsy, potentially as early as infancy, as the basis for activating access to early intervention services for children that can bolster their neuroplasticity and global development from an earlier age onward. We consolidate the existing literature on caregiver perceptions, beliefs and concerns surrounding earlier diagnosis of cerebral palsy and connect them to the recommendations in the revised guidelines. We also delineate several considerations surrounding education for healthcare providers and caregivers of children in navigating the chronicity of cerebral palsy in both community and healthcare contexts. There is a scant amount of literature on cerebral palsy across traditional and nontraditional sources of media in published studies, which we also review. Lastly, we present a wealth of recommendations for further research and practice that account for the revised 2022 guidelines, caregiver preferences and acceptability of care, and health equity as the bases for strengthening equitable access to care for children with cerebral palsy on a continuum as they transition into adulthood.

PMID: 37371227

19. Parents of Children Diagnosed with Congenital Anomalies or Cerebral Palsy: Identifying Needs in Interaction with Healthcare Services

Ana João Santos, Paula Braz, Teresa Folha, Ausenda Machado, Carlos Matias-Dias

Children (Basel). 2023 Jun 12;10(6):1051. doi: 10.3390/children10061051.

The changes deriving from the birth of a child with a congenital anomaly (CA) or cerebral palsy (CP) imply, in many cases, an increased interaction with health services. A cross-sectional descriptive study was conducted with a convenience sample of parents of children diagnosed with four groups of CA (severe heart anomalies, spina bifida, orofacial clefts, and Down syndrome) and/or CP. A semistructured online questionnaire to be answered by parents was sent by web link to focal points of five parent associations and professional institutions. Data were analyzed through thematic content analysis (open-ended questions) and descriptive analysis (closed-ended questions). The results indicate consistency of responses of parents of children diagnosed with different conditions, namely with respect to the perception of health services and professionals. Closed and open-ended responses indicated three main topics in the interaction between health services and parenthood: information, coordinated and integrated responses, and support. The less positive outcomes suggest unmet information needs, while positive aspects include confidence in the care provided and the "training" received from health professionals.

PMID: 37371282

20. Declining incidence of cerebral palsy in South Korea

Gun-Ha Kim, Gisu Lee, Sungyeon Ha, Geum Joon Cho, Yoon Ha Kim

Sci Rep. 2023 Jun 28;13(1):10496. doi: 10.1038/s41598-023-36236-8.

Presuming that the incidence of cerebral palsy (CP) in Korea is decreasing due to medical advances, we analyzed the trends and risk factors of CP in changing circumstances. We identified all women who delivered a singleton between 2007 and 2015 using the Korea National Health Insurance (KNHI). Information on pregnancy and birth was obtained by linking the KNHI claims database and data from the national health-screening program for infants and children. The 4-years incidence of CP decreased significantly from 4.77 to 2.52 per 1000 babies during the study period. The multivariate analysis revealed that the risk of developing CP was 29.5 times higher in preterm infants born before 28 weeks of gestational age, 24.5 times higher in infants born between 28 and 34 weeks, and 4.5 times higher in infants born between 34 and 36 weeks, compared to full-term appropriate for age (2.5 ~ 4 kg of body weight) infants. 5.6 times higher in those with birth weight < 2500 g, and 3.8 times higher in pregnancies with polyhydramnios. Additionally, respiratory distress syndrome increased the risk of developing CP by 2.04 times, while necrotizing enterocolitis was associated with a 2.80-fold increased risk of CP. In Korea, the incidence of CP in singleton decreased from 2007 to 2015. We need to continue to focus on developing medical technologies for the early detection of high-risk neonates and minimizing brain damage to reduce the incidence rate of CP effectively.

PMID: 37380633

21. Genetic testing in individuals with cerebral palsy

No authors listed

Dev Med Child Neurol. 2023 Jun 30. doi: 10.1111/dmcn.15699. Online ahead of print.

No abstract available

PMID: 37390221

22. Caregiver knowledge and preferences for gross motor function information in cerebral palsy

No authors listed

Dev Med Child Neurol. 2023 Jun 28. doi: 10.1111/dmcn.15686. Online ahead of print.

No abstract available

PMID: 37381628

23. Risk Factors for Mortality in Patients With Cerebral Palsy: A Systematic Review and Meta-Analysis

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Review Cureus. 2023 May 22;15(5):e39327. doi: 10.7759/cureus.39327. eCollection 2023 May.

Cerebral palsy (CP) is a developmental and physical disorder with different degrees of severity. Since CP manifests itself in early childhood, numerous research studies have concentrated on children with CP. Patients with CP encounter different severity of motor impairments attributed to the damage or disturbance to the fetal or infant developing brain, which begins in early childhood and persists through adulthood. Patients with CP are more prone to mortality compared to the general population. This systematic review and meta-analysis aimed to assess the risk factors that predict and influence mortality in patients with CP. Systematic search for studies assessing the risk factors for mortality in CP patients that were conducted from 2000 to 2023 in Google Scholar, PubMed, and Cochrane Library was performed. R-One Group Proportion was used for statistical analysis and Newcastle-Ottawa Quality Assessment Scale (NOS) for quality appraisal. Of the 1791 total database searches, nine studies were included. Based on the NOS tool for quality appraisal, seven studies were of moderate quality, and two studies were rated as of high quality. The risk factors included pneumonia and other respiratory infections, neurological disorders, circulatory diseases, gastrointestinal infections, and accidents. Pneumonia (OR = 0.40, 95% CI = 0.31 - 0.51), neurological disorders (OR = 0.11, 95% CI = 0.08 - 0.16), respiratory infections (OR = 0.36, 95% CI = 0.31 - 0.51), cardiovascular and circulatory diseases (OR = 0.11, 95% CI = 0.04 - 0.27), gastrointestinal and metabolic causes (OR = 0.12, 95% CI = 0.06 - 0.22), and accidents (OR = 0.05, 95% CI = 0.04 - 0.07) were the risk factors assessed. It was concluded that multiple factors predict the risk of mortality in patients with CP. Pneumonia and other respiratory infections are associated with a high risk of mortality. Cardiovascular and circulatory diseases, gastrointestinal and metabolic disorders, and accidents are strongly linked to mortality in CP patients.

PMID: 37378195

24. Arginase deficiency with parotid gland swelling and hyperamylasemia: A case report

Noboru Kuyama, Shigeru Nagaki, Akie Miyamoto, Kaoru Etou, Hiroshi Maruyama, Makiko Osawa

Case Reports SAGE Open Med Case Rep. 2023 Jun 23;11:2050313X231181836. doi: 10.1177/2050313X231181836. eCollection 2023.

Arginase deficiency is a progressive neurological disorder characterized by episodic hyperammonemia crises. Our patient had been diagnosed with cerebral palsy (spastic paraplegia) in childhood and received rehabilitation. She had suffered parotid swelling since the age of 5 years, prior to liver dysfunction becoming apparent, and then developed hyperamylasemia at 8 years of age. At age 25 years, she presented with hyperammonemia and elevations of aspartate aminotransferase and alanine aminotransferase. At age 27 years, she was diagnosed with arginase deficiency due to hyperargininemia and absent arginase activity in erythrocytes. Liver cirrhosis was also present. She was hospitalized several times for management of episodic hyperammonemia due to recurrent viral infections, an unbalanced diet, and poor compliance with medications.

PMID: 37377459

25. Juvenile Dermatomyositis and Infantile Cerebral Palsy: Aicardi-Gouteres Syndrome, Type 5, with a Novel Mutation in SAMHD1-A Case Report

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Case Reports Biomedicines. 2023 Jun 12;11(6):1693. doi: 10.3390/biomedicines11061693.

Introduction: Aicardi-Gouteres syndrome (AGS) is a monogenic interferonopathy characterized by early onset, dysregulation of skin (chilblain lesions), brain, and immune systems (fever, hepatomegaly, glaucoma, arthritis, myositis, and autoimmune activity). The disease looks like TORCH (Toxoplasmosis, Others, Rubella, Cytomegalovirus, Herpes) infection with early-onset encephalopathy resulting in severe neuropsychological disability. Case description: A six-year-old girl has been suffering from generalized seizures, fever episodes, severe psychomotor development delay, and spastic tetraparesis since the first year of her life. Her two elder brothers died at a young age from suspected infantile cerebral palsy (ICP). Other siblings (younger brother and two elder sisters) are as healthy as their parents. The girl was diagnosed with juvenile dermatomyositis at 5.5 years. Basal ganglia, periventricular, and cerebellum calcifications; hypoplasia of the corpus callosum; and leukodystrophy were detected on CT. The IFN-I score was 12 times higher than normal. The previously not described nucleotide variant c.434G > C (chr 20:36935104C > G; NM_015474) was detected in exon 4 of the SAMHD1 gene in the homozygous state, leading to amino acid substitution p.R145P. Aicardi-Goutières syndrome 5 was diagnosed. Her treatment included corticosteroids, methotrexate, and tofacitinib 5 mg twice a day and it contributed to health improvements. The following brain CT depicted the previously discovered changes without the sign of calcification spreading. Conclusions: Early diagnosis of AGS is highly important as it allows starting treatment in a timely manner. Timely treatment, in return, can help avoid the development/progression of end-organ damage, including severe neurological complications and early death. It is necessary to spread information about AGS among neurologists, neonatologists, infectious disease specialists, and pediatricians. A multidisciplinary team approach is required.

PMID: 37371788

26. Evidence for Using ACQUIRE Therapy in the Clinical Application of Intensive Therapy: A Framework to Guide Therapeutic Interactions

Stephanie C DeLuca, Mary Rebekah Trucks, Dorian Wallace, Sharon Landesman Ramey

Behav Sci (Basel). 2023 Jun 7;13(6):484. doi: 10.3390/bs13060484.

Intensive therapies have become increasingly popular for children with hemiparesis in the last two decades and are specifically recommended because of high levels of scientific evidence associated with them, including multiple randomized controlled trials and systematic reviews. Common features of most intensive therapies that have documented efficacy include: high dosages of therapy hours; active engagement of the child; individualized goal-directed activities; and the systematic application of operant conditioning techniques to elicit and progress skills with an emphasis on success-oriented play. However, the scientific protocols have not resulted in guiding principles designed to aid clinicians with understanding the complexity of applying these principles to a heterogeneous clinical population, nor have we gathered sufficient clinical data using intensive therapies to justify their widespread clinical use beyond hemiparesis. We define a framework for describing moment-by-moment therapeutic interactions that we have used to train therapists across multiple clinical trials in implementing intensive therapy protocols. We also document outcomes from the use of this framework during intensive therapies provided clinically to children (7 months-20 years) from a wide array of diagnoses that present with motor impairments, including hemiparesis and quadriparesis. Results indicate that children from a wide array of diagnostic categories demonstrated functional improvements.

PMID: 37366736

27. Factors Influencing Receipt and Type of Therapy Services in the NICU

Christiana D Butera, Shaaron E Brown, Jennifer Burnsed, Jodi Darring, Amy D Harper, Karen D Hendricks-Muñoz, Megan Hyde, Audrey E Kane, Meagan R Miller, Richard D Stevenson, Christine M Spence, Leroy R Thacker, Stacey C Dusing

Behav Sci (Basel). 2023 Jun 7;13(6):481. doi: 10.3390/bs13060481.

Understanding the type and frequency of current neonatal intensive care unit (NICU) therapy services and predictors of referral for therapy services is a crucial first step to supporting positive long-term outcomes in very preterm infants. This study enrolled 83 very preterm infants (<32 weeks, gestational age mean 26.5 ± 2.0 weeks; 38 male) from a longitudinal clinical trial. Race, neonatal medical index, neuroimaging, and frequency of therapy sessions were extracted from medical records. The Test of Infant Motor Performance and the General Movement Assessment were administered. Average weekly sessions of occupational therapy, physical therapy, and speech therapy were significantly different by type, but the magnitude and direction of the difference depended upon the discharge week. Infants at high risk for cerebral palsy based on their baseline General Movements Assessment scores received more therapy sessions than infants at low risk for cerebral palsy. Baseline General Movements Assessment was related to the mean number of occupational therapy sessions but not physical therapy or

speech therapy sessions. Neonatal Medical Index scores and Test of Infant Motor Performance scores were not predictive of combined therapy services. Medical and developmental risk factors, as well as outcomes from therapy assessments, should be the basis for referral for therapy services in the neonatal intensive care unit.

PMID: 37366732

28. Neurodevelopment and healthcare utilisation at age 5-6 years in bronchopulmonary dysplasia: an EPIPAGE-2 cohort study

Ludovic Tréluyer, Alexandra Nuytten, Isabelle Guellec, Pierre-Henri Jarreau, Valérie Benhammou, Gilles Cambonie, Patrick Truffert, Laetitia Marchand-Martin, Pierre Yves Ancel, Héloïse Torchin

Arch Dis Child Fetal Neonatal Ed. 2023 Jun 23;fetalneonatal-2023-325376. doi: 10.1136/archdischild-2023-325376. Online ahead of print.

Objective: We aimed to study neurodevelopmental outcomes and healthcare utilisation at age 5-6 years in very preterm children with bronchopulmonary dysplasia (BPD). Design: Prospective and national population-based study. Setting: All the neonatal units in 25 French regions (21 of the 22 metropolitan regions and 4 overseas regions). Patients: Children born before 32 weeks' gestation in 2011. Interventions: Blind, comprehensive and standardised assessment by trained neuropsychologists and paediatricians at age 5-6 years. Main outcome measures: Overall neurodevelopmental disabilities, behavioural difficulties, developmental coordination disorders, full-scale IQ, cerebral palsy, social interaction disorders, rehospitalisation in the previous 12 months and detailed developmental support. Results: Of the 3186 children included, 413 (11.7%) had BPD. The median gestational age of children with BPD was 27 weeks (IQR 26.0-28.0) and without BPD was 30 weeks (28.0-31.0). At age 5-6 years, 3150 children were alive; 1914 (60.8%) had a complete assessment. BPD was strongly associated with mild, moderate and severe overall neurodevelopmental disabilities (OR 1.49, 95% CI 1.05 to 2.20; 2.20, 1.41 to 3.42 and 2.71, 1.67 to 4.40). BPD was associated with developmental coordination disorders, behavioural difficulties, lower IQ score as well as rehospitalisation in the last 12 months and developmental support. The association between BPD and cerebral palsy was statistically significant before adjustment but not in adjusted analyses. Conclusions: BPD was strongly and independently associated with many neurodevelopmental disabilities. Improving medical and neurodevelopmental management of BPD in very preterm children should be a priority to reduce its long-term consequences.

PMID: 37364896

29. Implications of Genetic Variants in Cerebral Palsy

Ting Zhang, Tingsong Li

JAMA Pediatr. 2023 Jun 26. doi: 10.1001/jamapediatrics.2023.1864. Online ahead of print.

No abstract available

PMID: 37358873

30. Implications of Genetic Variants in Cerebral Palsy

Mark I Evans, David W Britt, Lawrence D Devoe

JAMA Pediatr. 2023 Jun 26. doi: 10.1001/jamapediatrics.2023.1861. Online ahead of print.

No abstract available

PMID: 37358861

31. Implications of Genetic Variants in Cerebral Palsy-Reply

Scott M Myers, Christa L Martin, Andres Moreno-De-Luca

JAMA Pediatr. 2023 Jun 26. doi: 10.1001/jamapediatrics.2023.1858. Online ahead of print.

No abstract available

PMID: 37358842

32. Long-Term Follow-Up of Pediatric Patients with Dyskinetic Cerebral Palsy and Deep Brain Stimulation

Anne Koy, Andrea A Kühn, Petra Schiller, Julius Huebl, Gerd-Helge Schneider, Matthias Eckenweiler, Cornelia Rensing-Zimmermann, Volker Arnd Coenen, Joachim K Krauss, Assel Saryyeva, Hans Hartmann, Delia Lorenz, Jens Volkmann, Cordula Matthies, Alfons Schnitzler, Jan Vesper, Alireza Gharabaghi, Daniel Weiss, Andrea Bevot, Warren Marks, Angela Howser, Elegast Monbaliu, Joerg Mueller, Reinhild Prinz-Langenohl, Veerle Visser-Vandewalle, Lars Timmermann; STIM-CP investigators

Mov Disord. 2023 Jun 26. doi: 10.1002/mds.29516. Online ahead of print.

Background: Deep brain stimulation (DBS) has been increasingly used in the management of dyskinetic cerebral palsy (DCP). Data on long-term effects and the safety profile are rare. Objectives: We assessed the efficacy and safety of pallidal DBS in pediatric patients with DCP. Methods: The STIM-CP trial was a prospective, single-arm, multicenter study in which patients from the parental trial agreed to be followed-up for up to 36 months. Assessments included motor and non-motor domains. Results: Of the 16 patients included initially, 14 (mean inclusion age 14 years) were assessed. There was a significant change in the (blinded) ratings of the total Dyskinesia Impairment Scale at 36 months. Twelve serious adverse events (possibly) related to treatment were documented. Conclusion: DBS significantly improved dyskinesia, but other outcome parameters did not change significantly. Investigations of larger homogeneous cohorts are needed to further ascertain the impact of DBS and guide treatment decisions in DCP.

PMID: 37358761

33. [Prenatal rescue dose of betamethasone in the preterm infant with intrauterine growth restriction] [Article in Spanish]

Natalia Saldaña-García, José David Martínez-Pajares, Mercedes Chaffanel-Peláez, Ma Del Mar Serrano-Martín, Ma Gracia Espinosa-Fernández, Elías Tapia-Moreno, Tomás Sánchez-Tamayo

Andes Pediatr. 2023 Apr;94(2):200-208. doi: 10.32641/andespediatr.v94i2.. Epub 2023 Feb 7.

Antenatal corticosteroids reduce mortality and respiratory distress syndrome (RDS) in preterm newborns. These benefits decrease after a week of administration, recommending a rescue therapy if there is a new threat of premature delivery. Repeated administration of antenatal corticosteroids may have deleterious effects and their benefits are controversial in intrauterine growth restriction (IUGR). Objective: to verify the effects in the IUGR population of antenatal betamethasone rescue therapy on neonatal morbidity and mortality, RDS, and neurodevelopment at 2 years. Patients and method: Retrospective study including ≤ 34 weeks and ≤ 1,500g preterm newborns divided according to antenatal betamethasone exposure: Single-cycle (2 doses) vs Rescue therapy (3 doses). Subgroups were created for those ≥ 30 weeks. Both cohorts were followed up to 24 months of corrected age. The Ages & Stages Questionnaires (ASQ)® was administered to assess neurodevelopment. Results: 62 preterm infants with a diagnosis of IUGR were included. The rescue therapy group compared with the single-dose group showed no differences in morbidity and mortality and less intubation rate at birth ($p = 0.02$), with no differences in respiratory support at 7 days of life. Preterm newborns ≥ 30 weeks exposed to rescue therapy showed higher morbidity and mortality ($p = 0.03$) and bronchopulmonary dysplasia (BPD) ($p = 0.02$), showing no differences in RDS. The rescue therapy group showed worse mean scores on the ASQ-3 scale, with no significant differences in cerebral palsy or sensory deficits. Conclusions: Rescue therapy reduces intubation at birth but does not reduce morbidity and mortality. However, at > 30 weeks, this benefit is not observed and the IUGR population exposed to rescue therapy presented more BPD and lower scores on the ASQ-3 scale at 2 years. Future studies should be aimed at the individualization of antenatal corticosteroid therapy.

PMID: 37358113

34. Bone Marrow-Derived Mononuclear Cells in the Treatment of Neurological Diseases: Knowns and Unknowns

Quyen Thi Nguyen, Liem Nguyen Thanh, Van T Hoang, Trang T K Phan, Michael Heke, Duc M Hoang

Review Cell Mol Neurobiol. 2023 Jun 25. doi: 10.1007/s10571-023-01377-x. Online ahead of print.

Bone marrow-derived mononuclear cells (BMMNCs) have been used for decades in preclinical and clinical studies to treat various neurological diseases. However, there is still a knowledge gap in the understanding of the underlying mechanisms of BMMNCs in the treatment of neurological diseases. In addition, prerequisite factors for the efficacy of BMMNC administration, such as the optimal route, dose, and number of administrations, remain unclear. In this review, we discuss known and unknown aspects of BMMNCs, including the cell harvesting, administration route and dose; mechanisms of action; and their applications in neurological diseases, including stroke, cerebral palsy, spinal cord injury, traumatic brain injury, amyotrophic lateral sclerosis, autism spectrum disorder, and epilepsy. Furthermore, recommendations on indications for BMMNC administration and the advantages and limitations of BMMNC applications for neurological diseases are discussed.

BMMNCs in the treatment of neurological diseases. BMMNCs have been applied in several neurological diseases. Proposed mechanisms for the action of BMMNCs include homing, differentiation and paracrine effects (angiogenesis, neuroprotection, and anti-inflammation). Further studies should be performed to determine the optimal cell dose and administration route, the roles of BMMNC subtypes, and the indications for the use of BMMNCs in neurological conditions with and without genetic abnormalities.

PMID: 37356043

Prevention and Cure

35. Effectiveness of Polyphenols on Perinatal Brain Damage: A Systematic Review of Preclinical Studies

Paula Brielle Pontes, Ana Elisa Toscano, Diego Cabral Lacerda, Eulália Rebeca da Silva Araújo, Paulo César Trindade da Costa, Swane Miranda Alves, José Luiz de Brito Alves, Raul Manhães-de-Castro

Review Foods. 2023 Jun 6;12(12):2278. doi: 10.3390/foods12122278.

Polyphenol supplementation during early life has been associated with a reduction of oxidative stress and neuroinflammation in diseases caused by oxygen deprivation, including cerebral palsy, hydrocephaly, blindness, and deafness. Evidence has shown that perinatal polyphenols supplementation may alleviate brain injury in embryonic, fetal, neonatal, and offspring subjects, highlighting its role in modulating adaptative responses involving phenotypical plasticity. Therefore, it is reasonable to infer that the administration of polyphenols during the early life period may be considered a potential intervention to modulate the inflammatory and oxidative stress that cause impairments in locomotion, cognitive, and behavioral functions throughout life. The beneficial effects of polyphenols are linked with several mechanisms, including epigenetic alterations, involving the AMP-activated protein kinase (AMPK), nuclear factor kappa B (NF-κB), and phosphoinositide 3-kinase (PI3K) pathways. To highlight these new perspectives, the objective of this systematic review was to summarize the understanding emerging from preclinical studies about polyphenol supplementation, its capacity to minimize brain injury caused by hypoxia-ischemia in terms of morphological, inflammatory, and oxidative parameters and its repercussions for motor and behavioral functions.

PMID: 37372488

36. Advances in neonatal cell therapies: Proceedings of the First Neonatal Cell Therapies Symposium (2022)

Atul Malhotra, Bernard Thebaud, Madison C B Paton, Bobbi Fleiss, Paris Papagianis, Elizabeth Baker, Laura Bennet, Tamara Yawno, Ngaire Elwood, Belinda Campbell, Kirat Chand, Lindsay Zhou, Tayla Penny, Timothy Nguyen, Salvatore Pepe, Alistair J Gunn, Courtney A McDonald

Review Pediatr Res. 2023 Jun 28. doi: 10.1038/s41390-023-02707-x. Online ahead of print.

Despite considerable advances, there is a need to improve the outcomes of newborn infants, especially related to prematurity, encephalopathy and other conditions. In principle, cell therapies have the potential to protect, repair, or sometimes regenerate vital tissues; and improve or sustain organ function. In this review, we present highlights from the First Neonatal Cell Therapies Symposium (2022). Cells tested in preclinical and clinical studies include mesenchymal stromal cells from various sources, umbilical cord blood and cord tissue derived cells, and placental tissue and membrane derived cells. Overall, most preclinical studies suggest potential for benefit, but many of the cells tested were not adequately defined, and the optimal cell type, timing, frequency, cell dose or the most effective protocols for the targeted conditions is not known. There is as yet no clinical evidence for benefit, but several early phase clinical trials are now assessing safety in newborn babies. We discuss parental perspectives on their involvement in these trials, and lessons learnt from previous translational work of promising neonatal therapies. Finally, we make a call to the many research groups around the world working in this exciting yet complex field, to work together to make substantial and timely progress to address the knowledge gaps and move the field forward. IMPACT: Survival of preterm and sick newborn infants is improving, but they continue to be at high risk of many systemic and organ-specific complications. Cell therapies show promising results in preclinical models of various neonatal conditions and early phase clinical trials have been completed or underway. Progress on the potential utility of cell therapies for neonatal conditions, parental perspectives and translational aspects are discussed in this paper.

PMID: 37380752