

Cerebral palsy research news

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Interventions and Management

Interventions and Management

1. Effectiveness of Game-Based Training of Selective Voluntary Motor Control in Children With Upper Motor Neuron Lesions: Randomized Multiple Baseline Design Study

Annina Fahr, Andrina Kläy, Larissa S Coka, Hubertus J A van Hedel

Randomized Controlled Trial JMIR Form Res . 2024 Nov 18:8:e47754. doi: 10.2196/47754.

Background: Selective voluntary motor control (SVMC) is the ability to control joint movements independently. Impairments in SVMC can affect functional activities, but only a few interventions directly target SVMC. Therefore, we developed a game -based intervention for children with upper motor neuron lesions to improve SVMC. The intervention trained selective activation of a muscle or joint movement while providing immediate feedback about involuntarily occurring muscle activations or movements in another joint. The intervention was provided in a playful manner with a custom-made game environment and a technology-based interface to capture muscle activation or joint movements.

Objective: This study aimed to investigate the effectiveness of this game-based intervention and explore treatment response-related factors in children with impaired SVMC undergoing inpatient neurorehabilitation.

Methods: We conducted a single-case research study with a randomized, nonconcurrent, multiple baseline design. The study consisted of a random-length baseline phase where no SVMC-specific intervention was provided and an intervention phase with additional SVMC training. Concurrently in both phases, children attended their individual multimodal rehabilitation program at our clinic, Swiss Children's Rehab. During the intervention phase, participants completed ten 45-minute sessions with our game-based SVMC training. SVMC was measured repeatedly throughout both phases and at the 3-month follow-up with a short custom-made assessment.

Results: Eighteen children with reduced SVMC from upper motor neuron lesions participated in the study. The mean age of the children was 12.7 (SD 2.9) years, and they mostly had spastic cerebral palsy. A linear mixed-effects model revealed a significant trend (P<.001) for improved SVMC already in the baseline phase. This trend did not change significantly (P=.15) when the game-based SVMC training was introduced in the intervention phase, suggesting no additional improvements due to the SVMC training. Although we could not find an overall treatment effect, we could explain 89.4% of the total random variation of the treatment effect by patient and therapy characteristics. Children with spasticity in the trained movement (20.1%), and those who trained the more affected side (23.5%) benefited most from the intervention. At the 3-month follow-up, SVMC had deteriorated compared to the end of the intervention but was still better than at the beginning of the study. Conclusions: The regular concomitant rehabilitation program already yielded improvements in SVMC, while the game-based SVMC training showed no additional effects. Although the intervention did not show a group effect, we could identify patient and therapy characteristics that determine who is likely to profit from the intervention.

PMID: 39556826

2. Effect of selective dorsal rhizotomy on neuromuscular symptoms, muscle morphology, and motor function in children with spastic cerebral palsy

Ineke Verreydt, Britta Hanssen, Guy Molenaers, Nathalie De Beukelaer, Ines Vandekerckhove, Eirini Papageorgiou, Catherine Huenaerts, Els Ortibus, Anja Van Campenhout, Kaat Desloovere Dev Med Child Neurol. 2024 Nov 18. doi: 10.1111/dmcn.16162. Online ahead of print.

Aim: To investigate the effect of selective dorsal rhizotomy (SDR) on an integrated outcome set 1-year post-SDR, in a cohort of children with spastic cerebral palsy (CP).

Method: Fifteen children with bilateral spastic CP (median age 8 years 8 months [interquartile range 3 years 3 months], 11 males, four females, eight in Gross Motor Function Classification System (GMFCS) level II, seven in GMFCS level III) were measured pre- and 1-year post-SDR. Clinical scales and goniometry assessed plantar flexor spasticity, range of motion, strength, and selectivity. Spasticity was also quantified via an instrumented assessment. Medial gastrocnemius macroscopic muscle morphology (absolute and normalized muscle belly, tendon and muscle-tendon unit length, cross-sectional area, muscle volume) was assessed using ultrasound. Gait profile score, ankle and knee gait variable scores, walking speed, cadence, and step length were extracted from gait analysis. Gross motor function was assessed using the Gross Motor Function Measure-66 item set. Wilcoxon signed-rank test was used to analyse pre- and post-SDR changes. A reference database was used to qualitatively judge muscle growth post-SDR with respect to muscle growth of children with spastic CP without SDR intervention.

Results: Significant changes (p < 0.05) were seen for spasticity, selectivity, all absolute morphology parameters, normalized tendon and muscle-tendon unit length, and all gait parameters, except walking speed and cadence. Muscle growth of children with and without SDR was comparable.

Interpretation: SDR is an effective spasticity reducing treatment and does not adversely affect natural muscle growth in spastic CP.

PMID: 39558556

3. Longitudinal relationship between hip displacement and hip function in children and adolescents with cerebral palsy: A scoping review

Ailish Malone, Giorgia Tanner, Helen P French

Dev Med Child Neurol. 2024 Nov 21. doi: 10.1111/dmcn.16175. Online ahead of print.

Aim: To identify, describe, and synthesize available evidence on the longitudinal relationship between hip displacement and hip function, using the International Classification of Functioning, Disability and Health (ICF) framework, in children and adolescents with cerebral palsy (CP) aged up to 18 years.

Method: Five databases were searched systematically from inception to May 2022. Study and sample characteristics, and hip displacement and hip function measures, mapped to the ICF domains, were extracted for narrative synthesis.

Results: Twenty-nine studies were included: four longitudinal registry-based studies; 12 prospective studies; 12 retrospective studies; and one randomized controlled trial. Sample size ranged from 11 to 267. Twenty-seven (93%) studies entailed an intervention: surgery (n = 16); rehabilitation (n = 2); nerve block or botulinum neurotoxin A injection (n = 4); and combined surgery and injection (n = 2). Twenty-six studies (90%) reported outcomes at the body structure and function and impairment domain of the ICF; 17 (59%) reported outcomes in the activity domain; and three (10%) included participation measures. The most common hip displacement measure was Reimers' migration percentage (79%).

Interpretation: Because of the inclusion of interventions in most studies, and the preponderance of retrospective studies, the relationship between hip displacement and hip function in CP is unclear. More high-quality prospective evidence on the natural history of hip displacement, and its effect on function, is needed to improve population-wide screening of children with CP. PMID: 39572923

4. Aerobic fitness in children with cerebral palsy compared to typically developing peers: A systematic review and meta -analysis

Emma J Wijnhoud, Arnoud M M Edelman Bos, Annemieke I Buizer, Heleen Beckerman Review Braz J Phys Ther . 2024 Nov 15;28(6):101142. doi: 10.1016/j.bjpt.2024.101142. Online ahead of print.

Background: In the public health domain, aerobic fitness is an important predictor of both health and disease. Objective: To determine aerobic fitness in children with cerebral palsy (CP) compared to typically developing (TD) peers measured with a maximal exercise test.

Methods: A systematic literature search was conducted in PubMed (MEDLINE), PsycArticles, PsycInfo, CINAHL, and SPORTDiscus (EBSCO). Original studies that reported findings on aerobic fitness expressed as peak oxygen uptake (VO2peak) during a maximal exercise test measured with a gas analysis system, in children with CP, aged 18 years or younger, were included. VO2peak values were pooled, using the generic inverse variance method, for type of maximal exercise test, Gross Motor Function Classification System (GMFCS) level, distribution of CP, and sex.

Results: Thirty-six studies with a total of 510 children with CP (GMFCS I-IV) and 173 TD peers were included. VO2peak was measured using cycle ergometer test (n = 16), treadmill exercise test (n = 13), arm crank ergometer test (n = 6), shuttle run test (n = 3), and shuttle ride test (n = 1). The overall pooled VO2peak in children with CP was 32.84 mL/kg/min (SE 1.28) and 45.02 mL/kg/min (SE 1.32) in TD peers, with a difference between CP and TD of -12.17 mL/kg/min (95 % CI: -16.70, -7.64). Subgroup analyses revealed that aerobic fitness was most compromised in children at higher GMFCS levels and boys with CP. Conclusion: Aerobic fitness is severely compromised in children with CP. Promoting a healthy lifestyle and increasing participation in physical activities for young people with CP is recommended. The study protocol was prospectively registered in the PROSPERO registry with reference number CRD42021292879.

PMID: 39549342

5. Exploring Ultrasonographic Diaphragmatic Function in Children With Cerebral Palsy

Maracy Balbino Morgado Sobreira, Thálita Raysa de Lima Crispim, Renata do Nascimento Silva, Francisco Locks, Helga Cecília Muniz de Souza, Paulo André Freire Magalhães

Pediatr Pulmonol . 2024 Nov 18. doi: 10.1002/ppul.27407. Online ahead of print.

No abstract available PMID: <u>39555706</u>

6. Pain and development: interacting phenomena

Katelynn E Boerner, Neil L Schechter, Tim F Oberlander

Review Pain. 2024 Nov 1;165(11S):S82-S91. doi: 10.1097/j.pain.000000000003304.

Abstract

For decades, clinicians and researchers have observed bidirectional relationships between child development and the pain experience in childhood. Pain in childhood is an inherently developmental phenomenon, embedded in an iterative, time-dependent process that reflects individual biological, behavioral, social, psychological, and environmental characteristics that unfold across the early life span. Childhood pain can have wide ranging effects on brain development in ways that contribute-for better and worse-to social, emotional, and cognitive well-being in childhood and on into adulthood. Atypical trajectories of development in the context of disorders such as autism, cerebral palsy, ADHD, and mood/anxiety disorders also contribute to unique childhood pain experiences. In this paper, pain will be considered as a determinant of development, and conversely development will be considered as a key determinant of a child's pain experience. We will discuss how intersectional identities (eg, gender, race, socioeconomic status) and associated social, structural, systemic, and physical environments influence the relationship between development and pain. Finally, we will identify what might be needed to think "developmentally" in ways that extend from the "bench side" in the lab to the "curb side" in the community, integrating a developmental perspective into research and clinical practice to achieve health accessibility and equity in pain care for all children across the developmental spectrum.

PMID: 39560419

7. Multi-session adaptation to audiovisual and sensorimotor biofeedback is heterogeneous among adolescents with cerebral palsy

Alyssa M Spomer, Benjamin C Conner, Michael H Schwartz, Zachary F Lerner, Katherine M Steele PLoS One. 2024 Nov 18;19(11):e0313617. doi: 10.1371/journal.pone.0313617. eCollection 2024.

Background: There is growing interest in the use of biofeedback-augmented gait training in cerebral palsy (CP). Audiovisual, sensorimotor, and immersive biofeedback paradigms are commonly used to elicit short-term gait improvements; however, outcomes remain variable. Because biofeedback training requires that individuals have the capacity to both adapt their gait in response to feedback and retain improvements across sessions, changes in either capacity may affect outcomes. Yet, neither has been explored extensively in CP.

Methods: In this study, we evaluated the extent to which adolescents with CP (7M/1F; 14 years (12.5,15.26)) could adapt gait and retain improvements across four, 20-minute sessions using combined audiovisual and sensorimotor biofeedback. Both systems were designed to target plantarflexor activity. Audiovisual biofeedback displayed real-time soleus activity and sensorimotor biofeedback was provided using a bilateral resistive ankle exoskeleton. We quantified the time-course of change in muscle activity within and across sessions and overground walking function before and after the four sessions. Results: All individuals were able to significantly increase soleus activity from baseline using multimodal biofeedback (p < 0.031) but demonstrated heterogeneous adaptation strategies. In-session soleus adaptation had a moderate positive correlation with short-term retention of the adapted gait patterns (0.40 $\le \rho \le 0.81$), but generally weak correlations with baseline walking function (GMFCS Level) and motor control complexity ($\rho \le 0.43$). The latter indicates that adaptation capacity may be a critical and unique metric underlying response to biofeedback. Notably, in-session gains did not correspond to significant improvements in overground walking function (p > 0.11).

Conclusions: This work suggests that individuals with CP have the capacity to adapt their gait using biofeedback, but responses are highly variable. Characterizing the factors driving adaptation to biofeedback may be a promising avenue to understand the heterogeneity of existing biofeedback training outcomes and inform future system optimization for integration into clinical care.

PMID: 39556530

8. Brain-computer interfaces patient preferences: a systematic review

Jamie F M Brannigan, Kishan Liyanage, Hugo Layard Horsfall, Luke Bashford, William Muirhead, Adam Fry J Neural Eng. 2024 Nov 19. doi: 10.1088/1741-2552/ad94a6. Online ahead of print.

Background
Brain-computer interfaces (BCIs) have the potential to restore motor capabilities and functional independence in individuals with motor impairments. Despite accelerating advances in the performance of various implanted devices, few studies have identified patient preferences underlying device design, and moreover, each study has typically captured a single actiology of motor impairment. We aimed to characterise BCI patient preferences in a large patient cohort across multiple aetiologies. & #xD; Methods & #xD; We performed a systematic review of all published studies reporting patient preferences for BCI devices. We searched MEDLINE, Embase, and CINAHL from inception to April 18th, 2023. We included any study reporting either qualitative or quantitative preferences concerning BCI devices. Article screening and data extraction were performed by two reviewers in duplicate. Extracted information included demographic information, current digital device use, device invasiveness preference, device design preferences, and device functional preferences. & #xD; Findings & #xD; Our search identified 1316 articles, of which 28 studies were eligible for inclusion. Preference information was captured from 1701 patients (mean age = 42.1-64.3 years). Amyotrophic lateral sclerosis was the most represented clinical condition (n = 15 studies, 53.6%), followed by spinal cord injury (n = 13 studies, 46.4%). We found that individuals with motor impairment prioritise device accuracy over other device design characteristics. We also found that the speed and accuracy of BCI systems in recent publications exceeds reported patient preferences, however this performance has been achieved with a level of training and setup burden that would not be tolerated by most patients. When comparing populations across studies, we found that patient preferences vary according to both disease actiology and the severity of motor

impairment.
Interpretation
Our findings support a greater research emphasis on minimising BCI setup and training burden, and they suggest future BCI devices may require bespoke configuration and training for specific patient groups.. PMID: 39569894

9. Changes in functional status during and after pregnancy in people with cerebral palsy: An international observational study

Georgia Condran, Hayley Lipworth, Anne Berndl

Obstet Med . 2024 Nov 13:1753495X241297560. doi: 10.1177/1753495X241297560. Online ahead of print.

Background: There is limited information surrounding physical changes people with cerebral palsy (CP) experience during pregnancy.

Methodology: This is a subgroup analysis of an international online questionnaire, developed with input from individuals with CP. Data collection included demographics, baseline functional status, and functional status changes during pregnancy. Descriptive analysis was used.

Results: 158 participants from 15 countries participated of which 30 had a total of 49 pregnancies resulting in birth. Worsened strength, spasticity, bladder function and fatigue occurred in 56.5% (13/23), 47.8% (11/23), 56.5% (13/23) and 87.0% (20/23) of participants. 9/23 (40.9%) required new mobility devices. Worsening of fatigue, strength, spasticity and need for a new mobility device was reported by all groups regardless of functional status.

Conclusions: People with CP may experience significant functional changes during pregnancy, even those who mobilized independently prior to pregnancy. These findings may inform obstetricians, nurses, neurologists and physiatrists, and contribute to preconception counselling.

PMID: 39553175

10. Prevalence of valgus and varus foot deformities in 2784 children with cerebral palsy, a register-based cross-sectional study

Evgenia Manousaki, Elisabet Rodby-Bousquet, Katina Pettersson, Jenny Hedberg-Graff, Erika Cloodt BMC Musculoskelet Disord . 2024 Nov 19;25(1):930. doi: 10.1186/s12891-024-08029-1

Background: Foot deformities, such as valgus and varus in the coronal plane and equinus in the sagittal plane, are common in children with cerebral palsy (CP). The purpose of this study was to describe the prevalence of coronal plane foot deformities and their association with the Gross Motor Function Classification System (GMFCS) level, age, CP subtype, and equinus in children with CP.

Methods: A cross-sectional study was performed of 2784 children (1644 boys, 1140 girls), mean age 10 years, 2 months (standard deviation, 4.83), from the Swedish CP Follow-up Program and registry for 2021-2023. Single and multiple binary regression analyses estimated the association between coronal plane foot deformities (valgus or varus) and sex, age, GMFCS level, CP subtype, and equinus.

Results: More than half (58%) the children with CP had valgus feet and 6% had varus feet. Valgus feet were more common in young children with high GMFCS levels, whereas the number of varus feet remained consistently low across all GMFCS levels. The prevalence of valgus feet was lower in older children at GMFCS I and II, but remained high in older children at

GMFCS III-V. Coronal plane foot deformities were associated with higher GMFCS levels (odds ratio [OR] 11, 95% confidence interval [CI] 8-15 for GMFCS V), lower age (OR 1.5, 95% CI 1.3-1.7), and equinus (OR 1.9, 95% CI 1.4-2.5). Conclusions: Most children with CP have a coronal plane foot deformity. Valgus is most commonly associated with higher GMFCS levels and lower age. These findings contribute to a mapping of the children with an increased risk of foot deformities and also highlight the need for continuous follow-up of foot deformities in children with CP. PMID: 39563276

11. T2/FLAIR mismatch and diffusion restriction as novel pathophysiological markers in MRI evaluation of central tegmental tract hyperintensity in pediatric patients

Emre Utkan Buyukceran, Seda Kaynak Sahap, Sinan Genc, Suat Fitoz Neuroradiology. 2024 Nov 21. doi: 10.1007/s00234-024-03509-6. Online ahead of print.

Introduction: Central tegmental tract hyperintensity (CTTH) on T2-weighted imaging is an uncommon neuroimaging finding in pediatric patients with unclear clinical significance. CTTH may represent either a physiological or pathological process. This study evaluates the relationship between CTTH and MRI sequences (FLAIR, DWI) to explore its diagnostic value. Methods: We retrospectively analyzed 3462 pediatric brain MRI scans conducted between July 2011 and January 2022, identifying 104 patients with bilateral CTTH. DWI, FLAIR sequences, and follow-up scans were visually assessed for T2/FLAIR mismatch and diffusion restriction. Clinical data were obtained from electronic patient records. Statistical analysis was performed using SPSS, with significance set at p < .05.

Results: A total of 104 pediatric patients with CTTH were included, ranging from 1 month to 16 years old (mean age: 31.34 months). Epilepsy, metabolic diseases, and cerebral palsy were the most common clinical diagnoses. Diffusion restriction was observed in 40.8% of patients, while 39.6% had FLAIR hyperintensity. T2/FLAIR mismatch, defined for the first time in CTTH, was found in 60.4% of patients. A significant correlation was found between T2/FLAIR mismatch and clinical diagnoses (p = .020), as well as between diffusion restriction and T2/FLAIR mismatch (p = .017).

Conclusion: CTTH in pediatric patients may arise from two distinct processes: a transient, developmental phenomenon or a pathological process marked by irreversible myelin degeneration. T2/FLAIR mismatch and diffusion restriction provide valuable diagnostic markers, offering insights into the severity and chronicity of CTTH. Further studies are needed to validate these findings and their clinical implications.

PMID: 39570401

12. Longitudinal Analysis of Amplitude-Integrated Electroencephalography for Outcome Prediction in Infants with Hypoxic-Ischemic Encephalopathy: A Validation Study

Mathies Rondagh, Linda S de Vries, Andrea van Steenis, Unoke Meder, Laszlo Szakacs, Agnes Jermendy, Sylke J Steggerda J Pediatr . 2024 Nov 15:114407. doi: 10.1016/j.jpeds.2024.114407. Online ahead of print

Objectives: To validate the prognostic accuracy of a previously published tool (HOPE calculator) using longitudinal analysis of amplitude-integrated electroencephalography (aEEG) background activity and sleep-wake cycling (SWC) to predict favorable or adverse 2-year neurodevelopmental outcome in infants with hypoxic-ischemic encephalopathy (HIE) undergoing therapeutic hypothermia (TH), and to evaluate the predictive value for outcome at 5 to 8 years of age.

Study design: Single-center retrospective cohort study in 117 infants who underwent TH for HIE between 2008 to 2022. We scored two-channel aEEG background patterns, SWC, and seizure activity at 6-hour intervals for 84 hours.

Neurodevelopmental outcome at 2 years was evaluated using the Bayley Scales of Infant Development-III (BSID-III), defining adverse outcome as death, cerebral palsy (CP) and/or cognitive/motor scores<85. Adverse outcome at 5 to 8 years was defined as total IQ score<85, Movement-ABC-2 score <p15, CP, severe sensory impairment, or death.

Results: The prediction model showed an area under the curve of 0.90~(95%~CI, 0.83-0.95) at 2 years and 0.83~(95%~CI, 0.73-0.92) at 5 to 8 years. Mean predicted probability of favorable outcome was 74.5%~(95%~CI, 69.4-79.6) in the favorable outcome group compared with 32.8%~(95%~CI, 23.5-42.2) in the adverse outcome group (p< 0.001) at 2 years (n=115) and 76.85%~(95%~CI, 70.0-83.4) compared with 40.7%~(95%~CI, 30.0-51.4) at 5 to 8 years (n=68).

Conclusion: Our study provided external validation of the HOPE calculator, assessing longitudinal aEEG background activity during TH in infants with HIE. The results suggest that this method can accurately predict favorable or adverse outcome not only at 2 but also at 5 to 8 years of age.

PMID: 39551094

13. Attention over vulnerable brain regions associating cerebral palsy disorder and biological markers

Muhammad Hassan, Jieqiong Lin, Ahmed Ameen Fateh, Wei Pang, Luning Zhang, Di Wang, Guojun Yun, Hongwu Zeng J Adv Res. 2024 Nov 16:S2090-1232(24)00534-4. doi: 10.1016/j.jare.2024.11.015. Online ahead of print.

Introduction: Cerebral palsy (CP) is a neurological disorder caused by cerebral ischemia and hypoxia during fetal brain development. Early intervention in CP favors medications and therapies; however, monitoring early brain development in children with CP is critical. It is essential to thoroughly examine brain-vulnerable regions associated with biological traits (BTs). Variations in BTs were evident in children with CP; however, it is critical to explore the BTs' impact on the brains of healthy controls (HC) and CP-disordered children.

Objective: This study associates BTs with HC and CP children. This study investigates the neurodevelopment of HC and CP underlying BTs. This study establishes a benchmark for the association of BT with HC and CP children.

Method: The proposed AWG-Net is composed of customized spatial-channel (CSC) and multi-head self (MHA) attentions, where CSC blocks are incorporated at the first few stages, MHA at later stages, and cumulative-dense structures to propagate susceptible regions to deeper layers. The training samples include T1-w, T2-w, Flair, and Sag, annotated with age, gender, and weight.

Results: The significant results for HC and CP are age (HC: MAE = 1.05, MCS10=85.63, R2=0.844; CP: MAE = 1.16, MCS10=84.79, R2=0.717), gender (HC: Acc = 82.98%, CP: Acc = 82.00%), and weight (HC: MAE = 4.65, MCS10=56.30, R2=0.78; CP: MAE = 2.85, MCS10=70.24, R2=0.82). Vulnerable regions for age are the cerebellar hemisphere, frontal, occipital, and parietal bones in HC and inconsistent in CP. HC and CP commonalities are in the frontal bone and cerebellar hemisphere with HC and discrepant in the occipital and temporal bones for CP. Similarly, gender differences are found for HC and CP.

Conclusion: Age and gender are marginally less affected by the brain regions vulnerable to CP than weight estimation. T1-w is appropriate for age, weight, and gender. The learned trends are different for HC and CP in brain development and gender while slightly different in the case of weight.

PMID: 39551127

Prevention and Cure

14. Systemic Postnatal Corticosteroids, Bronchopulmonary Dysplasia, and Survival Free of Cerebral Palsy

Lex W Doyle 1 2 3, Rheanna Mainzer 4 5, Jeanie L Y Cheong 1 2 3 5

JAMA Pediatr . 2024 Nov 18:e244575. doi: 10.1001/jamapediatrics.2024.4575. Online ahead of print.

Importance: Systemic postnatal corticosteroids have been shown to reduce rates of bronchopulmonary dysplasia (BPD) in infants born preterm, but both corticosteroids and BPD are associated with cerebral palsy.

Objective: To describe how the association between systemic postnatal corticosteroids and survival free of cerebral palsy varies with the risk of BPD in infants born preterm, and if the association differs between dexamethasone and hydrocortisone, or with age at starting treatment.

Design, setting, and participants: This comparative effectiveness research used weighted meta-regression analysis of eligible randomized clinical trials (RCTs) of systemic postnatal corticosteroids reported from June 1989 through March 2022 that included rates of all of BPD, mortality, and cerebral palsy in neonatal intensive care units in 10 countries. Infants born preterm at risk of BPD were included. Data were analyzed from April and July 2024.

Interventions: Systemic dexamethasone or hydrocortisone.

Main outcomes and measures: Type and timing of corticosteroid, control group rate of BPD, and risk difference in survival free of cerebral palsy between corticosteroid and control arms.

Results: Twenty-six RCTs with data on 3700 randomized infants were eligible; 18 (69%) investigated dexamethasone and 8 (31%) hydrocortisone; 12 (46%) started treatment in the first week after birth. There was evidence for a differential association of the type of corticosteroid with the effect of systemic dexamethasone on survival free of cerebral palsy and the risk of BPD in control groups (interaction coefficient, 0.54; 95% CI, 0.25-0.82; P = .001). For dexamethasone, for every 10-percentage point increase in the risk of BPD, the risk difference for survival free of cerebral palsy increased by 3.74% (95% CI, 1.54 to 5.93; P = .002). Dexamethasone was associated with improved survival free of cerebral palsy at a risk of BPD greater than 70%. Conversely, dexamethasone was associated with harm at a risk of BPD less than 30%. There was some evidence for a negative association with hydrocortisone, with possible benefit with risk of BPD less than 30%. There was no strong evidence for a differential effect of timing among those treated with dexamethasone (interaction coefficient, 0.13; 95% CI, -0.04 to 0.30; P = .14).

Conclusions and relevance: The findings suggest that dexamethasone (compared with control) was associated with improved rates of survival free of cerebral palsy in infants at high risk of BPD but should be avoided in those at low risk. A role for hydrocortisone is uncertain.

PMID: <u>3955604</u>