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Interventions and Management

1. Dev Neurorehabil. 2012;15(1):54-62.

Fatigue in cerebral palsy: A critical review.

Brunton LK, Rice CL.

Health and Rehabilitation Sciences .

Objective: Fatigue contributes to the deterioration or cessation of walking ability in adults with cerebral palsy (CP). However, conflict exists as to its role. Studies involving functional tasks reported increased, and earlier onset of, fatigue in CP, whereas laboratory studies have reported individuals with CP to be more fatigue-resistant than their peers. Methods: A critical review of the literature related to fatigue in CP was conducted. Results: This review describes factors that contribute to the observed fatigue resistance in laboratory tasks and how a decreased force-production in CP can result in higher energy expenditure to perform the same amount of work as their peers. Conclusion: More research regarding the process of fatigue and recovery for individuals with CP is needed; specifically studies that focus on functional movements requiring the integration of the whole body, thereby stressing the neuromuscular system in a different way than previously explored.

PMID: 22256835 [PubMed - in process]

2. Issues Compr Pediatr Nurs. 2012;35(1):24-44.

Parental stress in families of children with a genetic disorder/disability and the resiliency model of family stress, adjustment, and adaptation.

Hall HR, Neely-Barnes SL, Graff JC, Krcek TE, Roberts RJ, Hankins JS.

University of South Alabama.

Background: Research suggests that parents of children with disabilities endure increased amounts of stress but also experience positive outcomes. Purpose: To further investigate findings from focus group interviews that explored parental stress in families of children with disabilities using a sequential mixed methods design. Method: This study sought to model parental stress using the McCubbin and McCubbin (1993) Resiliency Model of Stress, Adjustment, and Adaptation using qualitative and quantitative data collected sequentially. Twenty-five parents of children with autism spectrum disorder, cerebral palsy, Down syndrome, and sickle cell disease participated in a 2-

step study that encompassed qualitative followed by quantitative data ascertainment. Results: Parents who quantitatively experienced high stress or low stress used different behavioral themes to describe their experience qualitatively. Positive appraisals, resources, and ability to engage in problem solving and coping were associated with family resiliency.

PMID: 22250965 [PubMed - in process]

3. Res Dev Disabil. 2012 Jan 11;33(3):832-840. [Epub ahead of print]

Medical expenditures attributable to cerebral palsy and intellectual disability among Medicaid-enrolled children.

Kancherla V, Amendah DD, Grosse SD, Yeargin-Allsopp M, Van Naarden Braun K.

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This study estimated medical expenditures attributable to cerebral palsy (CP) among children enrolled in Medicaid, stratified by the presence of co-occurring intellectual disability (ID), relative to children without CP or ID. The MarketScan(®) Medicaid Multi-State database was used to identify children with CP for 2003-2005 by using the International Classification of Diseases, Ninth Revision; Clinical Modification (ICD-9-CM) code 343.xx. Children with ID were identified for 2005 by using ICD-9-CM code 317.xx-319.xx. Children without CP or ID during the same period served as control subjects. Medical expenditures were estimated for case and control children for 2005. The difference between the average expenditures for children with and without CP was used as a proxy for attributable expenditures for the condition. The attributable expenditures of co-occurring ID were calculated similarly as the difference in average expenditures among children with CP with and without ID. A total of 9927 children with CP were identified. Among them, 2022 (20.3%) children had co-occurring ID recorded in medical claims. Children with CP but without ID incurred medical expenditures that were $15,047 higher than those of control children without CP or ID. By contrast, children with CP and co-occurring ID incurred costs that were $41,664 higher, compared with control children, and $26,617 more than children with CP but without ID. Administrative data from a large, multistate database demonstrated high medical expenditures for publicly insured children with CP. Expenditures approximately tripled for children with CP and co-occurring ID.

PMID: 22245730 [PubMed - as supplied by publisher]

4. J Paediatr Child Health. 2012 Jan;48(1):2-5. doi:10.1111/j.1440-1754.2011.02394.x.

Public services for children with special needs: Discrimination by diagnosis?

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In July 2011, the Australian federal government announced expansion of early intervention funding. Children diagnosed with cerebral palsy, Down syndrome, Fragile X syndrome and hearing and vision impairments are now eligible in addition to the existing funding for children diagnosed with autistic disorders. By deciding who gets the funding according to a set of accepted diagnoses, many children with equivalent if not greater levels of early intervention special need are excluded. In this viewpoint, we consider the fairness of this approach, and argue that while it may make sense from a political point of view, it is hard to justify, and possibly even discriminatory, from clinical, ethical and legal perspectives.

PMID: 22250827 [PubMed - in process]

5. J Med Case Reports. 2012 Jan 17;6(1):19. [Epub ahead of print]

Listening to the patient as a possible route to cost-effective rehabilitation: a case report.

Grandi A, Mazzola M, Angelini L, Chiappedi M.

INTRODUCTION: adolescents with Cerebral Palsy often do not need a specific rehabilitative treatment; however, when specific needs are expressed, clinicians should listen and try to answer them. Case presentation: we present the case of an Italian hemiplegic male 17 years old patient who had received standard physiotherapy, and ultimately, after a period of Adapted Physical Activity performed in a group, was under consideration for discharge. However, due to unsatisfactory hand control, he asked to be helped without surgery to reach a personal goal (i.e. the possibility to drive a motorbike). Functional taping showed efficacy, but was neither cost-effective nor practical for the patient and his family; by contrast a dynamic orthosis, associated with a training in real-life environment, was instead successful. Conclusion: the present case underlines the importance to consider solutions involving the motivation and compliance of the patient in order to improve his Activity and Participation.

PMID: 22251773 [PubMed - as supplied by publisher]

6. Conf Proc IEEE Eng Med Biol Soc. 2011 Aug;2011:7310-5.

Afferent and efferent activity control in the design of brain computer interfaces for motor rehabilitation.

Cho W, Vidaurre C, Hoffmann U, Birbaumer N, Ramos-Murguialday A.

Stroke is a cardiovascular accident within the brain resulting in motor and sensory impairment in most of the survivors. A stroke can produce complete paralysis of the limb although sensory abilities are normally preserved. Functional electrical stimulation (FES), robotics and brain computer interfaces (BCIs) have been used to induce motor rehabilitation. In this work we measured the brain activity of healthy volunteers using electroencephalography (EEG) during FES, passive movements, active movements, motor imagery of the hand and resting to compare afferent and efferent brain signals produced during these motor related activities and to define possible features for an online FES-BCI. In the conditions in which the hand was moved we limited the movement range in order to control the afferent flow. Although we observed that there is a subject dependent frequency and spatial distribution of efferent and afferent signals, common patterns between conditions and subjects were present mainly in the low beta frequency range. When averaging all the subjects together the most significant frequency bin comparing each condition versus rest was exactly the same for all conditions but motor imagery. These results suggest that to implement an on-line FES-BCI, afferent brain signals resulting from FES have to be filtered and time-frequency-spatial features need to be used.

PMID: 22256027 [PubMed - in process]

7. Conf Proc IEEE Eng Med Biol Soc. 2011 Aug;2011:6277-80.

An EEG-based brain computer interface for rehabilitation and restoration of hand control following stroke using ipsilateral cortical physiology.

Fok S, Schwartz R, Wronkiewicz M, Holmes C, Zhang J, Somers T, Bundy D, Leuthardt E.

The loss of motor control severely impedes activities of daily life. Brain computer interfaces (BCIs) offer new possibilities to treat nervous system injuries, but conventional BCIs use signals from primary motor cortex, the same sites most likely damaged in a stroke causing paralysis. Recent studies found distinct cortical physiology associated with contralesional limb movements in regions distinct from primary motor cortex. To capitalize on these findings, we designed and implemented a BCI that localizes and acquires these brain signals to drive a powered, hand orthotic which opens and closes a patient's hand.

PMID: 22255773 [PubMed - in process]

8. Conf Proc IEEE Eng Med Biol Soc. 2011 Aug;2011:1835-8.

Long-term hand tele-rehabilitation on the playstation 3: Benefits and challenges.

Burdea GC, Jain A, Rabin B, Pellosie R, Golomb M.

Rehabilitation interventions for the hand have shown benefits for children with Hemiplegia due to cerebral palsy or traumatic brain injury. Longer interventions are facilitated if training is provided in the patient's home, due to easier access to care and reduced impact on school or work activities. Providing remote rehabilitation over lengthy periods of time has however its own challenges. This paper presents two pediatric patients with hemiplegia, who practiced virtual hand rehabilitation games using a modified PlayStation 3 and 5DT sensing gloves. Despite severe initial hand spasticity, and occasional technology shortcomings, the subjects practiced for about 14 months, and 6 months, respectively. Game performance data for the second patient is presented. Follow-up evaluations 14 months from the removal of the PlayStation 3 from the home of the child with cerebral palsy showed that the patient had good retention in terms of grasp strength, hand function and bone health. Challenges of long-term home tele-rehabilitation are also discussed.

PMID: 22254686 [PubMed - in process]

9. Conf Proc IEEE Eng Med Biol Soc. 2011 Aug;2011:750-2.

Variable-arrival-time reaching with the brain-machine interface: Performance comparison on empirically-derived movements.

Srinivasan L.

Patients with paralysis will one day rely on clinically-available brain-machine interfaces (BMI) to facilitate activities of daily living. As such, the ability to generate dexterous reaching movements remains a prime target of BMI algorithms research. The Bayesian approach to BMI algorithms requires a statistical model to describe reaching movements. To date, available models have either required fixed targets or fixed arrival times, neither of which can be assumed under natural operating conditions. Recently, we described a generative reach model, GPFD-RSE, that simultaneously breaks both restrictions. This method combines the reach state equation (RSE) with General Purpose Filter Design (GPFD). In the following paper, we further compare GPFD-RSE against standard methods in simulated open-loop decoding using empirically-derived movements, as an adjunct to the idealized movements tested previously. Our results indicate that GPFD-RSE continues to outperform standard methods when reconstructing more realistic arm movements in simulation.

PMID: 22254419 [PubMed - in process]

10. Conf Proc IEEE Eng Med Biol Soc. 2011 Aug;2011:453-7.

Automatic classification of pathological gait patterns using ground reaction forces and machine learning algorithms.

Alaqtash M, Sarkodie-Gyan T, Yu H, Fuentes O, Brower R, Abdelgawad A.

An automated gait classification method is developed in this study, which can be applied to analysis and to classify pathological gait patterns using 3D ground reaction force (GRFs) data. The study involved the discrimination of gait patterns of healthy, cerebral palsy (CP) and multiple sclerosis subjects. The acquired 3D GRFs data were categorized into three groups. Two different algorithms were used to extract the gait features; the GRFs parameters and the discrete wavelet transform (DWT), respectively. Nearest neighbor classifier (NNC) and artificial neural networks (ANN) were also investigated for the classification of gait features in this study. Furthermore, different feature sets were formed using a combination of the 3D GRFs components (mediolateral, anterioposterior, and vertical) and their various impacts on the acquired results were evaluated. The best leave-one-out (LOO) classification accuracy 85% was achieved. The results showed some improvement through the application of a features selection algorithm based on M-shaped value of vertical force and the statistical test ANOVA of mediolateral and anterioposterior forces. The optimal feature set of six features enhanced the accuracy to 95%. This work can provide an automated gait classification tool that may be useful to the clinician in the diagnosis and

identification of pathological gait impairments.

PMID: 22254346 [PubMed - in process]

11. J Bone Joint Surg Am. 2012 Jan 18;94(2):121-30.

Development of knee function after hamstring lengthening as a part of multilevel surgery in children with spastic diplegia: a long-term outcome study.

Dreher T, Vegvari D, Wolf SI, Geisbüsch A, Gantz S, Wenz W, Braatz F.

BACKGROUND: Hamstring lengthening commonly is performed for the treatment of flexed knee gait in patients with spastic diplegic cerebral palsy. Satisfactory short-term results after hamstring lengthening have been demonstrated in various studies. However, evidence for the effectiveness of hamstring lengthening to correct flexed knee gait is scant because of small and inhomogeneous case series, different surgical techniques, and short follow-up. METHODS: The long-term results for thirty-nine patients with spastic diplegia and flexed knee gait who were managed with intramuscular hamstring lengthening as a part of multilevel surgery are presented. Standardized three-dimensional gait analyses and clinical examinations were performed for all patients preoperatively and at one, three, and six to twelve years postoperatively. RESULTS: Significant improvements in kinematic parameters and the popliteal angle were noted at short-term follow-up ($p < 0.01$), supporting the results of previous studies. Long-term results showed significant deterioration of minimum knee flexion in stance and the popliteal angle ($p < 0.01$), whereas the improvements in the Gross Motor Function Classification System and Gillette Gait Index were maintained. This recurrence of flexed knee gait is partial and measurable. Increased pelvic tilt was found in 49% of the limbs postoperatively, which may represent one factor leading to recurrence of flexed knee gait. Genu recurvatum was seen in eighteen patients (twenty-seven limbs; 35%) one year postoperatively, especially in the patients with a jump knee gait pattern preoperatively. At long-term follow-up, genu recurvatum resolved in many limbs,but 12% of the limbs showed residual genu recurvatum, indicating that overcorrection represents a problem following hamstring lengthening. CONCLUSIONS: The results of the present study are crucial for the prognosis of knee function after hamstring lengthening as a part of multilevel surgery. Recurrence and possible overcorrection should be considered in treatment planning. LEVEL OF EVIDENCE: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

PMID: 22257998 [PubMed - in process]

12. Res Dev Disabil. 2012 Jan 11;33(3):916-923. [Epub ahead of print]

To what extent is mean EMG frequency during gait a reflection of functional muscle strength in children with cerebral palsy?

Van Gestel L, Wambacq H, Aertbeliën E, Meyns P, Bruyninckx H, Bar-On L, Molenaers G, De Cock P, Desloovere K.

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The aim of the current paper was to analyze the potential of the mean EMG frequency, recorded during 3D gait analysis (3DGA), for the evaluation of functional muscle strength in children with cerebral palsy (CP). As walking velocity is known to also influence EMG frequency, it was investigated to which extent the mean EMG frequency is a reflection of underlying muscle strength and/or the applied walking velocity. Surface EMG data of the lateral gastrocnemius (LGAS) and medial hamstrings (MEH) were collected during 3DGA. For each muscle, 20 CP children characterized by a weak and 20 characterized by a strong muscle (LGAS or MEH) were selected. A weak muscle was defined as a manual muscle testing score <3; a strong muscle was defined as a manual muscle testing score ≥4. Patient selection was based on the following inclusion criteria: (a) predominantly spastic type of CP (3-15 years old), (b) either (near) normal muscle strength or muscle weakness in at least one of the studied lower limb muscles, (c) no lower limb Botulinum Toxin-A treatment within 6 months prior to the 3DGA, (d) no history of lower limb surgery, and (e) high-quality noise-free EMG-data. For each muscle, twenty age-related typically developing (TD) children were included as controls. In both muscles a consistent pattern of increasing mean EMG frequency with decreasing muscle strength was observed. This was significant in the LGAS (TD versus weak CP). Walking

velocity also had a significant effect on mean EMG frequency in the LGAS. Furthermore, based on R(2) and partial correlations, it could be concluded that both walking velocity and muscle strength have an impact on EMG, but the contribution of muscle strength was always higher. These findings underscore the potential of the mean EMG frequency recorded during 3DGA, for the evaluation of functional muscle strength in children with CP.

13. Eur J Paediatr Neurol. 2012 Jan 12. [Epub ahead of print]

Upper limb impairments and their impact on activity measures in children with unilateral cerebral palsy.

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BACKGROUND: Insights in upper limb impairments and their relationship with activity measures in children with unilateral cerebral palsy (CP) are important to optimize treatment interventions. AIMS: (1) To investigate upper limb impairments and activity limitations in children with unilateral CP; (2) to compare these according to the Manual Ability Classification System (MACS), timing of lesion (congenital/acquired) and age; (3) to determine the impact of impairments on activity measures. METHODS: Eighty-one children with unilateral CP aged 5-15 years (mean 9 years 11 months; congenital N=69, acquired N=12) were recruited. Body function measurements included passive range of motion (PROM), muscle tone, strength and sensibility. At activity level, the Melbourne Assessment, Assisting Hand Assessment (AHA) and Abilhand-Kids were assessed. RESULTS: Most PROM limitations were found for elbow extension and supination. Increased tone and weakness were most prominent in distal muscles. Stereognosis and two-point discrimination were mostly affected. Children with a lower MACS level or acquired lesion had significantly more impairments and activity limitations. In children with congenital lesions, best predictors for unimanual capacity (Melbourne Assessment) were wrist strength, stereognosis and proprioception, and for bimanual performance (AHA) wrist strength and grip strength, explaining 76% of the variance. For the Abilhand-Kids, wrist strength and stereognosis predicted 46% of the variance. CONCLUSIONS: Classification according to MACS and timing of lesion is important to differentiate within the wide range of impairments and activity limitations. In children with congenital lesions, unimanual capacity and bimanual performance are highly determined by distal strength, supporting the additional use of impairment-based interventions.

14. Conf Proc IEEE Eng Med Biol Soc. 2011 Aug;2011:8527-30.

Accuracy and reliability of haptic spasticity assessment using HESS (Haptic Elbow Spasticity Simulator).

Kim J, Park HS, Damiano DL.

Clinical assessment of spasticity tends to be subjective because of the nature of the in-person assessment; severity of spasticity is judged based on the muscle tone felt by a clinician during manual manipulation of a patient's limb. As an attempt to standardize the clinical assessment of spasticity, we developed HESS (Haptic Elbow Spasticity Simulator), a programmable robotic system that can provide accurate and consistent haptic responses of spasticity and thus can be used as a training tool for clinicians. The aim of this study is to evaluate the accuracy and reliability of the recreated haptic responses. Based on clinical data collected from children with cerebral palsy, four levels of elbow spasticity (1, 1+, 2, and 3 in the Modified Ashworth Scale [MAS]) were recreated by HESS. Seven experienced clinicians manipulated HESS to score the recreated haptic responses. The accuracy of the recreation was assessed by the percent agreement between intended and determined MAS scores. The inter-rater reliability among the clinicians was analyzed by using Fleiss's kappa. In addition, the level of realism with the recreation was evaluated by a questionnaire on "how realistic" this felt in a qualitative way. The percent agreement was high (85.7±11.7%), and for inter-rater reliability, there was substantial agreement (κ=0.646) among the seven clinicians.

The level of realism was 7.71±0.95 out of 10. These results show that the haptic recreation of spasticity by HESS has the potential to be used as a training tool for standardizing and enhancing reliability of clinical assessment.

PMID: 22256328 [PubMed - in process]

15. Clin Neurophysiol. 2012 Jan 12. [Epub ahead of print]

Comparison of a row-column speller vs. a novel lateral single-character speller: Assessment of BCI for severe motor disabled patients.

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OBJECTIVE: Non-invasive brain-computer interface (BCI) based on electroencephalography (EEG) offers a new communication channel for people suffering from severe motor disorders. This paper presents a novel P300-based speller called lateral single-character (LSC). The LSC performance is compared to that of the standard row-column (RC) speller. METHODS: We developed LSC, a single-character paradigm comprising all letters of the alphabet following an event strategy that significantly reduces the time for symbol selection, and explores the intrinsic hemispheric asymmetries in visual perception to improve the performance of the BCI. RC and LSC paradigms were tested by 10 able-bodied participants, seven participants with amyotrophic lateral sclerosis (ALS), five participants with cerebral palsy (CP), one participant with Duchenne muscular dystrophy (DMD), and one participant with spinal cord injury (SCI). RESULTS: The averaged results, taking into account all participants who were able to control the BCI online, were significantly higher for LSC, 26.11bit/min and 89.90% accuracy, than for RC, 21.91bit/min and 88.36% accuracy. The two paradigms produced different waveforms and the signal-to-noise ratio was significantly higher for LSC. Finally, the novel LSC also showed new discriminative features. CONCLUSIONS: The results suggest that LSC is an effective alternative to RC, and that LSC still has a margin for potential improvement in bit rate and accuracy. SIGNIFICANCE: The high bit rates and accuracy of LSC are a step forward for the effective use of BCI in clinical applications.

PMID: 22244868 [PubMed - as supplied by publisher]

16. JPEN J Parenter Enteral Nutr. 2012 Jan;36(1 Suppl):118S-23S.

Whey- vs Casein-Based Enteral Formula and Gastrointestinal Function in Children With Cerebral Palsy.

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Objectives: Children with severe cerebral palsy (CP) commonly have gastrointestinal (GI) dysfunction. Whey-based enteral formulas have been postulated to reduce gastroesophageal reflux (GOR) and accelerate gastric emptying (GE). The authors investigated whether whey-based (vs casein-based) enteral formulas reduce GOR and accelerate GE in children who have severe CP with a gastrostomy and fundoplication. Methods: Thirteen children received a casein-based formula for 1 week and either a 50% whey whole protein (50% WWP) or a 100% whey partially hydrolyzed protein (100% WPHP) formula for 1 week. Reflux episodes, gastric half-emptying time (GE t (1/2)), and reported pain and GI symptoms were measured. Results: Whey formulas emptied significantly faster than casein (median [interquartile range (IQR)] GE t(1/2), 33.9 [25.3-166.2] min vs 56.6 [46-191] min; P = .033). Reflux parameters were unchanged. GI symptoms were lower in children who received 50% WWP (visual analog symptom score, median [IQR], 0 [0-11.8]) vs 100% WPHP (13.0 [2.5-24.8]) (P = .035). Conclusion: This pilot study shows that in children who have severe CP with a gastrostomy and fundoplication, GE of the whey-based enteral formula is significantly faster than casein. The acceleration in GE does not alter GOR frequency, and there appears to be no effect of whey vs casein in reducing acid, nonacid, and total reflux episodes. The results indicate that

enteral formula selection may be particularly important for children with severe CP and delayed GE.

PMID: 22237871 [PubMed - in process]

Prevention and Cure

17. Lancet Neurol. 2012 Jan 17. [Epub ahead of print]

Genomic insights into the causes and classification of the cerebral palsies.

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Cerebral palsy-the most common physical disability of childhood-is a clinical diagnosis encompassing a heterogeneous group of neurodevelopmental disorders that cause impairments of movement and posture that persist throughout life. Despite being commonly attributed to a range of environmental factors, particularly birth asphyxia, the specific cause of cerebral palsy remains unknown in most individuals. A growing body of evidence suggests that cerebral palsy is probably caused by multiple genetic factors, similar to other neurodevelopmental disorders such as autism and intellectual disability. Recent advances in next-generation sequencing technologies have made possible rapid and cost-effective sequencing of the entire human genome. Novel cerebral palsy genes will probably be identified as more researchers and clinicians use this approach to study individuals with undiagnosed neurological disorders. As our knowledge of the underlying pathophysiological mechanisms of cerebral palsy increases, so will the possibility of developing genomically guided therapeutic interventions.

PMID: 22261432 [PubMed - as supplied by publisher]

18. Cochrane Database Syst Rev. 2012 Jan 18;1:CD007966.

Prophylactic phototherapy for preventing jaundice in preterm or low birth weight infants.

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South Africa, 7500.

BACKGROUND: Low birth weight and premature infants are at major risk for exaggerated hyperbilirubinaemia and jaundice that can lead to bilirubin encephalopathy. Phototherapy is the most common treatment for neonatal hyperbilirubinaemia and could be most effective in preventing the sequelae of hyperbilirubinaemia if initiated prophylactically. OBJECTIVES: To evaluate the efficacy and safety of prophylactic phototherapy for preterm (< 37 weeks gestational age) or low birth weight infants (birth weight < 2500 g). SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 3) on 31 March 2011, MEDLINE (1950 to 31 March 2011), EMBASE (1980 to 31 March 2011) and CINAHL (1982 to 31 March 2011). SELECTION CRITERIA: Randomised controlled trials or quasi-randomised controlled studies evaluating the effects of prophylactic phototherapy for preterm or low birth weight infants. DATA COLLECTION AND ANALYSIS: Two authors independently obtained data from published articles. We performed fixed-effect meta-analysis for the outcomes: rate of exchange transfusion, cerebral palsy or other neurodevelopmental impairment, peak serum bilirubin level and all-cause mortality. MAIN RESULTS: Nine studies of 3449 participants were included. The rate of exchange transfusion was reduced in one study with liberal transfusion criteria (risk ratio (RR) 0.20; 95% confidence interval (CI) 0.13 to 0.31) but not in the other two more recent studies with stringent criteria (typical RR 0.66; 95% CI 0.19 to 2.28). There was no statistically significant difference in the rate of cerebral palsy (typical RR 0.96; 95% CI 0.50 to 1.85; two studies, 756 participants). However, one large study that reported on neurodevelopmental impairment (a composite outcome including cerebral palsy) found a slightly lower rate of

neurodevelopmental impairment with prophylactic phototherapy (RR 0.85; 95% CI 0.74 to 0.99; 1804 participants). The prophylactic phototherapy group had lower peak bilirubin levels (mean difference (MD) -2.73; 95% CI -2.89 to -2.57; six studies, 2319 participants) and had fewer neonates with peak unconjugated serum bilirubin levels > 10 mg/dl (typical RR 0.27; 95% CI 0.22 to 0.33; three studies, 1090 participants) or peak unconjugated serum bilirubin levels > 15 mg/dl (typical RR 0.13; 95% CI 0.07 to 0.23; four studies, 1116 participants). There was no statistically significant difference in the rate of all-cause mortality between the two groups (typical RR 1.08; 95% CI 0.93 to 1.26; four studies, 3044 participants). AUTHORS' CONCLUSIONS: Prophylactic phototherapy helps to maintain a lower serum bilirubin concentration and may have an effect on the rate of exchange transfusion and the risk of neurodevelopmental impairment. However, further well-designed studies are needed to determine the efficacy and safety of prophylactic phototherapy on long-term outcomes including neurodevelopmental outcomes.

PMID: 22258977 [PubMed - in process]

19. J Clin Endocrinol Metab. 2012 Jan 18. [Epub ahead of print]

Neurodevelopmental Follow-Up at Five Years Corrected Age of Extremely Low Birth Weight Infants after Postnatal Replacement of 17β-Estradiol and Progesterone.

Trotter A, Steinmacher J, Kron M, Pohlandt F.

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Context: Extremely low birth weight (ELBW) infants are prone to impaired neurodevelopment.Objective:The aim was to determine long-term neurodevelopmental outcome in ELBW infants after postnatal 17β-estradiol (E2) and progesterone (P) replacement.Design:At 5-yr corrected age, ELBW infants were assessed for standardized cognitive and neurological outcome after postnatal randomized E2 and P replacement or placebo administration.Setting:The follow-up examination was performed in a neuropediatric ambulatory care center.Patients:Sixty-one of 71 surviving infants (86%) were available for follow-up.Main Outcome Measures:Cognitive and neurological outcome was evaluated using the Kaufmann Assessment Battery for Children, the Gross Motor Function Classification Scale, and clinical neurological examination.Results:No significant differences were found between the replacement and placebo groups for the Gross Motor Function Classification Scale, presence of paresis, cerebral palsy, spasticity, and ametropia. However, a significant time-response relationship was found with E2 and P replacement. Every day of treatment reduced the risk for cerebral palsy (P = 0.03), spasticity (P = 0.01), and ametropia (P = 0.01).Conclusion:Postnatal E2 and P replacement may have potential in improving neurodevelopmental outcome in ELBW infants. Larger trials are needed to test this new hypothesis.

PMID: 22259065 [PubMed - as supplied by publisher]

20. JAMA. 2012 Jan 18;307(3):275-82.

Survival without disability to age 5 years after neonatal caffeine therapy for apnea of prematurity.

Schmidt B, Anderson PJ, Doyle LW, Dewey D, Grunau RE, Asztalos EV, Davis PG, Tin W, Moddemann D, Solimano A, Ohlsson A, Barrington KJ, Roberts RS; Caffeine for Apnea of Prematurity (CAP) Trial Investigators.

Collaborators: Schmidt B, D'Ilario J, Cairnie J, Dix J, Adams B, Warriner E, Kim MH, Anderson P, Davis P, Doyle L, Argus B, Callanan K, Davis N, Duff J, McDonald M, Asztalos E, Hohn D, Lacy M, Haslam R, Barnett C, Goodchild L, Lontis R, Fraser S, Keng J, Saunders K, Opie G, Kelly E, Woods H, Marchant E, Turner AM, Davis N, Magrath E, Williamson A, Bairam A, Bélanger S, Fraser A, Lemyre B, Frank J, Solimano A, Synnes A, Grunau RE, Hubber-Richard P, Rogers M, Mackay M, Petrie-Thomas J, Butt A, van Wassenaer A, Nuytemans D, Houtzager B, van Sonderen L, Regev R, Itzchack N, Arnon S, Chalaf A, Ohlsson A, O'Brien K, Hamilton AM, Chan ML, Sankaran K, Morgan S, Proctor P, Golan A, Goldsch-Lerman E, Reynolds G, Dromgool B, Meskell S, Parr V, Maher C, Broom M, Kecskes Z, Ringland C, McMillan D, Schaab D, Spellen E, Sauve RS, Christianson H, Anseeuw-Deeks D, Creighton D, Heath J, Alvaro R, Chiu A, Porter C, Turner G, Moddemann D, Granke N, Penner K, Bow J, Mulder A, Wassenberg R, van der Hoeven M, Clarke M, Parfitt J, Parker K, Nwaesei C, Ryan H, Saunders C, Schulze A,

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CONTEXT: Very preterm infants are prone to apnea and have an increased risk of death or disability. Caffeine therapy for apnea of prematurity reduces the rates of cerebral palsy and cognitive delay at 18 months of age. OBJECTIVE: To determine whether neonatal caffeine therapy has lasting benefits or newly apparent risks at early school age. DESIGN, SETTING, AND PARTICIPANTS: Five-year follow-up from 2005 to 2011 in 31 of 35 academic hospitals in Canada, Australia, Europe, and Israel, where 1932 of 2006 participants (96.3%) had been enrolled in the randomized, placebo-controlled Caffeine for Apnea of Prematurity trial between 1999 and 2004. A total of 1640 children (84.9%) with birth weights of 500 to 1250 g had adequate data for the main outcome at 5 years. MAIN OUTCOME MEASURES: Combined outcome of death or survival to 5 years with 1 or more of motor impairment (defined as a Gross Motor Function Classification System level of 3 to 5), cognitive impairment (defined as a Full Scale IQ<70), behavior problems, poor general health, deafness, and blindness. RESULTS: The combined outcome of death or disability was not significantly different for the 833 children assigned to caffeine from that for the 807 children assigned to placebo (21.1% vs 24.8%; odds ratio adjusted for center, 0.82; 95% CI, 0.65-1.03; P = .09). The rates of death, motor impairment, behavior problems, poor general health, deafness, and blindness did not differ significantly between the 2 groups. The incidence of cognitive impairment was lower at 5 years than at 18 months and similar in the 2 groups (4.9% vs 5.1%; odds ratio adjusted for center, 0.97; 95% CI, 0.61-1.55; P = .89). CONCLUSION: Neonatal caffeine therapy was no longer associated with a significantly improved rate of survival without disability in children with very low birth weights who were assessed at 5 years.

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Long-term neurodevelopmental outcomes after intrauterine and neonatal insults: a systematic review.

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BACKGROUND: Neonatal interventions are largely focused on reduction of mortality and progression towards Millennium Development Goal 4 (child survival). However, little is known about the global burden of long-term consequences of intrauterine and neonatal insults. We did a systematic review to estimate risks of long-term neurocognitive and other sequelae after intrauterine and neonatal insults, especially in low-income and middle-income countries. METHODS: We searched Medline, Cumulative Index to Nursing and Allied Health Literature, the Cochrane Library, and Embase for studies published between Jan 1, 1966, and June 30, 2011, that reported neurodevelopmental sequelae after preterm or neonatal insult. For unpublished studies and grey literature, we searched Dissertation Abstracts International and the WHO library. We reviewed publications that had data for long-term outcome after defined neonatal insults. We summarised the results with medians and IQRs, and calculated the risk of at least one sequela after insult. FINDINGS: Of 28 212 studies identified by our search, 153 studies were suitable for inclusion, documenting 22 161 survivors of intrauterine or neonatal insults. The overall median risk of at least one sequela in any domain was 39·4% (IQR 20·0-54·8), with a risk of at least one severe impairment in any insult domain of 18·5% (7·7-33·3), of at least one moderate impairment of 5·0% (0·0-13·3%), and of at least one mild impairment of 10·0% (1·4-17·9%). The pooled risk estimate of at least one sequela (weighted mean) associated with one or more of the insults studied (excluding HIV) was 37·0% (95% CI 27·0-48·0%) and this risk was not significantly affected by region, duration of the follow-up, study design, or period of data collection. The most common sequelae were learning difficulties, cognition, or developmental delay (n=4032; 59%); cerebral palsy (n=1472; 21%); hearing impairment (n=1340; 20%); and visual impairment (n=1228; 18%). Only 40 (26%) studies

included data for multidomain impairments. These studies included 2815 individuals, of whom 1048 (37%) had impairments, with 334 (32%) having multiple impairments. INTERPRETATION: Intrauterine and neonatal insults have a high risk of causing substantial long-term neurological morbidity. Comparable cohort studies in resource-poor regions should be done to properly assess the burden of these conditions, and long-term outcomes, such as chronic disease, and to inform policy and programme investments. FUNDING: The Bill & Melinda Gates Foundation, Saving Newborn Lives, and the Wellcome Trust.

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