


INTRODUCTION: Motor impairment in children with spastic hemiparetic cerebral palsy (CP) is generally more prominent in the affected upper limb, leading to limitations in hand function stemming from deficiencies in motor coordination and selective motor control as well as muscle weakness, slower execution of movements and deficient integration of sensory-motor information. OBJECTIVE: Determine the effect of a single session of anodal transcranial direct current stimulation (tDCS) combined with functional training on the spatiotemporal variables of upper arm movements in children with spastic hemiparesis. METHOD: A randomized, sham-controlled trial with a blinded evaluator was conducted involving 20 children with CP between 6 and 12 years of age. The spatiotemporal variables of the upper limbs were analyzed by comparing the results of Evaluation 1 (before stimulation) and Evaluation 2 (immediately after stimulation). The protocol consisted of a 20-minute session of functional training of the paretic upper limb combined with tDCS administered over the primary motor cortex of the hemisphere contralateral to the motor impairment at an intensity of 1 mA. The participants were randomly allocated to two groups: experimental group (anodal tDCS) and control group (sham tDCS). RESULTS: Statistically significant (p < 0.05) reductions in total movement duration and returning movement duration were found in both the paretic and non-paretic limbs in the group submitted to active tDCS. No significant differences were found in the control group for any of the variables analyzed. CONCLUSION: A single session of anodal tDCS over the primary motor cortex of the hemisphere ipsilateral to the brain lesion led to momentary motor improvements in both upper limbs of the children with spastic hemiparetic CP analyzed in the present study.

PMID: 28632467

2. Commentary: Skilled Bimanual Training Drives Motor Cortex Plasticity in Children With Unilateral Cerebral Palsy.

Serrien DJ.


Comment on Skilled Bimanual Training Drives Motor Cortex Plasticity in Children With Unilateral Cerebral Palsy. [Neurorehabil Neural Repair. 2016]

PMID: 28638332
3. Hands Support and Postural Oscillation During Sit-to-Stand Movement in Children With Cerebral Palsy and Typical Children.

Pavão SL, Rocha NACF.


The authors aimed to compare the weight bearing on hands during sit-to-stand (STS) movement in children with cerebral palsy (CP) and typical children (TC), verify its effect on postural oscillation, and analyze the relationship between weight bearing on hands and postural oscillation. Twenty children with CP (Gross Motor Function Classification System levels I and II) and 35 TC performed STS with and without anterior hands support. Mann-Whitney test compared weight bearing between groups. Wilcoxon test investigated differences in postural oscillation between the conditions with and without anterior hand support for both groups. The Spearman correlation tested the relationship between weight-bearing and postural oscillation during the second phase of STS in both groups. In the CP group, greater weight bearing was related with lower postural oscillation in the beginning of STS. Although children with CP were able to perform STS without support, they bore more weight on their hands to perform the task than TC. Moreover, children with CP and TC use mechanical and somatosensory information to modulate their postural control during STS in different ways.

PMID: 28644922

4. Effects of the Integration of Dynamic Weight Shifting Training Into Treadmill Training on Walking Function of Children with Cerebral Palsy: A Randomized Controlled Study.

Wu M, Kim J, Arora P, Gaebler-Spira DJ, Zhang Y.


OBJECTIVE: The aim of the study was to determine whether applying an assistance force to the pelvis and legs during treadmill training can improve walking function in children with cerebral palsy. DESIGN: Twenty-three children with cerebral palsy were randomly assigned to the robotic or treadmill only group. For participants who were assigned to the robotic group, a controlled force was applied to the pelvis and legs during treadmill walking. For participants who were assigned to the treadmill only group, manual assistance was provided as needed. Each participant trained 3 times/wk for 6 wks. Outcome measures included walking speed, 6-min walking distance, and clinical assessment of motor function, which were evaluated before, after training, and 8 wks after the end of training, and were compared between two groups. RESULTS: Significant increases in walking speed and 6-min walking distance were observed after robotic training (P = 0.03), but no significant change was observed after treadmill training only. A greater increase in 6-min walking distance was observed after robotic training than that after treadmill only training (P = 0.01). CONCLUSIONS: Applying a controlled force to the pelvis and legs, for facilitating weight-shift and leg swing, respectively, during treadmill training may improve walking speed and endurance in children with cerebral palsy.

PMID: 28644244

5. To be active through indoor-climbing: an exploratory feasibility study in a group of children with cerebral palsy and typically developing children.

Schram Christensen M, Jensen T, Voigt CB, Nielsen JB, Lorentzen J.


BACKGROUND: Cerebral Palsy (CP) is the most common cause of motor disabilities in children and young adults and it is also often associated with cognitive and physiological challenges. Climbing requires a multifaceted repertoire of movements, participants at all levels of expertise may be challenged functionally and cognitively, making climbing of great potential interest in (re)habilitation settings. However, until now only few research projects have investigated the feasibility of climbing as a potential activity for heightening physical activity in children with CP and the possible beneficial effects of climbing activities in populations with functional and/or cognitive challenges. The aim of this study was therefore to test the feasibility of an intensive 3 weeks indoor-climbing training program in children with CP and typically developing (TD) peers. In addition we evaluated possible functional and cognitive benefits of 3 weeks of intensive climbing training in 11 children with cerebral...
palsy (CP) aged 11-13 years and six of their TD peers. METHOD: The study was designed as a feasibility and interventional study. We evaluated the amount of time spent being physically active during the 9 indoor-climbing training sessions, and climbing abilities were measured. The participants were tested in a series of physiological, psychological and cognitive tests: two times prior to and one time following the training in order to explore possible effects of the intervention. RESULTS: The children accomplished the training goal of a total of nine sessions within the 3-week training period. The time of physical activity during a 2:30 h climbing session, was comparably high in the group of children with CP and the TD children. The children with CP were physically active on average for almost 16 h in total during the 3 weeks. Both groups of participants improved their climbing abilities, the children with CP managed to climb a larger proportion of the tested climbing route at the end of training and the TD group climbed faster. For the children with CP this was accompanied by significant improvements in the Sit-to-stand test (p < 0.01), increased rate of force development in the least affected hand during an explosive pinch test and increased muscular-muscular coherence during a pinch precision test (p < 0.05). We found no improvements in maximal hand or finger strength and no changes in cognitive abilities or psychological well-being in any of the groups. CONCLUSIONS: These findings show that it is possible to use climbing as means to make children with CP physically active. The improved motor abilities obtained through the training is likely reflected by increased synchronization between cortex and muscles, which results in a more efficient motor unit recruitment that may be transferred to daily functional abilities.

PMID: 28619011


Shuman BR, Schwartz MH, Steele KM.


Muscle synergies calculated from electromyography (EMG) data identify weighted groups of muscles activated together during functional tasks. Research has shown that fewer synergies are required to describe EMG data of individuals with neurologic impairments. When considering potential clinical applications of synergies, understanding how EMG data processing impacts results and clinical interpretation is important. The aim of this study was to evaluate how EMG signal processing impacts synergy outputs during gait. We evaluated the impacts of two common processing steps for synergy analyses: low pass (LP) filtering and unit variance scaling. We evaluated EMG data collected during barefoot walking from five muscles of 113 children with cerebral palsy (CP) and 73 typically-developing (TD) children. We applied LP filters to the EMG data with cutoff frequencies ranging from 4 to 40 Hz (reflecting the range reported in prior synergy research). We also evaluated the impact of normalizing EMG amplitude by unit variance. We found that the total variance accounted for (tVAF) by a given number of synergies was sensitive to LP filter choice and decreased in both TD and CP groups with increasing LP cutoff frequency (e.g., 9.3 percentage points change for one synergy between 4 and 40 Hz). This change in tVAF can alter the number of synergies selected for further analyses. Normalizing tVAF to a z-score (e.g., dynamic motor control index during walking, walk-DMC) reduced sensitivity to LP cutoff. Unit variance scaling caused comparatively small changes in tVAF. Synergy weights and activations were impacted less than tVAF by LP filter choice and unit variance normalization. These results demonstrate that EMG signal processing methods impact outputs of synergy analysis and z-score based measures can assist in reporting and comparing results across studies and clinical centers.

PMID: 28634449


Alter KE, Gormley M Jr, Patel AT.


As seen in this CME online activity (available at http://courses.elseviercme.com/spasticity/662e), treatment of patients with spasticity due to upper motor neuron syndromes, including traumatic brain injury, stroke, and cerebral palsy, is multifaceted, involving chemodenervation, systemic medications, surgical therapy, rehabilitation efforts, and home care. Optimal care begins with the recognition that each patient's impairments are unique and must be assessed carefully to determine the impact of muscle overactivity, loss of dexterity, and weakness on passive and active function in the context of the patients' goals. While botulinum toxin plays a major role in providing symptomatic relief and functional improvement from hypertonia, it should rarely be used as a standalone treatment.

PMID: 28634003
8. Reliability, validity, and norms of the 2-min walk test in children with and without neuromuscular disorders aged 6-12.

Pin TW, Choi HL.


PURPOSE: The 2-min walk test may be more appropriate functional exercise test for young children. This study aimed to examine the 2-min walk test's reliability; validity; and minimal clinically important difference; and to establish norms for children aged 6-12. METHODS: Sixty-one healthy children were recruited to examine the 2-min walk test's reliability. Forty-six children with neuromuscular disorders (63% cerebral palsy) were recruited to test the validity. The normative study involved 716 healthy children without neuromuscular disorders (male = 51%, female = 49%). They walked at a self-selected speed for 2 min along a smooth, flat path 15 m in length. RESULTS: The mean distance covered in the 2-min walk test was 152.8 m (SD = 27.5). No significant difference was found in the children's test-retest results (p > 0.05). The intra- and inter-rater reliability were high (all intra-class correlation coefficients > 0.8). All children, except one with neuromuscular disorders, completed the 2-min walk test, of which the minimal clinically important difference at 95% confidence interval was 23.2 m for the entire group, 15.7 m for children walking with aids, and 16.6 m for those walking independently. CONCLUSIONS: The 2-min walk test is a feasible, reliable, and valid exercise test for children with and without neuromuscular disorders aged 6-12. The first normative references and minimal clinically important difference for children with neuromuscular disorders were established for children of this age group. Implications for rehabilitation The 2-min walk test is a feasible, safe, reliable, and valid time-based walk test for children aged 6-12 years. Normative references have been established for healthy children aged 6-12 years. Minimal clinically important difference at 95% confidence interval were calculated for children with neuromuscular disorders who walked without aids (i.e., independent and stand-by supervision) and those who walked with aids equal to 16.6 and 15.7 m, respectively. Distance covered by the healthy children in the 2 min did not correlate with age, gender, height, and weight of the children.

PMID: 28637155


Kainz H, Carty CP, Maine S, Walsh HPJ, Lloyd DG, Modenese L.


Joint kinematics can be calculated by Direct Kinematics (DK), which is used in most clinical gait laboratories, or Inverse Kinematics (IK), which is mainly used for musculoskeletal research. In both approaches, joint centre locations are required to compute joint angles. The hip joint centre (HJC) in DK models can be estimated using predictive or functional methods, while in IK models can be obtained by scaling generic models. The aim of the current study was to systematically investigate the impact of HJC location errors on lower limb joint kinematics of a clinical population using DK and IK approaches. Subject-specific kinematic models of eight children with cerebral palsy were built from magnetic resonance images and used as reference models. HJC was then perturbed in 6mm steps within a 60mm cubic grid, and kinematic waveforms were calculated for the reference and perturbed models. HJC perturbations affected only hip and knee joint kinematics in a DK framework, but all joint angles were affected when using IK. In the DK model, joint constraints increased the sensitivity of joint range-of-motion to HJC location errors. Mean joint angle offsets larger than 5° were observed for both approaches (DK and IK), which were larger than previously reported for healthy adults. In the absence of medical images to identify the HJC, predictive or functional methods with small errors in anterior-posterior and medial-lateral directions and scaling procedures minimizing HJC location errors in the anterior-posterior direction should be chosen to minimize the impact on joint kinematics.

PMID: 28641160
10. Effects of Participation in Sports Programs on Walking Ability and Endurance Over Time in Children With Cerebral Palsy.


OBJECTIVE: Children with cerebral palsy may benefit from maintaining a high level of physical fitness similar to typically developing children especially in terms of long-term physical performance, although in practice this is often difficult. The purpose of this study was to determine the effect of participation in sports programs on walking ability and endurance over time. DESIGN: A retrospective cohort study included participants with cerebral palsy, aged 6 to 20 yrs, who attended a summer sports program from 2004 to 2012. There were 256 participant sessions with pre/post data recorded. The participants consisted of a total of 97 children (mean age [SD] = 11.4 [3.1] yrs), many of whom attended multiple programs throughout the years. Programs were held 6 hrs/d, 5 d/wk for up to 4 wks. Outcome measures included the Timed Up and Go, modified 6-min walk, and 25-ft walk/run. RESULTS: The results showed significant improvements in the Timed Up and Go, modified 6-min walk distance and 25-ft walk/run over time. Children in Gross Motor Classification System level III made the largest gains. CONCLUSIONS: Walking ability and endurance seem to improve after participation in an intensive summer sports programs. Higher frequency of program attendance resulted in significant improvements in the Timed Up and Go. PMID: 28644242


BACKGROUND: Patellalowering aims to improve quadriceps function as a means of correcting crouch gait in patients with cerebral palsy (PC). Few studies have assessed the effects of patella lowering as a component of multilevel surgery. HYPOTHESIS: Including patella lowering into the components of multilevel surgery is beneficial in patients with crouch gait and patella alta. MATERIAL ET METHODS: In 12 lower limbs with patella alta (Caton-Deschamps index >1.4) in 41 children with cerebral palsy, patella lowering was performed, without distal femoral extension osteotomy or hamstring release. Among limbs with similar surgical procedures (e.g., hamstring lengthening, rectus femoris transfer) except for patella lowering, controls were selected retrospectively by matching on a propensity score for patella lowering. The propensity score was computed based on preoperative knee flexion contracture, knee extension lag, and minimum knee flexionat mid-stance. Clinical and 3D kinematic data were compared between the two groups. RESULTS: The improvement in minimum knee flexion at mid-stance was significantly greater in the group with patellar lowering (-24°±12°vs. -12°±7°). The Gait Deviation Index improved similarly in the two groups. Knee flexion contracture improved only in the group with patellar lowering. Extension lag did not improve in either group. Peak knee flexion during the swing phase remained unchanged in both groups. DISCUSSION: Patellar lowering is effective in diminishing minimum knee flexion at mid-stance in patients with patella alta and crouch gait due to cerebral palsy. Patellar lowering has not adverse effects on gait. These findings cannot be assumed to apply to patients with normal patellar height. PMID: 28629941


This preliminary study examined the effects of off-axis elliptical training on reducing transverse-plane gait deviations and improving gait function in 8 individuals with cerebral palsy (CP) (15.5 ± 4.1 years) who completed an training program using a custom-made elliptical trainer that allows transverse-plane pivoting of the footplates during exercise. Lower-extremity off-axis control during elliptical exercise was evaluated by quantifying the root-mean-square and maximal angular displacement of the footplate pivoting angle. Lower-extremity pivoting strength was assessed. Gait function and balance were evaluated using 10-m walk test, 6-minute-walk test, and Pediatric Balance Scale. Toe-in angles during gait were quantified. Participants with CP
demonstrated a significant decrease in the pivoting angle (root mean square and maximal angular displacement; effect size, 1.00-2.00) and increase in the lower-extremity pivoting strength (effect size = 0.91-1.09) after training. Reduced 10-m walk test time (11.9 ± 3.7 seconds vs. 10.8 ± 3.0 seconds; P = 0.004; effect size = 1.46), increased Pediatric Balance Scale score (43.6 ± 12.9 vs. 45.6 ± 10.8; P = 0.042; effect size = 0.79), and decreased toe-in angle (3.7 ± 10.5 degrees vs. 0.7 ± 11.7 degrees; P = 0.011; effect size = 1.22) were observed after training. We present an intervention to challenge lower-extremity off-axis control during a weight-bearing and functional activity for individuals with CP. Our preliminary findings suggest that this intervention was effective in enhancing off-axis control, gait function, and balance and reducing in-toeing gait in persons with CP.

PMID: 28628539

Syed YY.

AbobotulinumtoxinA (Dysport®) is currently the only botulinum toxin A formulation approved by the US FDA for the treatment of lower limb spasticity in pediatric patients aged ≥2 years. Intramuscular abobotulinumtoxinA was approved based on the results of a pivotal phase 3 trial in children with lower limb spasticity due to cerebral palsy. In this trial, a single treatment cycle with abobotulinumtoxinA 10-15 U/kg/leg injected into the gastrocnemius and soleus muscles significantly improved ankle plantar flexor muscle tone (primary endpoint), with abobotulinumtoxinA recipients showing a significant response to treatment relative to placebo. AbobotulinumtoxinA treatment also improved spasticity grade. The improvements in muscle tone and spasticity were associated with an improved ability to attain functional goals. Clinical benefits of abobotulinumtoxinA treatment lasted for 16-22 weeks in most patients, and were maintained with multiple treatment cycles during 1 year in an open-label extension study. AbobotulinumtoxinA was generally well tolerated, with a relatively low incidence of treatment-related adverse events. In summary, abobotulinumtoxinA is an effective and generally well tolerated treatment option for children with lower limb spasticity.

PMID: 28623614

14. Effect of neurodevelopmental treatment-based physical therapy on the change of muscle strength, spasticity, and gross motor function in children with spastic cerebral palsy.
Park EY, Kim WH.

[Purpose] This study aimed to investigate the effectiveness of neurodevelopmental treatment-based physical therapy on muscle tone, strength, and gross motor function in children with spastic cerebral palsy. [Subjects and Methods] One-hundred-seventy-five children with spastic cerebral palsy (88 diplegia; 78 quadriplegia) received neurodevelopmental treatment-based physical therapy for 35 minutes per day, 2-3 times per week for 1 year. Spasticity, muscle strength, and gross motor function were measured before and after treatment with the Modified Ashworth Scale, Manual Muscle Testing, and Gross Motor Function Measure, respectively. [Results] Spasticity was significantly reduced after 1 year of treatment. The Gross Motor Functional Classification System levels I-II group showed a significant increase in muscle strength compared with the Gross Motor Functional Classification System levels III-V, and the latter showed a significant decrease in spasticity compared with the former. [Conclusion] Neurodevelopmental treatment-based physical therapy in children with cerebral palsy seems to be effective in reducing spasticity, but does not improve gross motor function. Therefore, other interventional approaches are needed to improve gross motor function in children with cerebral palsy.

PMID: 28626301
15. The effects of dosage time and frequency on motor outcomes in children with cerebral palsy: A systematic review.

Cope S, Mohn-Johnsen S.


PURPOSE: Provide an updated review regarding treatment dosage for children with cerebral palsy (CP) by examining the variables of type, time, frequency, and intensity. METHODS: A systematic review was performed with 30 articles meeting the inclusion criteria. Two authors independently extracted data including information about risk of bias. Ten articles were included in the review. RESULTS: Eight studies manipulated time, two studies manipulated frequency, and three studies manipulated both variables. No studies investigated intensity. Findings suggest that manipulating time and/or frequency may result in better motor function for higher total dosing; however, benefits were not consistent across studies and few showed clinically significant improvements. CONCLUSION: This most current evidence regarding the effect of dosage on motor function for children with CP suggests that there is insufficient evidence to support implementing high-dosage therapy. Further research is needed to clarify the relationship between dosage variables on motor function for children with CP.

PMID: 28632463

16. Effectiveness of vitamin K2 on osteoporosis in adults with cerebral palsy.

Kodama Y, Okamoto Y, Kubota T, Hiroyama Y, Fukami H, Matsushita K, Kawano Y.


BACKGROUND: Osteoporosis can lead to spontaneous fractures in adults with cerebral palsy (CP). Undercarboxylated osteocalcin (ucOC) is a useful marker for vitamin K insufficiency in osteoporosis. The primary objective of this study was to determine the effect of vitamin K2 on bone mineral density (BMD) in adults with CP and vitamin K insufficiency. METHODS: Sixteen adults, median age of 56 years, with CP and osteoporosis in whom the serum ucOC concentration exceeded 4.5 ng/mL were included. All patients received 45 mg of vitamin K2 per day. BMD was measured and presented as a percentage of the young adult mean (%YAM). Serum levels of ucOC and BMD were measured at baseline and after 6 and 12 months. RESULTS: Serum levels of ucOC decreased from 7.8 ng/mL (range, 4.9-32) at baseline to 3.9 ng/mL (range, 1.9-6.8) after 6 months (P=0.001). BMD increased from 59%YAM (range, 45-67) at baseline to 68%YAM (range, 50-79) after 12 months (P=0.003). CONCLUSIONS: Vitamin K2 had a positive effect on BMD in osteoporotic adults with CP and high serum concentrations of ucOC, and might be useful as a first line treatment for osteoporotic adults with CP and vitamin K insufficiency.

PMID: 28624135

17. The Effect of a Comprehensive Care Transition Model on Cost and Utilization for Medically Complex Children With Cerebral Palsy.


INTRODUCTION: Our aim was to evaluate cost and acute care utilization related to an organized approach to care coordination and transitional care after major acute care hospitalization for children with medical complexities, including cerebral palsy. METHODS: A retrospective cohort of 32 patients from Ranken Jordan Pediatric Bridge Hospital (RJPBH) who received the Care Beyond the Bedside model was compared with 151 patients receiving standard care elsewhere across Missouri. Claims data (2007-2012) were obtained from MoHealthNet, Missouri's Medicaid program, for all children with moderate to severe cerebral palsy (defined using approximated Gross Motor Function Classification System levels) who had at least one hospital visit during the study period (N = 183). Risk-adjusted linear and Poisson regression models were used to analyze per-member-per-month costs and three indicators of acute care utilization (emergency department visits, readmissions, and inpatient days). RESULTS: RJPBH patients were associated with statistically significant reductions in per-member-per-month costs (-21%), hospital readmissions (-66%), and inpatient days (-57%). DISCUSSION: RJPBH's enhanced interprofessional medical home-like model, including intense care coordination, psychosocial therapy, family and caregiver empowerment, and transitional care, may be keys to reducing cost and unnecessary hospital use for children with medical complexities with cerebral palsy who receive Medicaid.

PMID: 28622983
Stadskleiv K, Jahnsen R, Andersen GL, von Tetzchner S.

PURPOSE: To explore factors contributing to variability in cognitive functioning in children with cerebral palsy (CP).
METHOD: A geographical cohort of 70 children with CP was assessed with tests of language comprehension, visual-spatial reasoning, attention, working memory, memory, and executive functioning. Mean age was 9;9 years (range 5;1-17;7), 54.3% were girls, and 50.0% had hemiplegic, 25.7% diplegic, 12.9% quadriplegic, and 11.4% dyskinetic CP. For the participants with severe motor impairments, assessments were adapted for gaze pointing. A cognitive quotient (CQ) was computed. RESULTS: Mean CQ was 78.5 (range 19-123). Gross motor functioning, epilepsy, and type of brain injury explained 35.5% of the variance in CQ (F = 10.643, p = .000). CONCLUSION: Twenty-four percent had an intellectual disability, most of them were children with quadriplegic CP. Verbal comprehension and perceptual reasoning scores did only differ for the 21% with an uneven profile, of whom two-thirds had challenges with perceptual reasoning.

PMID: 28632466

19. Stepping Up to Rethink the Future of Rehabilitation: IV STEP Considerations and Inspirations.
Kimberley TJ1, Novak I, Boyd L, Fowler E, Larsen D.

BACKGROUND AND PURPOSE: The IV STEP conference challenged presenters and participants to consider the state of science in rehabilitation, highlighting key area of progress since the previous STEP conference related to prediction, prevention, plasticity, and participation in rehabilitation. KEY POINTS: Emerging from the thought-provoking discussions was recognition of the progress we have made as a profession and a call for future growth. In this summary article, we present a recap of the key points and call for action. We review the information presented and the field at large as it relates to the 4 Ps: prediction, prevention, plasticity, and participation. RECOMMENDATIONS FOR PRACTICE: Given that personalized medicine is an increasingly important approach that was clearly woven throughout the IV STEP presentations, we took the liberty of adding a fifth "P," Personalized, in our discussion of the future direction of the profession.

PMID: 28628598

20. Impact of clinical and/or histological chorioamnionitis on neurodevelopmental outcomes in preterm infants: A literature review.
Maisonneuve E, Ancel PY, Foix-L'Hélias L, Marret S, Kayem G.

OBJECTIVE: To determine the impact of clinical and/or histological chorioamnionitis on neurodevelopmental outcomes in premature infants. METHODS: A review of the literature appeared in PubMed between 1997 and 2016 was conducted to examine the association between clinical and/or histological chorioamnionitis and neurologic impairment in the neonates (intraventricular hemorrhage, periventricular leukomalacia and white matter damage) and in infants (cerebral palsy and neurodevelopmental delay). RESULTS: The first meta-analysis published in 2000 observed that clinical chorioamnionitis was associated with cystic periventricular leukomalacia and cerebral palsy and that histologic chorioamnionitis was associated with periventricular leukomalacia only. A second meta-analysis in 2010 found that cerebral palsy was associated with both clinical and histological chorioamnionitis. But most recent studies over the last decade based on large cohorts found no effect of chorioamnionitis on neurological outcomes, even if they had several methodological limitations. CONCLUSION: According to the findings of the most recent studies, clinical or histological chorioamnionitis does not seem to be associated with neonatal white matter injuries, or with cerebral palsy. Further studies are needed to assess the impact of chorioamnionitis on long-term neurological development.

PMID: 28643657
21. Early Imaging and Adverse Neurodevelopmental Outcome in Asphyxiated Newborns Treated With Hypothermia.


BACKGROUND: Brain injury can be identified as early as day two of life in asphyxiated newborns treated with hypothermia, when using diffusion magnetic resonance imaging (MRI). However, it remains unclear whether these diffusion changes can predict future neurodevelopment. This study aimed to determine whether abnormal early diffusion changes in newborns treated with hypothermia are associated with adverse neurodevelopmental outcome at age two years. METHODS: Asphyxiated newborns treated with hypothermia were enrolled prospectively. They underwent magnetic resonance imaging (MRI) at specific time points over the first month of life, including diffusion-weighted imaging and diffusion-tensor imaging. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values were measured in different regions of interest. Adverse neurodevelopmental outcome was defined as cerebral palsy, global developmental delay, and/or seizure disorder around age two years. ADC and FA values were compared between the newborns developing or not developing adverse outcome. RESULTS: Twenty-nine asphyxiated newborns treated with hypothermia were included. Among the newborns developing adverse outcome, ADC values were significantly decreased on days two to three of life and increased around day ten of life in the thalamus, posterior limb of the internal capsule, and the lentiform nucleus. FA values decreased in the same regions around day 30 of life. These newborns also had increased ADC around day ten of life and around day 30 of life, and decreased FA around day 30 of life in the anterior and posterior white matter. CONCLUSIONS: Diffusion changes that were evident as early as day two of life, when the asphyxiated newborns were still treated with hypothermia, were associated with later abnormal neurodevelopmental outcome.

PMID: 28619376

22. Caffeine Protects Against Anticonvulsant-Induced Neurotoxicity in the Developing Rat Brain.

Endesfelder S, Weichelt U, Schiller C, Sifringer M, Bendix I, Bührer C.
Neurotox Res. 2017 Jun 22. doi: 10.1007/s12640-017-9768-z. [Epub ahead of print]

Phenobarbital is the most commonly used drug for the treatment of neonatal seizures but may induce neurodegeneration in the developing brain. Methylxanthine caffeine is used for the treatment of apnea in newborn infants and appears to be neuroprotective, as shown by antiapoptotic and anti-inflammatory effects in oxidative stress models in newborn rodents and reduced rates of cerebral palsy in human infants treated with caffeine. We hypothesized that caffeine may counteract the proapoptotic effects of phenobarbital in newborn rats. Postnatal day 4 (P4) rats received phenobarbital (50 mg/kg) +/- caffeine (10 mg/kg) for three consecutive days. Brains examined at 6, 12, and 24 h after last injection of phenobarbital showed a drastic increase of apoptotic cell death (TUNEL+), which was attenuated by co-treatment with caffeine at 6 and 24 h but not at 12 h. Phenobarbital also increased protein levels of apoptosis inducing factor (AIF) and cleaved caspase-3, which was reduced by caffeine co-administration at all time points investigated. RNA expression of the pro-inflammatory cytokines TNFα, IFNγ, and IL-1β, but not IL-18, was upregulated by phenobarbital. Co-treatment with caffeine significantly decreased these upregulations at all time points investigated, while caffeine without phenobarbital resulted in increased expression of TNFα, IL-1β, and IL-18, but not IFNγ at 6 h. Downregulation of the adenosine A1 and A2a receptors, both of which bind caffeine, by 24 h of phenobarbital exposure was partly antagonized by caffeine. These results raise the possibility that the phenobarbital-induced adverse effects could be reduced by a co-treatment with caffeine.

PMID: 28643232