1. Structural Brain Damage and Upper Limb Kinematics in Children with Unilateral Cerebral Palsy.


Background: In children with unilateral cerebral palsy (uCP) virtually nothing is known on the relation between structural brain damage and upper limb (UL) kinematics quantified with three-dimensional movement analysis (3DMA). This explorative study aimed to (1) investigate differences in UL kinematics between children with different lesion timings, i.e., periventricular white matter (PWM) vs. cortical and deep gray matter (CDGM) lesions and (2) to explore the relation between UL kinematics and lesion location and extent within each lesion timing group. Methods: Forty-eight children (age 10.4 ± 2.7 year; 29 boys; 21 right-sided; 33 PWM; 15 CDGM) underwent an UL 3DMA during a reach-to-grasp task. Spatiotemporal parameters [movement duration, (timing of) maximum velocity, trajectory straightness], the Arm Profile Score (APS) and Arm Variable Scores (AVS) were extracted. The APS and AVS refer to the total amount of movement pathology and movement deviations of the wrist, elbow, shoulder, scapula and trunk respectively. Brain lesion location and extent were scored based on FLAIR-images using a semi-quantitative MRI-scale. Results: Children with CDGM lesions showed more aberrant spatiotemporal parameters (p < 0.03) and more movement pathology (APS, p = 0.003) compared to the PWM group, mostly characterized by increased wrist flexion (p = 0.01). In the CDGM group, moderate to high correlations were found between lesion location and extent and duration, timing of maximum velocity and trajectory straightness (r = 0.53-0.90). Lesion location and extent were further moderately correlated with distal UL movement pathology (wrist flexion/extension, elbow pronation/supination, elbow flexion/extension; r = 0.50-0.65) and with the APS (r = 0.51-0.63). In the PWM group, only a few and low correlations were observed, mostly between damage to the PLIC and higher AVS of elbow flexion/extension, shoulder elevation and trunk rotation (r = 0.35-0.42). Regression analysis revealed damage to the temporal lobe with lesion timing as interactor (27%, p = 0.002) and the posterior limb of the internal capsule (PLIC) (7%, p = 0.04) as the strongest predictors, explaining 34% of the variance in APS. Conclusion: UL kinematic deviations are more influenced by lesion location and extent in children with later (CDGM) versus earlier lesions (PWM), except for proximal movement pathology. Damage to the PLIC is a significant predictor for UL movement pathology irrespective of lesion timing.

PMID: 29311871


Comment on Commentary: Skilled Bimanual Training Drives Motor Cortex Plasticity in Children With Unilateral Cerebral Palsy. [Front Hum Neurosci. 2017]

PMID: 29326574
3. A new strength assessment to evaluate the association between muscle weakness and gait pathology in children with cerebral palsy.

Goudriaan M, Nieuwenhuys A, Schless SH, Goemans N, Molenaers G, Desloovere K.


AIM: The main goal of this validation study was to evaluate whether lower limb muscle weakness and plantar flexor rate of force development (RFD) related to altered gait parameters in children with cerebral palsy (CP), when weakness was assessed with maximal voluntary isometric contractions (MVICs) in a gait related test position. As a subgoal, we analyzed intra- and intertester reliability of this new strength measurement method. METHODS: Part 1 - Intra- and intertester reliability were determined with the intra-class correlation coefficient (ICC2,1) in 10 typical developing (TD) children (age: 5-15). We collected MVICs in four lower limb muscle groups to define maximum joint torques, as well as plantar flexor RFD. Part 2 - Validity of the strength assessment was explored by analyzing the relations of lower limb joint torques and RFD to a series of kinematic- and kinetic gait features, the GDI (gait deviation index), and the GDI-kinetik in 23 children with CP (GMFCS I-II; age: 5-15) and 23 TD children (age: 5-15) with Spearman's rank correlation coefficients. RESULTS: Part 1 - The best reliability was found for the torque data (Nm), with the highest ICC2,1 (0.951) for knee extension strength (inter) and the lowest (0.693) for dorsiflexion strength (intra). For plantar flexor RFD, the most reliable window size was 300 milliseconds (ICC2,1: 0.828 (inter) and 0.692 (intra)). Part 2 - The children with CP were significantly weaker than the TD children (p <0.001). Weakness of the dorsiflexors and plantar flexors associated with delayed and decreased knee flexion angle during swing, respectively. No other significant correlations were found. CONCLUSION: While our new strength assessment was reliable, intra-joint correlations between weakness, RFD, and gait deviations were low. However, we found inter-joint associations, reflected by a strong association between plantar- and dorsiflexor weakness, and decreased and delayed knee flexion angle during swing.

PMID: 29324873


Yousef MAA, Rosenfeld S.


BACKGROUND: Scoliosis is a common deformity in patients with neuromuscular disorders which usually necessitates surgical correction. Patients with neuromuscular scoliosis are characterized by increased incidence of associated medical co-morbidities and higher postoperative complication rate; therefore, these patients are often managed with a wide multidisciplinary care team. Postoperative fever is a frequent complication after surgery which is often routinely investigated using different workup tests to rule out infection. These tests lack clear evidence on how they impact the patient care and are associated with increased cost and burden on the health system. OBJECTIVE: The objective of our study was to evaluate the incidence of postoperative fever after surgical correction of neuromuscular scoliosis and evaluate the clinical usefulness of fever diagnostic workup. METHODS: Demographic and clinical data on patients who underwent neuromuscular scoliosis corrective surgery between March 1, 2014 and February 28, 2017 were reviewed at a single institution. The occurrence of postoperative fever (defined by body temperature ≥ 38 °C during the 1st week after surgery) was characterized by maximum temperature (T max), postoperative day of occurrence (POD), and frequency as described by either single or multiple temperature spikes. The diagnostic tests performed for the assessment of postoperative fever were reviewed. The cost per health effect was calculated by dividing the total costs of performed fever workup tests by the number of tests that resulted in change of the patient care. RESULTS: Seventy-six patients (female and 29 males) were identified. Cerebral palsy was the most common aetiology in 40 patients (52.6%). The mean age at surgery was 13.5 years (range 3-18 years). The operative time was 490.34 ± 127.21 min. The intraoperative blood loss was 912.3 ± 627.8 cc. The hospital stay was 9.79 ± 5.3 days and the intensive care unit (ICU) stay was 3.26 ± 3.7 days. Wound drains were used in 71 patients for a period of 3.6 ± 2.3 days. Urinary catheters were used for a period of 3.6 ± 1.8 days. Forty-nine patients (64.5%) developed postoperative fever with a temperature of 38.7° ± 0.45° (range 38.10°-39.9°). The most frequent POD for occurrence of fever was the 2nd day in 22 patients (44.9%). The frequency of fever was in the form of multiple temperature spikes in 32 patients (65.3%) or in the form of a single spike in 17 patients (34.7%). There were a total of 20 positive tests out of 132 performed fever workup tests (15.2%). These included nine positive urine analysis (n = 32), five positive urine cultures (n = 28), one positive blood culture (n = 23), and two positive chest X-ray (n = 24). The occurrence of postoperative fever was statistically correlated with the operative time and increased hospital stay and ICU days. The most common identified cause of infection was urinary tract infection in 11 patients followed by respiratory tract infection in four patients and wound infection in one patient. The calculated cost per health effect was $3763. CONCLUSION: Sixty-four percent of patients who underwent surgical correction of neuromuscular scoliosis developed postoperative fever. Postoperative fever was sign of infection in 32.7% of patients and urinary tract infection was the most frequent finding. Only 15.2% of fever diagnostic workup tests were positive. Diagnostic urine tests account for 70% of the positive diagnostic workup. The routine use of blood cultures for the assessment of postoperative fever in such population should be avoided due to the low rate of positive tests and the associated high cost.

PMID: 29318413
Antunes D, Rossato M, Kons RL, Sakugawa RL, Fischer G.

Despite the evolution of runner performance in athletes with cerebral palsy (CP), little is known about neuromuscular parameters of sprinters from different classes, especially related to power output, muscular imbalances and asymmetry indexes in lower limbs. The aim of this study was to assess muscle power, muscular imbalance and asymmetry in sprinters with CP. Four male sprinters with CP (age, 18 to 27 years; body mass, 58.5 to 72.8 kg; height, 161.5 to 174 cm) classified as T38, T37, T36, T35 according to International Paralympic Committee functional classification, performed vertical counter movement jump and squat jump on force plate and isokinetic torque evaluations in both limbs. The concentric peak torque (PT) was measured at 60°/sec, 120°/sec and 180°/sec and PT eccentric at 60°/sec and 120°/sec. The asymmetry indexes, conventional and functional ratios were assessed. The results showed that athletes with more severe impairments (T35 and T36) showed worse performance to muscle power, more muscular imbalance and higher asymmetry in PT between limbs (> 10%). The exception was T37 athlete, who presented the better performance for all variables. It is concluded that CP athletes with more severe impairments showed lower jumping performance and torque production of knee extensors and flexors, they showed greater asymmetries between limbs. Finally, considering the results of T37 athlete, it seems that the athletic training for a longer period can reverse part of the neuromuscular impairments caused by CP.

PMID: 29326905

Cloodt E, Rosenblad A, Rodby-Bousquet E.

AIM: To identify the prevalence of knee contracture and its association with gross motor function, age, sex, spasticity, and muscle length in children with cerebral palsy (CP). METHOD: Cross-sectional data for passive knee extension were analysed in 3 045 children with CP (1 756 males, 1 289 females; mean age 8y 1mo [SD 3.84]). CP was classified using the Gross Motor Function Classification System (GMFCS) levels I (n=1 330), II (n=508), III (n=280), IV (n=449), and V (n=478). Pearson's χ2 test and multiple binary logistic regression were applied to analyse the relationships between knee contracture and GMFCS level, sex, age, spasticity, hamstring length, and gastrocnemius length. RESULTS: Knee contracture greater than or equal to 5 degrees occurred in 685 children (22%). The prevalence of knee contracture was higher in older children and in those with higher GMFCS levels. Odds ratios (ORs) for knee contracture were significantly higher for children at GMFCS level V (OR=13.17), with short hamstring muscles (OR=9.86), and in the oldest age group, 13 years to 15 years (OR=6.80). INTERPRETATION: Knee contracture is associated with higher GMFCS level, older age, and shorter muscle length; spasticity has a small effect. Maintaining muscle length, especially of the hamstrings, is important for reducing the risk of knee contracture. What this paper adds Knee contracture occurs in children with cerebral palsy at all Gross Motor Function Classification System (GMFCS) levels. Knee contracture in children is associated with short hamstring muscles, higher GMFCS level, and older age. Short hamstring muscles present a greater risk for knee contracture than spasticity.

PMID: 29318610

7. Toe Walking: A Neurological Perspective After Referral From Pediatric Orthopaedic Surgeons.
Haynes KB, Wimberly RL, VanPelt JM, Jo CH, Riccio AI, Delgado MR.

BACKGROUND: Toe walking (TW) in children is often idiopathic in origin. Our purpose was to determine the incidence of a neurological etiology for TW in patients seen in the neurology clinic after referral from pediatric orthopaedic surgeons. METHODS: We performed an Institutional Review Board approved retrospective review of 174 patients referred to the neurology clinic from orthopaedic surgeons at an academic pediatric tertiary care center between January 2010 and September 2015. Medical records were reviewed and data recorded including pertinent family history, birth history, age of initial ambulation, physical examination findings, and workup results including neuroimaging, neurophysiological studies, and findings of genetic testing and tissue biopsy. RESULTS: Sixty-two percent (108/174) of patients were found to have a neurological etiology for TW. Final pathologic diagnoses were: 37% (40/108) previously undiagnosed cerebral palsy (CP), 16.7% (18/108) peripheral neuropathy, 15.7% (17/108) autism spectrum disorder, 13.9% (15/108) hereditary spastic paraparesis, 8.3% (9/108) attention deficit hyperactivity disorder, 5.6% (6/108) syndromic diagnosis, and 2.8% (3/108) spinal cord abnormality. Ankle equinus contractures were noted in idiopathic and neurological patients and did not indicate a pathologic origin. Seventy-one percent of unilateral toe walkers and 32% of bilateral but asymmetric toe walkers were...
diagnosed with CP (P<0.001). Twenty-six percent of 145 brain magnetic resonance imaging studies diagnosed CP. Of the 125 (72%) with spinal imaging, 3 had spinal pathology to account for TW. Fourteen percent of 87 subjects with an electromyography/nerve conduction study had abnormal results indicating a peripheral polyneuropathy. CONCLUSIONS: An underlying pathologic diagnosis was found in 62% of patients referred to neurology for TW. A concerning birth history, delayed initial ambulation, unilateral TW, upper or lower motor neuron signs on examination, or behavioral features may suggest a pathologic diagnosis. Ankle contracture is not predictive of an abnormal diagnosis and can be found in idiopathic patients. CP, peripheral neuropathy, autism spectrum disorder, and hereditary spastic paraparesis are the most common pathologic diagnoses identified in our population. LEVEL OF EVIDENCE: Level III-retrospective cohort.

PMID: 29309384

Zhang J.

Cerebral palsy (CP), a common pediatric movement disorder, causes the most severe physical disability in children. Early diagnosis in high-risk infants is critical for early intervention and possible early recovery. In recent years, multivariate analytic and machine learning (ML) approaches have been increasingly used in CP research. This paper aims to identify such multivariate studies and provide an overview of this relatively young field. Studies reviewed in this paper have demonstrated that multivariate analytic methods are useful in identification of risk factors, detection of CP, movement assessment for CP prediction, and outcome assessment, and ML approaches have made it possible to automatically identify movement impairments in high-risk infants. In addition, outcome predictors for surgical treatments have been identified by multivariate outcome studies. To make the multivariate and ML approaches useful in clinical settings, further research with large samples is needed to verify and improve these multivariate methods in risk factor identification, CP detection, movement assessment, and outcome evaluation or prediction. As multivariate analysis, ML and data processing technologies advance in the era of Big Data of this century, it is expected that multivariate analysis and ML will play a bigger role in improving the diagnosis and treatment of CP to reduce mortality and morbidity rates, and enhance patient care for children with CP.

PMID: 29312134

Savage TA.
[No abstract available]

PMID: 2931378

10. Comparing impact on the family and insurance coverage in children with cerebral palsy and children with another special healthcare need.
Schaible B, Colquitt G, Caciula MC, Carnes A, Li L, Moreau N.
Child Care Health Dev. 2018 Jan 12. doi: 10.1111/cch.12547. [Epub ahead of print]

BACKGROUND: Families and caregivers of children with special healthcare needs (CSHCN) often experience financial difficulties, have unmet physical and mental health needs, and are at increased risk of marital problems due to the stress caused by caring for their child. Within the larger population of CSHCN, young people with cerebral palsy (CP) have more unmet needs due to the complexity and potential severity of the disability. The purpose of this study was to identify factors associated with differences in insurance coverage and impact on the family of children with CP and other CSHCN. METHODS: The data were taken from the National Survey of Children with Special Health Care Needs, which was designed to examine state- and national-level estimates of CSHCN. Three variables examined differences in insurance coverage between those children diagnosed with CP versus all other CSHCN: insurance coverage for the previous year, current insurance coverage, and adequacy of insurance coverage. Four variables representing different indicators of family impact were used to assess differences between children with CP versus all other CSHCN: out-of-pocket expenses for healthcare, family financial burden, hours per week that family members spent caring for the child, and impact on family work life. RESULTS: The results of this
study showed significant differences between households with a child with CP and a child with another health special need in terms of insurance coverage, indicating a tendency of children with CP to be insured the entire year. As for the impact on the family in households with children with CP versus other CSHCN, there were significant differences in all four variables that were analysed. CONCLUSIONS: There is limited evidence highlighting differences between the impact of caring for a child with CP and caring for other CSHCN. Caring for a child with CP has a significant impact on the family, despite insurance coverage.

PMID: 29327378

Shih STF, Tonmukayakul U, Imms C, Reddihough D, Graham HK, Cox L, Carter R.

AIM: Economic appraisal can help guide policy-making for purchasing decisions, and treatment and management algorithms for health interventions. We conducted a systematic review of economic studies in cerebral palsy (CP) to inform future research. METHOD: Economic studies published since 1970 were identified from seven databases. Two reviewers independently screened abstracts and extracted data following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Any discrepancies were resolved by discussion. RESULTS: Of 980 identified references, 115 were included for full-text assessment. Thirteen articles met standard criteria for a full economic evaluation, two as partial economic evaluations, and 18 as cost studies. Six were full economic evaluations alongside clinical studies or randomized controlled trials, whereas seven involved modelling simulations. The economic case for administration of magnesium sulfate for imminent preterm birth is compelling, achieving both health gain and cost savings. Current literature suggests intrathecal baclofen therapy and botulinum toxin injection are cost-effective, but stronger evidence for long-term effects is needed. Lifestyle and web-based interventions are inexpensive, but broader measurement of outcomes is required. INTERPRETATION: Prevention of CP would avoid significant economic burden. Some treatments and interventions have been shown to be cost-effective, although stronger evidence of clinical effectiveness is needed. What this paper adds Cost-effectiveness evidence shows prevention is the most significant strategy. Some treatments are cost-effective, but stronger evidence for long-term effectiveness is required. Comparison of treatment costs is challenging owing to variations in methodologies and varying clinical indications.

PMID: 29319155

Prevention and Cure

12. MAGnesium sulphate for fetal neuroprotection to prevent Cerebral Palsy (MAG-CP)-implementation of a national guideline in Canada.
De Silva DA, Synnes AR, von Dadelszen P, Lee T, Bone JN; MAG-CP, CPN and CNN collaborative groups, Magee LA.

BACKGROUND: Evidence supports magnesium sulphate (MgSO4) for women at risk of imminent birth at < 32-34 weeks to reduce the likelihood of cerebral palsy in the child. MAGnesium sulphate for fetal neuroprotection to prevent Cerebral Palsy (MAG-CP) was a multifaceted knowledge translation (KT) strategy for this practice. METHODS: The KT strategy included national clinical practice guidelines, a national online e-learning module and, at MAG-CP sites, educational rounds, focus group discussions and surveys of barriers and facilitators. Participating sites contributed data on pregnancies with threatened preterm birth. In an interrupted time-series study design, MgSO4 use for fetal neuroprotection (NP) was tracked prior to (Aug 2005-May 2011) and during (Jun 2011-Sept 2015) the KT intervention. Effectiveness of the strategy was measured by optimal MgSO4 use (i.e. administration when and only when indicated) over time, evaluated by a segmented generalised estimating equations logistic regression (p < 0.05 significant). Secondary outcomes included maternal effects and, using the Canadian Neonatal Network (CNN) database, national trends in MgSO4 use for fetal NP and associated neonatal resuscitation. With an anticipated recruitment of 3752 mothers over 4 years at Canadian Perinatal Network sites, we anticipated > 95% power to detect an increase in optimal MgSO4 use for fetal NP from < 5 to 80% (2-sided, alpha 0.05) and at least 80% power to detect any increases observed in maternal side effects from RCTs. RESULTS: Seven thousand eight hundred eighty-eight women with imminent preterm birth were eligible for MgSO4 for fetal NP: 4745 pre-KT (18 centres) and 3143 during KT (11 centres). The KT intervention was associated with an 84% increase in the odds of optimal use (OR 1.00 to 1.84, p < 0.001), a reduction in the odds of underuse (OR 1.00 to 0.47, p < 0.001) and an increase in suboptimal use (too early or at ≥ 32 weeks; OR 1.18 to 2.18, p < 0.001) of MgSO4 for fetal NP. Maternal hypotension was uncommon (7/1512, 0.5%). Nationally, intensive neonatal
resuscitation decreased (p = 0.024) despite rising MgSO4 use for fetal NP (p < 0.001). CONCLUSION: Multifaceted KT was associated with significant increases in use of MgSO4 for fetal NP, with neither important maternal nor neonatal risks.

PMID: 29325592

13. The emerging genetic landscape of cerebral palsy.

van Eyk CL, Corbett MA, Macleman AH.


Cerebral palsy (CP) is a broad clinical descriptor that encompasses a heterogeneous group of nonprogressive neurodevelopmental disabilities affecting movement and posture. While linked by the presence of damage to the developing brain, the etiology of CP is likely varied and the clinical outcomes are diverse. There is now a large body of evidence supporting a significant role for genetics in causation of CP. An increasing number of studies have identified likely causative genetic variants in families with CP, as well as in individual sporadic cases. Next-generation sequencing is now aiding clinicians in making specific molecular diagnoses, providing future opportunities for tailored treatments and for informed reproductive decisions.

PMID: 29325622

14. Targeted Knockdown of Bone Morphogenetic Protein Signaling within Neural Progenitors Protects the Brain and Improves Motor Function following Postnatal Hypoxia-Ischemia.

Dettman RW, Birch D, Fernando A, Kessler JA, Dizon MLV.


Hypoxic-ischemic injury (HI) to the neonatal human brain results in myelin loss that, in some children, can manifest as cerebral palsy. Previously, we had found that neuronal overexpression of the bone morphogenic protein (BMP) inhibitor noggin during development increased oligodendroglia and improved motor function in an experimental model of HI utilizing unilateral common carotid artery ligation followed by hypoxia. As BMPs are known to negatively regulate oligodendroglial fate specification of neural stem cells and alter differentiation of committed oligodendroglia, BMP signaling is likely an important mechanism leading to myelin loss. Here, we showed that BMP signaling is upregulated within oligodendroglia of the neonatal brain. We tested the hypothesis that inhibition of BMP signaling specifically within neural progenitor cells (NPCs) is sufficient to protect oligodendroglia. We conditionally deleted the BMP receptor 2 subtype (BMPR2) in NG2-expressing cells after HI. We found that BMPR2 deletion globally protects the brain as assessed by MRI and protects motor function as assessed by digital gait analysis, and that conditional deletion of BMPR2 maintains oligodendrocyte marker expression by immunofluorescence and Western blot and prevents loss of oligodendroglia. Finally, BMPR2 deletion after HI results in an increase in noncompacted myelin. Thus, our data indicate that inhibition of BMP signaling specifically in NPCs may be a tractable strategy to protect the newborn brain from HI.

PMID: 29324456

15. A Variant of the Autophagy-Related 5 Gene Is Associated with Child Cerebral Palsy.


Cerebral palsy (CP) is a major cause of childhood disability in developed and developing countries, but the pathogenic mechanisms of CP development remain largely unknown. Autophagy is a highly conserved cellular self-digestion of damaged organelles and dysfunctional macromolecules. Growing evidence suggests that autophagy-related gene 5 (ATG5)-dependent autophagy is involved in neural development, neuronal differentiation, and neurological degenerative diseases. The aim of this study was to analyze ATG5 protein expression and gene polymorphisms in Chinese patients with CP and to evaluate the importance of ATG5 in the development of CP. Five polymorphisms from different regions of the ATG5 gene (rs510432, rs3804338, rs573775, rs2299863, and rs6568431) were analyzed in 715 CP patients and 658 controls using MassARRAY. Of these, 58 patients and 56 controls were selected for measurement of plasma ATG5 level using ELISA. The relevance of disease-associated SNPs was evaluated using the SHEsis program. We identified a significant association between rs6568431 and CP (OR = 1.388, 95% CI = 1.173–1.643, Pallele = 0.0005, Pgenotype = 0.0015). Subgroup analysis showed a highly significant association of rs6568431 with spastic CP (n = 468, OR = 1.511, 95% CI = 1.251–1.824, Pallele = 8.50e-005, Pgenotype =
1.57e-004) and spastic quadriplegic (OR = 1.927, 95% CI = 1.533–2.421, Pallele = 7.35e-008, Pgenotype = 3.24e-009). Furthermore, mean plasma ATG5 levels were lower in CP patients than in controls, and individuals carrying the AA genotype of rs6568431 that was positively associated with CP had lower plasma ATG5 levels (P < 0.05). This study demonstrated an association of an ATG5 gene variant and low level of ATG5 protein with CP, and stronger associations with severe clinical manifestations were identified. Our results provide novel evidence for a role of ATG5 in CP and shed light on the molecular mechanisms underlying this neurodevelopmental disorder.

PMID: 29326554

16. Co-occurrence and Severity of Neurodevelopmental Burden (Cognitive Impairment, Cerebral Palsy, Autism Spectrum Disorder, and Epilepsy) at Age 10 Years in Children Born Extremely Preterm.


BACKGROUND: This study aims to determine the prevalence of neurodevelopmental impairments at age ten years among children born extremely preterm (less than 28 weeks gestational age) and to offer a framework for categorizing neurological limitations. METHODS: A multicenter, prospective cohort follow-up study recruited 889 ten-year-old children born from 2002 to 2004. We assessed prevalence of cognitive impairment, measured by intelligent quotient and tests of executive function, cerebral palsy (CP), autism spectrum disorder (ASD), and epilepsy singly and in combination. The three levels of impairment severity were: category I-no major neurodevelopmental impairment; category II-normal cognitive ability with CP, ASD, and/or epilepsy; and category III-children with cognitive impairment. RESULTS: A total 214 of 873 children (25%) had cognitive impairment, 93 of 849 children (11%) had CP, 61 of 857 children (7%) had ASD, and 66 of 888 children (7%) had epilepsy. Further, 19% of all children had one diagnosis, 10% had two diagnoses, and 3% had three diagnoses. Decreasing gestational age was associated with increasing number of impairments (P < 0.001). The children with cognitive impairment and one third of children with CP, ASD, or epilepsy had a single impairment. Six hundred one (68% [95% CI, 64.5%-70.7%]) children were in category I, 74 (8% [95% CI, 6.6%-10.3%]) were in category II, and 214 (24% [95% CI 21.7%-27.4%]) were in category III. CONCLUSIONS: Three quarters of children had normal intellect at age ten years; nearly 70% were free of neurodevelopmental impairment. Forty percent of children with impairments had multiple diagnoses.

PMID: 29310907

17. Two-year neurodevelopmental outcomes of extremely preterm infants treated with early hydrocortisone: treatment effect according to gestational age at birth.

Baud O, Trousson C, Biran V, Leroy E, Mohamed D, Alberti C; PREMILOC Trial group.


OBJECTIVE: To determine whether early hydrocortisone treatment in extremely preterm infants affects neurodevelopmental outcomes at 2 years of age according to gestational age at birth. PATIENTS AND METHODS: This is an exploratory analysis of neurodevelopmental outcomes by gestational age strata from the PREMILOC trial, in which patients were randomly assigned to receive either placebo or low-dose hydrocortisone and randomisation was stratified by gestational age groups (24-25 and 26-27 weeks of gestation). Neurodevelopmental impairment (NDI) was assessed using a standardised neurological examination and the revised Brunet-Lézine scale at 22 months of corrected age. RESULTS: A total of 379 of 406 survivors were evaluated, 96/98 in the gestational age group of 24-25 weeks and 283/308 in the gestational age group of 26-27 weeks. Among surviving infants born at 24-25 weeks, significant improvement in global neurological assessment was observed in the hydrocortisone group compared with the placebo group (P=0.02) with a risk of moderate-to-severe NDI of 2% and 18%, respectively (risk difference 16 (95% CI -28% to -5%). In contrast, no statistically significant difference between treatment groups was observed in infants born at 26-27 weeks (P=0.95) with a similar risk of moderate-to-severe NDI of 9% in both groups. The incidence of cerebral palsy or other major neurological impairments were found similar between treatment groups in each gestational group. CONCLUSIONS: In an exploratory analysis of neurodevelopmental outcomes from the PREMILOC trial, early low-dose hydrocortisone was associated with a statistically significant improvement in neurodevelopmental outcomes in infants born at 24 and 25 weeks of gestation.

PMID: 29321180
18. Are Extremely Low Gestational Age Newborns Born to Obese Women at Increased Risk of Cerebral Palsy at 2 Years?

van der Burg JW, O'Shea TM, Kuban K, Allred EN, Paneth N, Dammann O, Leviton A.


The authors hypothesized that the risk of cerebral palsy at 2 years in children born extremely preterm to overweight and obese women is increased relative to the risk among children born to neither overweight nor obese women. In a multicenter prospective cohort study, the authors created multinomial logistic regression models of the risk of diparetic, quadriparetic, and hemiparetic cerebral palsy that included the prepregnancy body mass index of mothers of 1014 children born extremely preterm, cerebral palsy diagnoses of children at 2 years, as well as information about potential confounders. Overweight and obese women were not at increased risk of giving birth to a child who had cerebral palsy. The risk ratios associated with overweight varied between 1.1 for quadriparesis (95% CI = 0.5, 2.1) to 2.0 for hemiparesis (95% CI = 0.4, 9.8). The risk ratios associated with obesity varied between 0.7 for diparesis (95% CI = 0.2, 2.5) to 2.5 for hemiparesis (95% CI = 0.4, 13).

PMID: 29322871


Lie RT, Moster D, Strand P, Wilcox AJ.


Ionizing radiation at high doses early in life may cause neurodevelopmental problems. Possible effects of lower doses are, however, controversial. We use carefully collected exposure data for Norway following the Chernobyl accident in April 1986 combined with population-based registries to assess long-term effects of fetal exposure on neurodevelopmental outcomes. Radiation doses were estimated for each Norwegian municipality for each calendar month from May 1986 to April 1989. We established a cohort of all Norwegian pregnancies during the three-year period of radiation measurement and compared them with appropriate unexposed groups. All cohorts were followed into adulthood. Risks of cerebral palsy, mental retardation, schizophrenia, epilepsy, vision or hearing problems, school dropout, and low income were estimated. We also conducted an analysis of mathematics and language grades using siblings born after the exposure period as comparison. There was little evidence of associations between radiation exposure and cerebral palsy, mental retardation, schizophrenia, epilepsy, or hearing or vision problems associated with radiation exposure. (p-values for trend with exposure dose were 0.27, 0.14, 0.83, 0.35 and 0.42.) Slightly more of the exposed failed to complete high school (p = 0.05), but there was no increase in the proportion with low income (p = 0.38). The natural advantage of older siblings over younger siblings in mathematics grades was diminished with exposure of older siblings (p = 0.003), but there was no association of exposure with Norwegian language grades (p = 0.37). There is scant evidence that the low-dose fallout from Chernobyl in Norway increased the risk for serious neurodevelopmental problems. We cannot exclude the possibility of lower mathematics grades with exposure, similar to a report from Sweden.

PMID: 29313167


Briana DD, Malamitsi-Puchner A.


This invited review aimed at presenting the evidence concerning neurodevelopmental outcomes, particularly cerebral palsy (CP), motor disability, cognitive impairment, mental retardation, any major disability, blindness and deafness in cases of twins, conceived after in vitro fertilization, presenting fetal/ intrauterine growth restriction (FGR/IUGR) or being prematurely born. FGR/IUGR, prematurity and zygosity affect neurodevelopmental outcome; CP is higher in term infants, those presenting with FGR/IUGR, as well as in survivors of intrauterine co-twin death; cognitive ability of twins versus singletons mainly relates to confounding factors, as FGR/IUGR and prematurity, while evidence for differences in behavioral and psychiatric disorders between twins and singletons is limited. The impact of IVF per se has not been documented. Nevertheless, available literature, usually of heterogeneous and retrospective nature, diverges in the criteria for neurodevelopmental delay. Furthermore, differences in selection/exclusion criteria and small mixed cohorts, including the full range of complications, make comparison of the existing studies difficult. Future studies should focus in confirming the lack of IVF impact on twins' neurodevelopment and general health, in comparing long-term outcome of naturally conceived twins with those conceived following assisted reproduction techniques and in including evaluation of individual, longitudinal trajectories of growth and development. In this respect, worldwide population-based registries will enable more precise description of neurodevelopmental outcomes among twins.

PMID: 29307249