1. Impaired Voluntary Movement Control and Its Rehabilitation in Cerebral Palsy.

Gordon AM.


Cerebral palsy is caused by early damage to the developing brain, as the most common pediatric neurological disorder. Hemiplegia (unilateral spastic cerebral palsy) is the most common subtype, and the resulting impairments, lateralized to one body side, especially affect the upper extremity, limiting daily function. This chapter first describes the pathophysiology and mechanisms underlying impaired upper extremity control of cerebral palsy. It will be shown that the severity of impaired hand function closely relates to the integrity of the corticospinal tract innervating the affected hand. It will also shown that the developing corticospinal tract can reorganize its connectivity depending on the timing and location of CNS injury, which also has implications for the severity of hand impairments and rehabilitation. The mechanisms underlying impaired motor function will be highlighted, including deficits in movement execution and planning and sensorimotor integration. It will be shown that despite having unimanual hand impairments, bimanual movement control deficits and mirror movements also impact function. Evidence for motor learning-based therapies including Constraint-Induced Movement Therapy and Bimanual Training, and the possible pathophysiological predictors of treatment outcome and plasticity will be described. Finally, future directions for rehabilitations will be presented.

PMID: 28035572


Curtis DJ, Woollacott M, Bencke J, Lauridsen HB, Saavedra S, Bandholm T, Sonne-Holm S.


PURPOSE: To determine whether segmental training is more effective in improving gross motor function in children and young people with moderate-to-severe cerebral palsy than conventional physiotherapy. METHODS: Twenty-eight participants were randomized to a segmental training or control group. Outcomes were Gross Motor Function Measure (GMFM), Pediatric Evaluation of Disability Inventory (PEDI), Segmental Assessment of Trunk Control (SATCo), and postural sway at baseline, at primary endpoint (6 months), and at follow-up (12 months). RESULTS: There were no significant differences in either GMFM, PEDI, or SATCo scores at primary endpoint or follow-up. There were significant reductions in anterior-posterior head angular sway and trunk sway in the segmental training group at primary endpoint but not at follow-up. CONCLUSION: Segmental training was not superior to usual care in improving GMFM. Improvements in head and trunk sway were greater in the segmental training group at primary endpoint but not at follow-up.

PMID: 28045553

Guo T, Zhu B, Zhang Q, Yang Y, He Q, Zhang X, Tai X.


BACKGROUND: Cerebral palsy (CP), a childhood disease of high morbidity and serious harmfulness, has no effective therapies to completely relieve the associated pain. Acupuncture has been used widely in China to alleviate several CP symptoms, such as pain and motion disorders, despite the deficiency of high-quality evidence related to this practice.

OBJECTIVE: The aim of this systematic review protocol is to assess the efficacy and safety of acupuncture for the treatment of children with CP. METHODS: The following electronic databases will be searched: Cochrane Library, Web of Science, EBASE, Springer, World Health Organization International Clinical Trials Registry Platform, China National Knowledge Infrastructure, Wan-fang database, Chinese Biomedical Literature Database, Chinese Scientific Journal Database, and other sources. All published randomized controlled trials from inception to December 2016 will be included. RevMan V.5.3 software will be implemented for the assessment of bias risk, data synthesis, subgroup analysis, and meta-analyses if inclusion conditions are met. Individuals recruited into the trials will include children with all types of CP, and these individuals will be involved as coresearchers to develop and evaluate the efficacy and safety of acupuncture for the treatment of children with CP. Due to language barriers, only English and Chinese articles will be retrieved. RESULTS: The systematic review will synthesize the available knowledge surrounding acupuncture for children with CP. The findings will be synthesized to determine the efficacy and safety of acupuncture for children with CP. CONCLUSIONS: The review has not been completed. This protocol presents a proper method to implement the systematic review, and ensures transparency for the completed review. Findings from the systematic review will be disseminated in a peer-reviewed journal and results will be presented at relevant conferences. The data of individual patients will not be included, so ethical approval is not required.

PMID: 28057608

4. The effectiveness of robotic-assisted gait training for paediatric gait disorders: systematic review.

Lefmann S, Russo R, Hillier S.


BACKGROUND: Robotic-assisted gait training (RAGT) affords an opportunity to increase walking practice with mechanical assistance from robotic devices, rather than therapists, where the child may not be able to generate a sufficient or correct motion with enough repetitions to promote improvement. However the devices are expensive and clinicians and families need to understand if the approach is worthwhile for their children, and how it may be best delivered. METHODS: The objective of this review was to identify and appraise the existing evidence for the effectiveness of RAGT for paediatric gait disorders, including modes of delivery and potential benefit. Six databases were searched from 1980 to October 2016, using relevant search terms. Any clinical trial that evaluated a clinical aspect of RAGT for children/adolescents with altered gait was selected for inclusion. Data were extracted following the PRISMA approach. Seventeen trials were identified, assessed for level of evidence and risk of bias, and appropriate data extracted for reporting. RESULTS: Three randomized controlled trials were identified, with the remainder of lower level design. Most individual trials reported some positive benefits for RAGT with children with cerebral palsy (CP), on activity parameters such as standing ability, walking speed and distance. However a meta-analysis of the two eligible RCTs did not confirm this finding (p = 0.72). Training schedules were highly variable in duration and frequency and adverse events were either not reported or were minimal. There was a paucity of evidence for diagnoses other than CP. CONCLUSION: There is weak and inconsistent evidence regarding the use of RAGT for children with gait disorders. If clinicians (and their clients) choose to use RAGT, they should monitor individual progress closely with appropriate outcome measures including monitoring of adverse events. Further research is required using higher level trial design, increased numbers, in specific populations and with relevant outcome measures to both confirm effectiveness and clarify training schedules.

PMID: 28057016
5. [Gait Analysis in Patients with Hip Disorders].

[Article in Czech]
Urbášek K, Poul J.

Recent studies have shown that the evaluation of both conservative and surgical therapy cannot do without gait analysis. Orthopaedic textbooks, with some exceptions, deal in great detail with a thorough clinical examination of the patient but gait assessment is mentioned only marginally. More attention is paid to gait analysis in rehabilitation medicine. Motion and gait analysis laboratories equipped with optoelectronic cameras and force platforms were first developed for cerebral palsy children. Recently, several studies have been published on the use of these methods in disorders of hip and knee joints or spine diseases. Key words: gait analysis, hip joint.

PMID: 28026724

6. Vector-field statistics for the analysis of time varying clinical gait data.
Donnelly CJ, Alexander C, Pataky TC, Stannage K, Reid S, Robinson MA.

BACKGROUND: In clinical settings, the time varying analysis of gait data relies heavily on the experience of the individual(s) assessing these biological signals. Though three dimensional kinematics are recognised as time varying waveforms (1D), exploratory statistical analysis of these data are commonly carried out with multiple discrete or 0D dependent variables. In the absence of an a priori 0D hypothesis, clinicians are at risk of making type I and II errors in their analysis of time varying gait signatures in the event statistics are used in concert with preferred subjective clinical assessment methods. The aim of this communication was to determine if vector field waveform statistics were capable of providing quantitative corroboration to practically significant differences in time varying gait signatures as determined by two clinically trained gait experts.

METHODS: The case study was a left hemiplegic Cerebral Palsy (GMFCS I) gait patient following a botulinum toxin (BoNT-A) injection to their left gastrocnemius muscle. FINDINGS: When comparing subjective clinical gait assessments between two testers, they were in agreement with each other for 61% of the joint degrees of freedom and phases of motion analysed. For tester 1 and tester 2, they were in agreement with the vector-field analysis for 78% and 53% of the kinematic variables analysed. When the subjective analyses of tester 1 and tester 2 were pooled together and then compared to the vector-field analysis, they were in agreement for 83% of the time varying kinematic variables analysed. INTERPRETATION: These outcomes demonstrate that in principle, vector-field statistics corroborates with what a team of clinical gait experts would classify as practically meaningful pre- versus post time varying kinematic differences. The potential for vector-field statistics to be used as a useful clinical tool for the objective analysis of time varying clinical gait data is established. Future research is recommended to assess the usefulness of vector-field analyses during the clinical decision making process.

PMID: 28024228


The objective of this investigation was to determine the outcome of spine fusion for neuromuscular (NM) scoliosis, using Unit Rod technique, with emphasis on complications related to preoperative general health. Between 1997 and 2007, 96 consecutive patients with neuromuscular scoliosis operated on with Unit Rod instrumentation were retrospectively reviewed. The inclusion criteria were diagnosis of NM scoliosis due to cerebral palsy (CP) and muscular dystrophy (DMD). Patient's preoperative general health, weight, and nutrition were collected. Different radiographic and clinical parameters were evaluated. There were 66 CP patients (59 nonwalking) and 30 DMD patients (24 nonwalking). Mean age at surgery was 16.5 years and 13.9 years, respectively. All radiographic measurements improved significantly. Wound infection rate was 16.7% (11% of reoperation rate in CP; 10% in DMD; 3 hardware removal cases). No pelvic fracture due to rod irritation was observed. Unit Rod technique provides good radiographic and clinical outcomes even if this surgery is associated with a high complication rate. It is a quick,
simple, and reliable technique. Perioperative management strategy should decrease postoperative complications and increases outcome. A standardized preoperative patient evaluation and preparation including respiratory capacity and nutritional, digestive, and musculoskeletal status are mandatory prior to surgery.

PMID: 28058256

8. Orthopaedic Surgery in Dystonic Cerebral Palsy.

Blumetti FC, Wu JC, Barzi F, Axt MW, Waugh MC, Selber P.


BACKGROUND: Outcomes after orthopaedic interventions in patients with dystonic cerebral palsy (DCP) are historically regarded as unpredictable. This study aims to evaluate the overall outcome of orthopaedic surgery in children with DCP.

METHOD: Children with DCP who underwent lower limb orthopaedic surgery with a minimum follow-up of 12 months were included. Data collected included age at time of surgery, surgical procedures performed, Gross Motor Function Classification System (GMFCS) level, and Barry Albright Dystonia Scale (BADS) score. The cohort was divided into 2 groups. Group 1 (GMFCS levels I to III), mean age 12 years 7 months and group 2 (GMFCS levels IV to V), mean age 10 years 7 months. Group 1 had surgery aimed at deformity correction to improve gait and mobility, and group 2 for the management or prevention of hip displacement. Outcome measures analyzed were: the incidence of unpredictable results related to surgery and early recurrence of deformity in both groups. Functional mobility scale scores were evaluated for group 1 and hip migration percentage for group 2. Linear mixed models were used to take into account repeated measures over time and correlations between measurements from the same patient.

RESULTS: Group 1 (n=18); had low BADS scores and were considered to have mild dystonia. Three children experienced unpredictable results, 2 had early recurrence of deformity, 3 had a decline, and 1 child improved in the functional mobility scale. Group 2 (n=19); had high BADS scores and were considered to have moderate to severe dystonia. Nine surgical events involved bony procedures and 15 were soft tissue surgery only. One surgical event lead to unpredictable results and 2 children had early recurrence of deformity. Postoperatively, a linear trend of increasing migration percentage [0.49% (95% confidence interval, 0.23-0.74; P=0.0002)] was seen up to 21 months. There was no significant change after 21 months [-0.08% (95% confidence interval, -0.24 to +0.041; P=0.18)].

CONCLUSIONS: This study suggests that unpredictable results and early recurrence of deformity following orthopaedic surgery in children with DCP are not as common as previously regarded. Furthermore, functional mobility and hip morphology can be improved.

PMID: 28027144

9. Optimizing bone health in cerebral palsy across the lifespan.

Trinh A, Fahey MC, Brown J, Fuller PJ, Milat F.


[No abstract available]

PMID: 28044317


Meyns P, Pans L, Plasmans K, Heyrman L, Desloovere K, Molenaers G.

Games Health J. 2017 Jan 4. doi: 10.1089/g4h.2016.0069. [Epub ahead of print]

OBJECTIVE: Impaired balance is disabling for children with cerebral palsy (CPc), especially for CPc who recently underwent lower limb surgery. Positive results of using virtual reality (VR) in balance rehabilitation have been published in several outpatient populations. We investigated the feasibility of applying additional VR training focused on sitting balance in CP inpatients of a rehabilitation center after lower limb surgery. Additionally, we investigated the rate of enjoyment of VR training
compared with conventional physiotherapy. MATERIALS AND METHODS: Eleven spastic CPc (4/7 males/females) following rehabilitation after lower limb orthopedic surgery were included (5-18 years). The control group received conventional physiotherapy. The intervention group received additional VR training. Balance was measured using the Trunk Control Measurement Scale every 3 weeks of the rehabilitation period. Enjoyment was analyzed using a 10-point Visual Analog Scale. RESULTS: Providing additional VR training was feasible in terms of recruitment, treatment adherence, and assessment adherence. Both groups improved sitting balance after therapy. The current games were not perceived as more enjoyable than conventional physiotherapy. CONCLUSION: Including additional VR training to conventional physiotherapy is feasible and might be promising to train sitting balance in CPc after lower limb surgery. Future research should take equal patient allocation and training duration between groups into consideration.

PMID: 28051880


Bonnechère B, Omelina L, Jansen B, Van Sint Jan S.


PURPOSE: Cerebral palsy (CP) leads to various clinical signs mainly induced by muscle spasticity and muscle weakness. Among these ones impaired balance and posture are very common. Traditional physical therapy exercise programs are focusing on this aspect, but it is difficult to motivate patients to regularly perform these exercises, especially at home without therapist supervision. Specially developed serious games (SG) could therefore be an interesting option to motivate children to perform specific exercise for balance improvement. METHOD: Ten CP children participated in this study. Patients received four sessions of SG included into conventional therapy (1 session of 30 min a week during 4 weeks). Trunk control and balance were assessed using Trunk Control Motor Scale (TCMS) before and after interventions. RESULTS: Children presented a significant improvement in TCMS global score after interventions [37.6 (8.7) and 39.6 (9.5) before and after interventions, respectively, p = 0.04]. CONCLUSION: SG could therefore be an interesting option to integrate in the conventional treatment of CP children. Implication for Rehabilitation Cerebral palsy (CP) leads to balance issues. Rehabilitation exercises are not performed (enough) at home. Serious games (SG) could increase patients' motivation. SG increase balance control of CP children.

PMID: 28033958


BACKGROUND: Early onset dystonia (dyskinesia) and deafness in childhood pose significant challenges for children and carers and are the cause of multiple disability. It is particularly tragic when the child cannot make use of early cochlear implantation (CI) technology to relieve deafness and improve language and communication, because severe cervical and truncal dystonia brushes off the magnetic amplifier behind the ears. Bilateral globus pallidus internus (GPI) deep brain stimulation (DBS) neuromodulation can reduce dyskinesia, thus supporting CI neuromodulation success. METHODS: We describe the importance of the order of dual neuromodulation surgery for dystonia and deafness. First with bilateral GPI DBS using a rechargeable ACTIVA-RC neurostimulator followed 5 months later by unilateral CI with a Harmony (BTE) Advanced Bionics Hi Res 90 K cochlear device. This double neuromodulation was performed in series in a 12.5 kg 5 year-old ex-24 week gestation-born twin without a cerebellum. RESULTS: Relief of dyskinesia enabled continuous use of the CI amplifier. Language understanding and communication improved. Dystonic storms abated. Tolerance of sitting increased with emergence of manual function. Status dystonicus ensued 10 days after ACTIVA-RC removal for infection-erosion at 3 years and 10 months. He required intensive care and DBS re-implantation 3 weeks later together with 8 months of hospital care. Today he is virtually back to the level of functioning before the DBS removal in 2012 and background medication continues to be slowly weaned. CONCLUSION: This case illustrates that early neuromodulation with DBS for dystonic cerebral palsy followed by CI
for deafness is beneficial. Both should be considered early i.e. under the age of five years. The DBS should precede the CI to maximise dystonia reduction and thus benefits from CI. This requires close working between the paediatric DBS and CI services.

PMID: 28017556


Schteinschnaider A.


In children, dystonia presents almost always as a severe, generalized and rapidly progressive condition. Response to pharmacological therapies is poor, making surgical treatment a better option. Originally, this was limited to basal ganglia neuroablative lesion surgery, but currently, Deep Brain Stimulation (DBS), a more conservative intervention which can be tailored to treat individual patient symptoms has become the standard of care worldwide, in particular GPi DBS, which is highly efficient in primary dystonia.

PMID: 28012698


Eken MM, Harlaar J, Dallmeijer AJ, de Waard E, van Bennekom CA, Houdijk H.


BACKGROUND: Knowledge on lower extremity strength is imperative to informed decision making for children with cerebral palsy (CP) with mobility problems. However, a functional and clinically feasible test is not available. We aimed to determine whether the squat test is suitable for this purpose by investigating test performance and execution in children with cerebral palsy and typically developing (TD) peers. METHODS: Squat test performance, defined by the number of two-legged squats until fatigue (max 20), was assessed in twenty children with bilateral CP (6-19 years; gross motor function classification system I-III) and sixteen TD children (7-16 years). Muscle fatigue was assessed from changes in electromyography (EMG). Joint range-of-motion and net torque were calculated for each single squat, to investigate differences between groups and between the 2nd and last squat. FINDINGS: Fifteen children with CP performed <20 squats (median=13, IQR=7-19), while all TD children performed the maximum of 20 squats. Median EMG frequency decreased and amplitude increased in mm. quadriceps of both groups. Ankle and knee range-of-motion were reduced in children with CP during a single squat by 10 to 15°. No differences between 2nd and last squat were observed, except for knee range-of-motion which increased in TD children and decreased in children with CP. INTERPRETATION: Squat test performance was reduced in children with CP, especially in those with more severe CP. Muscle fatigue was present in both children with CP and TD peers, confirming that endurance of the lower extremity was tested. Minor execution differences between groups suggest that standardized execution is important to avoid compensation strategies. It is concluded that the squat test is feasible to test lower extremity strength in children with CP in a clinically meaningful way. Further clinimetric evaluation is needed before clinical implementation.

PMID: 28040656

15. An aerobic exercise program for young people with cerebral palsy in specialist schools: A phase I randomized controlled trial.

Cleary SL, Taylor NF, Dodd KJ, Shields N.


PURPOSE: To evaluate the safety, adherence, and estimates of effect of an aerobic exercise program in specialist schools for young people with cerebral palsy. METHODS: Nineteen students with cerebral palsy were randomly allocated to an intervention group who completed an aerobic exercise program (27 sessions over nine weeks) or a control group who
completed social/art activities over the same time. RESULTS: There were no serious adverse events and the exercise program was completed with high rates of attendance (77%) and adherence to target heart rate zones (79%). Effect sizes favored the intervention group for measures of cardiovascular performance (sub-maximal treadmill test, effect size d = 0.7; muscle power sprint test, d = 0.9) and participation (Preference for Active-Physical Activities, d = 0.6). CONCLUSIONS: An aerobic exercise program in specialist schools for young people with cerebral palsy, that may improve measures of cardiovascular performance, can be completed safely, with moderately high levels of adherence.

PMID: 28045554


Sugden D.


This commentary is on the original article by Toovey et al.

PMID: 28039915

17. What is hippotherapy? The indications and effectiveness of hippotherapy.

Koca TT, Ataseven H.


Hippotherapy is a form of physical, occupational and speech therapy in which a therapist uses the characteristic movements of a horse to provide carefully graded motor and sensory input. A foundation is established to improve neurological function and sensory processing, which can be generalized to a wide range of daily activities. Unlike therapeutic horseback riding (where specific riding skills are taught), the movement of the horse is a means to a treatment goal when utilizing hippotherapy as a treatment strategy. Hippotherapy has been used to treat patients with neurological or other disabilities, such as autism, cerebral palsy, arthritis, multiple sclerosis, head injury, stroke, spinal cord injury, behavioral disorders and psychiatric disorders. The effectiveness of hippotherapy for many of these indications is unclear, and more research has been needed. Here, we purpose to give information about hippotherapy which is not known adequately by many clinicians and health workers.

PMID: 28058377

18. Longitudinal changes in health-related quality of life in preschool children with cerebral palsy of different levels of motor severity.

Lai CJ, Chen CY, Chen CL, Chan PS, Shen IH, Wu CY.


BACKGROUND: When setting goals for cerebral palsy (CP) interventions, health-related quality of life (HRQoL) is an important outcome. AIMS: To compare longitudinal changes in HRQoL in children with CP of different levels of motor severity. METHODS AND PROCEDURES: Seventy-three children with CP were collected and classified into three groups based on Gross Motor Function Classification System (GMFCS) levels. HRQoL was assessed by parent's proxy of the TNO-AZL Preschool Quality of Life (TAPQOL) at baseline and 6 months later. OUTCOMES AND RESULTS: Children with GMFCS level V had a lower total TAPQOL score and scores in all domains than those with level I-IV (p<0.01), except for the non-motor subdomain of physical functioning at follow-up. With regards to longitudinal changes, the children with GMFCS level V had greater improvements in physical (p=0.016) and cognitive functioning (p=0.042), but greater deterioration in emotional functioning (p=0.008) than those with levels I-II at 6 months of follow-up. CONCLUSIONS AND IMPLICATIONS: Motor severity was associated with TAPQOL scores in all domains and changes in some domains in
children with CP. Clinicians should early identify children at risk of a poor HRQoL and plan timely treatment strategies to enhance the HRQoL of children with CP.

PMID: 28040642

19. Invisible work of using and monitoring knowledge by parents (end-users) of children with chronic conditions.

Lagosy S, Bartlett D, Shaw L.


BACKGROUND: Parents who care for young children with chronic conditions are knowledge users. Their efforts, time, and energy to source, consider and monitor information add to the 'invisible' work of parents in making decisions about care, school transitions, and interventions. Little is known or understood about the work of parents as knowledge users. OBJECTIVE: To understand the knowledge use patterns and how these patterns may be monitored in parents caring for their young children with cerebral palsy (CP). METHODS: An embedded case study methodology was used. In-depth qualitative interviews and visual mapping were employed to collect and analyze data based on the experiences of three mothers of young children with CP. RESULTS: Knowledge use in parents caring for their young children with CP is multi-factorial, complex and temporal. Findings resulted in a provisional model elaborating on the ways knowledge is used by parents and how it may be monitored. CONCLUSIONS: The visual mapping of pathways and actions of parents as end users makes the processes of knowledge use more visible and open to be valued as well as appreciated by others. The provisional model has implications for knowledge mobilization as a strategy in childhood rehabilitation and the facilitation of knowledge use in the lives of families with children with chronic health conditions.

PMID: 28059821

Prevention and Cure

20. The genetic basis of cerebral palsy.

Fahey MC, Maclennan AH, Kretzschmar D, Gecz J, Krue MC.


Although prematurity and hypoxic-ischaemic injury are well-recognized contributors to the pathogenesis of cerebral palsy (CP), as many as one-third of children with CP may lack traditional risk factors. For many of these children, a genetic basis to their condition is suspected. Recent findings have implicated copy number variants and mutations in single genes in children with CP. Current studies are limited by relatively small patient numbers, the underlying genetic heterogeneity identified, and the paucity of validation studies that have been performed. However, several genes mapping to intersecting pathways controlling neurodevelopment and neuronal connectivity have been identified. Analogous to other neurodevelopmental disorders such as autism and intellectual disability, the genomic architecture of CP is likely to be highly complex. Although we are just beginning to understand genetic contributions to CP, new insights are anticipated to serve as a unique window into the neurobiology of CP and suggest new targets for intervention.

PMID: 28042670


Vilchez G, Dai J, Lagos M, Sokol RJ.


OBJECTIVE: Evidence supports the need of dose-adjustment of several drugs according to body mass index (BMI) to prevent toxicity in the underweight, and ensure efficacy in obese women. However, for MgSO4 neuroprotection, the effect of BMI on
maternal toxicity and fetal neuroprotection is understudied. We analyze the effect of BMI on maternal/infant outcomes after MgSO4. METHODS: Secondary analysis of a clinical trial that studied MgSO4 neuroprotection. Maternal side effects, magnesium cord levels, and offspring cerebral palsy/death were analyzed along BMI strata using ANOVA and chi-square test. Logistic regression was used to calculate adjusted odds ratios according to treatment and BMI, using non-obese that received placebo as reference. Interaction analyses were performed to validate differential efficacy of BMI. RESULTS: From 2,241 women, more side effects and higher magnesium cord levels were seen in underweight women (p = 0.05). MgSO4 neuroprotection was effective in the non-obese (p=.02), but not in obese women (p = 1.00). In multivariate analyses, MgSO4 significantly reduced cerebral palsy only in non-obese women. Interaction analyses showed the moderator effect of BMI (p=.169). Increasing MgSO4 dose in obese mothers may ensure neuroprotective efficacy without representing increased maternal risks. Considering costs of studying this association, current analysis may form the basis for reasonable practice.

PMID: 28056569

22. Intranasal C3a treatment ameliorates cognitive impairment in a mouse model of neonatal hypoxic-ischemic brain injury.
Morán J, Stokowska A, Walker FR, Mallard C, Hagberg H, Pekna M.

Perinatal asphyxia-induced brain injury is often associated with irreversible neurological complications such as intellectual disability and cerebral palsy but available therapies are limited. Novel neuroprotective therapies as well as approaches stimulating neural plasticity mechanism that can compensate for cell death after hypoxia-ischemia (HI) are urgently needed. We previously reported that single i.c.v. injection of complement-derived peptide C3a 1h after HI induction prevented HI-induced cognitive impairment when mice were tested as adults. Here, we tested the effects of intranasal treatment with C3a on HI-induced cognitive deficit. Using the object recognition test, we found that intranasal C3a treated mice were protected from HI-induced impairment of memory function assessed 6weeks after HI induction. C3a treatment ameliorated HI-induced reactive gliosis in the hippocampus, while it did not affect the extent of hippocampal tissue loss, neuronal cell density, expression of the pan-synaptic marker synapsin I or the expression of growth associated protein 43. In conclusion, our results reveal that brief pharmacological treatment with C3a using a clinically feasible non-invasive mode of administration ameliorates HI-induced cognitive impairment. Intranasal administration is a plausible route to deliver C3a into the brain of asphyxiated infants at high risk of developing hypoxic-ischemic encephalopathy.

PMID: 28062175

23. Long-term childhood outcomes of breech presentation by intended mode of delivery: a population record linkage study.
Bin YS, Ford JB, Nicholl MC, Roberts CL.

INTRODUCTION: There is a lack of information on long-term outcomes by mode of delivery for term breech presentation. We aimed to compare childhood mortality, cerebral palsy, hospitalizations, developmental, and educational outcomes associated with intended vaginal breech birth (VBB) compared to planned cesarean section. MATERIAL AND METHODS: Population birth and hospital records from New South Wales, Australia, were used to identify women with non-anomalous pregnancies eligible for VBB during 2001 to 2012. Intended mode of delivery was inferred from labor onset and management. Death, hospital, and education records were used for follow-up until 2014. Cox proportional hazards regression and modified Poisson regression were used for analysis. RESULTS: Of 15,340 women considered eligible for VBB, 7.8% intended VBB, 74.2% planned cesarean section, and intention was uncertain for 18.1%. Intended VBB did not differ from planned cesarean section on infant mortality (Fisher's exact p=0.55), childhood mortality (Fisher's exact p=0.50), cerebral palsy (Fisher's exact p=1.00), hospitalization in the first year of life (adjusted HR 1.04; 95% CI 0.90 - 1.20), hospitalization between the first and sixth birthdays (0.92; 0.82 - 1.04), being developmentally vulnerable (adjusted RR 1.22; 95% CI 0.48 - 1.88) or having special needs status (0.95; 0.48 - 1.88) when aged 4 - 6, scoring more than 1 standard deviation below the mean on tests of reading (1.10; 0.87 - 1.40) and numeracy (1.04; 0.81 - 1.34) when aged 7 - 9. CONCLUSIONS: Planned VBB confers no additional risks for child health, development, or educational achievement compared to planned cesarean section.

PMID: 28029180
24. Glucocorticoids Protect Neonatal Rat Brain in Model of Hypoxic-Ischemic Encephalopathy (HIE).

Harding B, Conception K, Li Y, Zhang L.


Hypoxic-ischemic encephalopathy (HIE) resulting from asphyxia in the peripartum period is the most common cause of neonatal brain damage and can result in significant neurologic sequelae, including cerebral palsy. Currently therapeutic hypothermia is the only accepted treatment in addition to supportive care for infants with HIE, however, many additional neuroprotective therapies have been investigated. Of these, glucocorticoids have previously been shown to have neuroprotective effects. HIE is also frequently compounded by infectious inflammatory processes (sepsis) and as such, the infants may be more amenable to treatment with an anti-inflammatory agent. Thus, the present study investigated dexamethasone and hydrocortisone treatment given after hypoxic-ischemic (HI) insult in neonatal rats via intracerebroventricular (ICV) injection and intranasal administration. In addition, we examined the effects of hydrocortisone treatment in HIE after lipopolysaccharide (LPS) sensitization in a model of HIE and sepsis. We found that dexamethasone significantly reduced rat brain infarction size when given after HI treatment via ICV injection; however it did not demonstrate any neuroprotective effects when given intranasally. Hydrocortisone after HI insult also significantly reduced brain infarction size when given via ICV injection; and the intranasal administration showed to be protective of brain injury in male rats at a dose of 300 µg. LPS sensitization did significantly increase the brain infarction size compared to controls, and hydrocortisone treatment after LPS sensitization showed a significant decrease in brain infarction size when given via ICV injection, as well as intranasal administration in both genders at a dose of 300 µg. To conclude, these results show that glucocorticoids have significant neuroprotective effects when given after HI injury and that these effects may be even more pronounced when given in circumstances of additional inflammatory injury, such as neonatal sepsis.

PMID: 28025500